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Generic Drug Formulations

Fine Chemicals
(2nd edition 1998)

BASF

1 Introduction

1.1 Preface

A selection of about 500 formulations of human and veterinary drugs are presented in this booklet. They have all been developed in the last 20 years in the Applications Laboratories of BASF AG and are in solid, liquid, and semi-solid form. However, emphasis is placed on tablets. Human and veterinary medicines have not been dealt with in separate chapters, because the technologies and excipients are the same.

Select the required formulation in the following list of all formulations by clicking with the cursor.

1.2 List of all formulations aranged alphabetically

A

Azithromycin Suspension (500 mg/10 ml)
Azulene solution (1%)

B

Barium Sulfate Oral Suspension (23%)
Basic Cream for Different Active Ingredients
Benzhexol Tablets (5 mg)
Benzoyl Peroxide + Alpha-Bisabolol Gel (5.0% + 0.2%)
Benzyl Benzoate Solution (10%)
Benzylpenicilline + Dihydrostreptomycin Injectable Suspension (200,000 units + 200 mg/ml)
Berberine Tablets (5 mg)
Beta Carotene + Vitamin C + Vitamin E Chewable Tablets (10 mg + 500 mg + 250 mg)
Beta Carotene + Vitamin C + Vitamin E Tablets (6 mg + 100 mg + 30 mg)
Beta Carotene + Vitamin C + Vitamin E Tablets (7 mg + 60 mg + 15 mg)
Beta Carotene + Vitamin C + Vitamin E Tablets (12 mg + 250 mg + 125 mg)
Beta Carotene Effervescent Tablets (7 mg)
Beta Carotene Tablets (15 mg)
Beta Carotene Tablets (20 mg)
Betamethasone + Neomycin Gel-Cream (0.1% + 0.6%)
Betamethasone Cream (0.1%)
Betamethasone Gel (0.1%)
Bifonazole Cream (1%)
Bran Tablets (250 mg), DC
Bran Tablets (250 mg), WG
Bromhexine Tablets (8mg)
Bromocriptine Tablet Cores (6 mg)

C

Calcium Carbonate Tablets (500 mg)
Calcium Effervescent Tablets (250 mg)
Calcium Gluconate Tablets (350 mg)
Calcium Glycerophosphate Tablets (200 mg)
Calcium Glycerophosphate Tablets (500 mg)
Calcium Pantothenate see Vitamin B_5
Calcium Phosphate Tablets for Cats and Dogs (400 mg)
Captopril Tablets (25 mg)
Carbamazepine Tablets (200 mg)
Carbonyl Iron + Manganese Sulfate + Copper Sulfate Tablets (24 mg + 3.5 mg + 0.16 mg)
Carnitine + Coenzym Q Solution (4.0% + 0.1%)
Caroate Dispersible Cleaning Tablets (880 mg)
Caroate Effervescent Cleaning Tablets (650 mg)
Charcoal Tablets (250 mg)
Chloramphenicol Ophthalmic Solution (3%)
Chloramphenicol Palmitate Oral or Topical Emulsion (2.5% = 250 mg/10 ml)
Chloramphenicol Palmitate Oral or Topical Emulsion (5.0% = 500 mg/10 ml)
Chlorhexidine Gel (2%)
Chlorhexidine Lozenges (5 mg)
Chloroquine Tablets (250 mg)
Choline Theophyllinate Tablets (100 mg)
Chymotrypsine Tablets (27 mg)
Cimetidine Tablets (200 mg)
Cimetidine Tablets (280 mg)
Cimetidine Tablets (400 mg)
Clenbuterol Tablets (20 µg)
Clobazam Tablets (10 mg)
Clomifen Tablets (50 mg)
Closantel Veterinary Injectable Solution (12 – 20 g/100 ml)
Clotrimazol Topical Solution (3%)

Clotrimazole Cream (1%)
Crospovidone Effervescent Tablets (1000 mg)
Crospovidone Water Dispersible Tablets (1000 mg)
Cyanocobalamin see Vitamin B_{12}
Cyproheptadine Tablet (4 mg)

D

Dexpanthenol Gel-Cream (5%)
Diazepam Injectable Solution (2.5 mg/ml)
Diazepam Tablet (10 mg)
Diclofenac Gel (1%)
Diclofenac Gel-Cream (1%)
Diclofenac Injectable Solution (75 mg/3 ml)
Diclofenac Oral Solution (1.5%)
Diclofenac Tablet Cores (50 mg)
Diclofenac Tablets (50 mg)
Diltiazem Tablets (50 mg)
Dimenhydrinate Tablet Cores (100 mg)
Dimenhydrinate Tablets (50 mg)

E

Enteric Film Coating
Ephedrine Tablets (100 mg)
Erythromycin Gel (1%)
Ethambutol Tablets (400 mg), DC
Ethambutol Tablets (400 mg), WG
Ethambutol Tablets (800 mg)
Etophylline + Theophylline Tablets (100 mg + 22 mg), DC
Etophylline + Theophylline Tablets (100 mg + 22 mg), WG
Eucalyptol Solution (8%)

F

Famotidine Tablets (40 mg)
Ferrous Fumarate Tablets (200 mg)
Ferrous Sulfate + Manganese Sulfate + Copper Sulfate Tablets (65 mg + 3.5 mg + 0.16 mg)
Ferrous Sulfate Tablets (200 mg)
Fir Needle Oil Solution (3%)
Folic Acid Tablets (5 mg)
Fucidine Tablet Cores (125 mg)
Furaltadone Injectable Solution (50 mg/ml)
Furosemide Tablets (40 mg)
Furosemide Tablets (200 mg)

G

Garlic Tablets Cores (100 mg)
Glibenclamide Tablets (5 mg)
Glutaminic Acid Tablets (550 mg)
Gramicidin Ophthalmic Solution (1.3 mg/10 ml)
Griseofulvin Tablets (125 mg)
Griseofulvin Tablets (500 mg)

H

Heparin Gel (30,000 i.u./100 g)
Horsetail Extract Tablets (450 mg)
Hydrochlorothiazide + Potassium Chloride Tablet Cores (50 mg + 300 mg)
Hydrochlorothiazide Tablets (50 mg), DC
Hydrochlorothiazide Tablets (50 mg), WG
Hydrocortisone Aqueous Gels (1%)
Hydrocortisone Cream (1%)
Hydrocortisone Ethanolic Gel (0.5%)

I

Ibuprofen Gel-Cream (5%)
Ibuprofen Gels (5%)
Ibuprofen Solution (2%)
Ibuprofen Suspension (4% = 400 mg/10 ml), I
Ibuprofen Suspension (4% = 400 mg/10 ml), II
Ibuprofen Tablets (400 mg), DC
Ibuprofen Tablets (400 mg), WG
Ibuprofen Tablets for Children (150 mg)

Indomethacin Gel (1%), I
Indomethacin Gel (1%), II
Indomethacin Powder for Hard Gelatin Capsules (160 mg)
Indomethacin Suppositories (50 mg)
Indomethacin Tablets (50 mg), DC
Indomethacin Tablets (50 mg), WG
Indomethacin Tablets (100 mg)
Inosin Tablet Cores (200 mg)
Isosorbide Dinitrate Tablets (5 mg)

K

Khellin Tablets (25 mg)

L

Levamisole Tablets (150 mg)
Levothyroxine Tablets (0.05 g)
Lidocain Gel (2%)
Lidocain Gel-Cream (5%)
Lisinopril Tablets (10 mg)

M

Magaldrate Chewable Tablets (500 mg)
Magaldrate Dispersible Tablets (700 mg)
Magaldrate Instant Powder or Dry Syrup
Magaldrate Suspension (10%)
Magnesium Carbonate Tablets (260 mg)
Mebendazol Tablets (100 mg)
Mebendazole Suspension (2% = 200 mg/10 ml)
Mefenamic Acid Tablets (250 mg)
Meprobamate + Phenobarbital Tablets (400 mg + 30 mg), DC
Meprobamate + Phenobarbital Tablets (400 mg + 30 mg), WG
Meprobamate Tablets (400 mg), DC
Meprobamate Tablets (400 mg), WG
Metamizol Tablets (500 mg)
Metformin Tablets (500 mg)
Methyl Cysteine Tablets (100 mg)
Methyl Salicylate + Menthol Gel (11% + 5%)
Metoclopramide Tablets (10 mg)
Metronidazole Effervescent Vaginal Tablets (500 mg)
Metronidazole Injectable Solution (500 mg/10 ml)
Metronidazole Tablet Cores (400 mg)
Metronidazole Tablets (200 mg)
Metronidazole Tablets (500 mg)
Metronidazole Vaginal Gel (1.2%)
Miconazole Cream (2%)
Miconazole Injectable Solution (1%)
Miconazole Mouth Gel (2%)
Mint Mouth Wash Solutions
Mint Oil Solution (3.5%)
Multivitamin + Calcium + Iron + Tablets
Multivitamin + Calcium Syrup
Multivitamin + Carbonyl Iron Tablets
Multivitamin + Minerals Tablets with Beta Carotene
Multivitamin Chewable Tablets for Children
Multivitamin Drops
Multivitamin Effervescent Granules
Multivitamin Effervescent Tablets with Beta Carotene (Food)
Multivitamin Effervescent Tablets (I)
Multivitamin Effervescent Tablets (II)
Multivitamin Injectable for Veterinary Application
Multivitamin Instant Granules
Multivitamin Oral Gel (vet.)
Multivitamin Oral Gel with Linoleic Acid and Linolenic Acid
Multivitamin Syrup, I
Multivitamin Syrup, II
Multivitamin Tablets (I)
Multivitamin Tablets (II)
Multivitamin Tablet Cores with Beta-Carotene
Multivitamin Tablets for Dogs
Multivitamin Tablets with Beta Carotene
Multivitamin Two Chamber Ampules

N

Nalidixic Acid Tablets (500 mg)
Naproxen Tablets (250 mg)
Naproxen Tablets (450 mg)
Neomycin Gel (0.05%)
Neomycin Tablets (250 mg)
Nicotinic Acid Tablets (200 mg)
Nicotinamide see Vitamin B_3
Nifedipine Tablet Cores (10 mg)
Nitrendipine Tablets (25 mg)
Nitrofurantoin Tablet Cores (100 mg)
Nitrofurantoin Tablets (100 mg)
Norephedrine Syrup (40 mg/10 g)
Nystatin Suspension (100,000 i.u./ml)
Nystatin Tabet Cores (200 mg)
Nystatin Tablets (50 mg and 100 mg)

O

Omega Fatty Acids Tablet Cores (10 mg EPA + DNA)
Oxytetracycline Injectable Solution for Veterinary Application (500 mg/10 ml)
Oxytetracycline Sustained Release Injectable for Veterinary Application (2.2 g/10 ml)
Oxytetracycline Tablets (250 mg)

P

Pancreatin Tablet Cores (30 mg)
Pancreatin Tablet Cores (130 mg)
Pancreatin Tablet Cores (300 mg)
Paracetamol (= Acetaminophen) + Caffeine Tablets (500 mg + 50 mg)
Paracetamol (= Acetaminophen) + Doxylamine + Caffeine Effervescent Granules (500 mg + 5 mg + 33 mg/2.1 g)
Paracetamol (= Acetaminophen) Instant Granules (250 mg or 500 mg)
Paracetamol (= Acetaminophen) + Ibuprofen + Orphenadin Tablets (250 mg + 200 mg + 100 mg)
Paracetamol (= Acetaminophen) + Norephedrine + Phenyltoloxamine Tablets (300 mg + 25 mg + 22 mg)
Paracetamol (= Acetaminophen) + Phenprobamat Tablets (200 mg + 200 mg)
Paracetamol (= Acetaminophen) Chewable Tablets (300 mg)
Paracetamol (= Acetaminophen) Effervescent Tablets (500 mg)
Paracetamol (= Acetaminophen) Instant Granules (500 mg)
Paracetamol (= Acetaminophen) Suppositories (150 mg and 500 mg)
Paracetamol (= Acetaminophen) Suspension (5% = 500 mg/10 ml)
Paracetamol (= Acetaminophen) Syrup (5% = 500 mg/10 g)
Paracetamol (= Acetaminophen) Syrup for Children (2.5% = 250 mg/10 ml)
Paracetamol (= Acetaminophen) Tablet Cores (500 mg)
Paracetamol (= Acetaminophen) Tablets (500 mg)
Paracetamol (= Acetaminophen) Tablets for Children (200 mg)
Phendimetrazin Tablets (35 mg)
Phenindion Tablets (50 mg)
Phenolphthalein Tablet Cores (200 mg)
Phenytoin Oral Suspension (5%)
Phenytoin Sodium Tablets (100 mg), DC
Phenytoin Sodium Tablets (100 mg), WG
Phenytoin Tablets (100 mg)
Piroxicam + Dexpanthenol Gel (0.5% + 5.0%)
Piroxicam Water Dispersible Tablets (20 mg)
Placebo Tablets
Polidocanol Wound Spray
Povidone-Iodine + Lidocain Gel (10%)
Povidone-Iodine Bar Soap (5%)
Povidone-Iodine Bar Soaps (5%)
Povidone-Iodine Concentrates for Broilers and Cattles (20%)

Povidone-Iodine Cream (10%)
Povidone-Iodine Effervescent Vaginal Tablets (350 mg)
Povidone-Iodine Foam Spray (10%)
Povidone-Iodine Gargle Solution Concentrate (10%)
Povidone-Iodine Gel-Cream (10%)
Povidone-Iodine Gels (10%)
Povidone-Iodine Glucose Ointment (2.5%(
Povidone-Iodine Lipstick or After Shave Stick (10%)
Povidone-Iodine Liquid Spray (10%)
Povidone-Iodine Lozenges (5 mg)
Povidone-Iodine Mastitis Cream (10%)
Povidone-Iodine Mouth Wash and Gargle Solution Concentrate (7.5%)
Povidone-Iodine Ophthalmic Solutions (0.4%)
Povidone-Iodine Ophthalmic Solutions (1.0%)
Povidone-Iodine Powder Spray
Povidone-Iodine Pump Spray (1%)
Povidone-Iodine Seamless Solutions (10%)
Povidone-Iodine Shampoo (7.5%)
Povidone-Iodine Soft Gel (1%)
Povidone-Iodine Solution (10%), I
Povidone-Iodine Solution (10%), II
Povidone-Iodine Surgical Scrubs (7.5%), I
Povidone-Iodine Surgical Scrubs (7.5%), II
Povidone-Iodine Teat-Dip Solution (3%)
Povidone-Iodine Transparent Ointment (10%)
Povidone-Iodine Vaginal Douche Concentrate (10%)
Povidone-Iodine Vaginal Ovula (5%)
Povidone-Iodine Vaginal Ovula (10%)
Povidone-Iodine Viscous Solution (1%)
Prazosin Tablets (5 mg)
Prednisolone Tablets (20 mg)
Prednisone Tablets (10 mg)
Probenecid Tablets (500 mg)
Procain Penicillin Injectable Suspension (300 mg/ml)
Propanidide Injectable Solution (50 mg/ml)
Propranolol Hydrochloride Tablets (10 mg, 50 mg and 100 mg)
Propranolol Tablets Cores (40 mg)
Protective Film Coating with Ethylcellulose + Kollidon VA 64
Protective Film Coating with HPC + Kollidon VA 64
Protective Film Coating with HPMC + Kollidon VA 64
Protective Film Coating with Kollidon VA 64
Protecitive Filmcoating with Polyvinyl Alcohol + Kollidon VA 64
Protective Film Coating with Shellac + Kollidon 30
Pseudoephedrine Tablets (60 mg)
Pyrazinamide Tablets (500 mg), DC
Pyrazinamide Tablets (500 mg), WG
Pyridoxine see Vitamin B_6

R

Ranitidine Tablet Cores (150 mg)
Ranitidine Tablet Cores (300 mg)
Riboflavin see Vitamin B_2
Rifampicin Tablets (450 mg)

S

Saccharin Effervescent Tablets (15 mg)
Saccharin Tablets (15 mg)
Selegiline Tablets (5 mg)
Serratio Peptidase Tablets (10 mg)
Silimarin Tablets (35 mg)
Simethicone Chewable Tablets (70 mg)
Simethicone Chewable Tablets (80 mg)
Simethicone Instant Granules (6%)
Sobrerol Injectable Solution (75 mg/5 ml)

Sodium Fluoride Tablets (0.5 mg)
Sodium Fluoride Tablets (1.3 mg)
Spironolactone Tablets (25 mg)
Spirulina Extract Chewable Tablets (250 mg)
Subcoating of tablets Cores
Sucralfate Tablets (500 mg)
Sugar Coating, automatic
Sugar Coating, manual
Sugar Film Coating
Sulfadiazine + Trimethoprim Veterinary Oral Suspension (40% + 8%)
Sulfadiazine Tablets (450 mg)
Sulfadimethoxine Veterinary Injectable Solution (250 mg/10 ml)
Sulfadimidine Tablets (500 mg)
Sulfadoxine + Trimethoprim Veterinary Injectable Solution (1000 mg + 200 mg/10 ml)
Sulfadoxine Solution (2% = 20 mg/ml)
Sulfamethoxazole + Trimethoprim Tablets (400 mg + 80 mg)
Sulfamethoxazole + Trimethoprim Dry Syrup (400 mg + 80 g/10 ml)
Sulfamethoxazole + Trimethoprim Oral Suspension (400 mg + 80 mg/5 ml)
Sulfamoxole + Trimethoprim Veterinary Injectable Solution (400 mg + 80 mg/10 ml)
Sulfathiazole Tablets (250 mg)
Sulfathiazole Veterinary Injectable Solution (8 mg/ml)
Sulfathiazole Veterinary Oral Solution (8 mg/ml)

T

Tannin-Crospovidone Complex Tablets (55 mg + 230 mg)
Terazosin Tablets (1 mg and 5 mg)
Terfenadine Suspension (60 mg/5 ml = 1.2%)
Terfenadine Tablets (60 mg)
Tetracycline Tablets (125 mg)
Tetracycline Tablets (250 mg)
Tetrazepam Tablets (50 mg)
Theophylline + Ephedrine Tablets (130 mg + 15 mg)
Theophylline Tablets (100 mg)
Theophylline Injectable Solution (200 mg/5 ml)
Thiamine see Vitamin B_1
Tretinoin + Alpha Bisabolol Gel (50 mg + 100 mg/100 g)
Tretinoin + Dexpanthenol Gel (50 mg + 2.5 g/100 g)
Tretinoin Cream (50 mg/100 g)
Tretinoin Gel (50 mg/100 g)
Tretinoin Solution (50 mg/100 g)
Triamcinolone Tablets (4 mg)
Trifluoperazine Tablets (5 mg)
Trihexylphenidyl see Benzhexol

U

Ultrasonic Adhesive Gel

V

Valeriana Extract + Passiflora Extract Tablet Cores (44 mg + 30 mg)
Valproate Sodium Tablets (500 mg)
Verapamil Tablets (120 mg)
Vitamin A + Vitamin B_6 + Vitamin E Tablets (40,000 i.u. + 40 mg + 35 mg)
Vitamin A + Vitamin C + Vitamin D_3 Chewable Tablets for Children (2,000 i.u. + 30 mg + 200 i.u.)
Vitamin A + Vitamin C + Vitamin E Tablets (1,200 i.u. + 60 mg + 30 mg)
Vitamin A + Vitamin D_3 + Calcium + Magnesium Injectable Solution (33,000 i.u. + 6,000 i. u. + 100 mg + 200 mg/g)
Vitamin A + Vitamin D_3 + Vitamin E + Beta Carotene Veterinary Injectable Solution (100,000 i.u. + 20,000 i.u. + 10 mg + 8 mg/g)

Vitamin A + Vitamin D_3 + Vitamin E Aqueous Injectable Emulsion for Cattles (500,000 i.u. + 75,000 i.u. + 50 mg/ml with Solutol HS 15)
Vitamin A + Vitamin D_3 + Vitamin E Aqueous Injectable Emulsion for Cattles (500,000 i.u. + 75,000 i.u. + 50 mg/ml with Cremophor EL)
Vitamin A + Vitamin D_3 + Vitamin E Concentrates, Water-miscible (120,000 i.u. + 60,000 i.u. + 40 mg/ml)
Vitamin A + Vitamin D_3 + Vitamin E Injectable Solution in Organic Solvents for Cattles (500,000 i.u. + 75,000 i.u. + 50 mg/ml)
Vitamin A + Vitamin D_3 + Vitamin E Veterinary Injectable Solution (100,000 i.u. + 20,000 i.u. + 10 mg/g)
Vitamin A + Vitamin D_3 Concentrate, Water-miscible (100,000 i. u. + 20,000 i. u./ml)
Vitamin A + Vitamin D_3 Concentrate, Water-miscible (120,000 i. u. + 12,000 i.u./g)
Vitamin A + Vitamin D_3 Drops (30,000 i.u. + 3,000 i.u./g)
Vitamin A + Vitamin D_3 Injectable Solutions (30,000 i.u. + 5,000 or 10,000 i.u./ml)
Vitamin A + Vitamin D_3 Oral Solution for Children (1,000 i.u. + 100 i.u./ml)
Vitamin A + Vitamin D_3 Syrup (30,000 i.u. + 10,000 i.u./ml)
Vitamin A + Vitamin E Chewable Tablets (30,000 i.u. + 35 mg)
Vitamin A + Vitamin E Drops (25,000 i. u. + 50 mg/ml)
Vitamin A + Vitamin E Drops (5,000 i.u. + 50 mg/ml)
Vitamin A + Vitamin E Injectable Solution for Sheeps (250,000 i.u. + 25 mg/ml)
Vitamin A + Vitamin E Tablets (33,000 i.u. + 70 mg)
Vitamin A Chewable Tablets (100,000 i.u.)
Vitamin A Concentrate, Water-miscible (100,000 i. u./ml)
Vitamin A Drops (50,000 i. u./ml)
Vitamin A Ethanolic Veterinary Injectable Solution (500,000 i.u./ml)
Vitamin A Suppositories (150,000 i.u.)
Vitamin A Tablet Cores (50,000 i.u.)
Vitamin A Tablets (25,000 i.u.)
Vitamin A Tablets (50,000 i.u.)
Vitamin B Complex + Amino Acid + Magnesium Effervescent Granules
Vitamin B Complex + Carnitine Tablet Cores
Vitamin B Complex + Minerals + Linoleic/Linolenic Acid Syrup
Vitamin B Complex + Vitamin C + Calcium Effervescent Tablets
Vitamin B Complex + Vitamin C + Ferrous Sulfate Tablets
Vitamin B Complex + Vitamin C Effervescent Tablets
Vitamin B Complex + Vitamin C Instant Granules
Vitamin B Complex + Vitamin C Syrup, I
Vitamin B Complex + Vitamin C Syrup, II
Vitamin B Complex + Vitamin C Tablets
Vitamin B Complex Injectable Solution
Vitamin B Complex Syrup
Vitamin B Complex Tablets I
Vitamin B Complex Tablets II
Vitamin B_1 + Caffeine Tablets (500 mg + 100 mg)
Vitamin B_1 + Vitamin B_2 + Vitamin B_3 + Vitamin B_6 Injectable Solution (100 mg + 6 mg + 40 mg + 4 mg/2 ml)
Vitamin B_1 + Vitamin B_6 + Vitamin B_{12} Tablets (100 mg + 10 mg + 100 µg)
Vitamin B_1 + Vitamin B_6 + Vitamin B_{12} Tablets (100 mg + 200 mg + 100 µg)

Vitamin B_1 + Vitamin B_6 + Vitamin B_{12} Tablets (250 mg + 250 mg + 1 mg)
Vitamin B_1 Tablets (50 mg), I
Vitamin B_1 Tablets (50 mg), II
Vitamin B_1 Tablets (100 mg), DC
Vitamin B_1 Tablets (100 mg), WG
Vitamin B_1 Tablets (300 mg)
Vitamin B_{12} Tablets, Coloured (50 µg)
Vitamin B_2 Tablets (3 mg)
Vitamin B_2 Tablets (10 mg)
Vitamin B_2 Tablets (75 mg)
Vitamin B_2 Tablets (100 mg)
Vitamin B_2 Tablets (150 mg)
Vitamin B_3 (Nicotinamide) Tablets (300 mg)
Vitamin B_5 (Calcium D-Pantothenate) Chewable Tablets (600 mg)
Vitamin B_5 (Calcium D-Pantothenate) Tablets (100 mg)
Vitamin B_5 (Calcium D-Pantothenate) Tablets (280 mg)
Vitamin B_5 (Calcium D-Pantothenate) Tablets (300 mg)
Vitamin B_6 Tablets (40 mg), DC
Vitamin B_6 Tablets (40 mg), WG
Vitamin B_6 Tablets (100 mg)
Vitamin B_6 Tablets (250mg)
Vitamin B_6 Tablets (300 mg)
Vitamin C + Calcium Carbonate Effervescent Tablets (500 mg + 300 mg)
Vitamin C + Vitamin E Lozenges (100 mg + 50 mg)
Vitamin C Chewable Tablets (100 mg, 500 mg, 1,000 mg)
Vitamin C Chewable Tablets (500 mg)
Vitamin C Chewable Tablets with Dextrose (100 mg)
Vitamin C Chewable Tablets with Fructose (120 mg)
Vitamin C Chewable Tablets with Sucrose (500 mg)
Vitamin C Effervescent Tablets (100 mg and 1000 mg)
Vitamin C Effervescent Tablets (500 mg)
Vitamin C Tablets (100 mg)
Vitamin C Tablets (200 mg)
Vitamin C Tablets (250 mg)
Vitamin C Tablets (400 mg)
Vitamin E + Benzocaine Solution (5% + 2%)
Vitamin E + Selenium Veterinary Injectable Solution (60 mg E + 3 mg Se/ml)
Vitamin E Chewable Tablets (100 mg)
Vitamin E Chewable Tablets (150 mg)
Vitamin E Chewable Tablets (200 mg)
Vitamin E Chewable Tablets (400 mg)
Vitamin E Concentrate, Water-miscible (10% = 100 mg/ml)
Vitamin E Drops (50 mg/ml)
Vitamin E Gel-Cream (10%)
Vitamin E Solution with Ethanol (0.01% = 1 mg/10 ml)
Vitamin E Tablets (50 mg)
Vitamin K_1 Phytomenadion) Injectable Solution (10 mg and 20 mg/ml)

1.3 Size and optimization of the formulations

All the formulations were developed exclusively on a laboratory scale of the order of 1 kg maximum. For this reason, scale-up for production must therefore be checked and revised, as necessary.

It is only in very exceptional cases that the formulations have been optimized by a systematic study involving a comparison between different excipients or by varying the amounts of excipients. Thus, the formulations are merely suggestions that require further optimization.

1.4 Active substances

The active substances are almost exclusively generic. They were mostly supplied free of charge as samples by pharmaceutical companies. Since the manufacturer's name was mostly not mentioned, it unfortunately cannot be listed here.

Significant differences in the properties of the preparations may occur if the same active substance is used, but has a different grain size or originates from another manufacturer. The reason for this is that the difference in physical properties may exert a strong effect particularly on solid drugs (cf. Chapter 2.5).

1.5 Excipients

As far as possible, the manufacturer's name and the registered trademark are given for excipients.
The excipients mostly used in the formulations and their suppliers are listed in Table 1. The serial numbers in the left-hand column of this table are quoted in the formulations.

Table 1

	Supplier and address	Excipients
[1]	BASF AG Department MER 67056 Ludwigshafen, Germany or BASF subsidiary in the country concerned	Cremophor® products Kollicoat® products Kollidon® products Ludipress® Lutrol® products Propylene glycol Pharma Sicovit® Soluphor® P Solutol® HS 15
[2]	Bärlocher GmbH 80992 Munich, Germany	Calcium arachinate Magnesium stearate
[3]	Cerestar GmbH Düsseldorferstrasse 191 47809 Krefeld, Germany	 Potato starch Corn starch
[4]	Degussa AG GB Industry + Fine Chemicals Postfach 1345 63457 Hanau, Germany	 Aerosil® 200
[5]	FMC Corp. Food + Pharmaceutical Products 735 Market Street Philadelphia, PA 19103, USA	 Avicel® products Ac-Di-Sol®
[6]	Hüls AG Postfach 45674 Marl, Germany	 Polyethylene glycol 6000, powder
[7]	Mallincrodt Inc. P.O. Box 5439 675 McDonnel Boulevard St. Louis, MO 63134, USA	 Stearic acid
[8]	Meggle Milchindustrie GmbH Postfach 40 83512 Wasserburg, Germany	 Lactose Monohydrate D 20 Tablettose®

[9]	Rhône-Poulenc 15, Rue Pierre Pays B.P. 52 69660 Collonges-au Mont d'Or, France	Dicalcium phosphate, $CaHPO_4$ (DITAB®)
[10]	Riedel-de-Haen AG Wunstdorferstrasse 40 30926 Seelze, Germany	Sorbitol, crystalline Talc

1.6 Stability data

It is only in exceptional cases or when certain groups of active substances are present that data are given on the chemical and/or the physical stability of the formulations. The reasons are as follows.

a. The formulations are practically always modified by the customer when they are scaled up to meet the demands of industry.

b. Aromas or colorants are added to the formulations in amounts depending on the particular taste of the target group.

c. In view of the very number of formulations presented here and for capacity reasons, the long-term stability of all of them cannot be checked.

The stability of the preparation may change as a result of items a. and b. Thus the final formulation must be checked in any event.

Data on the chemical stability are often available for sensitive materials, e. g. PVP-iodine or vitamins. They mostly concern either storage at room temperature (20 – 25 °C) over a period of one year or a stress test that lasts at least just as long.

In a number of formulations, data are also listed on the physical stability.

2 Tablets

2.1 Size of formulations and measured values

The formulations were developed on a laboratory scale in which case 200 – 1,000 g of the mixtures to be tabletted were used. Normally, the amounts weighed out in the formulations correspond to the amount in the tablets multiplied by a factor of 1,000. The weight, hardness, disintegration, and chipping of the tablets and the data on their release are measured values.

2.2 Direct compression

The technology involved in direct compression assumes great importance in the tablet formulations, because it is often the cheapest means, particularly in the production of generics, that the active substance permits. The limiting factors are the physical properties of the active substance and its concentration in the tablets (cf. Chapter 2.5). Even substances such as ascorbic acid that are hardly suitable for direct tabletting owing to the friability of their crystals can normally be directly pressed into tablets at concentrations of 30 – 40 %. However, this technique is not as suitable if the content of ascorbic acid is higher. This limit may be shifted upwards by special direct compression auxiliaries, e. g. Ludipress. Two important alternatives, viz. Ludipress and Kollidon VA 64, can be found in the BASF line of pharmaceutical excipients for direct compression.

A. Ludipress

Ludipress is a speciality derived from lactose, Kollidon 30, and Kollidon CL. It thus combines the properties of a filler, binder, disintegrant, and flowability agent and also often acts as a release accelerator. By virtue of its versatility formulations containing it are usually very simple. It can also be combined with almost all active substances with the exception of those that enter into a chemical interaction with lactose (Maillard reaction).

Active substances, e. g. many analgetics, behave very differently with Ludipress when the dosage is extremely high. Acetylsalicylic acid and metamizole can be pressed when little Ludipress has been added; ibuprofen requires a larger amount; and the fraction of Ludipress required in the tablets is too large for paracetamol (= acetaminophen).

B. Kollidon VA 64

An alternative to Ludipress is the outstanding dry binder Kollidon VA 64 together with excipients, e. g. calcium phosphate, microcrystalline cellulose, lactose, or starch, and a disintegrant, e. g. Kollidon CL. This combination even allows 500 mg of paracetamol to be pressed into good tablets with a weight of 700 mg.

No other dry binder has a binding power and plasticity comparable to those of Kollidon VA 64. Plasticity, in particular, is an important parameter in direct compression. As can be seen in Fig. 1, this property of Kollidon VA 64 is not adversely effected by increasing the pressure. The beneficial properties of Kollidon VA 64 can

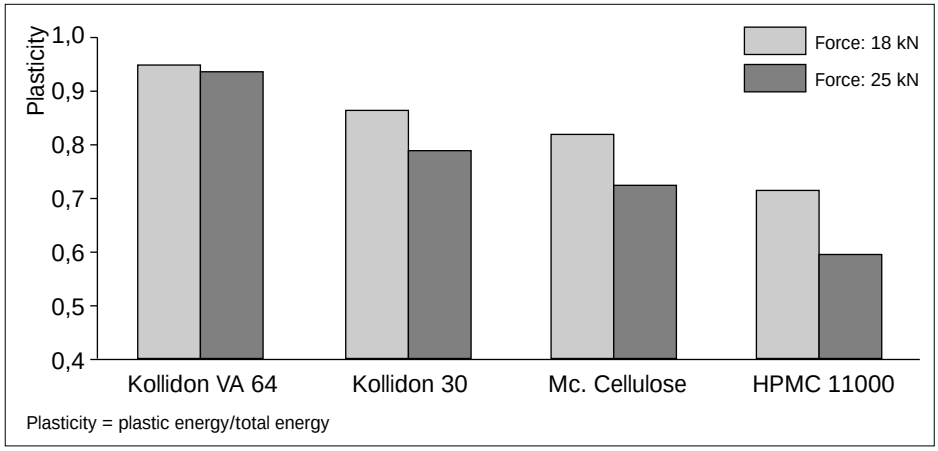


Fig. 1 Plasticity of dry binders in tablets
(99.5% binder + 0.5% magnesium stearate)

also be exploited for the production of concentrated active substance that is subsequently used for direct tabletting.

Obviously, Kollidon VA 64 and Ludipress can also be combined with one another.

2.3 Wet granulation

Great significance is still attached to wet granulation, because direct compressing is not the most suitable technology for many active substances that are in high dosages or in fine powder form. Even if the active substance is sensitive to hydrolysis, modern equipment, e.g. in a fluidized bed, eliminates all problems in wet granulation.

The granules for tabletting of the presented formulations were mostly produced by traditional means, i.e. moistening, screening, drying, and again screening. Fluidized-bed granulation was resorted to only in exceptional cases in view of the amounts needed.

Various alternatives to wet granulation in general are offered by BASF pharmaceutical excipients:

- granulation with a Kollidon solution
- granulation of a dry mixture of the active substance and (filler and) Kollidon with water/solvent
- granulation in which some of the Kollidon is mixed with the active substance and the rest is dissolved in the solution used for granulation

The last the of the three alternatives is preferred if the amount of liquid required for granulation is restricted and therefore the viscosity of the solution containing all of the Kollidon would be too high.

Other alternatives consist of using different grades of Kollidon. Substituting Kollidon 25 or Kollidon 30 by Kollidon 90 F would be particularly interesting for obtaining greater hardness without increasing the pressure. The example of a placebo tablet illustrated in Fig. 2 shows that tablets of twice the hard-

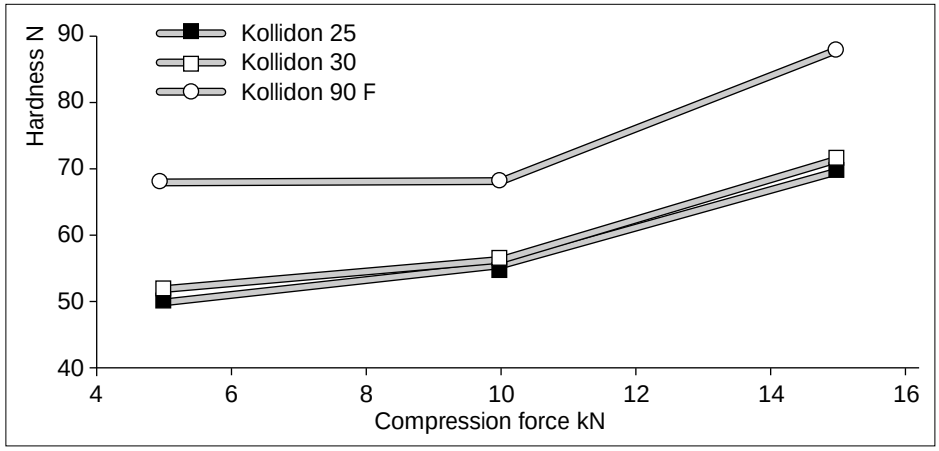


Fig. 2 Hardness of lactose tablets containing various Kollidon products (wet granulation)

ness of those obtained by Kollidon 25 can be achieved by using Kollidon 90 F at low pressures.

Conversely, there would be some point in changing over from Kollidon 90 F to Kollidon 25 or 30 if the viscosity of the solution used in granulation is too high. In practice, however, the same hardness is usually achieved by increasing the amount of Kollidon.

2.4 Tablet press

All the formulations were devised on rotary tabletting presses that were fitted with 10 – 20 punches.

2.5 Effect of the physical properties of the active substance

In the manufacture of tablets it is important to define and appreciate the

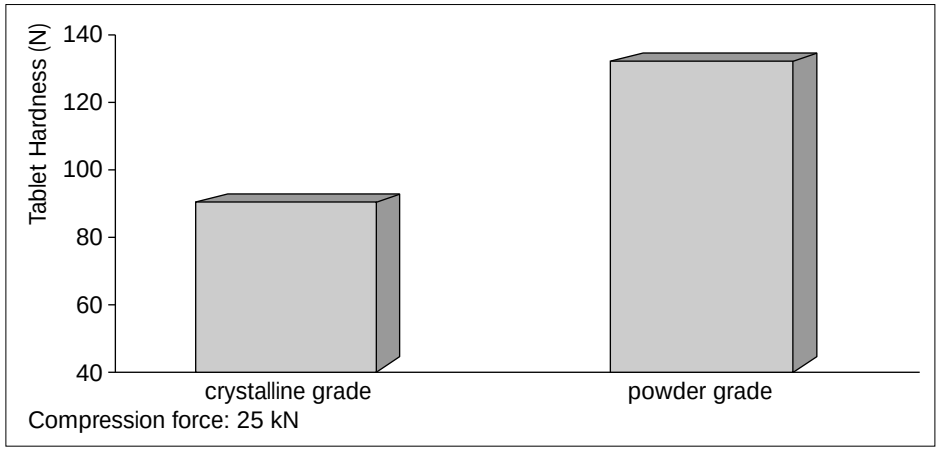


Fig. 3 Direct compression of different types of ascorbic acid
(40% ascorbic acid, 5% Kollidon VA 64)

physical properties of the active substance. This particularly concerns the particle size.

Fig. 3 shows the difference that can occur when ascorbic acid tablets of the same composition are produced at the same pressure, but when the active substance consists of crystals of two different sizes (crystalline = > 150 µm; powder = < 150 µm).

2.6 Effect of the physical properties of the excipients

Characterization of the physical properties of excipients is also important. This is demonstrated in Table 2 in the light of the example of hydrochlorothiazide. Tablets of greater hardness are obtained if fine instead of coarse Povidone K 90 is taken. To a certain extent, the disintegration and the release are also affected.

2.7 Methods of measuring the properties of tablets

The general instructions for the determination of the corresponding properties of tablets are contained in the Pharmacopoeiae (Ph.Eur. or USP). If it is not stated to the contrary, the disintegration time is measured in artificial gastric juice. The release is determined by the methods laid down in the corresponding monographs for the tablets (usually USP) and in the prescribed medium.

2.8 Information on dissolution of active substance

Nowadays it is standard practice and/or laid down that the in-vitro release of active substance be checked. Unfortunately, these data cannot be given for all formulations. This is particularly the case when the active substance is sufficiently soluble or when the formulation was developed

Table 2

Influence of the particle size of Povidone K 90 on the properties of hydrochlorothiazide tablets (solvent granulation)

Formulation	I	Hydrochlorothiazide	50.0 mg
		Povidone K 90	7.5 mg
		Lactose monohydrate	422.5 mg
	II	Water	37.5 mg
	III	Magnesium stearate	2.5 mg

Tablet properties

Binder	Hardness	Disintegration time	Dissolution (30 min)
Povidone K 90 95 % > 250 µm	66 N	18 min	23 %
Povidone K 90 15 % > 250 µm	97 N	22 min	19 %

in a time when this parameter was not yet demanded.

2.9 Formulations

The formulations in this chapter have been arranged in the alphabetic order of their active substances.

3 Coating of tablets and capsules

3.1 Size of formulations and amounts used

The formulations were developed on a laboratory scale.

The batches usually consisted of ca. 1 kg of spray solution or spray suspension and 5 kg of tablet cores.

3.2 Equipment

The tests were mostly performed in the Accela-Cota 241, for which the minimum amount of cores is 5 kg. In a few cases, the fluidized-bed granulator WSG Glatt 15 or a traditional coating pan was used.

3.3 Conditions for spraying

Whenever they are of importance, the conditions for processing the formulations on a given scale have been quoted.

3.4 Colour additives

Normally the colorants added were Sicovit colour lakes or Sicovit pigments. To a certain extent, these two are interchangeable.

3.5 Formulations

The formulations in this chapter have been arranged in the alphabetic order of their function.

4 Granules, powders, dry syrups and lyophilisates

4.1 Size of formulations and amounts used

The formulations were developed on a laboratory scale.

Normally the amounts used were those required for a trial of 50 – 500 g. Larger batches, e.g. in fluidized-bed granulation, were only resorted to in exceptional cases.

4.2 Methods of granulation

The granules were mostly produced by traditional means, i.e. moistening, screening, drying, and again screening. Fluidized-bed granulation was resorted to only in exceptional cases in view of the amounts needed.

4.3 Assessment of the properties of the granules

Most of the cases concerned granules that were suspended in water before the administration. Consequently, the properties of the suspension thus formed were assessed. The parameters that attracted most attention were the relative sediment volume (volume of sediment/total volume) and the redispersability. See Chapter 5.3 for details on the suspensions.

4.4 Formulations

The formulations in this chapter have been arranged in alphabetical order of their active substances.

5 Liquid preparations

5.1 Size of formulations and amounts used

The formulations were developed on a laboratory scale.

The batches were of 50 –1,000 g size.

5.2 Solubilization of insoluble active substances

In order to solubilize insoluble lypophilic or hydrophobic active substances in an aqueous medium, BASF Pharmaceutical Excipients offer several possibilities and mechanisms.

A Microemulsions

Cremophor RH 40, Cremophor EL, and Solutol HS 15 act as surface-active solubilizers in water and form the structures of micelles. The micelle that envelops the active substance is so small that it is invisible or perhaps visible in the form of an opalescence.

Typical fields of application are oil-soluble vitamins, antimycotics of the miconazole type, mouth disinfectants, e.g. hexiditin, and etherian oils or fragrances.

Solutol HS 15 is recommended for parenteral use of this solubilizing system and has been specially developed for this purpose.

B Formation of complexing compounds

The soluble Kollidon products form reversible complexes with many hydrophobic active substances, and clear solutions in water are thus obtained. This may be affected by the molecular weight. The longer the chains or the higher the K-value of the Kollidon type, the stronger is the solubility effect and thus the greater the solubility that can be obtained by the active substance. In practice, this effect was mostly exploited for the solubilization of antibiotics in human and veterinary medicine. Details are given in the book “Kollidon – Polyvinylpyrrolidone for the pharmaceutical industry”.

There are also restrictions on the use of this auxiliary in human parenterals. It is laid down in many countries that the K-value must not exceed 18, and there is also a restriction on the amount to be used for each dose administered in intramuscular application.

C Hydrophilization

Active substances can also be solubilized by Lutrol F 68 in addition to the Cremophor and Kollidon products. The mechanism is probably based, for the most part, on the principle of hydrophilization. Micelle formation is certainly of minor significance, if it exists at all.

5.3 Stabilizing suspensions

Various BASF pharmaceutical excipients with different functions can be used for stabilizing suspensions.

5.3.1 Oral and topical suspensions

The following groups of products can be offered for stabilizing oral and topical suspensions.

A. Soluble Kollidon products

Low concentrations, i.e. 2 – 5 %, of Kollidon 90 F suffice to stabilize aqueous suspensions. Fig. 4 demonstrates that it can completely prevent sedimentation. The example taken was a crospovidone suspension.

A combination consisting of 2 % of Kollidon 90 F and 5 – 9 % of Kollidon CL-M has proved to be an effective system for stabilizing suspensions.

Kollidon 30 is also used for this purpose. It can be combined with all conventional suspension stabilizers (thickeners, surfactants, etc.).

B. Kollidon CL-M

The use of Kollidon CL-M as a suspension stabilizer has nothing whatever to do with the principle of increasing the viscosity. The addition of 5 – 9 % has practically no effect in changing the viscosity, but strongly reduces the rate of sedimentation and facilitates the redispersability, in particular, an effect that is consistent with the low viscosity. One of the reasons for this Kollidon CL-M effect is its low (bulk) density, which is only half of that of conventional crospovidone, e.g. Kollidon CL. It can clearly be seen from Fig. 5 that a relative volume of sediment of normal micronized crospovidone of high bulk density (= Crospovidone M) is less and more compact that of Kollidon CL-M, which undergoes hardly any sedimentation.

In this book, a number of formulations for made-up suspensions or extemporaneous suspensions produced from instant granules or dry syrups

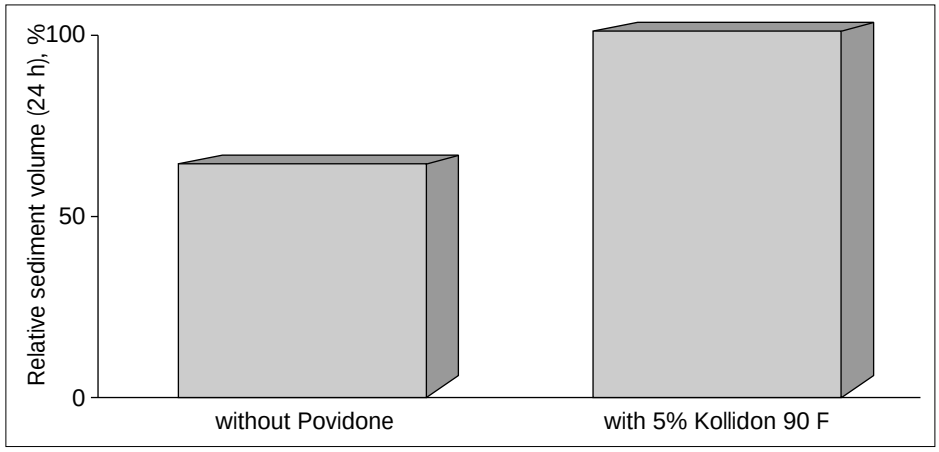


Fig. 4 Effect of Kollidon 90 F on the volume of sediment in a crospovidone suspension (7.5 % in water)

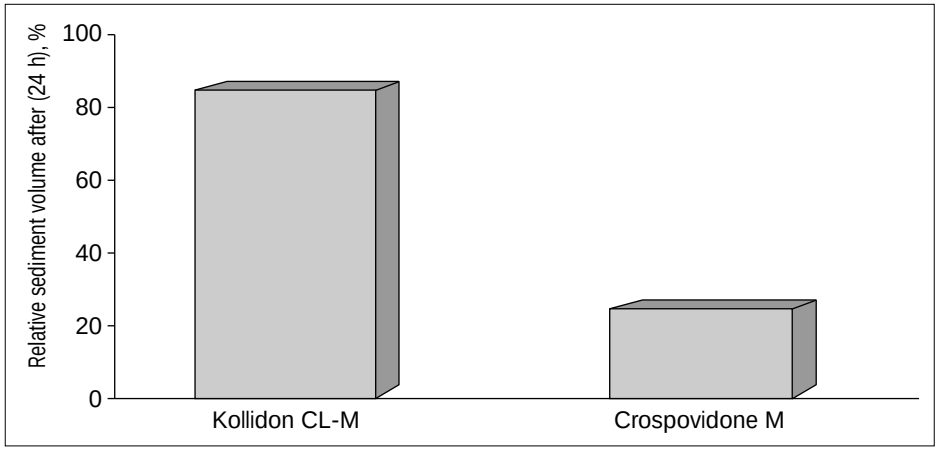


Fig. 5 Volume of sediment of various micronized crospovidone types (7.5 % in water + 5 % Lutrol F 127)

(see Chapter 4) illustrate the use of Kollidon CL-M.

C Lutrol F products

The polyoxamers, Lutrol F 68 and Lutrol F 127, in concentrations of 2 – 5 %, expressed in terms of the final weight of the suspension, offer a further opportunity of stabilizing suspensions. They also do not increase the viscosity when used in these amounts and can be combined with all other conventional suspension stabilizers.

5.3.2 Parenteral suspensions

Kollidon 17 PF is eminently suitable for improving the wetability of the active substance in parenteral suspensions, e.g. penicillin ampoules. It reduces the sedimentation rate and improves the dispersability. Kollidon 17 PF, in the amounts used for this purpose, exerts practically no influence on the viscosity.

Solutol HS 15 can also be used.

5.3.3 Dispersions for tablet coating

Kollidon 25 or Kollidon 30 are particularly suitable for stabilizing pigment suspensions. Examples are given in Chapter 3.4.

5.4 Aromas and dyes

Aromas and dyes are quoted in only exceptional cases, because they depend strongly on the taste of the target group concerned and are often specific for a particular country. They can be included in the formulations if this is wished.

5.5 Preservation

In a few cases, preservatives have been already integrated in the formulations. In difficult cases, e.g., antiacid suspensions with a pH more than 7, the preservative system i.e. bacteria-free or low-bacteria production, should be the subject of accurate research.

5.6 Physical stability

The most important parameters for the physical stability of suspensions are the relative volume of sediment (= volume of sediment/total volume) and the redispersability. They are tested after 1 – 4 weeks have elapsed.

5.7 Chemical stability

Data on the chemical stability at room temperature have been compiled almost exclusively for vitamins. A stress test was almost always performed for PVP-iodine preparations, and this corresponds to at least one year at room temperature.

5.8 Formulations

The formulations mentioned in this chapter are arranged in alphabetical order of their active substances.

6 Semi-solid drugs (gels, creams, suppositories and ovula)

6.1 Size of formulations and amounts used

The formulations were developed on a laboratory scale.

The size of the batch was usually 100 g, with the result that care must be exercised in scaling up from a laboratory to a production scale.

6.2 Emulsifying agents in pharmaceutical creams

The Cremophor types, Cremophor A 6 and Cremophor A 25 are the most suitable in the BASF line of excipients for the development of macroemulsions with the appearance and the consistency of a cream. They allow the production of physically stable formulations when they are used in low concentrations in the vicinity of 1 – 4 %.

6.3 Excipients as a base for suppositories and ovula

In the formulations presented here, mixtures of the polyethylene glycols, Lutrol E 400, Lutrol E 1500, Lutrol E 4000, and Lutrol E 6000, are intended as water-soluble base for suppositories and ovula.

6.4 Gel formers

At the present time, gels are growing in importance in the pharmaceutical industry, because, in contrast to pastes and creams, it can be visually ascertained that the active substance is dissolved. This is often coupled with a guarantee of superior absorption.

The BASF line of pharmaceutical excipients includes a gel former, viz. the

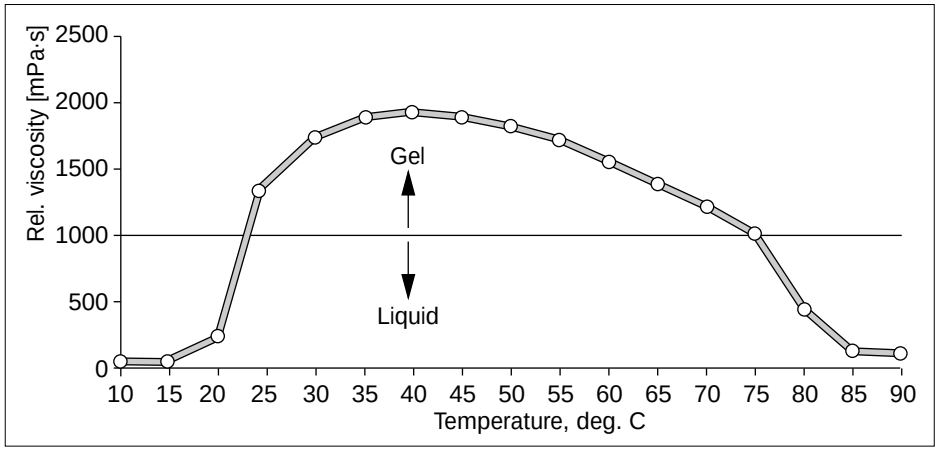


Fig. 6 Influence of the temperature on the consistency of 20 % Lutrol F 127 in water (rotary viscometer, 250 rpm)

polyoxamer Lutrol F 127. It allows the production of gels whose structures are stable in a pH range of 4 – 8. No neutralization whatever is necessary. A feature of these gels is their thermoreversible consistency. It is apparent from Fig. 6 that the gels are liquid at low temperatures i.e. below 15 °C and at temperatures above 75 °C. In between these two values, a gel reversibly exists whose consistency depends on the concentration of the Lutrol F 127.

6.5 Preservatives and fragrances

Preservatives and fragrances were not always added. Consequently, this point must be worked out in the final formulation. For the gels based on Lutrol F 127 the addition of 0.2% sorbic acid is recommended.

6.6 Stability

Data on the chemical stability are scanty. Preparations with PVP-iodine as disinfectant are an exception, in which case a stress test was always performed whose results represent a period of much more than 12 months at room temperature (20 – 25 °C).

The physical stability, on applying heat at 45 °C, was mainly determined on creams.

6.7 Formulations

The formulations given in this chapter have been arranged in alphabetical order of their active substances.

2.9 Tablet formulations (Lab Scale)

Aceclofenac Gel-Cream (1.5 %)

1. Formulation

I.	Aceclofenac	1.5 g
	Miglyol® 812 (Dynamit-Nobel)	9.9 g
	Lutrol E 400 [1]	4.9 g
II.	Water	64.0 g
III.	Lutrol F 127 [1]	19.7 g

2. Manufacturing

Mix the components I with water and cool to about 5 °C. Add slowly Lutrol F 127 and continue stirring until Lutrol F 127 is dissolved. Maintain cool until the air bubbles escaped.

3. Properties of the gel

A milky, firm gel was obtained.

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Aceclofenac Instant Granules (50 mg)

1. Formulation (granules)

I.	Aceclofenac	1.3 g
	Orange flavour	4.3 g
	Sorbit	85.6 g
II.	Lutrol F 68 [1]	4.4 g
	Cremophor RH 40 [1]	4.4 g
	Water	about 50 g

2. Manufacturing

Granulate mixture I with solution II, pass through a 0.8 mm screen, dry and sieve again. Fill 3.9 g in sachets corresponding to 50 mg aceclofenac.

3. Properties of the granules

Free flowing, water dispersible granules having almost no bitter taste.

2.9 Tablet formulations (Lab Scale)

Acetylsalicylic Acid + Paracetamol (= Acetaminophen) + Caffeine Tablets (250 mg + 250 mg + 50 mg)

1. Formulation

I.	Acetylsalicylic acid, crystalline (Merck)	250 g
	Paracetamol, crystalline (Merck)	250 g
	Caffeine (Knoll)	50 g
II.	Kollidon 90 F [1]	50 g
	Isopropanol	q. s.
III.	Magnesium stearate [2]	5 g
	Kollidon CL [1]	16 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry and sieve through a 0.8 mm screen, add the components III and press with high compression force.

3. Tablet properties

Weight	670 mg
Form	biplanar
Diameter	12 mm
Hardness	45 N
Disintegration	6 min
Friability	0.7%

4. Physical stability (12 months, 20–25 °C)

Weight	670 mg
Hardness	65 N
Disintegration	4 min
Friability	0.9%

2.9 Tablet formulations (Lab Scale)

Acetylsalicylic Acid + Paracetamol (= Acetaminophen) + Caffeine Tablets (400 mg + 100 mg + 30 mg)

Formulation

Acetylsalicylic acid, crystalline	400 g
Paracetamol, crystalline (Merck)	100 g
Caffeine (Knoll)	30 g
Ludipress [1]	100 g
Kollidon CL [1]	20 g
Polyethylene glycol 6000, powder [6]	30 g
Stearic acid [7]	5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with low compression force.

3. Tablet properties

Weight	683 mg
Diameter	12 mm
Form	biplanar
Hardness	116 N
Disintegration	1 – 2 min
Friability	0.3 %

2.9 Tablet formulations (Lab Scale)

Acetylsalicylic Acid + Paracetamol (= Acetaminophen) Tablets (250 mg + 250 mg)

Formulation

Acetylsalicylic acid, crystalline (Merck) .....250 g
Paracetamol, crystalline (Merck) .....250 g
Avicel PH 101 [5].....60 g
Kollidon 30 (or Kollidon VA 64) [1].....15 g
Kollidon CL [1] .....25 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

Weight .....605 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....90 N
Disintegration .....< 1 min
Friability.....0.7%

4. Chemical stability of formulation No. 2 (20–25 °C, closed)

	0 Months	6 Months	12 Months
Acetylsalicylic acid	100%	100%	100%
Vitamin C	100%	100%	96%
Free acetic acid	< 0,01%		< 0.01%
Free salicylic acid	< 0,01%		< 0.01%

2.9 Tablet formulations (Lab Scale)

Acetylsalicylic Acid + Vitamin C Tablets (325 mg + 250 mg)

1. Formulations

	No. 1	No. 2
Acetylsalicylic acid, crystalline (Merck)	325 g	325 g
Ascorbic acid, powder (BASF)	250 g	250 g
Sorbitol, crystalline [10]	120 g	–
Avicel PH 101 [5]	40 g	100 g
Kollidon VA 64 [1]	25 g	12 g
Kollidon CL [1]	20 g	30 g
Magnesium stearate [2]	2 g	3 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium/high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	790 mg	726 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	92 N	100 N
Disintegration	2 min	< 1 min
Friability	1%	1%

4. Chemical stability of formulation No. 2 (20–25 °C)

	0 Months	6 Months	12 Months
Acetylsalicylic acid	100 %	100 %	100 %
Vitamin C	100 %	100 %	96 %
Free acetic acid	< 0,01 %		< 0.01 %
Free salicylic acid	< 0,01 %		< 0.01 %

2.9 Tablet formulations (Lab Scale)

Acetylsalicylic Acid Tablets (400 mg)

1. Formulation

Acetylsalicylic acid, crystalline (Merck) .....400 g
Ludipress [1] .....99 g
Stearic acid [7] .....1 g
Kollidon CL [1].....15 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....516 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....90 N
Disintegration .....<1 min
Friability.....0.4 %
Dissolution, 15 min.....84 %
30 min .....97 %

4. Chemical stability

Storage time	RT	40 °C
0 months	100.0 %	100.0 %
6 months	100.0 %	100.0 %
12 months	98.4 %	100.0 %

The content of free salicylic acid remained always below 0.2 %.

2.9 Tablet formulations (Lab Scale)

Acetylsalicylic Acid Tablets (500 mg)

1. Formulation

Acetylsalicylic acid (Merck).....500 g
Avicel PH 101 [5].....200 g
Kollidon 30 [1].....15 g
Kollidon CL [1].....25 g
Magnesium stearate [2].....3 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight.....707 mg
Diameter.....12 mm
Form.....biplanar
Hardness.....61 N
Disintegration.....<1 min
Friability.....0.7%

5.8 Liquid Formulations (Lab scale)

Acyclovir Oral Suspension (2 % = 200 mg/10 ml)

1. Formulation

Acyclovir	2.0 g
Kollidon CL-M [1]	6.0 g
Kollidon 30 [1]	3.0 g
Sorbitol [10]	28.0 g
Citric acid	0.5 g
Preservative	q.s.
Water	60.5 g

2. Manufacturing

Suspend acyclovir and Kollidon CL-M in the solution of the other components under vigorous stirring.

3. Properties of the solution

Colour	white
Relative sediment volume after 14 days	96 %
Redispersibility after 14 days	easy

4. Remarks

- The substitution of Kollidon 30 by Kollidon 90F gives a more compact sediment.
- The deletion of citric acid gives a much more compact sediment.
- The substitution of citric acid by sodium citrate impairs strongly the redispersibility.

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Albendazole Dry Syrup or Instant Granules (200 mg)

1. Formulation

I.	Albendazole	4 g
	Citric acid	3 g
	Sodium citrate	3 g
	Sorbitol, crystalline [10]	88 g
II.	Ethanol 96 %	22 g
	Lutrol F 68 [1]	2 g

2. Manufacturing

Granulate mixture I with solution II, pass through a 0.8 mm screen, dry and sieve again.

Fill 50 g of the granules in a 100 ml flask (= dry syrup) or 5 g in sachets (= instant granules)

3. Administration forms

Dry syrup (200 mg albendazole /10 ml):
Fill the flask containing 50 g of granules with water to the 100 ml mark. The obtained suspension has no bitter taste.

Instant granules (200 mg albendazole sachet):
Suspend 5 g of the granules (= 200 mg albendazol) in a glass of water. The suspension has no bitter taste.

2.9 Tablet formulations (Lab Scale)

Albendazole Tablets, (100 mg)

1. Formulation

Albendazole .....100 g
Ludipress [1] .....288 g
Magnesium stearate [2] .....4 g
Aerosil 200 [4].....8 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....400 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....99 N
Disintegration .....2 min
Friability.....0.1%

2.9 Tablet formulations (Lab Scale)

Alginic Acid + Aluminium Hydroxide + Magnesium Silicate Tablets (500 mg + 100 mg + 25 mg)

1. Formulation

Alginic acid	500 g
Aluminium hydroxide dried gel (Giulini)	100 g
Magnesium trisilicate	25 g
Sodium bicarbonate	170 g
Sorbitol, crystalline [10]	160 g
Sucrose, crystalline	627 g
Ludipress [1]	900 g
Kollidon VA 64 [1]	70 g
Magnesium stearate [2]	50 g
Vanillin	5 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight	2.55 g
Diameter	20 mm
Form	biplanar
Hardness	120 N
Friability	1.3 %

6.7 Formulations of semi-solid drugs (Lab scale)

Aloe Vera Gel

1. Formulation

I.	Aloe vera extract 200 fold	0.4 g
	Propylene glycol Pharma [1]	5.0 g
	Preservative	q.s.
	Water	73.6 g
II.	Cremophor RH 40 [1]	1.1 g
	Perfume	q.s.
III.	Lutrol F 127 [1]	20.0 g

2. Manufacturing

Prepare the solutions I and II separtely and add I onto II. Cool this mixture to < 10 °C (or heat to 70 – 80 °C) and dissolve III. Maintain the temperature until the air bubbles escaped.

3. Properties of the gel

Appearance	clear ·
Viscosity	about 60 Pa · s
pH	about 5.5
Physical stability	no change of appearance after 4 weeks at room temperature

5.8 Liquid Formulations (Lab scale)

Alpha-Bisabolol Aqueous Mouth Wash Solution (0.2 %)

1. Formulation

I.	Alpha-Bisabolol, natural (BASF)	0.2 g
	Flavour	q.s
	Cremophor RH 40 [1]	2.5 g
II.	Glycerol	5.0 g
	Saccharin sodium	0.1 g
	Preservative	q.s.
	Water	92.2 g

2. Manufacturing

Heat mixture I to about 60 °C and add slowly the warm solution II (60 °C).

3. Properties of the solution

Clear, colourless liquid having a low viscosity.

5.8 Liquid Formulations (Lab scale)

Alpha-Bisabolol Buccal or Topical Solution (0.1%)

1. Formulation

I.	Alpha-Bisabolol, racemic (BASF)	0.12 g
	Cremophor RH 40 [1]	1.00 g
	Butylhydroxytoluene	0.01 g
II.	Preservative	q.s.
	Water	99 g

2. Manufacturing

Heat mixture I to about 60 °C, stirr well and add slowly the warm solution II. A clear solution is obtained.

3. Chemical stability (40 °C)

No loss of alpha-Bisabolol after 3 months.

5.8 Liquid Formulations (Lab scale)

Alpha-Bisabolol Ethanolic Mouth Wash Solution (1%)

1. Formulation

I.	Alpha-Bisabolol, racemic (BASF)	1.0 g
	Flavour	10.0 g
	Cremophor RH 40 [1]	6.0 g
II.	Glycerol	1.0 g
	Saccharin sodium	0.2 g
	Ethanol, 96%	81.8 g

2. Manufacturing

Heat mixture I to about 60 °C and add slowly the warm solution II.

3. Properties of the solution

Clear, colourless liquid which can be diluted with water.

5.8 Liquid Formulations (Lab scale)

Alpha-Bisabolol Mouth Wash Solution (0.5 %)

1. Formulation

I.	(-)Alpha-Bisabolol, natural (BASF)	0.5 g
	Lutrol F 127 [1]	5.0 g
	Flavour	q.s.
	Propylene glycol Pharma [1]	10.0 g
	Ethanol 96 %	30.0 g
II.	Water	54.5 g

2. Manufacturing

Prepare solution I and add slowly the water.

3. Properties of the solution

The clear colourless solution had got the pH 8.

4. Remark

The neutralisation to pH 5 – 7 would be recommended.

2.9 Tablet formulations (Lab Scale)

Alpha-Methyldopa Tablet Cores (250 mg), DC

1. Formulation

Alpha-Methyldopa	250 g
Ludipress [1]	350 g
Stearic acid [7]	15 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	620 mg
Diameter	11 mm
Form	biconvex
Hardness	123 N
Disintegration	6 min
Friability	0.2 %
Dissolution (10 min)	91 %
(20 min)	98 %

4. Physical stability (20 months, 20–25 °C)

Weight	620 mg
Hardness	115 N
Disintegration	7 min
Friability	0.5 %
Dissolution (10 min)	91 %
(20 min)	100 %

Alpha-Methyldopa Tablet Cores (250 mg), WG

1. Formulations

		No. 1	No. 2
I.	Alpha-Methyldopa	275 g	275 g
	Lactose monohydrate [8]	55 g	–
	Calcium phosphate, dibasic [9]	–	55 g
II.	Kollidon 30 [1]	15 g	15 g
	Isopropanol	80 ml	80 ml
III.	Kollidon CL [1]	8 g	8 g
	Magnesium stearate [2]	2 g	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a sieve, mix the dry granules with III and press with medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	361 mg	362 mg
Diameter	11 mm	11 mm
Hardness	118 N	156 N
Disintegration	5 min	4 min
Friability	<0.1%	<0.1%
Dissolution (10 min)	45%	55%
(20 min)	82%	90%
(30 min)	90%	98%

2.9 Tablet formulations (Lab Scale)

Alpha-Methyldopa Tablets (500 mg), DC

1. Formulations

	No. 1	No. 2
Alpha-Methyldopa (Alpha Chemicals)	500 g	500 g
Avicel PH 101 [5]	54 g	200 g
Kollidon VA 64 [1]	20 g	30 g
Kollidon CL [1]	20 g	20 g
Talc [10]	90 g	8 g
Aerosil 200 [4]	7 g	1 g
Magnesium stearate [2]	2 g	–
Calcium arachinate [2]	–	1 g

2. Manufacturing (Direct compression)

Pass magnesium stearate trough a 0.2 mm sieve and the other components through a 0.5 mm sieve, mix and press with high compression force (Formulation No. 1) and low compression force (Formulation No. 2).

3. Tablet properties

		No. 1	No. 2
Weight		693 mg	750 mg
Diameter		12 mm	12 mm
Form		biplanar	biplanar
Hardness		80 N	113 N
Disintegration		<1 min	1 – 2 min
Friability		0.4 %	0.8 %
Dissolution,	4 min	86 %	–
	16 min	92 %	–

4. Remark

In the case of formulation No. 1 it was not possible to press tablet cores of a biconvex form because some capping effect was observed.

2.9 Tablet formulations (Lab Scale)

Alpha-Methyldopa Tablets (500 mg), WG

1. Formulations

		No. 1	No. 2
I.	Alpha-Methyldopa	500 g	500 g
	Lactose monohydrate [8]	200 g	–
	Corn starch [3]	–	200 g
II.	Kollidon 30 [1]	30 g	–
	Kollidon 90 F [1]	–	10 g
	Isopropanol	35 ml	q.s.
III.	Kollidon CL	20 g	15 g
	Talc [10]	–	8 g
	Aerosil 200 [4]	5 g	2 g
	Magnesium stearate [2]	8 g	–
	Calcium arachinate [2]	–	2 g

2. Manufacturing (Wet granulation)

Granulate the mixture I with solution II, pass through a 0.8 mm sieve, mix with III and press with low/medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	790 mg	696 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	80 N	95 N
Disintegration	5 min	4 min
Friability	0.5 %	0.98 %

4. Remark

For the production of tables cores for coating purposes the oblong form would be better.

2.9 Tablet formulations (Lab Scale)

Alprazolam Tablets (0.5 mg)

1. Formulation

Alprazolam	0.5 g
Ludipress [1]	148 g
Magnesium stearate [2]	1 g

2. Manufacturing (Direct compression)

Mix all components, sieve through a 0.8 mm screen and press with low compression force.

3. Tablet properties

Weight	158 mg
Diameter	8 mm
Form	biplanar
Hardness	106 N
Disintegration	3 min
Friability	<0.1%

4. Remark

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

2.9 Tablet formulations (Lab Scale)

Aluminium Acetylsalicylate Tablets (250 mg)

1. Formulation

I.	Aluminium acetylsalicylate	255 g
	Mannitol	213 g
	Corn starch [3]	28 g
II.	Kollidon 90 F [1]	10 g
	Lutrol E 6000 [1]	5 g
	Isopropanol	about 50 g
III.	Kollidon CL [1]	23 g
	Magnesium stearate [2]	5 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with medium compression force.

3. Tablet properties

Weight	540 mg
Diameter	12 mm
Form	biplanar
Hardness	110 N
Disintegration	1 – 2 min
Friability	0.4 %

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Aluminium Hydroxide + Magnesium Carbonate Dry Syrup (12.5 % + 12.5 %)

1. Formulation

I.	Aluminium hydroxide dry gel (Giulini)	25.0 g
	Basic Magnesium carbonate	25.0 g
	Kollidon CL-M [1]	29.0 g
	Sorbitol, crystalline [10]	25.6 g
	Orange flavour	5.0 g
II.	Kollidon 30 [1]	10.0 g
	Coconut flavour	0.4 g
	Banana flavour	0.5 g
	Saccharin sodium	0.5 g
	Water	0.1 g
		about 36.0 g

2. Manufacturing

Granulate mixture I with solution II, pass through a sieve and dry.

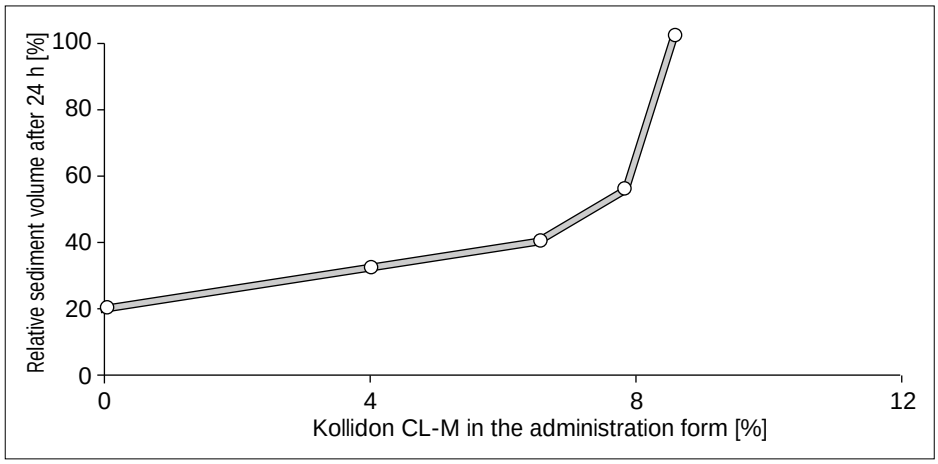
3. Preparation of the suspension for administration

Shake 58 g of the granules with 100 ml of water.

4. Properties of the suspension

- Homogeneous and without sedimentation during more than 24 h.
- Redispersibility very easy.

5. Influence of the amount of Kollidon Cl-M on the sedimentation of the obtained suspension



2.9 Tablet formulations (Lab Scale)

Aluminium hydroxide + Magnesium carbonate/oxide + Simethicone Tablets (150 mg + 250 mg + 90 mg)

1. Formulation

I.	Sucrose	576 g
	Aluminium hydroxide	157 g
	Magnesium carbonate	160 g
	Magnesium oxide	97 g
	Kollidon 90 F [1]	45 g
	Aerosil 200 [4]	22 g
II.	Simethicone, suspension 30%	300 g
III.	Menthol	9 g
	Saccharin sodium	1 g
	Talc [10]	49 g
	Magnesium stearate [2]	13 g

2. Manufacturing (Wet granulation)

Granulate mixture I with the simethicone suspension II, dry, sieve through a 0.8 mm screen, add III and press with high compression force.

3. Properties of the tablets pressed with two different diameters

	12 mm	20 mm
Weight	1200 mg	1295 mg
Form	biplanar	biplanar
Hardness	130 N	55 N
Disintegration	30 min	7 min
Friability	0.1%	0.7%

5.8 Liquid Formulations (Lab scale)

Aluminium Hydroxide + Magnesium Hydroxide + Simethicone Suspension (8 % + 8 % + 0.8 %)

1. Formulation

I.	Simethicone 30 %	2.7 g
	Cremophor RH 40 [1]	3.0 g
	Water	7.0 g
II.	Aluminium hydroxide dry gel (Giulini)	8.0 g
	Magnesium hydroxide	8.0 g
	Kollidon CL-M [1]	8 –10.0 g
	Sorbitol, crystalline [10]	10.0 g
	Banana flavour	0.4 g
	Coconut flavour	0.5 g
	Saccharin sodium	0.1 g
	Water	ad 100 ml
III.	Citric acid	q. s. to adust pH 9

2. Manufacturing

I. Mix Cremophor RH 40 with simethicone, heat to about 50 °C stirring well and add the warm water.
II. Dissolve the flavours and saccharin in water and suspend aluminium hydroxide, magnesium hydroxide and Kollidon CL-M.
III. Add emulsion I to the stirred suspension II and adjust the pH to about 9 with citric acid if needed.

3. Properties of the suspension

Colour: White
Aspect: Homogeneous, milky
Relative sediment volume (1 day): 99 %

Aluminium Hydroxide + Magnesium Hydroxide Chewable Tablets (200 mg + 200 mg)

1. Formulation

I.	Aluminium hydroxide (Rorer)	200 g
	Magnesium hydroxide (Rorer)	200 g
	Lactose monohydrate [8]	100 g
II.	Kollidon VA 64 [1]	30 g
	Water	260 g
III.	Sucrose, crystalline	315 g
	Sorbitol, crystalline (Merck)	100 g
	Polyethylene glycol 6000, powder [6]	60 g
	Aerosil 200 [4]	12 g
	Talc [10]	6 g
	Magnesium stearate [2]	6 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add III and press with high compression force (20 kN).

3. Tablet properties

Weight	1013 mg
Diameter	16 mm
Form	biplanar
Hardness	131 N
Disintegration	27 min
Friability	0.2 %

5.8 Liquid Formulations (Lab scale)

Aluminium Hydroxide + Magnesium Hydroxide Suspension (4 % + 4 %)

1. Formulation

Aluminium hydroxide	4.0 g
Magnesium hydroxide	4.0 g
Cremophor RH 40 [1]	5.0 g
Silicon oil DC 200 (Serva)	0.1 g
Kollidon CL-M [1]	10.0 g
Water	76.9 g

2. Manufacturing

Mix Cremophor RH 40 well with the silicon oil, add the water and suspend the solid substances.

3. Properties of the suspension

There was only a slow sedimentation during storage and the redispersibility after weeks was excellent.

2.9 Tablet formulations (Lab Scale)

Aluminium Hydroxide + Magnesium Silicate Chewable Tablets (120 mg + 250 mg)

1. Formulation

Aluminium hydroxide dried gel (Giulini) ...120.0 g
Magnesium trisilicate .....250.0 g
Ludipress [1] .....232.0 g
Aerosil 200 [4].....6.0 g
Magnesium stearate [2].....6.0 g
Cyclamate sodium .....12.0 g
Menthol .....1.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with a compression force of 20 kN.

3. Tablet properties

Weight .....640 mg
Diameter .....16 mm
Form .....biplanar
Hardness.....83 N

4. Remarks

Due to the poor flowability of the powder the tabletting machine should be equipped with a special technical device providing a continuous and homogenous filling of the dies.

2.9 Tablet formulations (Lab Scale)

Ambroxol Tablets (30 mg)

1. Formulation

Ambroxol hydrochloride .....30.0 g
Ludipress [1].....217.5 g
Magnesium stearate [2].....2.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....250 mg
Diameter .....8 mm
Form .....biplanar
Hardness .....115 N
Disintegration .....7 min
Friability.....0.2 %
Dissolution, 30 min .....82 %

2.9 Tablet formulations (Lab Scale)

Aminophylline Tablets (90 mg)

1. Formulations

		No. 1	No. 2
I.	Aminophylline, hydrous powder (Knoll)	90 g	90 g
	Potato starch [3]	80 g	–
	Corn starch [3]	–	74 g
	Kollidon VA 64 [1]	3 g	3 g
II.	Kollidon VA 64 [1]	3 g	3 g
	Water	30 g	27 g
III.	Magnesium stearate [2]	1 g	–
	Talc [10]	4 g	–
	Polyethylene glycol 6000, powder [6]	–	10 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, dry, mix with III, pass through a 0.5 mm sieve and press to tablets with medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	179 mg	180 mg
Diameter	8 mm	8 mm
Form	biplanar	biplanar
Hardness	80 N	72 N
Disintegration	3 – 4 min	6 – 7 min
Friability	0.4 %	0.4 %

Aminophylline Tablets (100 mg), I

1. Formulation

Aminophylline powder (Knoll).....100 g
Avicel PH 200 [5].....200 g
Kollidon VA 64 [1].....6 g
Magnesium stearate [2] .....2 g
Aerosil 200 [4] .....12 g

2. Manufacturing (Direct compression)

Mix all components, sieve and press on a rotary press to tablets with low compression force.

3. Tablet properties

Weight .....318 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....124 N
Disintegration.....1 – 2 min
Friability.....0.2 %

4. Remarks

Due to the reduced flowability the tabletting machine should be equipped with a special technical device providing a continuous and homogenous filling of the molds.

2.9 Tablet formulations (Lab Scale)

Aminophylline Tablets (100 mg), II

1. Formulation

Aminophylline (Knoll)	100 g
Ludipress [1]	150 g
Aerosil 200 [4]	2 g
Magnesium stearate [2]	2 g

2. Manufacturing (Direct compression)

Mix all components, pass through sieve and press with low compression force.

3. Tablet properties

Weight	254 mg
Diameter	8 mm
Form	biplanar
Hardness	97 N
Disintegration	10 min
Friability	0.2 %
Dissolution 10 min:	87 %
15 min:	100 %

4. Colour stability

After 2 weeks at room temperature no change of the colour of the tablets was observed but the long term compatibility between aminophylline and lactose should be controlled.

Amitryptylline Tablets (10 mg and 25 mg)

1. Formulations

	No. 1: 10 mg	No. 2: 25 mg
Amitryptylline	10 mg	25 mg
Ludipress [1]	139 mg	124 mg
Magnesium stearate [2]	1 g	1 mg

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix intensively and press with low compaction force (8 kN).

3. Tablet properties

	No. 1	No. 2
Weight	152 mg	157 mg
Diameter	8 mm	8 mm
Form	biplanar	biplanar
Hardness	70 N	92 N
Disintegration	1 – 2 min	3 min
Friability	0.3 %	0.2 %

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Amoxicillin Dry Syrup (5 % = 500 mg/10 ml)

1. Formulation

Amoxicillin trihydrate	5.0 g
Sodium citrate	5.0 g
Citric acid, crystalline	2.1 g
Sodium gluconate	5.0 g
Sorbitol crystalline [10]	40.0 g
Kollidon CL-M [1]	6.0 g
Orange flavour	1.5 g
Lemon flavour	0.5 g
Saccharin sodium	0.4 g

2. Manufacturing

Mix all components and fill in a flask.

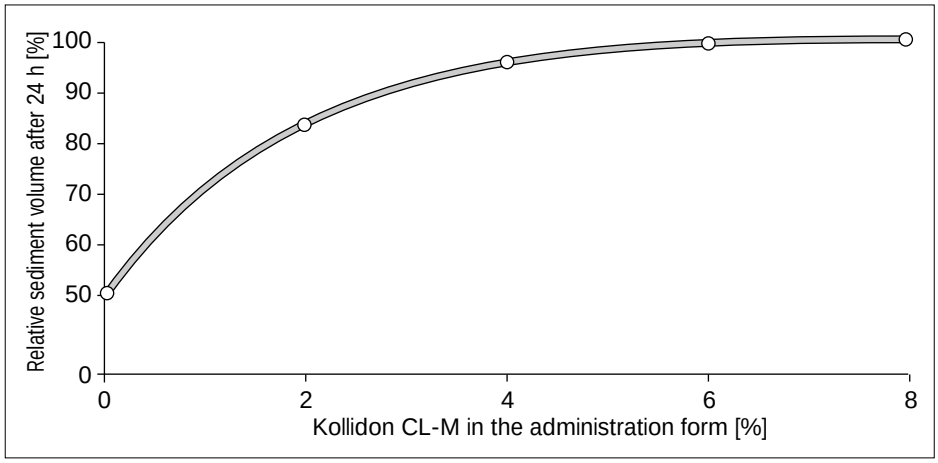
3. Preparation of the suspension for administration

To 66 g of the powder add water to fill to a total volume of 100 ml shaking very well.

4. Properties of the suspension

The pH of the suspension is about 4.9.
No sedimentation could be observed during more than 24 hours.
The redispersibility is very easy after 2 weeks.

5. Influence of the amount of Kollidon CL-M on the sedimentation of the obtained suspension



Amoxicillin Lyophylisate for Injection (250 mg)

(according to Eur. Patent 0.012.495 + 0.012.496, 1979, Beecham)

1. Formulation

Amoxicillin sodium	6.25 g
Kollidon 12 PF [1]	7.50 g
Water for injections	add 100.00 ml

2. Manufacturing

Dissolve the active ingredient in the well stirred solution of Kollidon 12 PF and after freeze-drying, fill 500-mg-portions of the dry lyophilisate into ampoules.

3. Administration

Prior to administration, the dry content of an ampoule is mixed with 1.9 ml of water to give a clear injection solution.

2.9 Tablet formulations (Lab Scale)

Amoxicillin Tablets (125 mg)

1. Formulation

I.	Amoxicillin	125 g
	Corn starch [3]	148 g
II.	Kollidon 30 [1]	9 g
	Water	about 60 g
III.	Kollidon CL [1]	15 g
	Magnesium stearate [2]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, sieve and mix with III. Press with low compression force.

3. Tablet properties

Weight	297 mg
Diameter	12 mm
Form	biplanar
Hardness	62 N
Disintegration	4 min
Friability	0.2 %

5.8 Liquid Formulations (Lab scale)

Ampicillin + Cloxacillin Oily Suspension (1.5 % + 4.0 %)

1. Formulation

I.	Ampicillin sodium	1.5 g
	Cloxacillin sodium	4.0 g
II.	Lutrol F 68 [1]	3.0 g
III.	Antioxidant	q. s.
	Castor oil	91.5 g

2. Manufacturing

Heat the mixture III to 50 °C and dissolve II. Add the components I and stir during cooling to room temperature.

3. Properties of the suspension

A homogeneous suspension was obtained.

4. Remark

The castor oil should not be heated to more than 50 °C because at higher temperature a strong thickening effect was observed.

Ampicillin Dry Syrup (5 % = 500 mg/10 ml)

1. Formulation

Ampicillin trihydrate	5.0 g
Sodium citrate	5.0 g
Citric acid, crystalline	2.1 g
Sodium gluconate	5.0 g
Sorbitol crystalline [10]	40.0 g
Kollidon CL-M [1]	6.0 g
Orange flavour	1.5 g
Lemon flavour	0.5 g
Saccharin sodium	0.4 g

2. Manufacturing

Mix all components and fill in a flask.

3. Preparation of the suspension for administration

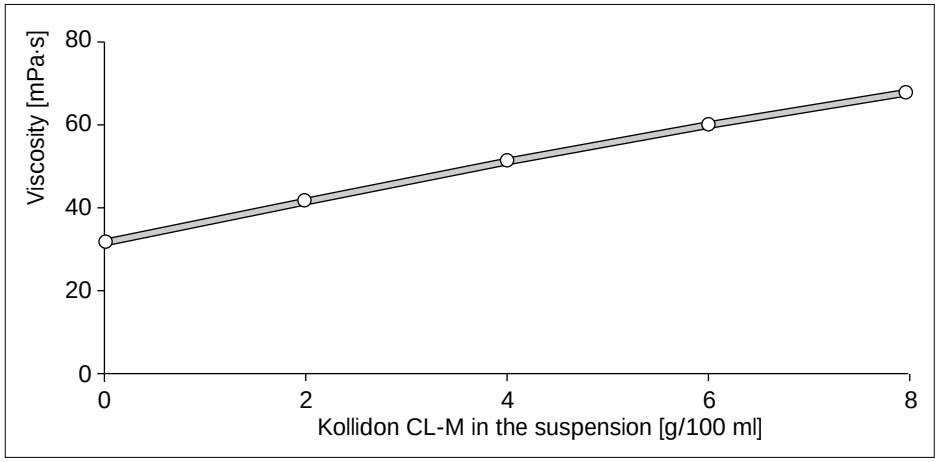
To 66 g of the powder add water to fill to a total volume of 100 ml shaking very well.

4. Properties of the suspension

The pH of the suspension is about 4.9.
No sedimentation could be observed during more than 24 hours.
The redispersibility is very easy after 2 weeks.

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

5. Influence of the amount of Kollidon CL-M on the viscosity of the obtained suspension



2.9 Tablet formulations (Lab Scale)

Ampicillin Tablets (250 mg)

1. Formulation

Ampicillin trihydrate .....250 g
Ludipress [1] .....250 g
Magnesium stearate [2].....10 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with low compression force.

3. Tablet properties

Weight .....500 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....84 N
Disintegration .....4 min
Friability.....0.4 %

Ampicillin Tablets (500 mg)

1. Formulations

		No. 1	No. 2
I.	Ampicillin trihydrate	500 g	500 g
	Corn starch [3]	242 g	–
	Sorbitol, crystalline [10]	–	242 g
II.	Kollidon VA 64 [1]	25 g	25 g
	Isopropanol or water	q. s.	q.s.
III.	Kollidon CL [1]	12 g	12 g
	Magnesium stearate [2]	10 g	10 g
	Aerosil 200 [4]	8 g	8 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with high/medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	798 mg	822 mg
Diameter	16 mm	16 mm
Hardness	170 N	154 N
Disintegration	5 min	11 min
Friability	0.4 %	0.2 %

5.8 Liquid Formulations (Lab scale)

Anise Oil Solution (1%)

1. Formulation

I.	Anise oil	1.0 g
	Cremophor RH 40 [1]	1.7 g
II.	Ethanol	34.0 g
	Preservatives	q.s.
	Water	63.3 g

2. Manufacturing

Mix the anise oil with Cremophor RH 40, heat to about 65 °C, stir strongly and add slowly the hot solution II.

3. Properties

Clear or slightly opalescent, colourless liquid.

Asparagus Extract + Parsley Extract Tablets (200 mg + 200 mg)

1. Formulation

Asparagus extract, powder	200 g
Parsley extract, powder	200 g
Sorbitol, crystalline [10]	200 g
Kollidon VA 64 [1]	20 g
Kollidon CL [1]	10 g
Magnesium stearate [2]	4 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight	636 mg
Diameter	12 mm
Form	biplanar
Hardness	49 N
Disintegration	9 min
Friability	0 %

2.9 Tablet formulations (Lab Scale)

Aspartame Effervescent Tablets (20 mg)

1. Formulation

Aspartame	20.0 g
Sorbitol, crystalline [10]	10.4 g
Tartaric acid, powder	14.3 g
Sodium bicarbonate	18.7 g
Kollidon 25 [1]	1.7 g
Polyethylene glycol 6000, powder [6]	1.1 g

2. Manufacturing (Direct compression)

Mix , pass through a 0.5 mm sieve and press to tablets.

3. Tablet properties

Weight	66 mg
Diameter	6 mm
Form	biplanar
Hardness	25 N
Disintegration	<1 min
Friability	0.7%

Aspartame Tablets (25 mg), DC

1. Formulation

Aspartame	27 g
Ludipress [1]	76 g
Kollidon CL [1]	12 g
Magnesium stearate [2]	1 g
Lutrol F 68 [1]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with low compression force.

3. Tablet properties

Weight	120 mg
Diameter	8 mm
Form	biplanar
Hardness	65 N
Disintegration	<1 min
Friability	0.1%

Aspartame Tablets (25 mg), WG

1. Formulation

I.	Aspartame	25 g
	Dibasic calcium phosphate [9]	25 g
	Kollidon VA 64 [1]	3 g
II.	Water	10 g
III.	Kollidon CL [1]	3 g
	Polyethylene glycol 6000, powder [6]	3 g

2. Manufacturing (Wet granulation)

Granulate the mixture I with II, pass through a 0.8 mm sieve, mix with III and press to tablets.

3. Tablet properties

Weight	60 mg
Diameter	5 mm
Form	biplanar
Hardness	60 N
Disintegration	1 min
Friability	< 0.1%

Atenolol Tablets (90 mg)

1. Formulation

Atenolol (Stober)	93.0 g
Ludipress [1]	287.0 g
Kollidon CL [1]	52.0 g
Magnesium stearate [2]	2.2 g
Aerosil 200 [4]	0.9 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with low compression force.

3. Tablet properties

Weight	436 mg
Diameter	12 mm
Form	biplanar
Hardness	85 N
Disintegration	2 – 3 min
Friability	<0.1%

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Azithromycin Dry Syrup (5 % = 500 mg/10 ml)

1. Formulation

I.	Azithromycin dihydrate	5.0 g
	Sodium citrate	5.0 g
	Citric acid	2.0 g
	Sucrose	60.0 g
	Sodium cyclamate	0.5 g
	Kollidon CL-M [1]	9.0 g
II.	Ethanol	9.0 g
	Menthol, crystalline	0.5 g
	Cremophor RH 40 [1]	0.3 g

2. Manufacturing

The mixture I is granulated with the solution II. The obtained granules are passed through a 1.0 mm sieve and dried at room temperature. Fill 83 g of the granules in a 100 ml flask.

3. Administration

Shake 83 g of the granules with drinking water and fill the flask until the 100 ml mark.

4. Properties of the the suspension

White suspension showing no sedimentation during 24 hours and good redispersibility. The bitter taste Azithromycin is almost completely masked.

5.8 Liquid Formulations (Lab scale)

Azithromycin Suspension (5 % = 500 mg/10 ml)

1. Formulations

I.	Azithromycin dihydrate	5.0 g
	Sodium citrate	5.0 g
	Citric acid	2.0 g
	Sucrose	60.0 g
	Kollidon CL-M [1]	9.0 g
II.	Cremophor RH 40 [1]	0.5 g
	Chocolate flavour	0.2 g
	Water	10.0 g
III.	Water	ad 100 ml

2. Manufacturing

Add the mixture I to the solution II and fill with water to a total volume of 100 ml shaking very well.

3. Properties of the suspensions

Light-brown suspension showing no sedimentation during 24 hours and good redispersibility. The bitter taste of Azithromycin is almost completely masked.

5.8 Liquid Formulations (Lab scale)

Azulene solution (1%)

1. Formulation

Azulene.....1.0 g
Cremophor RH 40 [1] .....3.0 g
Water.....ad 100 ml

2. Manufacturing

Mix azulene and Cremophor RH 40 and heat to about 60 °C. Add slowly the water (60 °C) and cool to room temperature

3. Properties

A clear solution was obtained.

5.8 Liquid Formulations (Lab scale)

Barium Sulfate Oral Suspension (23 %)

1. Formulation

Barium sulfate	100.0 g
Kollidon 90 F [1]	5.0 g
Carboxymethylcellulose sodium	0.4 g
Sodium bisulfite	< 0.5 g
Preservatives	q. s.
Water	320.0 g

2. Manufacturing

Dissolve the preservatives and the carboxy methylcellulose sodium in the hot water and add Kollidon 90 F and sodium bisulfite. In the obtained clear solution suspend barium sulfate.

3. Properties of the suspension

White homogeneous suspension having a viscosity of about 160 mPa · s.

6.7 Formulations of semi-solid drugs (Lab scale)

Basic Cream for Different Active Ingredients

1. Formulation

I.	Cetylstearyl alcohol	7.0 g
	Cremophor A 6 [1]	1.5 g
	Cremophor A 25 [1]	1.5 g
	Liquid paraffin	12.0 g
	Parabene(s)	0.2 g
II.	Water	67.8 – 69.7 g
III.	Propylene glycol [1]	8.0 g
	Active ingredient	0.1 – 2.0 g

2. Manufacturing

Heat the mixture I and the water II separately to about 80 °C. Add the water II to the obtained solution I with rigorous stirring. Heat III until the active ingredient is dissolved, mix with I/II and continue to stir during cooling to room temperature.

This basic cream was tested with different active ingredients soluble in 1,2-propylene glycol.

3. Properties

White cream.

4. Physical stability

No change of appearance were observed during 6 weeks at 45 °C.

2.9 Tablet formulations (Lab Scale)

Benzhexol Tablets (5 mg)

1. Formulations

	No. 1	No. 2
Benzhexol chloride (= trihexylphenidyl hydrochloride)	5.0 g	5.0 g
Ludipress [1]	114.0 g	100.0 g
Corn starch [3]	–	14.5 g
Magnesium stearate [2]	0.6 g	0.5 g
Aerosil 200 [4]	–	1.5 g

2. Manufacturing (Direct compression)

Mix all components for 10 minutes in a turbula mixer and press with low compression force.

3. Tablet properties

	No. 1	No. 2
Weight	120 mg	121 mg
Diameter	5 mm	5 mm
Form	biplanar	biplanar
Hardness	120 N	113 N
Disintegration	7 min	3 min
Friability	< 0.06 %	0.4 %

6.7 Formulations of semi-solid drugs (Lab scale)

Benzoyl Peroxide + Alpha-Bisabolol Gel (5.0 % + 0.2 %)

1. Formulation

I.	Alpha-Bisabolol, natural (BASF)	0.2 g
	Propylene glycol Pharma [1]	6.0 g
	Triethanolamine	1.0 g
	Cremophor RH 40 [1]	3.0 g
	Kollidon 30 [1]	3.0 g
	Water	40.8 g
II.	Carbopol® 940 (Goodrich)	1.0 g
	Water	40.0 g
III.	Benzoyl peroxide	5.0 g

2. Manufacturing

Prepare suspension II and let swell during one hour. Add this suspension to the well stirred solution I. Add III.

3. Properties of the gel

Colourless transparent gel.

5.8 Liquid Formulations (Lab scale)

Benzyl Benzoate Solution (10 %)

1. Formulation

I.	Benzyl benzoate	10 g
	Cremophor RH 40 [1]	22 g
	Ethanol 96 %	41 g
	Water	27 g

2. Manufacturing

Heat the mixture of benzyl benzoate and Cremophor RH 40 to about 60 °C, stir strongly and add slowly the water. Finally add the ethanol.

3. Properties of the solution

Clear, colourless liquid.

5.8 Liquid Formulations (Lab scale)

Benzylpenicilline + Dihydrostreptomycin Injectable Suspension (200,000 units + 200 mg/ml)

1. Formulation

I.	Procain benzylpenicilline	20.0 g
	Dihydrostreptomycin sulfate	20.0 g
II.	Kollidon 12 PF [1]	0.5 g
	Carboxymethyl cellulose sodium	0.5 g
	Sodium citrate	0.6 g
	Parabene	q.s.
	Water for injectables	ad 100 ml

2. Manufacturing

Prepare solution II, add the components I to the well stirred solution II and pass through a colloid mill.

3. Properties

A white homogeneous suspension was obtained.

4. Remark

To prevent of discolouration of Kollidon in the solution during storage 0.2 to 0.5% of cysteine could be added as antioxidant.

2.9 Tablet formulations (Lab Scale)

Berberine Tablets (5 mg)

1. Formulation

Berberine sulfate .....5.7 g
Lactose monohydrate [8].....54.1 g
Ludipress [1] .....54.1 g
Magnesium stearate [2].....1.2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight.....115 mg
Diameter .....6 mm
Form .....biplanar
Hardness.....40 N
Disintegration .....1 min
Friability.....0.1%

2.9 Tablet formulations (Lab Scale)

Beta Carotene + Vitamin C + Vitamin E Chewable Tablets (10 mg + 500 mg + 250 mg)

1. Formulation

Beta Carotene dry powder 10%	100 g
Ascorbic acid, crystalline (BASF)	250 g
Sodium ascorbate, crystalline	280 g
Vitamin E acetate dry powder SD 50 (BASF)	500 g
Sorbitol, crystalline [10]	600 g
Ludipress [1]	500 g
Fructose	350 g
Polyethylene glycol 6000, powder [6]	50 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with high compression force.

3. Tablet properties

Weight	2,600 mg
Diameter	20 mm
Form	biplanar
Hardness	122 N
Disintegration (water)	15 – 20 min
Friability	0.4%

2.9 Tablet formulations (Lab Scale)

Beta Carotene + Vitamin C + Vitamin E Tablets (6 mg + 100 mg + 30 mg)

1. Formulation

	No. 1	No. 2
Betavit® dry powder 10 % (BASF)	65 g	65 g
Ascorbic acid, powder (BASF)	100 g	100 g
Vitamin E acetate dry powder 50 %	60 g	60 g
Ludipress [1]	369 g	–
Sorbitol, crystalline (Merck)	–	233 g
Kollidon VA 64 [1]	–	30 g
Kollidon CL [1]	–	8 g
Magnesium stearate [2]	6 g	4 g

2. Manufacturing (Direct compression)

Pass all components through o 0.8 mm sieve, mix and press with medium or high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	599 mg	502 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	60 N	59 N
Disintegration (water)	7 min	7 min
Friability	0.3 %	0.2 %

4. Chemical stability of beta carotene in Formulation No. 1 (40 °C, closed)

	0 weeks	15 weeks
Beta carotene/tablet	80 mg	78 mg

5. Remarks

A colourant pigment should be added to obtain a homogeneous appearance of the tablets.

The tablets of Formulation No. 1 could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Beta Carotene + Vitamin C + Vitamin E Tablets (7 mg + 60 mg + 25 mg)

1. Formulation

Betavit® dry powder 10% (BASF) .....75 g
Ascorbic acid, powder (BASF).....60 g
Vitamin E acetate dry powder 50% .....50 g
Sorbitol, crystalline [10].....240 g
Kollidon CL [1] .....30 g
Magnesium stearate [2] .....5 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight .....497 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....55 N
Disintegration .....8 min
Friability.....< 0.1%

4. Remarks

A colourant pigment should be added to obtain a homogeneous appearance of the tablets.

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Beta Carotene + Vitamin C + Vitamin E Tablets (12 mg + 250 mg + 125 mg)

1. Formulation

Beta Carotene dry powder 10% .....125 g
Ascorbic acid, crystalline (BASF) .....125 g
Sodium ascorbate, crystalline (BASF).....141 g
Vitamin E acetate dry powder SD 50 .....250 g
(BASF)
Ludipress [1] or Sorbitol, crystalline [10] ....119 g
Polyethyleneglycol 6000, powder [10].....5 g
Orange flavour (FDO) .....15 g
Sodium cyclamate .....10 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with medium compression force.

3. Tablet properties

Weight .....790 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....50 N
Disintegration .....not tested
Friability.....< 0.1%

2.9 Tablet formulations (Lab Scale)

Beta Carotene Effervescent Tablets (7 mg)

1. Formulation

Lucarotin® dry powder 10% CWD (BASF)	70 g
Ludipress [1]	113 g
Citric acid, anhydrous	200 g
Sodium bicarbonate	120 g
Sodium carbonate	12 g
Sodium cyclamate	20 g
Aspartame	15 g
Orange flavour	20 g
Polyethylene glycol 6000, powder [6]	30 g

2. Manufacturing (Direct compression)

Pass all components through o 0.8 mm sieve, mix and press with medium or high compression force at maximum 30% of relative atmospheric humidity.

3. Tablet properties

	Compression force 18 kN	26 kN
Weight	602 mg	605 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Colour	brown	brown
Hardness	81 N	108 N
Disintegration (water)	45 sec	50 sec
Friability	0.4%	0.2%

Beta Carotene Tablets (15 mg)

1. Formulation

	No. 1	No. 2
Beta carotene dry powder 10%	160.0 g	150.0 g
Ludipress [1]	240.0 g	–
Dicalcium phosphate [9], granulated with 5% Kollidon 30	–	175.0 g
Avicel PH 101 [5]	–	100.0 g
Kollidon CL [1]	6.0 g	5.0 g
Aerosil 200 [4]	–	2.5 g
Talc [10]	–	20.0 g
Calcium arachinate [2]	–	2.5 g
Magnesium stearate [2]	2.0 g	–

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with a medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	400 mg	502 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	59 N	57 N
Disintegration	12 min	1 min
Friability	0.1%	0%

2.9 Tablet formulations (Lab Scale)

4. Chemical and physical stability (20–25 °C)

Formulation No. 1:	**6 Months**	**12 Months**
Loss of beta carotene	3 %	4 %
Hardness	60 N	59 N
Disintegration	9 min	7 min
Friability	0.15 %	0.16 %

Formulation No. 2:	**6 Months**	**12 Months**
Loss of beta carotene	< 8 %	9 %

2.9 Tablet formulations (Lab Scale)

Beta Carotene Tablets (20 mg)

1. Formulation

Beta carotene dry powder 10 %.....220 g
Avicel PH 101 [5].....250 g
Kollidon CL [1] .....20 g
Aerosil 200 [4].....2 g

2. Manufacturing (Direct compression)

Mix all components and press with a low compression force.

3. Tablet properties

Weight .....518 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....90 N
Disintegration .....< 1 min
Friability.....0.5 %

4. Chemical stability (20–25 °C, protected from light)

0 Months: .....110 % (= 22 mg)
6 Months: ..... 95 % (= 19 mg)
9 Months: ..... 95 % (= 19 mg)
12 Months: ..... 95 % (= 19 mg)

5. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

6.7 Formulations of semi-solid drugs (Lab scale)

Betamethasone + Neomycin Gel-Cream (0.1 % + 0.6 %)

1. Formulation

Betamethasone valerate	0.13 g
Neomycin sulfate	0.65 g
Lutrol E 400 [1]	15.00 g
Miglyol® 812 (Dynamit-Nobel)	10.00 g
Lutrol F 127 [1]	20.00 g
Water	ad 100.00 g

2. Manufacturing

Dissolve betamethasone valerate in the mixture of Lutrol E 400 and Miglyol 812.
Dissolve Lutrol F 127 and neomycin sulfate in water at 5–10°C. Mix both solutions. Maintain cool until the air bubbles disappeared.

3. Properties of the gel-cream

A milky white soft gel-cream is obtained.

Betamethasone Cream (0.1%)

1. Formulation

I.	Cetylstearyl alcohol	7.0 g
	Cremophor A 6 [1]	1.5 g
	Cremophor A 25 [1]	1.5 g
	Liquid paraffin	12.0 g
	Parabene(s)	0.2 g
II.	Water	69.7 g
III.	Propylene glycol [1]	8.0 g
	Betamethasone	0.1 g

2. Manufacturing

Heat the mixture I and the water II separately to about 80 °C. Add the water II to the obtained solution I with rigorous stirring. Heat III until the active ingredient is dissolved, mix with I/II and continue to stir during cooling to room temperature.

3. Properties

White cream.

4. Physical stability

No change of appearance or crystallization were observed during 6 weeks at 45 °C.

5. Remark

This formulation could be used for other active ingredients too.

Betamethasone Gel (0.1%)

1. Formulation

I.	Betamethasone valerate	0.1 g
	Ethanol 96%	10.0 g
	Propylene glycol Pharma [1]	20.0 g
II.	Lutrol F 127 [1]	22.0 g
	Water	47.0 g

2. Manufacturing

Prepare the solution I at room temperature and solution II at about 6 °C (or at > 70 °C). Mix both solutions. Maintain the temperature until the air bubbles disappeared.

3. Properties of the gel

The obtained gel is clear and colourless.

4. Remark

Perhaps a certain amount of propylene glycol could be substituted by water.

Bifonazole Cream (1%)

1. Formulation

I.	Cetylstearyl alcohol	7.0 g
	Cremophor A 6 [1]	1.5 g
	Cremophor A 25 [1]	1.5 g
	Liquid paraffin	12.0 g
	Parabene(s)	0.2 g
II.	Water	68.8 g
III.	Propylene glycol [1]	8.0 g
	Bifonazole	1.0 g

2. Manufacturing

Heat the mixture I and the water II separately to about 80 °C. Add the water II to the obtained solution I with rigorous stirring. Heat III until the active ingredient is dissolved, mix with I/II and continue to stir during cooling to room temperature.

3. Properties

White cream.

4. Physical stability

No change or appearance or crystallization were observed during 6 weeks at 45 °C.

5. Remark

This formulation could be used for other active ingredients too.

2.9 Tablet formulations (Lab Scale)

Bran Tablets (250 mg), DC

1. Formulation

Bran wheat (milled <1 mm)	250 g
Ludipress [1]	200 g
Kollidon 30 [1]	5 g
Aerosil 200 [4]	4 g
Magnesium stearate [2]	4 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with medium compression force.

3. Tablet properties

Weight	477 mg
Diameter	12 mm
Form	biplanar
Hardness	52 N
Disintegration	3 min
Friability	0.4 %

4. Remark

If the bran is not milled, the hardness of tablet is higher but the content uniformity is less.

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Bran Tablets (250 mg), WG

1. Formulation

I.	Bran wheat (milled <1 mm)	250 g
	Dibasic calcium phosphate [9]	200 g
II.	Kollidon 90 F [1]	12 g
	Water	3 g
III.	Polyethylene glycol 6000, powder [6]	q.s.
	Magnesium stearate [2]	4 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a sieve, mix with III and press with medium compression force.

3. Tablet properties

Weight	467 mg
Diameter	12 mm
Form	biplanar
Hardness	70 N
Disintegration	3 min
Friability	0.4 %

Bromhexine Tablets (8 mg)

1. Formulations

	No. 1	No. 2
Bromhexine	8 g	8 g
Dicalcium phosphate [9]	179 g	–
Ludipress [1]	–	190 g
Kollidon VA 64 [1]	7 g	–
Kollidon CL [1]	5 g	–
Magnesium stearate [2]	1 g	1 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low/ medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	204 mg	202 mg
Diameter	8 mm	8 mm
Form	biplanar	biplanar
Hardness	70 N	70 N
Disintegration	< 1 min	1 – 2 min
Friability	0.2 %	0.2 %

2.9 Tablet formulations (Lab Scale)

Bromocriptine Tablet Cores (6 mg)

1. Formulation

Bromocriptine mesylate .....6.1 g
Ludipress [1] .....205.5 g
Magnesium stearate [2].....2.2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

Weight .....214 mg
Diameter .....9 mm
Form .....biconvex
Hardness.....88 N
Disintegration .....4 min
Friability.....0.7%
Dissolution (10 min.).....95.6%

2.9 Tablet formulations (Lab Scale)

Calcium Carbonate Tablets (500 mg)

1. Formulation

I.	Calcium carbonate, precipitated	500 g
	Kollidon 30 [1]	65 g
II.	Water	97 g
III.	Kollidon CL [1]	32 g
	Ludipress [1]	53 g

2. Manufacturing (Wet granulation)

Granulate mixture I with the water II, pass through a sieve, mix the dry granules with III and press with low compression force.

3. Tablet properties

Weight	656 mg
Diameter	12 mm
Form	biplanar
Hardness	120 N
Disintegration	10 min
Friability	0.1%

2.9 Tablet formulations (Lab Scale)

Calcium Effervescent Tablets (250 mg Ca)

1. Formulation

I.	Calcium lactate	650 g
	Calcium gluconate	625 g
	Calcium carbonate	190 g
	Sodium bicarbonate	410 g
	Tartaric acid	480 g
	Kollidon 30 [1]	48 g
II.	Kollidon 30 [1]	12 g
	Isopropanol	q.s.
III.	Kollidon CL [1]	100 g
	Polyethylene glycol 6000, powder [6]	48 g
	Flavour	q.s.

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, sieve, mix with III and press with low compression force.

3. Tablet properties

Weight	2560 mg
Diameter	20 mm
Form	biplanar
Hardness	193 N
Disintegration (water)	2 – 3 min
Friability	0.5 %

2.9 Tablet formulations (Lab Scale)

Calcium Gluconate Tablets (350 mg)

1. Formulation

I.	Calcium gluconate, powder	360 g
	Lactose monohydrate [8]	117 g
II.	Kollidon 30 [1]	11 g
	Isopropanol	90 g
III.	Kollidon CL [1]	25 g
	Magnesium stearate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with high compression force.

3. Tablet properties

Weight	500 mg
Diameter	12 mm
Form	biplanar
Hardness	118 N
Disintegration (water)	16 min
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Calcium Glycerophosphate Tablets (200 mg)

1. Formulation

Calcium glycerophosphate	200.0 g
Ludipress [1]	297.5 g
Magnesium stearate [2]	2.5 g
Aerosil 200 [4]	q.s.

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight	470 mg
Diameter	12 mm
Form	biplanar
Hardness	131 N
Disintegration	7 min
Friability	0.1%

2.9 Tablet formulations (Lab Scale)

Calcium Glycerophosphate Tablets (500 mg)

1. Formulation

I.	Calcium glycerophosphate	500.0 g
	Corn starch [3]	117.5 g
II.	Kollidon 90 F [1]	15.0 g
	Water	60.0 g
III.	Kollidon CL [1]	15.0 g
	Magnesium stearate [2]	2.5 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, sieve and mix with III. Press with medium to high compression force.

3. Tablet properties

Weight	650 mg
Diameter	12 mm
Form	biplanar
Hardness	220 N
Disintegration	7 min
Friability	0.1%

2.9 Tablet formulations (Lab Scale)

Calcium Phosphate Tablets for Cats and Dogs (400 mg)

1. Formulation

		No. 1	No. 2
I.	Dicalcium phosphate [9]	400 g	400 g
	Wheaten flour	100 g	100 g
	Citric acid crystalline	1 g	1 g
	Lactose monohydrate [8]	272 g	262 g
	Flavours	q.s.	q.s.
II.	Kollidon 30 F [1]	–	30 g
	Kollidon 90 F [1]	20 g	–
	Water	–	150
III.	Magnesium stearate [2]	4 g	4 g

2.Manufacturing (Direct compression/Wet granulation)

Formulation No. 1 (Direct compression)
Pass all components through a 0.8 mm sieve, mix and press with medium to high compression force (20 kN).

Formulation No. 2 (Wet granulation)
Granulate mixture I with solution II, dry and pass through a 0.8 mm sieve, add III and press with medium to high compression force (20 kN).

3. Tablet properties

	No. 1	No. 2
Weight	800 mg	800 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	85 N	180 N
Disintegration	1 min	8 – 9 min
Friability	0.2 %	0.1 %

Captopril Tablets (25 mg)

1. Formulation

Captopril	25 g
Ludipress [1]	91 g
Kollidon CL [1]	2 g
Magnesium stearate [2]	2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight	122 mg
Diameter	8 mm
Form	biplanar
Hardness	49 N
Disintegration	1 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Carbamazepine Tablets (200 mg)

1. Formulation

Carbamazepine .....200 g
Ludipress [1] .....300 g
Magnesium stearate [2] .....2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....496 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....128 N
Disintegration .....1 min
Friability.....0.3 %
Dissolution 10 min:.....75 %
30 min: .....83 %
60 min: .....86 %

2.9 Tablet formulations (Lab Scale)

Carbonyl Iron + Copper Sulfate + Manganese Sulfate Tablets (24 mg + 0.16 mg + 3.5 mg)

1. Formulation

Carbonyl iron OF (BASF) .....24.0 g
Copper sulfate.....0.16 g
Manganese sulfate .....3.5 g
Ludipress [1] .....100.0 g
Magnesium stearate [2].....2.0 g

2. Manufacturing (Direct compression)

Pass all components through a 0.5 mm sieve, mix and press with medium compression force.

3. Tablet properties

Weight .....131 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....95 N
Disintegration.....2 – 3 min
Friability.....0.3 %

5.8 Liquid Formulations (Lab scale)

Carnitine + Coenzym Q Solution (4.0 % + 0.1 %)

1. Formulation

I.	Coenzym Q 10	0.1 g
	Lutrol E 400 [1]	0.1 g
	Cremophor RH 40 [1]	0.4 g
II.	Preservative	q.s.
	Water	95.4 g
III.	Carnitine	4.0 g

2. Manufacturing

Heat the mixture I to 60 °C, stir well and add solution II (60 °C). Cool and dissolve III.

3. Properties of the solution

Clear, colourless liquid.

4. Physical stability (6–8 °C)

No change of clarity after one month.

2.9 Tablet formulations (Lab Scale)

Caroate Dispersible Cleaning Tablets (880 mg)

1. Formulation

I.	Sodium chloride	884 g
II.	Kollidon VA 64 [1]	47 g
	Ethanol or Isopropanol	q.s.
III.	Caroate	884 g
	Kollidon CL [1]	93 g
	Polyethylene glycol 6000, powder	93 g

2. Manufacturing (Wet granulation)

Granulate I with soluton II, pass through a 0.8 mm sieve, dry, mix with the components III and press to tablets.

3. Tablet properties

Weight	2,000 mg
Diameter	20 mm
Form	biplanar
Hardness	130 N
Disintegration (water)	< 30 sec
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Caroate Effervescent Cleaning Tablets (650 mg)

1. Formulation

I.	Sodium chloride	488 g
II.	Kollidon VA 64 [1]	49 g
	Ethanol or Isopropanol	q.s.
III.	Caroate	650 g
	Tartaric acid	325 g
	Sodium bicarbonate	407 g
	Polyethylene glycol 6000, powder	81 g

2. Manufacturing (Wet granulation)

Granulate I with soluton II, pass through a 0.8 mm sieve, dry, mix with the components III and press to tablets.

3. Tablet properties

Weight	2,000 mg
Diameter	20 mm
Form	biplanar
Hardness	140 N
Disintegration (water)	2 min
Friability	0.3 %

2.9 Tablet formulations (Lab Scale)

Charcoal Tablets (250 mg)

1. Formulation

I.	Activated charcoal (Carbo medicinalis, Merck)	250 g
	Bolus alba (Merck)	150 g
II.	Kollidon 25 [1]	28 g
	Acacia gum	38 g
	Water + isopropanol (10 + 3)	575 ml
III.	Cremophor EL [1]	15 g
	Isopropanol	300 ml

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 1 mm sieve, dry until the relative powder humidity of 90 % is reached, add solution III and pass again through a sieve. Dry the granules and press with low compression force. Dry the obtained tablets.

3. Tablet properties

Weight	481 mg
Diameter	12 mm
Form	biplanar
Hardness	55 N
Disintegration	1 min

5.8 Liquid Formulations (Lab scale)

Chloramphenicol Ophthalmic Solution (3 %)

1. Formulation

Chloramphenicol .....3.0 g
Kollidon 25 [1] .....15.0 g
Preservative .....q.s.
Water .....add 100.0 g

2. Manufacturing

Dissolve the preservative in hot water, cool, dissolve Kollidon 25, add chloramphenicol and stir until a clear solution is obtained.

3. Properties

Clear colourless solution having a low viscosity.

4. Remark

To prevent of discolouration of Kollidon in the solution during storage 0.2 to 0.5 % of cysteine could be added as antioxidant.

5.8 Liquid Formulations (Lab scale)

Chloramphenicol Palmitate Oral or Topical Emulsion (2.5 % = 250 mg/10 ml)

1. Formulation

I.	Chloramphenicol palmitate	2.5 g
	Lutrol E 400 [1]	4.0 g
	Cremophor RH 40 [1]	4.0 g
II.	Sucrose, crystalline	40.0 g
	Water	40.0 g
III.	Water	ad 100 ml

2. Manufacturing

Mix components I at 70°C to obtain a clear solution. Cool to 40 °C and add this solution slowly to the well stirred solution II. Fill up with III to 100 ml.

3. Properties

White, homogeneous emulsion without foam formation.

5.8 Liquid Formulations (Lab scale)

Chloramphenicol Palmitate Oral or Topical Emulsion (5.0 % = 500 mg/10 ml)

1. Formulation

I.	Chloramphenicol palmitate	5 g
	Lutrol E400 [1]	6 g
	Cremophor RH 40 [1]	4 g
II.	Sucrose, crystalline	40 g
	Preservative	q.s.
	Water	45 g

2. Manufacturing

Mix components I at 70°C to obtain a clear solution and cool to about 40 °C. Add the warm solution II slowly to the well stirred solution I.

3. Properties

White, milky emulsion

4. Physical Stability

After 3 weeks at room temperature and at 45 °C no change of appearance and viscosity was observed.

Chlorhexidine Gel (2 %)

1. Formulation

Chlorhexidin diacetate .....2 g
1,2-Propylene glycol Pharma [1].....30 g
Lutrol F 127 [1].....22 g
Water.....46 g

2. Manufacturing

Dissolve chlorhexidin diacetate in propylene glycol at > 70 °C, stir well and add slowly Lutrol F 127 and water. Maintain the temperature until the air bubbles escaped.

3. Properties of the gel

A clear colourless gel is obtained.

4. Physical stability (4 months, 40 °C)

No change of the appearance.

2.9 Tablet formulations (Lab Scale)

Chlorhexidine Lozenges (5 mg)

1. Formulation

Chlorhexidine (Sigma)	5.0 g
Sorbitol, crystalline [10]	150. g
Kollidon VA 64 [1]	5.0 g
Menthol, crystalline	5.0 g
Eucalyptol, crystalline	5.0 g
Aspartame, potassium	1.0 g
Saccharin, sodium	0.1 g
Aerosil 200 [4]	2.0 g
Magnesium stearate [2]	1.0 g

2. Manufacturing

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight	175 mg
Diameter	8 mm
Form	biplanar
Hardness	63 N
Disintegration	> 10 min
Friability	0.3 %

2.9 Tablet formulations (Lab Scale)

Chloroquine Tablets (250 mg)

1. Formulation

I.	Chloroquine diphosphate	250 g
	Dicalcium phosphate, Ditab [9]	100 g
II.	Kollidon 30 [1]	10 g
	Isopropanol	83 g
III.	Kollidon CL [1]	10 g
	Aerosil 200 [4]	2 g
	Talc [10]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add the mixture III and press with low compression force.

3. Tablet properties

Weight	361 mg
Diameter	8 mm
Form	biplanar
Hardness	202 N
Disintegration	8 min
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Choline Theophyllinate Tablets (100 mg)

1. Formulation

Choline theophyllinate .....100 g
Ludipress [1] .....244 g
Magnesium stearate [2] .....6 g

2. Manufacturing (Direct compression)

Pass all components through a 0.5 mm sieve mix and press with very low compression force.

3. Tablet properties

Weight .....350 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....70 N
Disintegration .....4 min
Friability .....< 0.1%

2.9 Tablet formulations (Lab Scale)

Chymotrypsine Tablets (27 mg)

1. Formulation

Chymotrypsine .....27.5 g
Ludipress [1] .....71.5 g
Magnesium stearate [2].....1.0 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm screen and press with low compression force.

3. Tablet properties

Weight .....100 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....67 N
Disintegration .....6 min
Friability .....< 0.1%

Cimetidine Tablets (200 mg)

1. Formulation

Cimetidine.....200 g
Ludipress [1] .....295 g
Magnesium stearate [2] .....5 g

2. Manufacturing (Direct compression)

Pass the mixture through a 0.8 mm screen and press with low compression force.

3. Tablet properties

Weight .....510 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....92 N
Disintegration .....1 min
Friability.....0.2 %
Dissolution (15 min).....88 %

2.9 Tablet formulations (Lab Scale)

Cimetidine Tablets (280 mg)

1. Formulation

I.	Cimetidine	288 g
	Corn starch [3]	122 g
II.	Kollidon 30 [1]	14 g
	Water	72 g
III.	Magnesium stearate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, add III and press to tablets with low compression force.

3. Tablet properties

Weight	427 mg
Diameter	12 mm
Form	biplanar
Hardness	108 N
Disintegration	3 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Cimetidine Tablets (400 mg)

1. Formulation

I.	Cimetidine	400 g
	Corn starch [3]	170 g
II.	Kollidon VA 64 [1]	20 g
	Water	100 g
III.	Magnesium stearate [2]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, add III and press to tablets with low compression force.

3. Tablet properties

Weight	601 mg
Diameter	12 mm
Form	biplanar
Hardness	91 N
Disintegration	4 min
Friability	0.5 %
Dissolution (10 min)	62 %
(20 min)	91 %
(30 min)	100 %

2.9 Tablet formulations (Lab Scale)

Clenbuterol Tablets (20 µg)

1. Formulation

Clenbuterol hydrochloride .....0.02 g
Ludipress [1] .....99.00 g
Magnesium stearate [2].....1.00 g

2. Manufacturing (Direct compression)

Mix all components in a turbula mixer and press to tablets with a compression force of 20 kN.

3. Tablet properties

Weight .....100 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....75 N
Disintegration .....3 min

4. Remark

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of clenbuterol hydrochloride with a small part of the Ludipress before mixing with the other components of the tabletting mixture.

2.9 Tablet formulations (Lab Scale)

Clobazam Tablets (10 mg)

1. Formulation

Clobazam	10.0 g
Dicalcium phosphate DI-TAB [9]	135.0 g
Kollidon VA 64 [1]	7.0 g
Kollidon CL [1]	7.0 g
Magnesium stearate [2]	1.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force (15 kN).

3. Tablet properties

Weight	165 mg
Diameter	8 mm
Form	biplanar
Hardness	44 N
Disintegration	< 1 min
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Clomifen Citrate Tablets (50 mg)

1. Formulation

Clomifen citrate .....50 mg
Ludipress [1].....100 mg
Magnesium stearate [2].....1 mg

2. Manufacturing (Direct compression)

Mix all components, sieve and press with low compression force.

3. Tablet properties

Weight .....154 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....82 N
Disintegration .....6 min
Friability.....0.13 %
Dissolution (60 min).....100 %

5.8 Liquid Formulations (Lab scale)

Closantel Veterinary Injectable Solution (12 – 20 g/100 ml)

1. Formulation

I.	Closantel	12.0 – 20.0 g
II.	Kollidon 12 PF or Kollidon 17 PF [1]	9.0 – 12.0 g
	Sodium hydroxide, 50 % in water	2.5 – 3.0 g
	Propylene glycol Pharma [1]	ca. 60 g
III.	Sodium bisulfite	0.01 – 0.04 g
	Water for injectables	ca. 20 g

2. Manufacturing

Dissolve Closantel in solution II and add solution III.
The sterilisation can be done by heating (120 °C, 20 min)

3. Properies of the solution

Clear yellow solution

4. Remarks

The function of Kollidon 12 PF or Kollidon 17 PF is to reduce strongly the local side effects (e.g. formation of oedemas) and to increase the retention time in the tissue.

5.8 Liquid Formulations (Lab scale)

Clotrimazol Topical Solution (3 %)

1. Formulation

I.	Clotrimazol	3.0 g
	Cremophor RH 40	30.0 g
II.	Preservative	q. s.
	Ethanol 96 %	34 g
	Water	33 g

2. Manufacturing

Dissolve Clotrimazol in Cremophor RH 40 at about 60 °C, stir strongly and add slowly the hot solution II.

3. Properties

Clear, colourless, viscous liquid.

Clotrimazole Cream (1%)

1. Formulation

I.	Cetylstearyl alcohol	7.0 g
	Cremophor A 6 [1]	1.5 g
	Cremophor A 25 [1]	1.5 g
	Liquid paraffin	12.0 g
	Parabene(s)	0.2 g
II.	Water	68.8 g
III.	Propylene glycol [1]	8.0 g
	Clotrimazole	1.0 g

2. Manufacturing

Heat the mixture I and the water II separately to about 80 °C. Add the water II to the obtained solution I with rigorous stirring. Heat III until the active ingredient is dissolved, mix with I/II and continue to stir during cooling to room temperature.

3. Properties

White cream.

4. Physical stability

No change of appearance or crystallization were observed during 6 weeks at 45 °C.

5. Remark

This formulation could be used for other active ingredients too.

2.9 Tablet formulations (Lab Scale)

Crospovidone Effervescent Tablets (1000 mg)

1. Formulation

I.	Crospovidone, micronized (Kollidon CL-M, BASF)	1000 g
	Citric acid	150 g
	Aerosil 200 [4]	25 g
II.	Sucrose, crystalline	100 g
	Saccharin sodium	1 g
	Water	q.s.
III.	Magnesium stearate [2]	5 g
	Sodium bicarbonate	125 g
	Flavour mixture	65 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a sieve, mix the dry granules with III and press with medium compression force.

3. Tablet properties

Weight	1590 mg
Diameter	20 mm
Form	biplanar
Hardness	111 N
Disintegration	1 min
Friability	0.4 %

4. Remark

The dosage may be increased to 2000 mg crospovidone by increasing the tablet weight to 3200 mg.

2.9 Tablet formulations (Lab Scale)

Crospovidone Water Dispersible Tablets (1000 mg)

1. Formulation

I.	Crospovidone M (BASF)	1000 g
	Aerosil 200 [4]	50 g
II.	Sucrose, crystalline	250 g
	Saccharin sodium	5 g
	Flavours	2-3 g
	Water	380 g
III.	Magnesium stearate [2]	5 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a sieve, mix the dry granules with III and press with low compression force.

3. Tablet properties

Weight	1280 mg
Diameter	20 mm
Form	biplanar
Hardness	103 N
Disintegration	1 – 2 min
Friability	0.6 %

4. Remark

The dosage may be increased to 2000 mg Crospovidone by increasing the tablet weight to 2600 mg.

2.9 Tablet formulations (Lab Scale)

Cyproheptadine Tablet (4 mg)

1. Formulation

Cyproheptadine .....4 g
Ludipress [1] .....194 g
Magnesium stearate [2] .....2 g

2. Manufacturing (Direct compression)

Pass all ingredients through a 0.8 mm sieve. Mix and press with very low compression force (4 kN).

3. Tablet properties

Weight .....202 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....46 N
Disintegration ..... 3 min
Friability.....0.5 %

4. Remark

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

6.7 Formulations of semi-solid drugs (Lab scale)

Dexpanthenol Gel-Cream (5 %)

1. Formulation

Dexpanthenol (BASF).....5 g
Liquid paraffin .....10 g
Lutrol E 400 [1].....15 g
Lutrol F 127 [1].....18 g
Water.....52 g

2. Manufacturing

Dissolve dexpanthenol and Lutrol E 400 in water, add liquid paraffin and stir heating to 60 – 70°C. Add slowly Lutrol F 127 and stir until it is dissolved. Cool to room temperature stirring continously when the air bubbles disappeared.

3. Properties of the gel

Soft turbid gel-cream.

4. Physical stability (3 months, 40 °C)

No change of the appearance and viscosity.

5.8 Liquid Formulations (Lab scale)

Diazepam Injectable Solution (2.5 mg/ml)

1. Formulation

I.	Diazepam	0.25 g
	Solutol HS 15 [1]	4.00 g
	Lecithin	4.00 g
II.	Water for injectables	ad 100 ml
	Preservative	q.s.

2. Manufacturing

Heat mixture I to 60 – 70 °C, stirr well and add very slowly the hot solution II.

3. Properties of the solution

A clear colourless solution of very low viscosity was obtained.

2.9 Tablet formulations (Lab Scale)

Diazepam Tablet (10 mg)

1. Formulation

Diazepam.....10 g
Ludipress .....100 – 480 g
Magnesium stearate .....0.5 – 2.0 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium
compactation force.

3. Tablet properties

Weight .....110 – 490 mg
.....according to the formulation
Form .....biplanar
Hardness .....> 100 N
Disintegration.....< 5 min
Friability .....< 0.1%
Dissolution (10 min) 100%

Diclofenac Gel (1%)

1. Formulation

Diclofenac sodium	1 g
Propylene glycol Pharma [1]	20 g
Lutrol F 127 [1]	22 g
Water	57 g

2. Manufacturing

Dissolve Lutrol F 127 in water at 4 – 6 °C (or at > 70 °C) and mix with the solution of diclofenac sodium in propylene glycol. Maintain the temperature until the air bubbles disappeared.

3. Properties

Colourless clear gel.

6.7 Formulations of semi-solid drugs (Lab scale)

Diclofenac Gel-Cream (1%)

1. Formulation

Diclofenac sodium	1 g
Propylene glycol Pharma [1]	15 g
Miglyol® 812 (Dynamit-Nobel)	10 g
Lutrol F 127 [1]	20 g
Water	54 g

2. Manufacturing

Dissolve diclofenac sodium in propylene glycol, add the mixture of water and Miglyol 812. Dissolve Lutrol F 127 in this well stirred mixture at 4 – 6 °C (or at > 70 °C). Maintain the temperature until the air bubbles escaped.

3. Properties

White, turbid gel-cream.

5.8 Liquid Formulations (Lab scale)

Diclofenac Injectable Solution (75 mg/3 ml)

1. Formulation

Diclofenac sodium	7.5 g
Propylene glycol Pharma [1]	50.0 g
Kollidon 17 PF [1]	5.0 g
Benzyl alcohol	12.0 g
Water for injectables	to 300 ml

2. Manufacturing

Dissolve Kollidon 17 PF in the mixture of propylene glycol, benzyl alcohol and water, add diclofenac sodium and stir until a clear solution is obtained.

The sterilisation could be made by aseptic filtration (0.2 µm).

5.8 Liquid Formulations (Lab scale)

Diclofenac Oral Solution (1.5 %)

1. Formulations

	No. 1	No. 2
Diclofenac sodium	1.5 g	1.5 g
Kollidon 30 [1]	2.5 g	1.5 g
Cremophor RH 40 [1]	–	0.5 g
Sucrose, crystalline	40.0 g	40.0 g
Water	56.0 g	56.5 g

2. Manufacturing

Dissolve diclofenac sodium in the aqueous solution of the auxiliaries.

3. Physical stability

There was no crystallisation after the storage of 2 weeks at 6 °C.

2.9 Tablet formulations (Lab Scale)

Diclofenac Tablet Cores (50 mg)

1. Formulation

I.	Diclofenac sodium (Chemag)	50 g
	Calcium phosphate, dibasic [9]	132 g
	Kollidon 30 [1]	6 g
II.	Ethanol 96 %	q.s.
III.	Kollidon CL [1]	10 g
	Magnesium stearate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solvent II, pass through a 0.8 mm sieve, add III and press with low compression force.

3. Tablet properties

Weight	209 mg
Diameter	8 mm
Form	biconvex
Hardness	72 N
Disintegration	7 min
Friability	0.4 %

2.9 Tablet formulations (Lab Scale)

Diclofenac Tablets (50 mg)

1. Formulation

Diclofenac sodium	50.0 g
Ludipress [1]	150.0 g
Magnesium stearate [2]	1.5 g
Polyethylene glycol 6000, powder [6]	15.0 g
Kollidon CL [1]	10.0 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	226 mg
Diameter	8 mm
Form	biplanar
Hardness	72 N
Disintegration	16 min
Friability	<0.1%
Dissolution (10 min)	58%
(15 min)	77%
(30 min)	99%

2.9 Tablet formulations (Lab Scale)

Diltiazem Tablets (50 mg)

1. Formulation

Diltiazem	60 g
Ludipress [1]	141 g
Polyethylene glycol 6000, powder [6]	5 g
Aerosil 200 [4]	1 g
Magnesium stearate [2]	1 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with low compression force.

3. Tablet properties

Weight	215 mg
Diameter	8 mm
Form	biplanar
Hardness	> 100 N
Disintegration	6 min
Friability	0.1%

2.9 Tablet formulations (Lab Scale)

Dimenhydrinate Tablet Cores (100 mg)

1. Formulation

I.	Dimenhydrinate	100 g
	Lactose monohydrate [8]	40 g
	Corn starch [3]	40 g
	Kollidon 90 F [1]	6 g
II.	Isopropanol	30 g
III.	Kollidon CL [1]	14 g
	Talc [10]	16 g
	Aerosil 200 [4]	2 g
	Calcium arachinate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with low compression force.

3. Tablet properties

Weight	210 mg
Diameter	9 mm
Form	biconvex
Hardness	27 N
Disintegration	< 1 min
Friability	1%

Dimenhydrinate Tablets (50 mg)

1. Formulation

Dimenhydrinate .....50 g
Ludipress [1] .....245 g
Magnesium stearate [2] .....5 g

2. Manufacturing (Direct compression)

Mix all components, sieve and press with low compression force.

3. Tablet properties

Weight .....300 mg
Diameter .....8 mm
Form .....biplanar
Hardness .....144 N
Disintegration .....10 min
Friability.....0.5 %

3.5 Coating formulations (Lab Scale)

Enteric Film Coating

1. Formulations

		No. 1	No. 2
I.	Sicovit Titanium dioxide [1]	5 g	10 g
	Talc [10]	20 g	90 g
	Sicovit Iron oxide Red 30 [1]	5 g	10 g
	Kollidon 25 or Kollidon 30 [1]	5 g	12 g
	Propylene glycol Pharma [1]	–	6 g
	Silicone emulsion	–	2 g
	Water	100 g	420 g
II.	Kollicoat MAE 30 DP [1]	500 g	200 g
	Triethyl citrate (Merck)	15 g	–
	Water	350 g	400 g

2. Manufacturing of the suspension

Prepare the suspensions I and II separately, mix both and homogenize in a disk mill or in a colloid mill.

3. Coating procedure (Accela Cota 24″)

Tablet core loading	5 kg
Core size	9 mm biconvex
Quantity of suspension applied	1,890 g
Quantity of solids/cm^2	9 mg
Quantity of film-forming agent/cm^2	6 mg
Speed of the coating pan	12 rpm
Spray nozzle	0.8 mm
Spraying pressure	2.0 bar
Type of spraying	continuous
Inlet air temperature	50 °C
Outlet air temperature	approx. 30 °C
Spraying time	approx. 60 min
Spraying rate	approx. 30 g/min

Ephedrine Tablets (100 mg)

1. Formulation

l-Ephedrine hydrochloride (Knoll) .....100.0 g
Ludipress [1].....397.5 g
Magnesium stearate [2].....2.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight .....524 mg
Diameter .....12 mm
Form .....biplanar
Hardness .....> 150 N
Disintegration .....7 min
Friability.....0.1%

6.7 Formulations of semi-solid drugs (Lab scale)

Erythromycin Gel (1%)

1. Formulation

I.	Erythromycin base	1 g
	Lutrol E 400 [1]	20 g
	Propylene glycol Pharma [1]	20 g
II.	Lutrol F 127 [1]	20 g
III.	Water	39 g

2. Manufacturing

Heat solution I to about 70 °C, dissolve II, mix with III and cool when the air bubbles escaped.

3. Properties of the gel

A clear soft gel is obtained.

Ethambutol Tablets (400 mg), DC

1. Formulation

Ethambutol	400 g
Sorbitol, crystalline [10]	200 g
Kollidon VA 64 [1]	20 g
Kollidon CL [1]	10 g
Magnesium stearate [2]	10 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium/high compression force.

3. Tablet properties

Weight	620 mg
Diameter	12 mm
Form	biplanar
Hardness	82 N
Disintegration	10 min
Friability	0.8 %

2.9 Tablet formulations (Lab Scale)

Ethambutol Tablets (400 mg), WG

1. Formulation

I.	Ethambutol	400 g
	Kollidon CL [1]	40 g
II.	Mannitol	200 g
III.	Kollidon 30 [1]	7 g
	Water	q.s.
IV.	Magnesium stearate [2]	10 g

2. Manufacturing (Wet granulation)

Granulate mannitol II with solution III, dry, pass through a 0.8 mm sieve, mix with the components I and IV and press with high compression force.

3. Tablet properties

Weight	622 mg
Diameter	12 mm
Form	biplanar
Hardness	97 N
Disintegration	9 min
Friability	0.4 %

2.9 Tablet formulations (Lab Scale)

Ethambutol Tablets (800 mg)

1. Formulation

I.	Ethambutol (Helm)	800 g
	Dicalcium phosphate, DI-TAB [9]	200 g
II.	Kollidon 30 [1]	30 g
	Isopropanol	q.s.
III.	Kollidon CL [1]	50 g
	Magnesium stearate [2]	15 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add III and press with high compression force.

3. Tablet properties

Weight	1,112 mg
Diameter	20 mm
Form	oblong
Hardness	78 N
Disintegration	2 min
Friability	1.1%

2.9 Tablet formulations (Lab Scale)

Etophylline + Theophylline Tablets (100 mg + 22 mg), DC

1. Formulation

Etophylline, powder (Knoll) .....101 g
Theophylline, anhydrous 0,2/0,7 (Knoll) .....23 g
Ludipress [1] .....53 g
Magnesium stearate [2] .....1 g
Aerosil 200 [4].....2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with low compression force.

3. Tablet properties

Weight .....175 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....102 N
Disintegration.....7 – 8 min
Friability.....0.2 %

4. Remark

To enhance the flowability of the tabletting mixture the amount of Aerosil 200 could be increased.

2.9 Tablet formulations (Lab Scale)

Etophylline + Theophylline Tablets (100 mg + 22 mg), WG

1. Formulation

I.	Etophylline, powder (Knoll)	100 g
	Theophylline, anhydrous 0.2/0.7 (Knoll)	23 g
	Corn starch or potato starch	50 g
	Kollidon VA 64 [1]	3 g
II.	Kollidon VA 64 [1]	4 g
	Water	35 g
III.	Magnesium stearate [2]	1 g
	Talc [10]	5 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, dry, mix with III, pass through a 0.5 mm sieve and press with medium compression force.

3. Tablet properties

Weight	183 mg
Diameter	8 mm
Form	biplanar
Hardness	92 N
Disintegration	3 – 4 min
Friability	0.3 %

5.8 Liquid Formulations (Lab scale)

Eucalyptol Solution (8 %)

1. Formulation

I.	Eucalyptol	8.0 g
	Cremophor RH 40 [1]	4.0 g
II.	Preservative	q.s.
	Water	ad 100 ml

2. Manufacturing

Mix eucalyptol and Cremophor at 65 °C, stir well and add slowly the warm solution II.

3. Properties of the solution

Clear or slightly opalescent, colourless liquid.

Famotidine Tablets (40 mg)

1. Formulations

	No. 1	No. 2
Famotidine	40 g	40 g
Ludipress [1]	105 g	104 g
Magnesium stearate [2]	3 g	–
Stearic acid [7]	–	2 g
Aerosil 200 [4]	4 g	4 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

	No. 1	No. 2
Weight	149 mg	148 mg
Diameter	8 mm	8 mm
Form	biplanar	biplanar
Hardness	74 N	49 N
Disintegration (gastric juice)	3 min	1 min
Friability	<0.1%	0.3%
Dissolution (10 min)	63%	not tested
(30 min)	95%	not tested

2.9 Tablet formulations (Lab Scale)

Ferrous Fumarate Tablets (200 mg)

1. Formulation

Ferrous fumarate .....200 g
Ludipress [1] .....295 g
Magnesium stearate [2] .....5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....509 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....92 N
Disintegration .....1 min
Friability.....0.2 %

2.9 Tablet formulations (Lab Scale)

Ferrous Sulfate + Manganese Sulfate + Copper Sulfate Tablets (65 mg + 3.5 mg + 0.16 mg)

1. Formulation

Ferrous sulfate, anhydrous	65.0 g
Manganese sulfate	3.5 g
Copper sulfate	0.16 g
Ludipress [1]	70.0 g
Kollidon 30 [1]	10.0 g
Magnesium stearate [2]	2.0 g
Aerosil 200 [4]	3.0 g

2. Manufacturing (Direct compression)

Pass all components through a 0.5 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight	149 mg
Diameter	8 mm
Form	biplanar
Hardness	28 N
Disintegration	3 – 4 min
Friability	0.4 %

2.9 Tablet formulations (Lab Scale)

Ferrous Sulfate Tablets (200 mg)

1. Formulation

Ferrous sulfate, anhydrous	203 g
Ludipress [1]	185 g
Kollidon VA 64 [1]	15 g
Magnesium stearate [2]	4 g
Talc [10]	4 g
Aerosil 200 [4]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with medium compression force.

3. Tablet properties

Weight	413 mg
Diameter	8 mm
Form	biplanar
Hardness	110 N
Disintegration	13 min
Friability	0.2 %

5.8 Liquid Formulations (Lab scale)

Fir Needle Oil Solution (3 %)

1. Formulation

Fir needle oil (Frey & Lau)	3.0 g
Camphora	5.0 g
Cremophor RH 40 [1]	6.0 g
Ethanol 96 %	40.3 g
Water	45.7 g

2. Manufacturing

Mix the active ingredients with Cremophor RH 40 and heat to 50 – 60 °C. Add the ethanol and slowly the warm water to the well stirred solution.

3. Properties of the solution

Clear or slightly opalescent liquid.

4. Remark

The needed amount of Cremophor RH 40 depends on the type of fir needle oil.

2.9 Tablet formulations (Lab Scale)

Folic Acid Tablets (5 mg)

1. Formulation

Folic acid .....5.0 g
Ludipress [1] .....195.0 g
Magnesium stearate [2].....1.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with medium compression force.

3. Tablet properties

Weight .....213 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....205 N
Disintegration .....7 min
Friability .....< 0.1%

4. Remark

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

2.9 Tablet formulations (Lab Scale)

Fucidine Tablet Cores (125 mg)

1. Formulation

I.	Fucidine	125.0 g
	Dicalcium phosphate, DI-TAB [9]	63.0 g
II.	Kollidon 90 F [1]	2.5 g
	Isopropanol	30 ml
III.	Kollidon CL [1]	6.2 g
	Aerosil 200 [4]	1.3 g
	Magnesium stearate [2]	3.0 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add the mixture III and press with low compression force.

3. Tablet properties

Weight	200 mg
Diameter	9 mm
Form	biconvex
Hardness	55 N
Disintegration	25 min
Friability	0 %

4. Remark

To accelerate the disintegration the amount of Kollidon 90 F should be reduced and Kollidon CL should be applied in intra- and extragranular form.

5.8 Liquid Formulations (Lab scale)

Furaltadone Injectable Solution (50 mg/ml)

1. Formulation

Furaltadone.....5.00 g
Tartaric acid .....1.25 g
Kollidon 12 PF [1] .....25.00 g
Water of injectables .....ad 100 ml

2. Manufacturing

Dissolve the solid substances in water at about 50 °C.

The sterilisation can be made by aseptic filtration or by heating (120 °C, 20 min).

3. Remark

To prevent of discolouration of Kollidon in the solution during storage 0.2 to 0.5% of cysteine could be added as antioxidant.

2.9 Tablet formulations (Lab Scale)

Furosemide Tablets (40 mg)

1. Formulation

Furosemide .....40 g
Ludipress [1] .....158 g
Magnesium stearate [2] .....2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....205 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....81 N
Disintegration .....2 min
Friability.....0.1%

2.9 Tablet formulations (Lab Scale)

Furosemide Tablets (200 mg)

1. Formulation

Furosemide	200 g
Ludipress [1]	388 g
Magnesium stearate [2]	6 g
Aerosil 200 [4]	6 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	618 mg
Diameter	12 mm
Form	biplanar
Hardness	159 N
Disintegration	3 – 4 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Garlic Tablets Cores (100 mg)

1. Formulation

I.	Calcium phosphate, dibasic [9]	95 g
	Lactose monohydrate [8]	94 g
II.	Kollidon 30 [1]	9 g
	Water	25 g
III.	Dried garlic powder	100 g
	Magnesium stearate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, add III and press with low compression force.

3. Tablet properties

Weight	312 mg
Diameter	9 mm
Form	biconvex
Hardness	98 N
Disintegration	23 min
Friability	0.3 %

4. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Glibenclamide Tablets (5 mg)

1. Formulation

	No. 1	No. 2
Glibenclamide micronized (Guidotti)	5.0 g	–
Glibenclamide	–	5.0 g
Ludipress [1]	120.0 g	194.0 g
Magnesium stearate [2]	0.5 g	1.0 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force (about 10 kN).

3. Tablet properties

	No. 1	No. 2
Weight	125 mg	201 mg
Diameter	7 mm	8 mm
Form	biplanar	biplanar
Hardness	80 N	107 N
Disintegration	2-3 min	3 – 4 min
Friability	< 0.2 %	< 0.1 %
Dissolution (10 min)	50 %	–
(30 min)	69 %	–
(60 min)	75 %	–

4. Influence of the compression force on the physical tablet properties (Formulation No. 2)

Property	Compression force 5 kN	10 kN	20 kN	25 kN
Hardness	47 N	107 N	158 N	191 N
Disintegration	2 – 3 min	3 – 4 min	3 – 4 min	5 min
Friability	< 0.1%	< 0.1%	< 0.1%	< 0.1%

2.9 Tablet formulations (Lab Scale)

Glutaminic Acid Tablets (550 mg)

1. Formulation

I.	Glutaminic acid	573 g
	Sorbitol, crystalline [10]	115 g
II.	Kollidon 30 [1]	17 g
	Water	q.s.
III.	Kollidon CL [1]	11 g
	Magnesium stearate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve and mix with III. Press with low compression force to tablets.

3. Tablet properties

Weight	719 mg
Diameter	12 mm
Form	biplanar
Hardness	138 N
Disintegration	6 min
Friability	0.2 %

5.8 Liquid Formulations (Lab scale)

Gramicidin Ophthalmic Solution (1.3 mg/10 ml)

1. Formulation

I.	Gramicidin	13 mg
	Cremophor RH 40 [1]	0.1 g
II.	Ethanol 96 %	1.0 g
	Preservatives	q. s.
	Water	98.8 g

2. Manufacturing

Mix gramicidin and Cremophor RH 40, heat to about 65 °C, stir and add slowly the heat solution II.

3. Properties

Clear solution.

2.9 Tablet formulations (Lab Scale)

Griseofulvin Tablets (125 mg)

1. Formulation

Griseofulvin, micronized (Aldrich) .....125 g
Ludipress [1] .....250 g
Polyethylene glycol 6000, powder [6].....10 g
Aerosil 200 [4] .....19 g

2. Manufacturing (Direct compression)

Pass all components through a 0.5 mm sieve, mix and press with low compression force applying a vibrating hopper.

3. Tablet properties

Weight .....367 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....79 N
Disintegration .....1 min
Friability.....0.3 %
Dissolution, 20 min .....78 %
40 min .....88 %
60 min .....92 %

4. Remark

The flowability of the tabletting mixture should be increased by higher amounts of Ludipress or/and Aerosil 200.

2.9 Tablet formulations (Lab Scale)

Griseofulvin Tablets (500 mg)

1. Formulation

I.	Griseofulvin	500 g
	Kollidon VA 64 [1]	100 g
II.	Dimethyl formamide	7,500 g
III.	Kollidon CL [1]	75 g
	Lactose monohydrate [8]	75 g
	Magnesium stearate [2]	5 g
	Aerosil 200 [4]	5 g

2. Manufacturing (Wet granulation)

Dissolve mixture I in the solvent II, evaporate to dryness, pass the obtained coprecipitate through a 0.5 mm sieve, mix with III and press with low compression force.

3. Tablet properties

Weight	751 mg
Diameter	12 mm
Form	biplanar
Hardness	62 N
Disintegration	2 min
Friability	0.5 %

Heparin Gel-Cream (300 i.u./g)

1. Formulation

Heparin sodium	186 mg
Lutrol E 400 [1]	15 g
Liquid paraffin	10 g
Lutrol F 127 [1]	23 g
Water	ad 100 g

2. Manufacturing

Dissolve heparin sodium in water, add Lutrol E 400 and liquid paraffin, stir and cool to 6 °C. Add slowly Lutrol F 127 and stir until it is dissolved. Heat to room temperature when the air bubbles escaped.

2.9 Tablet formulations (Lab Scale)

Horsetail Extract Tablets (450 mg)

1. Formulation

I.	Horsetail extract, powder	456 g
II.	Kollidon VA 64 [1]	14 g
	Lutrol F 68 [1]	5 g
	Isopropanol	about 120 g
III.	Kollidon CL [1]	14 g
	Magnesium stearate [2]	q.s.

2. Manufacturing (Wet granulation)

Granulate the extract I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with high compression force.

3. Tablet properties

Weight	489 mg
Diameter	12 mm
Form	biplanar
Hardness	75 N
Disintegration	2 – 3 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Hydrochlorothiazide + Potassium Chloride Tablet Cores (50 mg + 300 mg)

1. Formulation

Hydrochlorothiazide	50 g
Potassium chloride	300 g
Kollidon CL [1]	15 g
Aerosil 200 [4]	2 g
Magnesium stearate [2]	2 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press.

3. Tablet properties

Weight	369 mg
Diameter	9 mm
Form	biconvex
Hardness	88 N
Disintegration	< 1 min
Dissolution of hydrochlorothiazide, 10 min	89 %

Hydrochlorothiazide Tablets (50 mg), DC

1. Formulation

Hydrochlorothiazide	50 g
Ludipress [1]	280 g
Magnesium stearate [2]	2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	328 mg
Diameter	8 mm
Form	biplanar
Hardness	70 N
Disintegration	3 min
Friability	0.1%

2.9 Tablet formulations (Lab Scale)

Hydrochlorothiazide Tablets (50 mg), WG

1. Formulation

I.	Hydrochlorothiazide (Chemag)	50 g
	Lactose monohydrate [8]	422 g
	Kollidon 90 F [1]	8 g
II.	2-Propanol	38 ml
III.	Kollidon CL [1]	15 g
	Magnesium stearate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, add III and press with low compression force.

3. Tablet properties

Weight	495 mg
Diameter	12 mm
Form	biplanar
Hardness	55 N
Disintegration	< 1 min
Friability	< 0.1%
Dissolution (30 min)	92%
(60 min)	100%

Hydrocortisone Aqueous Gels (1%)

1. Formulations

		No. 1	No. 2
I.	Hydrocortisone acetate	1.0 g	1.0 g
II.	Lutrol E 400 [1]	10.0 g	–
	Cremophor A 25 [1]	–	15.0 g
	Cremophor RH 40 [1]	5.0 g	20.0 g
III.	Carpopol 940 (Goodrich)	0.5 g	–
	Water	49.5 g	–
IV.	Preservative	q.s.	q.s.
	Water	26.0 g	64.0 g
V.	Triethanolamine	0.8 g	–
	Water	7.2 g	–

2. Manufacturing

Formulation No. 1:
Suspend I in the mixture II at 70 °C. Prepare solution II, dilute with the solution IV, heat to 70 °C, and add slowly to the hot mixture I/II. Add solution V and continue to stir until the gel is cool.

Formulation No. 2:
Suspend I in the mixture II at 70 °C. Prepare solution IV, heat to 70 °C and add slowly to the hot mixture I/II. Continue to stir until the gel is cool.

3. Properties

Clear colourless gels.

Hydrocortisone Cream (1%)

1. Formulation

I.	Cetylstearyl alcohol	7.0 g
	Cremophor A 6 [1]	1.5 g
	Cremophor A 25 [1]	1.5 g
	Liquid paraffin	12.0 g
	Parabene(s)	0.2 g
II.	Water	68.8 g
III.	Propylene glycol [1]	8.0 g
	Hydrocortisone	1.0 g

2. Manufacturing

Heat the mixture I and the water II separately to about 80 °C. Add the water II to the obtained solution I with rigorous stirring. Heat III until the active ingredient is dissolved, mix with I/II and continue to stir during cooling to room temperature.

3. Properties

White cream.

4. Physical stability

No change of appearance or crystallization were observed during 6 weeks at 45 °C.

5. Remark

This formulation could be used for other active ingredients too.

Hydrocortisone Ethanolic Gel (0.5 %)

1. Formulation

I.	Hydrocortisone acetate	0.5 g
	Cremophor RH 40 [1]	6.0 g
	Triethanolamine	0.9 g
	Water	7.6 g
	Ethanol 96 %	60.0 g
II.	Carbopol 940 (Goodrich)	0.5 g
	Water	24.5 g

2. Manufacturing

Prepare solution II and mix slowly with solution I.

3. Properties

Clear, colourless gel.

6.7 Formulations of semi-solid drugs (Lab scale)

Ibuprofen Gel-Cream (5 %)

1. Formulation

I.	Ibuprofen (Knoll-Boots)	5 g
	Propylene glycol Pharma [1]	12 g
	Isopropanol	12 g
II.	Lutrol F 127 [1]	12 g
III.	Water	44 g
IV.	Nonionic hydrophilic Cream (DAB 1996)*	15 g

2. Manufacturing

Prepare solution I and coll to about 8°C. Dissolve II and add III and IV. Maintain cool until the air bubbles escaped.

Nichtionische hydrophile Creme (DAB 1996)

Polysorbat 60.....5 Teile
Cetylstearylalkohol.....10 Teile
Glycerol 85%.....10 Teile
Weißes Vaselin.....25 Teile
Wasser.....50 Teile

In das auf dem Wasserbad auf etwa 70 °C erwärmte Gemisch von Polysorbat 60, Cetylstearylalkohol und Weißem Vaselin wird die auf gleiche Temperatur erwärmte Mischung der übrigen Bestandteile in Anteilen eingearbeitet. Das für die Herstellung verwendete Wasser soll vor Gebrauch frisch aufgekocht werden. Die Creme wird bis zum Erkalten gerührt und das verdampfte Wasser ersetzt. Die Creme kann mit 0,1 Prozent Sorbinsäure konserviert werden.

Ibuprofen Gels (5 %)

1. Formulations

		No. 1	No. 2
I.	Ibuprofen (Knoll-Boots)	5 g	5 g
	Ethanol 96 %	10 g	10 g
	Propylene glycol Pharma [1]	20 g	10 g
II.	Lutrol F 127 [1]	22 g	15 g
III.	Isopropyl myristate	–	1 g
	Preservative	q. s.	q. s.
	Water	43 g	59 g

2. Manufacturing

Heat solution I to 70 – 80 °C, dissolve II, add III and cool.

3. Properties of the gel

A colourles clear gel was obtained.
The gel of formulation No. 2 is less adhesive than formulation No. 1.

4. Remark

The function of isopropyl myristate is the reduction of the adhesive properties of Lutrol F 127.

5.8 Liquid Formulations (Lab scale)

Ibuprofen Solution (2 %)

1. Formulation

I.	Ibuprofen (Knoll-Boots)	2 g
	Cremophor RH 40 [1]	20 g
II.	Preservatives	q. s.
	Water	78 g

2. Manufacturing

Suspend Ibuprofen in the hot Cremophor RH 40 (about 60 °C) and add slowly the hot solution II.

3. Physical stability

The solution remained clear more than one week at 6 °C.

5.8 Liquid Formulations (Lab scale)

Ibuprofen Suspension (4 % = 400 mg/10 ml), I

1. Formulation

Ibuprofen (Knoll-Boots).....4 g
Sucrose.....25 g
Kollidon CL-M [1].....8 g
Kollidon 90 F [1].....2 g
Sodium citrate.....2 g
Water.....ad 100 ml

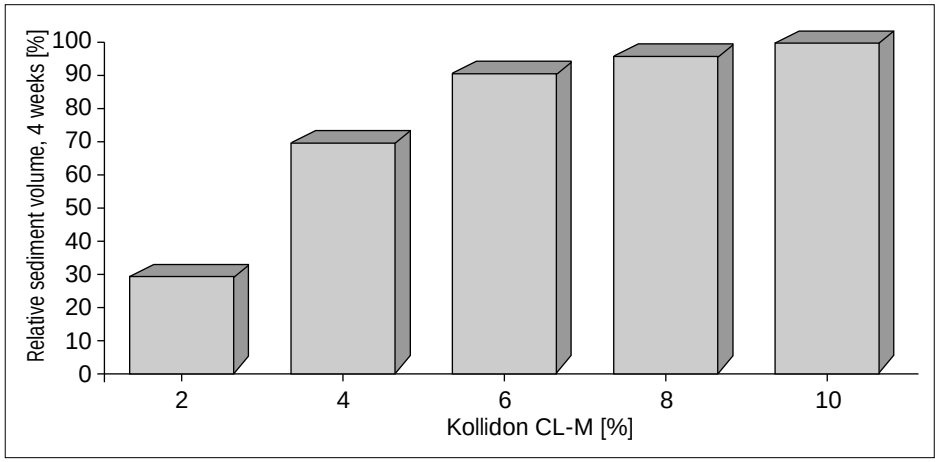
2. Manufacturing

Dissolve sucrose, Kollidon 90 F and sodium citrate in about 40 ml of water, suspend Kollidon CL-M and ibuprofen in this solution by stirring and add the rest of water.

3. Suspension properties

Color.....white
Aspect.....Homogeneous
Viscosity.....low
Rel. sediment volume.....100 %
(after 1 day)
Rel. sediment volume.....94 %
(after 4 weeks)
Redispersibility.....very easy
(after 4 weeks)

4. Influence of the amount of Kollidon CL-M on the sedimentation



5.8 Liquid Formulations (Lab scale)

Ibuprofen Suspension (4 % = 400 mg/10 ml), II

1. Formulation

I.	Ibuprofen (Knoll-Boots)	4.0 g
	Cremophor RH 40 [1]	10.0 g
II.	Lutrol F 68 [1]	5.0 g
	Preservative	q.s.
	Water	81 g

2. Manufacturing

Dissolve Lutrol F 68 and the preservative in water II and ibuprofene in Cremophor RH 40 (I). Add the solution II slowly to the ibuprofene-Cremophor RH 40 mixture I whilst stirring.

3. Properties of the suspension

The redispersibility of the suspension is very easy after 14 days at room temperature. The viscosity is low.

2.9 Tablet formulations (Lab Scale)

Ibuprofen Tablets (400 mg), DC

1. Formulations

	No. 1	No. 2
Ibuprofen 50 (Knoll-Boots)	400 g	–
Ibuprofen (Francis)	–	400 g
Aerosil 200 [4]	6 g	4 g
Avicel PH 102 [5]	79 g	–
Kollidon VA 64 [1]	27 g	–
Ludipress [1]	–	342 g
Kollidon CL [1]	18 g	8 g
Magnesium stearate [2]	3 g	8 g

2. Manufacturing (Direct compression)

No. 1: Mix ibuprofen with Aerosil 200, add the other components and press with low compression force.

No. 2: Pass ibuprofen and magnesium stearate through a 200 µm sieve, mix with the other components and press with medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	533 mg	752 mg
Diameter	12 mm	16 mm
Hardness	93 N	112 N
Disintegration	< 1 min	2 – 3 min
Friability	0.3 %	0.4 %
Dissolution, 10 min	98 %	82 %
15 min	99 %	91 %

4. Physical stability of formulation No. 2 (20–25ºC)

	6 Months	8 Months	12 Months
Hardness	–	121 N	120 N
Disintegration	–	2 – 3 min	–
Friability	–	0.4 %	0.2 %
Dissolution, 10 min	85 %	–	89 %
20 min	87 %	91 %	88 %

2.9 Tablet formulations (Lab Scale)

Ibuprofen Tablets (400 mg), WG

1. Formulations

		No. 1	No. 2
I.	Mannitol	330 g	–
	Dicalcium phosphate [9]	–	289 g
II.	Kollidon 30 [1]	12 g	15 g
	Water	q.s.	q.s.
III.	Ibuprofen (Knoll-Boots)	400 g	400 g
	Kollidon CL [1]	16 g	38 g
	Aerosil 200 [4]	8 g	
	Magnesium stearate [2]	8 g	8 g

2. Manufacturing (Wet granulation)

Granulate mannitol or dicalcium-phosphate with solution II, pass through a 0.8 mm sieve, add III and press with low compression force.

3. Tablet properties

	No. 1	No. 2
Weight	774 mg	741 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	90 N	177 N
Disintegration	2 min	1-2 min
Friability	0.4%	0.3%
Dissolution (30 min)	85%	–

4. Dissolution stability of formulation No. 1 (3 months, 20–25 °C)

Dissolution (30 min)	81%

2.9 Tablet formulations (Lab Scale)

Ibuprofen Tablets for Children (150 mg)

1. Formulation

I.	Ibuprofen	150,0 g
	Potato starch [3]	18.0 g
	Lactose monohydrate [8]	20.0 g
	Avicel PH 101 [5]	20.0 g
II.	Kollidon 30 [1]	3.0 g
	Water	52.0 g
III.	Avicel PH 102 [5]	76.0 g
	Croscarmelose [5]	1.7 g
	Magnesium stearate [2]	2.0 g
	Aerosil 200 [4]	0.2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with medium compression force (17 kN).

3. Tablet properties

Weight	290 mg
Diameter	10 mm
Form	biplanar
Hardness	108 N
Disintegration	11 min
Friability	0.2 %
Dissolution, 10 min	95 %
20 min	100 %

4. Remark

Croscarmelose could be substituted by Kollidon CL.

6.7 Formulations of semi-solid drugs (Lab scale)

Indomethacin Gel (1%), I

1. Formulation

Indomethacin	1 g
Cremophor RH 40 [1]	10 g
Lutrol F 127 [1]	15 g
Water	74 g

2. Manufacturing

Dissolve indomethacin in Cremophor RH 40 at 60 – 70°C, add slowly the water (60 – 70°C) stirring well the mixture and dissolve Lutrol F 127. Cool to room temperature.

3. Properties of the gel

A clear soft gel was obtained.

4. Physical stability (4 weeks, 40 °C)

No change of appearance.

Indomethacin Gel (1%), II

1. Formulations

		No. 1	No. 2
I.	Indomethacin	1.0 g	1.0 g
	Propylene glycol Pharma [1]	20.0 g	– g
	Ethanol 96%	–	15.0 g
	Lutrol E 400 [1]	20.0 g	22.0 g
II.	Lutrol F 127 [1]	21.0 g	23.0 g
III.	Water	38.0 g	39.0 g

2. Manufacturing

Heat solution I to about 70°C, dissolve II well stirring about 30 minutes, mix with III and cool. It forms a clear yellow gel.

3. Physical stability

Formulation No. 1: No change during 1 year at room temperature.

Formulation No. 2: No change during 12 weeks at 40 °C, 23 °C and 6 °C.

4. Chemical stability

Lutrol F 127 (= Pluronic® F 127) stabilizes indomethacin against hydrolisis as shown in the following publication summary:

Hydrolysis of Indomethacin in Pluronic F 127 Gels
Tomida H., Kuwada N., Kiryu S.: Acta Pharm. Suec. 25, No. 2, 87 – 96 (1988)

„In drug stability studies, the rates of hydrolysis of indomethacin (Sigma-Chem.) were considerably slower in Pluronic F 127 (BASF) gels than in buffer alone. The degradation of indomethacin followed 1st order kinetics, with linear plots of the 1st order rate constant vs. pH in both Pluronic and aqueous solutions, allowing prediction of the time required for degradation of indomethacin."

Indomethacin Powder for Hard Gelatin Capsules (160 mg)

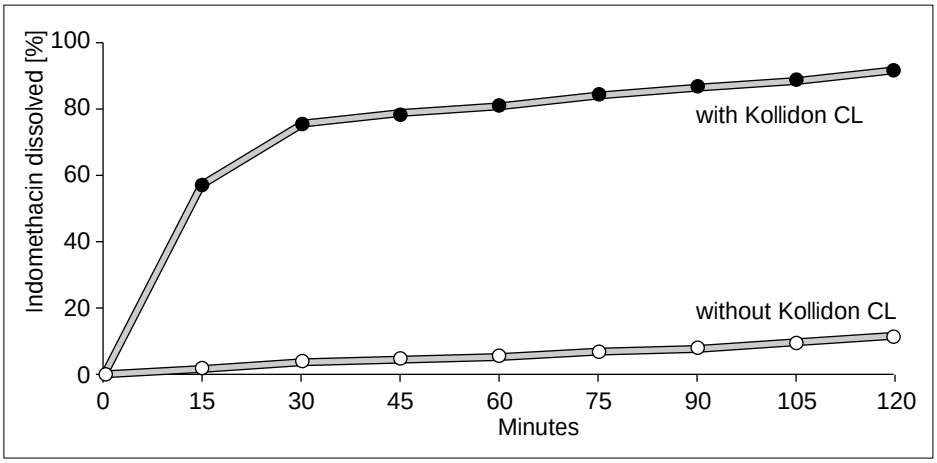
1. Formulation

Indomethacin .....160 g
Kollidon CL [1].....320 g
Aerosil 200 [4].....q.s.

2. Manufacturing

Mix the components for about 10 min and fill in hard gelatin capsules to obtain 160 mg indomethacin in each capsule.

3. Dissolution



Indomethacin Suppositories (50 mg)

1. Formulation

I.	Indomethacin	5.0 g
	Butylhydroxytoluene	8.3 mg
	Lutrol E 4000 [1]	141.0 g
	Lutrol E 6000 [1]	14.0 g
II.	EDTA	16.3 mg
	Water	3.0 g

2. Manufacturing

Prepare solution II, mix with the melted mixture I and fill into the moulds of suppositories.

3. Properties of the suppositories

Weight:	1.6 g
Colour:	slightly yellowish

2.9 Tablet formulations (Lab Scale)

Indomethacin Tablets (50 mg), DC

1. Formulation

Indomethacin	50 g
Ludipress [1]	227 g
Kollidon CL [1]	20 g
Magnesium stearate [2]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight	303 mg
Diameter	8 mm
Form	biplanar
Hardness	176 N
Disintegration	3 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Indomethacin Tablets (50 mg), WG

1. Formulation

I.	Indomethacin	50 g
	Lactose monohydrate [8]	300 g
II.	Kollidon 30 [1]	10 g
	Water	30 g
III.	Kollidon CL [1]	12 g
	Aerosil 200 [4]	2 g
	Magnesium stearate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, add III and press with low compression force.

3. Tablet properties

Weight	372 mg
Diameter	12 mm
Form	biplanar
Hardness	72 N
Disintegration	<1 min
Friability	0.1%
Dissolution, 10 min	75%
20 min	88%

4. Physical stability (20–25°C)

Storage time	Hardness	Disintegration	Friability
6 Months	70 N	<1 min	0.1%
12 Months	55 N	<1 min	0.1%

2.9 Tablet formulations (Lab Scale)

Indomethacin Tablets (100 mg)

1. Formulation

Indomethacin .....100 g
Ludipress [1] .....397 g
Magnesium stearate [2] .....3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....500 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....61 N
Disintegration .....5 min
Friability.....0.4 %

2.9 Tablet formulations (Lab Scale)

Inosin Tablet Cores (200 mg)

1. Formulation

I.	Inosin (Ribaxin, Russia)	200 g
	Lactose monohydrate [8]	51 g
	Kollidon 90 F [1]	6 g
II.	Isopropanol	60 ml
III.	Kollidon CL [1]	10 g
	Magnesium stearate [2]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with the solvent II, dry, pass through a 0.8 mm sieve, add the components III and press with low compression force.

3. Tablets properties

Weight	270 mg
Diameter	9 mm
Form	biconvex
Hardness	55 N
Disintegration	3 – 4 min
Friability	0 %

2.9 Tablet formulations (Lab Scale)

Isosorbide Dinitrate Tablets (5 mg)

1. Formulation

Isosorbide dinitrate + Lactose (4+6).....12.5 g
Lactose monohydrate [8].....152.1 g
Kollidon 30 [1].....5.4 g
Kollidon CL [1] .....9.0 g
Magnesium stearate [2].....1.0 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....184 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....45 N
Disintegration .....< 1 min
Friability.....0.1%

Khellin Tablets (25 mg)

1. Formulation

Khellin .....25 g
Ludipress [1] .....124 g
Magnesium stearate [2] .....1 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix intensively and press with low compression force (10 kN).

3. Tablet properties

Weight .....150 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....65 N
Disintegration.....about 1 min
Friability.....0.25 %

2.9 Tablet formulations (Lab Scale)

Levamisole Tablets (150 mg)

1. Formulation

Levamisole hydrochloride.....150 g
Ludipress [1] .....300 g
Magnesium stearate [2] .....4 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....458 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....80 N
Disintegration .....3 – 4 min
Friability.....0.2 %

2.9 Tablet formulations (Lab Scale)

Levothyroxine Tablets (0.05 mg)

1. Formulations

		No. 1	No. 2
I.	Levothyroxine sodium	0.05 g	0.05 g
	Citric acid, anhydrous	–	10.00 g
	Magnesium stearate	1.00 g	1.00 g
II.	Ludipress [1]	99.00 g	89.00 g

2. Manufacturing (Direct compression)

Prepare premix I, add II and pass the mixture through a 0.8 mm sieve. Mix and press with low compression force.

3. Tablet properties

	No. 1	No. 2
Weight	103 mg	101 mg
Diameter	6 mm	6 mm
Form	biplanar	biplanar
Hardness	52 N	45 N
Disintegration	1 – 2 min	4 min
Friability	0.1%	< 0.1%
Content uniformity	not controlled	

4. Remarks

If the content uniformity of formulation No. 1 does not meet the requirements it would be recommended to add a small part of Ludipress (= part II) to the premix I.

The function of citric acid in formulation No. 2 is the stabilization of the active ingredient. The effectiveness was not controlled in this formulation.

6.7 Formulations of semi-solid drugs (Lab scale)

Lidocain Gel (2 %)

1. Formulation

I.	Lidocain hydrochloride	2 g
	Water	56 g
	Propylene glycol Pharma [1]	20 g
II.	Lutrol F 127 [1]	22 g

2. Manufacturing

Prepare solution I at room temperature, heat to 70 °C or cool to 6 °C and add slowly II to the well stirred solution until it is dissolved. Maintain the temperature until the air bubbles escaped.

3. Properties of the gel

A clear colourless gel was obtained.

4. Physical stability (3 months, 20–25°C)

No change was observed.

Lidocain Gel-Cream (5 %)

1. Formulation

I.	Lidocain hydrochloride	5 g
	Water	50 g
	Propylene glycol Pharma [1]	15 g
II.	Liquid paraffin	10 g
III.	Lutrol F 127 [1]	20 g

2. Manufacturing

Prepare solution I at room temperature and mix with II. Heat to 70 °C or cool to 6 °C and add slowly III to the well stirred solution until it is dissolved. Maintain cool until the air bubbles escaped.

3. Physical stability (3 months, 20–25°C)

No change was observed.

Lisinopril Tablets (10 mg)

1. Formulation

Lisinopril .....10 g
Ludipress [1] .....139 g
Magnesium stearate [2] .....1 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix intensively and press with low compactation force (10 kN).

3. Tablet properties

Weight .....152 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....94 N
Disintegration.....2 – 3 min
Friability.....0.2 %

Magaldrate Chewable Tablets (500 mg)

1. Formulation

I.	Magaldrate USP	500 g
	Lactose monohydrate [8]	400 g
	Orange flavour (FDO)	50 g
II.	Kollidon 90 F [1]	20 g
	Banana flavour (FDO)	6 g
	Cocos flavour (FDO)	6 g
	Saccharin sodium	1 g
	Water	180 g
III.	Aerosil 200 [4]	5 g
	Magnesium stearate [2]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, dry, mix with III and press with low compression force.

3. Tablet properties

Weight	1000 mg
Diameter	16 mm
Form	biplanar
Hardness	72 N
Disintegration (water)	60 min
Friability	< 0.1%
Taste	good

2.9 Tablet formulations (Lab Scale)

Magaldrate Dispersible Tablets (700 mg)

1. Formulation

Magaldrate	700 g
Lactose monohydrate [8]	435 g
Kollidon 90 F [1]	10 g
Kollidon CL [1]	50 g
Magnesium stearate [2]	5 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force (4 – 6 kN).

3. Tablet properties

Weight	1,200 mg
Diameter	16 mm
Form	biplanar
Hardness	125 N
Disintegration (water)	25 sec
Friability	0.1%

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Magaldrate Instant Powder or Dry Syrup (800 mg)

1. Formulation

I.	Magaldrate USP	100.0 g
	Kollidon CL-M [1]	80.0 g
	Sorbitol, crystalline [10]	50.0 g
	Orange flavour	10.0 g
II.	Kollidon 90 F [1]	10.0 g
	Coconut flavour	1.0 g
	Banana flavour	1.0 g
	Saccharine sodium	0.2 g
	Water	about 70 ml

2. Manufacturing

Granulate mixture I with solution II and pass through a 0.8 mm sieve to obtain free-flowing granules. Fill 2 g in sachets or 20 g in a 100 ml flask.

3. Administration

- *Instant granules in sachets:*
  Suspend 2 g (= 1 sachet) in a glass of water (= 800 mg Magaldrate)

- *Dry syrup:*
  Fill the flask with drinking water until the mark of 100 ml and shake well. 10 ml of the suspension correspond to 800 mg Magaldrate.

5.8 Liquid Formulations (Lab scale)

Magaldrate Suspension (10 %)

1. Formulation

Magaldrate USP	10.0 g
Kollidon CL-M [1]	8.0 g
Kollidon 90 F [1]	2.0 g
Orange flavour	1.0 g
Coconut flavour	0.05 g
Banana flavour	0.08 g
Saccharine sodium	0.02 g
Preservatives	q.s.
Water	ad 100 ml

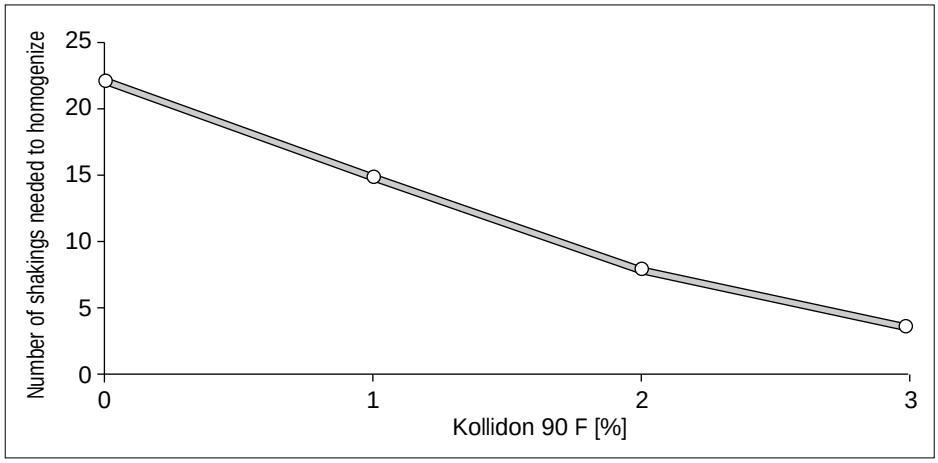
2. Manufacturing

Dissolve or suspend all the solids in water under aseptic conditions.

3. Properties of the suspension

- White homogeneous suspension practically without sedimentation during 24 hours.
- Very easy to redisperse by shaking after the storage of more than 2 weeks.
- pH value about 9.

4. Influence of the Kollidon 90 F concentration on the redispersibility after 7 days



2.9 Tablet formulations (Lab Scale)

Magnesium Carbonate Tablets (260 mg)

1. Formulation

Magnesium carbonate USP.....262 g
Ludipress [1].....238 g
Magnesium stearate [2].....4 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight.....499 mg
Diameter.....12 mm
Form.....biplanar
Hardness.....168 N
Disintegration.....1 min
Friability.....< 0.1%

2.9 Tablet formulations (Lab Scale)

Mebendazol Tablets (100 mg)

1. Formulation

Mebendazol .....100 g
Ludipress [1] .....196 g
Magnesium stearate [2] .....4 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....294 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....73 N
Disintegration .....2 min
Friability.....0.5 %

5.8 Liquid Formulations (Lab scale)

Mebendazole Suspension (2 % = 200 mg/10 ml)

1. Formulation

Mebendazole	2 g
Lutrol F 127 [1]	3 g
Methylparaben	0.18 g
Propylparaben	0.02 g
Water	ad 100 g

2. Manufacturing

Dissolve the parabens in water at 80 °C. After cooling to room temperature add Lutrol F 127 whilst stirring. When the Lutrol F 127 is completely dissolved suspend Mebendazole in the solution.

3. Properties of the suspension

After one day of storage at room temperature no sedimentation could be observed.

After some weeks of storage at room temperature some sedimentation occurred but the redispersibility was very easy.

2.9 Tablet formulations (Lab Scale)

Mefenamic Acid Tablets (250 mg)

1. Formulation

I.	Mefenamic acid	250 g
	Corn starch [3]	40 g
II.	Kollidon 90 F [1]	5 g
	Isopropanol	q.s.
III.	Kollidon CL [1]	12 g
	Avicel PH 101 [5]	85 g
	Magnesium stearate [2]	5 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, sieve, dry, add mixture III and press with medium compression force.

3. Tablet properties

Weight	404 mg
Diameter	12 mm
Form	biplanar
Hardness	70 N
Disintegration	2 min
Friability	0.8 %

2.9 Tablet formulations (Lab Scale)

Meprobamate + Phenobarbital Tablets (400 mg + 30 mg), DC

1. Formulation

Meprobamate	400 g
Phenobarbital	30 g
Avicel PH 101 [5]	76 g
Kollidon VA 64 [1]	13 g
Kollidon CL [1]	21 g
Talc [10]	8 g
Aerosil 200 [4]	1 g
Calcium arachinate [2]	1 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight	551 mg
Diameter	12 mm
Form	biplanar
Hardness	87 N
Disintegration	< 1 min
Friability	0.9 %

2.9 Tablet formulations (Lab Scale)

Meprobamate + Phenobarbital Tablets (400 mg + 30 mg), WG

1. Formulation

I.	Meprobamate	400 g
	Phenobarbital	30 g
II.	Kollidon VA 64 [1]	13 g
	Isopropanol	q.s.
III.	Kollidon CL [1]	21 g
	Corn starch [3]	50 g
	Avicel PH 101 [5]	60 g
	Talc [10]	8 g
	Aerosil 200 [4]	1 g
	Calcium arachinate [2]	1 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with low compression force.

3. Tablet properties

Weight	559 mg
Diameter	12 mm
Form	biplanar
Hardness	131 N
Disintegration	< 1 min
Friability	0.4 %

2.9 Tablet formulations (Lab Scale)

Meprobamate Tablets (400 mg), DC

1. Formulation

Meprobamate	400 g
Avicel PH 101 [5]	80 g
Corn starch [3]	30 g
Kollidon VA 64 [1]	20 g
Kollidon CL [1]	20 g
Talc [10]	7 g
Magnesium stearate [2]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force (20 KN).

3. Tablet properties

Weight	560 mg
Diameter	12 mm
Form	biplanar
Hardness	90 N
Disintegration	< 10 min
Friability	0.6 %

Meprobamate Tablets (400 mg), WG

1. Formulations

		No. 1	No. 2
I.	Meprobamate	400.0 g	400.0 g
	Corn starch [3]	100.0 g	100.0 g
II.	Kollidon 25 [1]	15.0 g	–
	Kollidon VA 64 [1]	–	15.0 g
	Lutrol E 400 [1]	4.5 g	–
	Isopropanol	q.s.	q.s.
III.	Talc [10]	2.0 g	2.0 g
	Aerosil 200 [4]	0.2 g	0.2 g
	Calcium arachinate [2]	0.3 g	0.3 g

2. Manufacturing (Wet granulation)

Granulate the mixture I with solution II, pass through a 0.8 mm sieve, add III and press.

3. Tablet properties

	No. 1	No. 2
Weight	520 mg	500 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	95 N	88 N
Disintegration	5 min	3 – 4 min
Friability	0.5 %	< 0.1 %

2.9 Tablet formulations (Lab Scale)

Metamizol Tablets (500 mg)

1. Formulations

	No. 1	No. 2
Metamizol sodium (= Dipyrone)	500 g	500 g
Ludipress [1]	100 g	–
Avicel PH 101 [5]	–	100 g
Kollidon 30 [1]	–	15 g
Kollidon CL [1]	10 g	25 g
Magnesium stearate [2]	10 g	–
Aerosil 200 [4]	5 g	1 g
Talc [10]	–	8 g
Calcium arachinate [2]	–	1 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.5 mm sieve and press with low compression force.

3. Tablet properties

	No. 1	No. 2
Weight	625 mg	654 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	120 N	62 N
Disintegration	5 min	2 min
Friability	0.3%	1%

2.9 Tablet formulations (Lab Scale)

Metformin Tablets (500 mg)

1. Formulation

I.	Metformin hydrochloride	500 g
	Dicalcium phosphate [9]	100 g
	Kollidon 90 F [1]	15 g
II.	Kollidon 90 F [1]	8 g
	Isopropanol	90 g
III.	Kollidon CL [1]	5 g
	Polyethylene glycol 6000, powder [6]	15 g

2. Manufacturing (Wet granulation)

Granulate the mixture I with solution II, mix with III, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight	650 mg
Diameter	12 mm
Form	biplanar
Hardness	> 200 N
Disintegration	6 min
Friability	0.3 %

4. Remark

Due to the high hardness the amount of Kollidon 90 F could be reduced.

2.9 Tablet formulations (Lab Scale)

Methyl Cysteine Tablets (100 mg)

1. Formulation

Methyl cysteine hydrochloride .....100 g
Ludipress [1] .....200 g
Magnesium stearate [2].....3 mg
Menthol .....4 mg

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....307 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....55 N
Disintegration.....2 – 3 min
Friability.....0.3 %

4. Physical stability (12 months, 20–25 ºC)

Weight .....307 mg
Hardness.....85 N
Disintegration.....2 – 3 min
Friability.....0.2 %

6.7 Formulations of semi-solid drugs (Lab scale)

Methyl Salicylate + Menthol Gel (11 % + 5 %)

1. Formulation

I.	Methyl salicylate	11 g
	Menthol	5 g
	Lutrol E 400 [1]	20 g
	Cremophor RH 40 [1]	6 g
	Propylene glycol Pharma [1]	7 g
II.	Lutrol F 127 [1]	32 g
III.	Water	19 g

2. Manufacturing

Dissolve II in solution I and mix with III. The clear gel can be diluted with water.

3. Properties of the gel

Due to the high concentration of the active ingredients and of Lutrol F 127 the consistency of the colourless clear gel is extremely hard.

4. Remark

Reducing the concentration of the active ingredients the amount of Lutrol F 127 could be reduced too and the consistency of the gel will be normal.

2.9 Tablet formulations (Lab Scale)

Metoclopramide Tablets (10 mg)

1. Formulation

Metoclopramide hydrochloride .....10.0 g
Ludipress [1] .....89.5 g
Magnesium stearate [2].....0.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight .....100 mg
Diameter .....6 mm
Form .....biplanar
Hardness.....35 N
Disintegration (gastric juice).....3 min
Friability.....0.1%
Dissolution (15 min) 100%

4. Physical stability (18 months, 20–25 ºC)

Weight .....100 mg
Hardness.....35 N
Disintegration (gastric juice).....3 min
Friability.....0.1%
Dissolution (15 min) 100%

2.9 Tablet formulations (Lab Scale)

Metronidazole Effervescent Vaginal Tablets (500 mg)

1. Formulation

I.	Metronidazole	500 g
	Sodium bicarbonate	600 g
	Kollidon 30 [1]	30 g
II.	Kollidon 30 [1]	10 g
	Isopropanol	150 ml
III.	Tartaric acid, crystalline	500 g
	Polyethylene glycol 6000, powder [6]	50 g

2. Manufacturing (Wet granulation)

Granulate I with solution II, pass through a 0.8 mm sieve, mix with III and press.

3. Tablet properties

Weight	1700 mg
Diameter	16 mm
Form	biplanar
Hardness	113 N
Disintegration	4 min
Friability	1.8 %

5.8 Liquid Formulations (Lab scale)

Metronidazol Injectable Solution (500 mg/10 ml)

1. Formulation

I.	Metronidazol	5.0 g
II.	Kollidon 12 PF [1]	25.0 g
	Propylene glycol Pharma [1]	25.0 g
	Lutrol E 400 [1]	25.0 g
	Water for injectables	20.0 g
III.	Hydrochloric acid 0.1 N	q.s.

2. Manufacturing

Suspend I in the solution II, adjust pH 4.4 with III and heat until metronidazol is dissolved.

3. Properties of the solution

A clear solution was obtained. It can be diluted with water without precipitation.

4. Remark

To prevent of discolouration of Kollidon in the solution during storage 0.2 to 0.5% of cysteine could be added as antioxidant.

2.9 Tablet formulations (Lab Scale)

Metronidazole Tablet Cores (400 mg)

1. Formulation

Metronidazole .....400 g
Avicel PH 102 [5] .....150 g
Kollidon VA 64 [1].....25 g
Kollidon CL [1].....15 g
Aerosil 200 [4].....5 g
Polyethylene glycol 6000, powder [6].....50 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force (25 – 30 kN).

3. Tablet properties

Weight .....645 mg
Diameter .....12 mm
Form .....biconvex
Hardness.....87 N
Disintegration.....1 – 2 min
Friability .....< 0.1%

2.9 Tablet formulations (Lab Scale)

Metronidazole Tablets (200 mg)

1. Formulation

Metronidazole	200 g
Avicel PH 101 [5]	200 g
Kollidon 30 [1]	6 g
Kollidon CL [1]	10 g
Aerosil 200 [4]	5 g
Magnesium stearate [2]	5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force (25 – 30 kN).

3. Tablet properties

Weight	426 mg
Diameter	12 mm
Form	biplanar
Hardness	133 N
Disintegration	1 – 2 min
Friability	< 0.1%

Metronidazole Tablets (500 mg)

1. Formulation

I.	Metronidazole	500 mg
	Sorbitol, crystalline [10]	220 mg
II.	Kollidon 90 F [1]	10 mg
	Ethanol 96 %	ca. 75 mg
III.	Kollidon CL [1]	20 mg
	Talc [10]	4 mg
	Aerosil 200 [4]	0.5 mg
	Calcium arachinate [2]	0.5 mg

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, dry, mix with III and press with medium compression force.

3. Tablet properties

Weight	755 mg
Diameter	16 mm
Form	biplanar
Hardness	178 N
Disintegration	6 min
Friability	0.6 %

6.7 Formulations of semi-solid drugs (Lab scale)

Metronidazol Vaginal Gel (1.2 %)

1. Formulation

I.	Metronidazol	1.2 g
	Lutrol F 127 [1]	21.0 g
	Lutrol E 400 [1]	40.0 g
II.	Water	37.8 g

2. Manufacturing

Heat mixture I to 70 – 80 °C and slowly add the water heated to about 70 °C. Maintain the temperature until the air bubbles disappeared.

3. Properties of the gel

A clear colourless gel was obtained.

Miconazole Cream (2 %)

1. Formulation

I.	Cetylstearyl alcohol	7.0 g
	Cremophor A 6 [1]	1.5 g
	Cremophor A 25 [1]	1.5 g
	Liquid paraffin	12.0 g
	Parabene(s)	0.1 g
II.	Water	67.8 g
III.	Propylene glycol [1]	8.0 g
	Micronazole nitrate	2.0 g

2. Manufacturing

Heat the mixture I and the water II separately to about 80 °C. Add the water II to the obtained solution I with rigorous stirring. Heat III until the active ingredient is dissolved, mix with I/II and continue to stir during cooling to room temperature.

3. Properties

White cream.

4. Physical stability

No change of appearance or crystallization were observed during 6 weeks at 45 °C.

5. Remark

This formulation could be used for other active ingredients too.

5.8 Liquid Formulations (Lab scale)

Miconazole Injectable Solution (1%)

1. Formulation

I.	Miconazole	1.0 g
	Cremophor EL [1]	12.0 g
II.	Parabenes	q.s.
	Water for injectables	ad 100 ml

2. Manufacturing

Heat mixture I to about 65 °C, stir well and add slowly the hot solution II.

After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occurred. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the solution

Clear colourless liquid having a low viscosity.

4. Remark

In Germany Cremophor EL must be declared on the labels of the injectables.

6.7 Formulations of semi-solid drugs (Lab scale)

Miconazole Mouth Gel (2 %)

1. Formulation

I.	Miconazole nitrate (Sigma)	2.0 g
	Orange flavour	0.1 g
II.	Lutrol F 127 [1]	20.0 g
	Cremophor RH 40 [1]	10.0 g
	Propylene glycol Pharma [1]	10.0 g
III.	Kollidon 90 F [1]	5.0 g
	Saccharine sodium	0.3 g
	Water	52.6 g

2. Manufacturing

Dissolve I in the molten mixture II. Heat solution III to 90 °C and mix slowly with I/II. Let cool to room temperature when the air bubbles escaped.

3. Properties of the gel

A colourless, clear and soft gel was obtained having a orange like taste and a slightly bitter after taste.

5.8 Liquid Formulations (Lab scale)

Mint Mouth Wash Solutions

1. Formulations

		No. 1	No. 2
I.	Mint oil	2.0 g	–
	Menthol	0.04 g	1.0 g
	Eucalyptus oil	0.09 g	1.0 g
	alpha-Bisabolol (BASF)	–	1.0 g
	Thymian oil	0.06 g	–
	Cremophor RH 40 [1]	4.0 g	4.0 g
II.	Saccharin sodium	0.45 g	0.45 g
	Sodium citrate	0.20 g	0.20 g
	Citric acid	0.50 g	0.50 g
	Sodium fluoride	–	0.02 g
	Glycerol	–	5.0 g
	Lutrol F 127 [1]	5.0 g	5.0 g
	Salicylic acid	0.06 g	–
	Benzoic acid	0.10 g	–
	Sorbitol, crystalline [10]	17.5 g	–
	Ethanol 96 %	21.6 g	6.7 g
	Sicovit colorant [1]	q. s.	q. s.
	Water	48.4 g	80.1 g

2. Manufacturing

Mix the components I and heat to about 60 °C. Prepare solution II, heat to about 60 °C and add it slowly to the well stirred mixture I.

3. Properties of the solutions

Clear, coloured liquids having a fresh mint taste.

5.8 Liquid Formulations (Lab scale)

Mint Oil Solution (3.5 %)

1. Formulation

Peppermint oil	3.5 g
Cremophor RH 40 [1]	13.8 g
Ethanol 96 %	52.0 g
Water	30.7 g

2. Manufacturing

Mix the peppermint oil with Cremophor RH 40, stir well and add slowly ethanol and water.

3. Properties of solution

Clear, colourless liquid of low viscosity.

2.9 Tablet formulations (Lab Scale)

Multivitamin + Calcium + Iron Tablets (1 RDA of Vitamins)

1. Formulation

Vitamin A acetate dry powder 500,000 i. u./g (BASF)	5.0 g
Vitamin D dry powder 100,000 i. u./g (BASF)	2.0 g
Thiamine mononitrate (BASF)	1.2 g
Riboflavin (BASF)	1.8 g
Nicotinamide	12.0 g
Vitamin E acetate dry powder SD 50 (BASF)	4.0 g
Ascorbic acid, powder (BASF)	50.0 g
Ferrous fumarate	60.0 g
Dibasic calcium phosphate [9], granulated with 5% Kollidon 30 [1]	200.0 g
Calcium carbonate	125.0 g
Avicel PH 101 [5]	45.0 g
Aerosil 200 [4]	1.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press to tablets.

3. Tablet properties

Weight	500 mg
Diameter	11 mm
Form	biplanar
Hardness	75 N
Disintegration (water)	2 – 3 min
Friability	0.3%

5.8 Liquid Formulations (Lab scale)

Multivitamin + Calcium Syrup (1 RDA of Vitamins/20 ml)

1. Formulation

I.	Vitamin A palmitate 1.7 Mio. i. u./g (BASF)	10.0 mg
	Vitamin D 40 Mio. i.u./g	0.05 mg
	Vitamin E acetate (BASF)	100.0 mg
	Butylhydroxytoluene	2.0 mg
	Cremophor RH 40 [1]	4.5 g
II.	Water	10.0 g
III.	Saccharose	45.0 g
	Methyl parabene	200.0 mg
	Citric acid	80.0 mg
IV.	Glycerol	9.6 g
	Calcium gluconate	70 mg
	Water	25.0 g
V.	Thiamine hydrochloride (BASF)	15.0 mg
	Riboflavin 5'-phosphate sodium	15.0 mg
	Nicotinamide	55.0 mg
	Pyridoxine hydrochloride (BASF)	15.0 mg
	Ascorbic acid, crystalline (BASF)	300.0 mg
	Sorbic acid	100.0 mg
	Propylene glycol Pharma [1]	5.0 g
	Total amount	100 g

2. Manufacturing

Heat I and II separately to about 60 °C and mix slowly well stirring to obtain a clear solution. Dissolve III in the hot solution IV to obtain a clear solution. Mix the cool solutions I/II, III/IV and V and adjust the pH value to 4.0 – 4.1. Pass during 10 min nitrogen through the solution and fill in flasks under nitrogen.

3. Chemical stability (20–25 °C; HPLC methods)

The following stability data were obtained with the same syrup but without calcium gluconate:

	(9 months)	(12 months)
Vitamin A	86 %	73 %
Vitamin B_1	88 %	83 %
Vitamin B_2	96 %	92 %
Vitamin C	78 %	77 %

2.9 Tablet formulations (Lab Scale)

Multivitamin + Carbonyl Iron Tablets (1 – 2 RDA of Vitamins)

1. Formulation

Vitamin A acetate dry powder 500,000 i. u./g (BASF)	10.0 g
Thiamine mononitrate (BASF)	2.2 g
Riboflavin (BASF)	2.2 g
Nicotinamide	16.5 g
Calcium D-pantothenate (BASF)	11.5 g
Pyridoxine hydrochloride (BASF)	2.2 g
Cyanocobalamin, dry powder 0.1%	6.0 g
Ascorbic acid, powder (BASF)	85.0 g
Vitamin E acetate dry powder SD 50 (BASF)	31.0 g
Ludipress [1]	311.0 g
Carbonyl iron powder OF (BASF)	10.0 g
Magnesium stearate [2]	3.0 g
Orange flavour	7.2 g
Saccharin sodium	2.5 g

2. Manufacturing (Direct compression)

Mix all ingredients, pass through a 0.8 mm sieve, mix and press with high compression force (20 kN).

3. Tablet properties

Weight	500 mg
Diameter	12 mm
Form	biplanar
Hardness	69 N
Disintegration	12 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Multivitamin + Minerals Tablets with Beta Carotene (2 RDA of Vitamins)

1. Formulation

	No. 1	No. 2
Beta carotene dry powder 10%	150.0 g	50.0 g
Thiamine mononitrate (BASF)	2.5 g	3.0 g
Riboflavin (BASF)	2.9 g	3.0 g
Pyridoxine hydrochloride (BASF)	2.0 g	3.0 g
Nicotinamide	22.0 g	22.0 g
Calcium D-pantothenate (BASF)	12.0 g	12.0 g
Ascorbic acid for direct compression (Roche)	110.0 g	100.0 g
Calcium phosphate, dibasic [9]	550.0 g	550.0 g
Ferrous fumarate	82.0 g	80.0 g
Magnesium oxide	166.0 g	160.0 g
Cupric sulfate	2.5 g	2.0 g
Manganese sulfate	13.8 g	14.0 g
Potassium chloride	57.2 g	50.0 g
Zinc sulfate	37.0 g	37.0 g
Avicel PH 102 [5]	57.0 g	60.0 g
Kollidon CL [1]	50.0 g	50.0 g
Stearic acid [7]	5.7 g	6.0 g
Magnesium stearate [2]	5.0 g	5.0 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	1300 mg	1205 mg
Diameter	16 mm	16 mm
Form	biplanar	biplanar
Hardness	94 N	88 N
Disintegration (water)	< 1 min	< 1 min
Friability	1%	< 0.1%

4. Chemical stability of formulation No. 2 (20–25°C)

Storage time	Beta Carotene	B_1	B_2	B_5	B_6	C
6 Months	100%	98%	98%	100%	97%	95%
12 Months	92%	96%	92%	99%	96%	94%

5. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Multivitamin Chewable Tablets for Children

1. Formulation

Vitamin A acetate dry powder 500,000 i. u./g (BASF)	7.0 g
Thiamine mononitrate (BASF)	1.2 g
Riboflavin (BASF)	1.2 g
Nicotinamide	20.0 g
Pyridoxine hydrochloride (BASF)	1.8 g
Cyanocobalamin 0.1% dry powder (BASF)	6.5 g
Ascorbic acid, powder (BASF)	60.0 g
Vitamin D_3 acetate dry powder 100,000 i. u./g (BASF)	5.0 g
Vitamin E acetate dry powder SD 50 (BASF)	31.0 g
Sorbitol, crystalline [10]	200.0 g
Sucrose, crystalline	200.0 g
Kollidon VA 64 [1]	20.0 g
Aerosil 200 [4]	1.0 g
Orange flavour, dry powder	30.0 g
Raspberry flavour, dry powde	6.0 g
Passion fruit flavour, dry powder	3.0 g
Cyclamate sodium	2.0 g

2. Manufacturing (Direct compression)

Mix all ingredients, pass through a 0.8 mm sieve and press with medium to high compression force (20 kN).

3. Tablet properties

Weight	575 mg
Diameter	12 mm
Form	biplanar
Hardness	100 N
Disintegration	7 min
Friability	0.2 %

5.8 Liquid Formulations (Lab scale)

Multivitamin Drops

1. Formulation

I.	Vitamin A palmitate 1.7 Mio. i. u./g (BASF)	0.8 g
	Vitamin D_3 40 Mio. i. u./g	0.013 g
	Vitamin E acetate (BASF)	0.5 g
	Cremophor EL (or Cremophor RH 40) [1]	15.0 g
II.	Parabenes	0.2 g
	Water	52.5 g
III.	Thiamine hydrochloride (BASF)	0.4 g
	Riboflavin 5-phosphate sodium	0.2 g
	Pyridoxine hydrochloride (BASF)	0.2 g
	Nicotinamide	0.2 g
	Sodium bisulfite	0.02 g
	Propylene glycol Pharma [1]	20.0 g
	Water	10.0 g
IV.	Hydrochloric acid	q.s.
	Total amount	100 g

2. Manufacturing

Heat mixture I to about 60 °C, stir strongly and add slowly solution II (60 °C). To the obtained clear solution add solution III. Adjust the pH with IV to about 4.

3. Properties

Clear or slightly opalescent yellow liquid of low viscosity and pH 4.

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Multivitamin Effervescent Granules (1 RDA of Vitamins)

1. Formulation

I.	Thiamin hydrochloride (BASF)	0.26 g
	Riboflavin (BASF)	0.30 g
	Nicotinamide	1.10 g
	Pyridoxine hydrochloride (BASF)	0.25 g
	Calcium D-pantothenate (BASF)	1.50 g
	Ascorbic acid, powder (BASF)	20.00 g
	Citric acid	50.00 g
	Sucrose	130.00 g
	Fructose	80.00 g
	Kollidon CL-M [1]	20.00 g
	Flavours	25.00 g
	Cyclamate sodium	2.00 g
	Saccharine sodium	0.10 g
II.	Kollidon VA 64 [1]	15.00 g
	Isopropanol	35.00 g
III.	Vitamin A acetate dry powder 325,000 I.U./g CWD (BASF)	1.50 g
	Vitamin D_3 dry powder 100,000 I.U./g CWD (BASF)	0.80 g
	Vitamin E acetate dry powder 50%	2.10 g
	Cyanocobalamin gelatin coated 0.1% (BASF)	0.66 g
	Sodium bicarbonate	40.00 g

2. Manufacturing

Granulate mixture I with solution II, pass through a 0.8 mm sieve, dry well and mix with III.
Fill 3 – 4 g in sachets.

3. Properties of the granules

Colour:	Yellow granules
Flowability:	Very good
Dispersibility:	4 g disperse homogeneously in water after about 40 seconds.

4. Administration

3 – 4 g of the granules (= 1 sachet) correspond to about 1 RDA of the vitamins

2.9 Tablet formulations (Lab Scale)

Multivitamin Effervescent Tablets with Beta Carotene, Food (1 – 2 RDA of Vitamins)

1. Formulation

I.	Thiamine mononitrate (BASF)	2 g
	Riboflavin (BASF)	2 g
	Pyridoxine hydrochloride (BASF)	2 g
	Nicotinamide	22 g
	Calcium D-pantothenate (BASF)	11 g
	Tartaric acid powder	400 g
	Lactose monohydrate [8]	300 g
	Corn starch [3]	100 g
II.	Corn starch [3]	3 g
	Water	50 g
III.	Beta carotene dry powder 10% CWD Food grade (BASF)	23 g
	Cyanocobalamin, powder 0.1% (BASF)	6 g
	Ascorbic acid, powder (BASF)	85 g
	Vitamin E acetate dry powder 50%	40 g
	Sodium bicarbonate	600 g
	Flavours	80 g
	Saccharin sodium	q.s.

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II prepared at 70 °C, dry and sieve, add III, pass through a 0.4 mm sieve and press with high compression force at maximum 30% of relative atmospheric humidity.

3. Tablet properties

Weight	1630 mg
Diameter	16 mm
Form	biplanar
Hardness	107 N
Disintegration (water)	1 min
Friability	0.9%

4. Remark

All components of this formulation are allowed in Europe for food application.

2.9 Tablet formulations (Lab Scale)

Multivitamin Effervescent Tablets I

1. Formulation

I.	Thiamine mononitrate (BASF)	13 mg
	Riboflavin (BASF)	4 mg
	Pyridoxine hydrochloride (BASF)	11 mg
	Nicotinamide	66 mg
	Calcium D-pantothenate (BASF)	17 mg
	Tartaric acid, powder	360 mg
	Sodium bicarbonate	550 mg
	Sucrose, crystalline	300 mg
	Sucrose, powder	300 mg
	Kollidon 30 [1]	35 mg
II.	Kollidon 30 [1]	5 mg
	Isopropanol	about 80 mg
III.	Riboflavin (BASF)	6 mg
	Ascorbic acid, powder (BASF)	550 mg
	Cyanocobalamin 0.1% dry powder	20 mg
	Vitamin A palmitate 250000 i.u./g dry powder CWD (BASF)	12 mg
	Vitamin E acetate dry powder 50%	60 mg
	Polyethylene glycol 6000, powder [6]	80 mg
	Kollidon CL [1]	100 mg

2. Manufacturing (Wet granulation)

Granulate the mixture I with solution II, dry at 60 ºC with vacuum, mix with III and press with high compression force at maximum 30% of relative atmospheric humidity.

3. Tablet properties

Weight	2500 mg
Diameter	20 mm
Form	biplanar
Hardness	140 N

Disintegration (water).....1 – 2 min
Friability.....1%

4. Chemical and physical stability (20–25 ºC)

	6 Months	**12 Months**
Ascorbic acid	100 %	92 %
Cyanocobalamin	91%	92 %
Vitamin A	80 %	69 %
All other vitamins	> 94 %	> 94 %
Hardness	140 N	

2.9 Tablet formulations (Lab Scale)

Multivitamin Effervescent Tablets II (3 – 4 RDA of Vitamins)

1. Formulations

	No. 1	No. 2
Thiamine mononitrate (BASF)	5.5 g	5.5 g
Ribolfavin (BASF)	5.5 g	5.5 g
Pyridoxine hydrochloride (BASF)	6.5 g	6.5 g
Nicotinamide	60.0 g	60.0 g
Calcium D-pantothenate (BASF)	30.0 g	30.0 g
Ascorbic acid, powder (BASF)	200.0 g	200.0 g
Cyanocobalamin 0.1% dry powder	20.0 g	20.0 g
Vitamin A palmitate dry powder 325000 i.u./g CWD (BASF)	30.0 g	30.0 g
Vitamin E acetate dry powder 50%	110.0 g	50.0 g
Citric acid, powder	–	500.0 g
Tartaric acid, powder	400.0 g	–
Sodium bicarbonate	500.0 g	500.0 g
Ludipress [1]	600.0 g	500.0 g
Polyethylene glycol 6000, powder [6]	70.0 g	70.0 g
Saccharin sodium	0.5 g	0.5 g
Cyclamate sodium	40.0 g	40.0 g
Sucrose, crystalline	200.0 g	200.0 g
Fructose	200.0 g	200.0 g
Flavours (Firmenich)	100.0 g	100.0 g

2. Manufacturing (Direct compression)

Mix all components, sieve through a 0.8 mm screen and press with high compression force at maximum 30% relative atmospheric humidity.

3. Tablet properties

	No. 1	No. 2
Weight	2200 mg	2495mg
Diameter	20 mm	20 mm
Form	biplanar	biplanar
Hardness	98 N	197 N
Disintegration (water)	1 – 2 min	2 min
Friability	1.0 %	0.4 %

4. Chemical stability of formulation No. 1 (after 12 months at 20–25 ºC; HPLC)

Vitamin B_1	93 %
Vitamin B_6	89 %
Vitamin B_{12}	88 %
Vitamin A	79 %
All other vitamins	> 95 %

5.8 Liquid Formulations (Lab scale)

Multivitamin Injectable for Veterinary Application

1. Formulations

		No. 1 Emulsion	No. 2 Solution
I.	Vitamin A propionate 2.5 Mio. i. u./g (BASF)	4.5 g	4.5 g
	Vitamin D_3 (Cholecaciferol) 40 Mio. i. u./g	27 mg	27 mg
	Vitamin E acetate (BASF)	2.1 g	2.1 g
	Butylhydroxytoluene	0.5 g	0.5 g
	Benzyl alcohol	1.0 g	1.0 g
	Solutol HS 15 [1]	6.0 g	22.0 g
II.	Preservative	q.s.	q.s.
	Water for injectables	ad 90 ml	ad 90 ml
III.	Nicotinamide	1.1 g	1.1 g
	Thiamine hydrochloride	0.6 g	0.6 g
	Riboflavin phosphate sodium	0.1 g	0.1 g
	Pyridoxine hydrochloride	0.5 g	0.5 g
	Dexpanthenol	0.6 g	0.6 g
	EDTA sodium	10 mg	10 mg
	Water	ad 10 ml	ad 10 ml
	Total amount	100 ml	100 ml

2. Manufacturing

Heat mixture I to about 65 °C, stir well and add very slowly the hot solution II. Prepare solution III and add to the cool mixture I/II.

3. Properties

Emulsion (formulation No. 1)
A yellow milky emulsion was obtained having a viscosity below 5 mPa · s and a pH of 4.1.

Solution (formulation No. 2)
A clear yellow solution was obtained having a viscosity of about 7 mPa · s and a pH of 4.5.

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Multivitamin Instant Granules (2 – 4 RDA of Vitamins)

1. Formulation

I. Vitamin A+D dry powder 250,000
+ 50,000 I.U./g CWD (BASF) ..... 200 g
Thiamine mononitrate (BASF) ..... 26 g
Riboflavin (BASF) ..... 33 g
Nicotinamide ..... 110 g
Pyridoxine hydrochloride (BASF) ..... 22 g
Calcium D-pantothenate (BASF) ..... 150 g
Cyanocobalamin 0.1% ..... 66 g
gelatin coated (BASF)
Ascorbic acid powder (BASF) ..... 1,150 g
Vitamin E acetate dry powder ..... 210 g
SD 50 (BASF)
Sucrose, finely ground ..... 20,000 g
Kollidon CL-M [1] ..... 5,000 g
Orange flavour ..... 1,000 g

II. Kollidon VA 64 [1] ..... 2,000 g
Ethanol or Isopropanol ..... approx. 7 l

2. Manufacturing

Pass mixture through a 0.8 mm sieve and granulate with solution II in the fluidized bed. Fill 6 – 12 g of the granules in sachets.

If the technology of a fluidized bed is not available, the dry powders of vitamin A, E and B_{12} should be added after the granulation of the other components.

3. Administration

Suspend 6 – 12 g (= 1 sachet) in a glass of water corresponding to 2 – 4 RDA of vitamins.

4. Properties of the suspension

The multivitamin suspension is prepared prior to application by shaking the granules with water. The uniform, yellow suspension thus obtained shows no sedimentation over a period of some hours. The redispersibility is very easy.

5. Stability (after 12 months, 20–25 °C, HPLC)

Vitamin C.....91%
Calcium pantothenate .....not tested
All other vitamins.....> 95 %

6.7 Formulations of semi-solid drugs (Lab scale)

Multivitamin Oral Gel (vet.)

1. Formulation

I.	Vitamin A palmitate 1.7 Mio. i.u./g (BASF)	110 mg
	Vitamin E acetate (BASF)	1,060 mg
	Butylhydroxytoluene	500 mg
	Cremophor RH 40 [1]	20 g
II.	Water	725 g
III.	Thiamine hydrochloride (BASF)	355 mg
	Riboflavin (BASF)	35 mg
	Pyridoxin hydrochloride (BASF)	177 mg
	Cyanocobalamin gelatin coated 1% (BASF)	35 mg
	Nicotinamide	353 mg
	Folic acid	35 mg
	Dexpanthenol (BASF)	353 mg
	EDTA sodium	300 mg
	Ferrous sulfate (7 H_2O)	438 mg
	Manganese chloride (4 H_2O)	638 mg
	Potassium iodide	115 mg
IV.	Kollidon 90 F [1]	50 g
	Lutrol F 127 [1]	100 g
V	Lutrol F 127 [1]	100 g
	Total amount:	about 1000 g

2. Manufacturing

Heat mixture I to about 60 °C to obtain a clear solution, add slowly the water II to the well stirred solution I, dissolve III and IV in this mixed solution at room temperature, cool to about 6 °C, add V and stirr until all Lutrol F 127 is dissolved. Maintain the cool temperature until the air bubbles escaped.

3. Properties of the gel

Colour .....yellow-orange
Clarity .....opalescent
pH-value.....4.3
Consistency.....semi-solid

6.7 Formulations of semi-solid drugs (Lab scale)

Multivitamin Oral Gel with Linoleic Acid and Linolenic Acid

1. Formulation

I.	Evening Primrose Oil (Epopure®, Prima Rosa/SA)	5.0 ml
	Vitamin A palmitate 1.7 Mio. i.u./g (BASF)	30 mg
	Vitamin E acetate (BASF)	19 mg
	Vitamin D_3 40 Mio i.u./g	150 µg
	Cremophor RH 40 [1]	20.0 g
II.	Water	55.0 g
III.	Thiamine hydrochloride (BASF)	3 mg
	Riboflavin (BASF)	3 mg
	Pyridoxin hydrochloride (BASF)	15 mg
	Cyanocobalamin, crystalline	10 µg
	Calcium D-pantothenate (BASF)	10 mg
	Nicotinamide	50 mg
	Ascorbic acid, crystalline (BASF)	1.0 g
	Lutrol F 127 [1]	14.0 g
IV.	Lutrol F 127 [1]	5.0 g
	Total amount:	about 100 g

2. Manufacturing

Prepare mixture I and heat to about 65 °C. Add the warm water II (65 °C) slowly to the well stirred mixture I. Dissolve at 20 – 25 °C the components III in this clear solution I/II. Cool the obtained solution to about 5 °C and dissolve the rest of Lutrol F 127 (= IV). Maintain the cool temperature until the air bubbles escaped.

3. Properties

A clear yellow gel was obtained.

4. Remark

5 ml of Evening Primrose Oil Epopure contains 3.5 g linoleic acid and 0.45 g gamma-linolenic acid.

5.8 Liquid Formulations (Lab scale)

Multivitamin Syrup, I (1 – 2 RDA/20 ml)

1. Formulation

I.	Vitamin A palmitate 1.7 Mio. i. u./g (BASF)	10.0 mg
	Vitamin D 40 Mio. i.u./g	0.05 mg
	Vitamin E acetate (BASF)	100.0 mg
	Butylhydroxytoluene	2.0 mg
	Cremophor RH 40 [1]	4.5 g
II.	Water	10.0 g
III.	Saccharose	45.0 g
	Methyl parabene	200.0 mg
	Citric acid	80.0 mg
IV.	Glycerol	9.6 g
	Water	25.0 g
V.	Thiamine hydrochloride (BASF)	15.0 mg
	Riboflavin 5'-phosphate sodium	15.0 mg
	Nicotinamide	55.0 mg
	Pyridoxine hydrochloride (BASF)	15.0 mg
	Ascorbic acid, crystalline (BASF)	300.0 mg
	Sorbic acid	100.0 mg
	Propylene glycol Pharma [1]	5.0 g
	Total amount	100 g

2. Manufacturing

Heat I and II separately to about 60 °C and mix slowly well stirring to obtain a clear solution. Dissolve III in the hot solution IV to obtain a clear solution. Mix the cool solutions I/II, III/IV and V and adjust the pH value to 4.0 – 4.2. Pass during 10 min nitrogen through the solution and fill in flasks under nitrogen.

3. Chemical stability (20–25 °C; HPLC methods)

	(9 months)	(12 months)
Vitamin A	86 %	73 %
Vitamin B_1	88 %	83 %
Vitamin B_2	96 %	92 %
Vitamin C	78 %	77 %

5.8 Liquid Formulations (Lab scale)

Multivitamin Syrup, II

1. Formulation

I.	Vitamin A palmitate	17.0 mg
	1.7 Mio i.u./g (BASF)	
	Vitamin D_3 40 Mio i. u./g	0.1 mg
	Butylhydroxytoluene	1.0 mg
	Cremophor RH 40 [1]	3.00 g
II.	Parabenes	0.10 g
	Water	17.00 g
III.	Thiamine hydrochloride (BASF)	0.05 g
	Riboflavin phosphate sodium	0.02 g
	Pyridoxine hydrochloride (BASF)	0.02 g
	Ascorbic acid, crystalline (BASF)	0.25 g
	Water	5 g
IV.	Sugar syrup USP	ad 100 ml

2. Manufacturing

Heat mixture I to about 65 °C, stir well and add very slowly the warm solution II (65 °C). Mix with solution III and add the syrup IV.

3. Properties of the syrup

Clear, yellow viscous liquid.

4. Physical stability (20–25 °C protected from light)

No change of the appearance after 3 months.

2.9 Tablet formulations (Lab Scale)

Multivitamin Tablets I (1 – 2 RDA of Vitamins)

1. Formulation

	No. 1	No. 2
Vitamin A acetate dry powder 500,000 i. u./g (BASF)	10.0 g	10.0 g
Thiamine mononitrate (BASF)	2.2 g	2.2 g
Ribolfavin (BASF)	2.2 g	2.2 g
Nicotinamide	16.5 g	16.5 g
Calcium D-pantothenate (BASF)	11.5 g	11.5 g
Pyridoxine hydrochloride (BASF)	2.2 g	2.2 g
Cyanocobalamin 0.1% dry powder	6.0 g	6.0 g
Ascorbic acid, powder (BASF)	85.0 g	85.0 g
Vitamin E acetate dry powder SD 50 (BASF)	31.0 g	31.0 g
Ludipress [1]	321.0 g	–
Microcrystalline cellulose, Vitacel® (Rettenmaier)	–	300.0 g
Kollidon VA 64 [1]	–	21.0 g
Magnesium stearate [2]	3.0 g	3.0 g
Orange flavour	7.2 g	7.2 g
Saccharin sodium	2.5 g	2.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve, mix and press with medium compression force (15 kN).

3. Tablet properties

	No. 1	No. 2
Weight	500 mg	501 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	68 N	195 N
Disintegration (water)	5 min	6 min
Friability	0.2 %	< 0.1 %

4. Chemical stability of formulation No. 1 (after 12 months at 20–25 ºC)

Vitamin A	88 %
Vitamin B_6	94 %
Calcium D-pantothenate	92 %
Vitamin B_{12}	90 %
All other vitamins	> 95 %

2.9 Tablet formulations (Lab Scale)

Multivitamin Tablets II (1 – 2 RDA of Vitamins)

1. Formulation

I.	Thiamine hydrochloride (BASF)	2.2 g
	Riboflavin (BASF)	2.2 g
	Calcium D-pantothenate (BASF)	11.0 g
	Pyridoxine hydrochloride (BASF)	2.2 g
	Mannitol	300.0 g
II.	Kollidon 30 [1] or Kollidon VA 64 [1]	20.0 g
	Isopropanol	ca. 80 g
III.	Vitamin A acetate + Vitamin D_3 dry powder 500,000 + 50,000 i. u./g (BASF)	11.0 g
	Vitamin E acetate dry powder SD 50 (BASF)	31.0 g
	Cyanocobalamin gelatin coated 0.1% (BASF)	6.0 g
	Ascorbic acid, crystalline (BASF)	80.0 g
	Nicotinamide	20.0 g
	Avicel PH 101 [5]	65.0 g
	Orange flavour	7.0 g
	Saccharin sodium	2.0 g
	Magnesium stearate [2]	3.0 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with the components III and press with medium compression force.

3. Tablet properties

Weight	560 mg
Diameter	12 mm
Form	biplanar
Hardness	100 N
Disintegration (water)	1 – 2 min
Friability	< 0.1%

4. Chemical stability of vitamins A and C (20–25°C, closed)

	0 Months	3 Months	6 Months
Vitamin A	15,500 i. u./g = 100 %	15,500 i. u./g = 100 %	14,300 i. u./g = 92 %
Vitamin C	85 mg = 106 %	82 mg = 102 %	77 mg = 96 %

2.9 Tablet formulations (Lab Scale)

Multivitamin Tablet Cores with Beta-Carotene (1 – 2 RDA of Vitamins)

1. Formulation

Vitamin mixture (BASF, see “Remark”)....270.2 g
Ludipress [1] .....69.1 g
Magnesium stearate [2].....3.3 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight .....459 mg
Diameter .....11 mm
Form .....biconvex
Hardness.....97 N
Disintegration (water).....13 min
Friability .....0 %
Content uniformity of Vitamin B_1, B_2, B_6 and folic acid .....conform to DAB

4. Remark

The used vitamin mixture had the following composition:

Vitamin A acetate dry powder 1.27%
500,000 i. u./g
Beta carotene dry powder BetaVit 10%.....11.50%
Thiamine mononitrate.....1.24%
Riboflavin 0.96%
Nicotinamide.....11.50%
Calcium D-pantothenate 1.91%
Pyridoxine hydrochloride 1.15%
Cyanocobalamin gelatin coated 1%.....2.86%
D-Biotin, 1% trituration 1.91%
Folic acid 0.09%
Ascorbic acid.....38.20%
Vitamin D_3 dry powder 100,000 i. u./g.....0.76%
Vitamin E acetate dry powder 50 DC.....28.40%
Phytomenadione dry powder 5% GFP.....0.19%

2.9 Tablet formulations (Lab Scale)

Multivitamin Tablets for Dogs

1. Formulation

Vitamin A + D_3 dry powder 500,000 + 50,000 i. u./g (BASF)	4.0 g
Thiamine mononitrate (BASF)	0.5 g
Riboflavin (BASF)	0.7 g
Nicotinamide	5.0 g
Calcium D-pantothenate (BASF)	1.0 g
Pyridoxine hydrochloride (BASF)	0.5 g
Cyanocobalamin gelatin coated 1% (BASF)	0.5 g
Folic acid	0.05 g
Choline bitartrate	20.0 g
Vitamin E acetate dry powder SD 50 (BASF)	20.0 g
Ludipress [1]	196.0 g
Magnesium stearate [2]	2.0 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight	250 mg
Diameter	8 mm
Form	biplanar
Hardness	77 N
Disintegration (water)	7 min
Friability	0 %

2.9 Tablet formulations (Lab Scale)

Multivitamin Tablets with Beta Carotene (1 – 2 RDA of Vitamins)

1. Formulations

	No. 1	No. 2
Beta Carotene dry powder 10% Betavit® (BASF)	10.0 g	–
Beta Carotene dry powder 10% Pharma (BASF)	–	70.0 g
Thiamine mononitrate (BASF)	2.0 g	2.2 g
Riboflavin (BASF)	2.0 g	2.2 g
Nicotinamide	16.0 g	6.5 g
Calcium D-pantothenate (BASF)	11.0 g	11.5 g
Pyridoxine hydrochloride (BASF)	2.0 g	2.2 g
Cyanocobalamin 0.1% dry powder	6.0 g	6.0 g
Ascorbic acid, powder (BASF)	85.0 g	85.0 g
Vitamin E acetate dry powder SD 50 (BASF)	31.0 g	32.0 g
Ludipress [1]	321.0 g	210.0 g
Kollidon VA 64 [1]	–	7.0 g
Magnesium stearate [2]	3.0 g	3.0 g
Orange flavour	7.0 g	7.0 g
Saccharin sodium	2.0 g	2.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	508 mg	449 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	72 N	47 N
Disintegration (water)	5 min	10 min
Friability	< 0.1%	0.15%

4. Chemical stability of vitamins in formulation No. 1 (20–25°C, HPLC)

Storage time	Beta Carotene	B_1	B_2	B_5	B_6	C
6 Months	100%	100%	90%	100%	98%	96%
12 Months	100%	98%	87%	100%	97%	94%

5. Remark

Formulation No. 1 could be commercialized in Europe as dietary food because all components are allowed for this application.

5.8 Liquid Formulations (Lab scale)

Multivitamin Two Chamber Ampules

1. Formulations

Chamber 1:

I.	Vitamin A palmitate 1.7 Mio. i.u./g (BASF)	40 mg
	Vitamin E acetate (BASF)	200 mg
	Vitamin D_2 40 Mio. i.u./g	0.2 mg
	Butylhydroxytoluene	2.6 mg
	Butylhydroxyanisol	1.4 mg
	Solutol HS 15 [1]	4.0 g
	Lutrol E 400 [1]	2.0 g
II.	Water	70.0 g
III.	Sodium ascorbate crystalline	2.2 g
	Dexpanthenol (BASF)	300 mg
	Folic acid	0.8 mg
	Propylene glycol Pharma [1]	30.0 ml

Chamber 2:

I.	Thiamine hydrochloride (BASF)	110 mg
	Riboflavin phosphate sodium	66 mg
	Nicotinamide	440 mg
	Pyridoxine hydrochloride (BASF)	44 mg
II.	Parabenes	18 mg
	Citric acid	252 mg
	Sodium hydroxide, solution 1 molar	2.4 ml
	Hydrochloric acid, 0.1 molar	8.0 ml
	Water for injectables	9.6 ml

2. Manufacturing

Chamber 1: Heat mixture I to 60 °C, add slowly the water of the same temperature and mix with solution III. Adjust the pH to about 7, pass nitrogen through the solution and fill in ampules under nitrogen. Sterilize at 120 °C during 10 min.

Chamber 2: Dissolve the mixture I in the buffer solution II, keep it during 5 min under nitrogen bubbles, filter through a 0.2 µm membrane and fill in ampules under nitrogen. The pH-value is about 4.

3. Chemical stability (Vitamin contents after 12 months at 20–25°C, HPLC)

Vitamin A: .....not determined
Folic acid:.....75 %
Dexpanthenol: .....91 %
Vitamin B_1: .....93 %
Vitamin B_2: .....90 %
Nicotinamide:.....100 %
Vitamin B_6: .....97 %
Vitamin C: .....94 %

2.9 Tablet formulations (Lab Scale)

Nalidixic Acid Tablets (500 mg)

1. Formulation

I.	Nalidixic acid	500 g
II.	Kollidon 30 [1]	15 g
	Water	125 g
III.	Kollidon CL [1]	25 g
	Magnesium stearate [2]	5 g

2. Manufacturing (Wet granulation)

Granulate I with the solution II, dry and pass through a 0.8 mm-sieve, add the mixture III, mix during 10 minutes, pass again through a 0.8 mm-sieve and press with low compression force (10 kN).

3. Tablet properties

Weight	545 mg
Diameter	12 mm
Form	biplanar
Hardness	104 N
Disintegration (water)	1 min
Friability	0.4 %
Dissolution (30 min)	59 %
(60 min)	73 %

2.9 Tablet formulations (Lab Scale)

Naproxen Tablets (250 mg)

1. Formulation

I.	Naproxen (Midas)	250 g
	Kollidon 90 F [1]	6 g
II.	Kollidon 90 F [1]	4 g
	Cremophor RH 40 [1]	4 g
	Water	41 g
III.	Tablettose [8]	150 g
	Stearic acid [7]	1 g
	AcDiSol [5]	10 g
	Magnesium stearate [2]	1 g
	Polyethylene glycol 6000, powder [6]	10 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add III and press with low compression force.

3. Tablet properties

Weight	441 mg
Diameter	12 mm
Form	biplanar
Hardness	47 N
Disintegration	2 min
Friability	0.5 %

2.9 Tablet formulations (Lab Scale)

Naproxen Tablets (450 mg)

1. Formulations

		No. 1	No. 2
I.	Naproxen (Syntex)	457.5 g	457.5 g
	Kollidon CL [1]	10.0 g	–
II.	Kollidon 30 [1]	25.0 g	25.0 g
	Water	90.0 g	90.0 g
III.	Magnesium stearate (Merck)	2.5 g	2.5 g
	Kollidon CL [1]	–	10.0 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, add III and press to tablets with low compression force.

3. Tablet properties

	No. 1	No. 2
Weight	496 mg	511 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	100 N	95 N
Disintegration	4 min	3 min
Friability	0.3%	0.3%
Dissolution, pH 7.4 (10 min)	85.5%	86.9%
(30 min)	95.2%	94.3%

Neomycin Gel (0.05 %)

1. Formulation

Neomycin sulfate	0.05 g
Propylene glycol Pharma [1]	5.0 g
Parabenes	0.5 g
Lutrol F 127 [1]	20.0 g
Water	74.5 g

2. Manufacturing

Dissolve the parabenes and Lutrol F 127 in water heated to about 80 °C, add the propylene glycol and dissolve neomycin sulfate. Cool to room temperature when the air bubbles escaped.

Alternative:
Dissolve parabenes in hot water, cool to 5-10 °C, dissolve Lutrol F 127, add propylene glycol and dissolve neomycin sulfate. Maintain the cool temperature until the air bubbles escaped.

3. Properties of the gel

A clear semisoft gel was obtained.

4. Physical stability (6 weeks)

No change at 6 °C and 23 °C. Yellowish at 45 °C.

2.9 Tablet formulations (Lab Scale)

Neomycin Tablets (250 mg)

1. Formulation

Neomycin sulfate	250 g
Ludipress [1]	334 g
Magnesium stearate [2]	6 g
Aerosil 200 [4]	10 g

2. Manufacturing (Direct compression)

Mix all componnents, pass through a 0.8 mm-sieve and press to tablets with low compression force.

3. Tablet properties

Weight	600 mg
Diameter	12 mm
Form	biplanar
Hardness	76 N
Disintegration	14 min
Friability	0.8 %

2.9 Tablet formulations (Lab Scale)

Nicotinic Acid (= Niacin) Tablets (200 mg)

1. Formulation

Nicotinic acid (Lonza).....200.0 g
Ludipress [1].....200.0 g
Kollidon CL [1].....5.0 g
Magnesium stearate [2].....1.5 g
Aerosil 200 [4].....3.0 g
Polyethylene glycol 6000, powder [6].....10.0 g

2. Manufacturing (Direct compression)

Pass all componts through a 0.5 mm sieve, mix and press with very low compression force.

3. Tablet properties

Weight .....419 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....144 N
Disintegration .....1 min
Friability .....0.2 %

2.9 Tablet formulations (Lab Scale)

Nifedipine Tablet Cores (10 mg)

(According to Ph.Eur. Patent 0078.430, 1982)

1. Formulation

I.	Nifedipine	10.0 g
	Kollidon 25 [1]	40.0 g
II.	Methylene chloride	180.0 g
III.	Microcrystalline Cellulose [5]	105.0 g
	Corn starch [3]	20.0 g
	Kollidon CL [1]	25.0 g
IV.	Magnesium stearate	0.4 g

2. Manufacturing (Wet granulation)

Dissolve mixture I in II. Granulate mixture III with solution I/II, sieve, dry the obtained coprecipitate, add IV and press with low to medium compression force.

3. Tablet properties

Weight	223 mg
Diameter	8 mm
Form	biconvex
Hardness	132 N
Disintegration	about 10 min
Friability	< 0.1%
Dissolution (20 min)	90%

Nitrendipine Tablets (25 mg)

1. Formulation

Nitrendipine	26.0 g
Ludipress [1]	53.0 g
Kollidon CL [1]	1.5 g
Magnesium stearate [2]	0.5 g

2. Manufacturing (Direct compression)

Pass all components through a 0.5 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight	82 mg
Diameter	6 mm
Form	biplanar
Hardness	63 N
Disintegration	< 1 min
Friability	0.3 %

2.9 Tablet formulations (Lab Scale)

Nitrofurantoin Tablet Cores (100 mg)

(According to E.A.Hosny, A.M.S. Ahmed, Drug Dev. Ind. Pharm 20(9), 1631 – 38, 1994)

1. Formulation

I.	Nitrofurantoin	100 g
	Corn starch [3]	20 g
	Lactose [8]	38 g
II.	Kollidon 30 [1]	10 g
	Water	q.s.
III.	Kollidon CL [1]	5 g
	Corn starch [3]	8 g
	Talc [10]	3 g
	Magnesium stearate [2]	1 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, sieve, mix with III and press.

3. Tablet properties

Weight	180 mg
Diameter	8 mm
Form	biconvex
Disintegration	5 min
Dissolution (60 min)	78 %
(120 min)	93 %

2.9 Tablet formulations (Lab Scale)

Nitrofurantoin Tablets (100 mg)

1. Formulation

Nitrofurantoin .....100 g
Ludipress [1] .....200 g
Magnesium stearate [2] .....2 g
Aerosil 200 [4].....3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....307 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....85 N
Disintegration.....1 – 2 min
Friability.....0.5 %

5.8 Liquid Formulations (Lab scale)

Norephedrine Syrup (40 mg/10 g)

1. Formulation

DL-Norephedrine hydrochloride.....0.4 g
Parabenes (Nipa).....0.1 g
Saccharin sodium.....0.5 g
Kollidon 90 F [1].....3.0 g
Sorbitol solution .....50.0 g
(Karion® F liquid, Merck)
Water.....46.0 g

2. Manufacturing

Dissolve the parabenes in the hot water, add the sorbitol, cool to room temperature and dissolve the other components.

3. Properties of the syrup

Appearance .....clear solution
Taste.....reasonable

4. Remarks

To prevent of discolouration of Kollidon in the solution during storage 0.1 to 0.5% of cysteine could be added as antioxidant.

Flavours should be added to adjust the required taste.

Nystatin Suspension (100,000 i.u./ml)

1. Formulation

Nystatin	2.25 g
Kollidon CL-M [1]	5.75 g
Kollidon 90 F [1]	2.00 g
Sorbitol [10]	24.80 g
Citric acid	0.50 g
Water	64.70 g

2. Manufacturing

Nystatin, Kollidon CL-M, sorbitol and citric acid are suspended in water. Kollidon 90 F is added slowly in small portions under vigorous stirring.

3. Properties of the suspension

Colour	yellow
Viscosity (25 °C)	60 mPa · s
Sedimentation	not observed after one week
Redispersibility	easy

2.9 Tablet formulations (Lab Scale)

Nystatin Tabet Cores (200 mg)

1. Formulation

I.	Nystatin	200 g
	Lactose monohydrate [8]	51 g
II.	Isopropanol	40 ml
III.	Kollidon CL [1]	10 g
	Magnesium stearate [2]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with the solvent II, dry, pass through a 0.8 mm sieve, add the components III and press with medium compression force.

3. Tablet properties

Weight	270 mg
Diameter	9 mm
Form	biconvex
Hardness	40 N
Disintegration	14 min
Friability	0 %

2.9 Tablet formulations (Lab Scale)

Nystatin Tablets (50 mg and 100 mg)

1. Formulations

	50 mg	100 mg
Nystatin	55.0 g	110.0 g
Ludipress [1]	110.0 g	220.0 g
Aerosil 200 [4]	1.0 g	2.0 g
Magnesium stearate [2]	1.3 g	2.5 g

2. Manufacturing (Direct compression)

Mix the components, pass through a 0.8 mm sieve and press with very low compression force.

3. Tablet properties

	50 mg	100 mg
Weight	175 mg	339 mg
Diameter	8 mm	10 mm
Form	biplanar	biplanar
Hardness	54 N	66 N
Disintegration	10 min	9 min
Friability	0.6 %	0.3 %

2.9 Tablet formulations (Lab Scale)

Omega Fatty Acids Tablet Cores (10 mg EPA + DHA)

1. Formulation

Omega Fatty Acids Dry N-3 (BASF).....140.0 g
Avicel PH 101 [5] .....140.0 g
Kollidon VA 64 [1].....8.4 g
Magnesium stearate [2].....2.0 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight .....289 mg
Diameter .....9 mm
Form .....biconvex
Hardness.....71 N
Friability.....< 0.15

4. Remarks

– The dry powder *Omega Fatty Acids Dry N-3* contains 25% fish oil. This fish oil consists of about 30% EPA+DHA.

– These tablet cores could be coated with an enteric coating of Kollicoat MAE 30 D [1] (see chapter 3).

5.8 Liquid Formulations (Lab scale)

Oxytetracycline Injectable Solution for Veterinary Application (500 mg/10 ml)

1. Formulation

I.	Oxytetracycline hydrochloride	5.7 g
II.	Kollidon 17 PF [1]	10.0 g
	Reducing agent	0.5 g
	(e.g. Rongalite® C, BASF)	
	Water for injectables	ad 100 ml
III.	Magnesium oxide	0.46 g
IV.	Ethanolamine	to adjust pH 8.8

2. Manufacturing

Suspend III in solution II, pass continously nitrogen through the solution to avoid oxidation and add slowly I to the well stirred solution. Adjust the pH with IV.

3. Properties of the solution

Yellow clear solution.

4. Remarks

The absence of oxygen during manufacturing and in the final packaging and a good quality of oxytetracycline HCl are essential to avoid the oxidation (= dark solution).

The function of Kollidon 17 PF not only is the solubilisation of oxytetracycline but also the reduction of its local toxicity.

The reducing agent must be selected in accordance with the legislation of the corresponding country.

5.8 Liquid Formulations (Lab scale)

Oxytetracycline Sustained Release Injectable for Veterinary Application (2.2 g/10 ml)

(According to US-Patent 4.018.889 (1976)

1. Formulation

Oxytetracycline	22.65 g
Magnesium oxide	1.92 g
Soluphor P [1]	40.00 g
Kollidon 17 PF [1]	5.00 g
Sodium formaldehyde sulfoxylate	0.44 g
2-Aminoethanol	3.84 g
Water of injectables	q.s. ad 100.00 ml

2. Manufacturing

Mix the water and the Soluphor P, and dissolve the Kollidon 17 PF in the mixture. Heat the solution to 75 °C. Add the sodium formaldehyde sulfoxylate and stir until dissolved. After the magnesium oxide has been suspended, slowly stir in the oxytetracycline until a clear solution is obtained. After the solution has cooled, set to pH 8.5 with aminoethanol.

3. Remarks

The quality of the oxytetracycline and the complete absence of oxygen during the manufacturing and packaging of the solution is essential to obtain a acceptable chemical stability and no dark colour.

The reducing agent e.g. sodium formaldehyde sulfoxylate (Rongalite, C, BASF) must be selected in accordance with the legislation of the corresponding country.

Oxytetracycline Tablets (250 mg)

1. Formulation

Oxytetracycline hydrochloride .....250 g
Ludipress [1] .....230 g
Magnesium stearate [2] .....6 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with very low compression force.

3. Tablet properties

Weight .....495 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....86 N
Disintegration .....4 min
Friability.....0.1%

2.9 Tablet formulations (Lab Scale)

Pancreatin Tablet Cores (30 mg)

1. Formulation

Pancreatin (Knoll) .....30 g
Ludipress [1] .....308 g
Kollidon CL [1].....10 g
Magnesium stearate [2] .....2 g

2. Manufacturing (Direct compression)

Mix the components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....355 mg
Diameter .....8 mm
Form .....biconvex
Hardness.....76 N
Disintegration .....4 – 5 min
Friability .....< 0.1%

4. Enteric coating

See Chapter 3.

2.9 Tablet formulations (Lab Scale)

Pancreatin Tablet Cores (130 mg)

1. Formulation

Pancreatin (Knoll)	130 g
Cholic acid	2 g
Avicel PH 101 [5]	127 g
Lactose monohydrate [8]	56 g
Magnesium stearate (Merck)	2 g
Aerosil 200 [4]	3 g

2. Manufacturing (Direct compression)

Mix the components and press with high compression force.

3. Properties of the cores

Weight	324 mg
Diameter	9 mm
Form	biconvex
Hardness	177 N
Friability	< 0.1%

4. Enteric coating

See Chapter 3.

2.9 Tablet formulations (Lab Scale)

Pancreatin Tablet Cores (300 mg)

1. Formulation

Pancreatin (Knoll) .....300 g
Ludipress [1] .....290 g
Kollidon CL [1] .....25 g
Magnesium stearate [2] .....3 g

2. Manufacturing (Direct compression)

Mix the components, pass through a 0.8 mm sieve and press to tablets with low compression force.

3. Tablet properties

Weight .....615 mg
Diameter 11mm
Form .....biconvex
Hardness.....74 N
Friability.....< 0.1%

4. Enteric coating

See Chapter 3.

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) + Caffeine Tablets (500 mg + 50 mg)

1. Formulation

Paracetamol, crystalline	500 g
Caffeine (Knoll)	50 g
Avicel PH 101 [5]	90 g
Kollidon 30 [1]	10 g
Kollidon CL [2]	20 g
Polyethylene glycol 6000, powder [6]	10 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve of 0.8 mm and press with high compression force.

3. Tablet properties

Weight	683 mg
Diameter	12 mm
Form	biplanar
Hardness	56 N
Disintegration	< 1 min
Friability	0.9 %
Dissolution, 15 min	91%

4. Remark

If the flowability of the powder mixture for tabletting is not high enough some Aerosil 200 [4] should be added.

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Paracetamol (= Acetaminophen) + Doxylamine + Caffeine Effervescent Granules (500 mg + 5 mg + 33 mg/2.1 g)

1. Formulation

I.	Paracetamol, powder	500 g
	Doxylamine succinate	5 g
	Caffeine (Knoll)	33 g
	Tartaric acid	391 g
	Sodium hydrogen carbonate	417 g
II.	Kollidon 30 [1]	6 g
	Isopropanol (or Ethanol)	q.s.
III.	Sodium citrate	30 g
	Sugar	707 g

2. Manufacturing

Granulate mixture I with solution II, dry at 60°C under vacuum conditions, sieve and mix with III.
Fill 2.1 g in sachets at maximum 30% of relative atmospheric humidity.

3. Properties

Free flowing granules.

4. Remark

If the solvent insopropanol is replaced by water the granulation should be done in a fluidized bed.

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Paracetamol (= Acetaminophen) Instant Granules (250 mg or 500 mg)

1. Formulations

		No. 1	No. 2
I.	Paracetamol, fine powder	50 g	50 g
	Sucrose, fine powder	128 g	–
	Sorbitol Instant (Merck)	–	130 g
	Kollidon CL-M [1]	90 g	50 g
	Aspartame	7 g	7 g
	Orange flavour	5 g	5 g
	Strawberry flavour	5 g	5 g
	Sodium citrate	–	3 g
	Citric acid	–	3 g
II.	Kollidon 30 [1]	12 g	–
	Kollidon 90 F [1]	–	8 g
	Ethanol 96%	75 g	50 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, and pass through a 0.8 mm sieve.
Formulation No. 1: Fill 1.5 g or 3.0 g in sachets.
Formulation No. 2: Fill 1.3 g or 2.6 g in sachets.

3. Properties of the granules

The free flowing granules are very well dispersible in cold water.

4. Administration

Formulation No. 1: Suspend 1.5 g or 3.0 g of the granules (= 250 mg or 500 mg paracetamol) in a glass of water.
Formulation No. 2: Suspend 1.3 g or 2.6 g of the granules (= 250 mg or 500 mg paracetamol) in a glass of water.

5. Properties of the suspensions

Yellowish, milky appearance with ***a sweet and fruity taste.*** No sedimentation within two hours.

6. Chemical stability of the granules (Formulation No. 1)

No loss of paracetamol after 2 months at 60 °C.

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) + Ibuprofen + Orphenadin Tablets (250 mg + 200 mg + 100 mg)

1. Formulation

Paracetamol, powder < 300 µm .....250 g
Ibuprofen .....200 g
Orphenadine hydrochloride .....100 g
Ludipress [1] .....200 g
Magnesium stearate [2] .....5 g
Aerosil 200 [4].....5 g

2. Manufacturing (Direct compression)

Pass all components through a 0.5 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight .....761 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....74 N
Disintegration .....6 min
Friability.....0.7%

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) + Norephedrine + Phenyltoloxamine Tablets (300 mg + 25 mg + 22 mg)

1. Formulation

I.	Paracetamol, crystalline (Merck)	300 g
	Norephedrine hydrochloride (Knoll)	25 g
	Phenyltoloxamine	22 g
	Corn starch [3]	200 g
II.	Kollidon 30 [1]	25 g
	Ethanol 96 %	q.s.
III.	Kollidon CL [1]	25 g
	Magnesium stearate [2]	5 g

2. Manufacturing (Wet formulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add III and press with high compression force.

3. Tablet properties

Weight	601 mg
Diameter	12 mm
Form	biplanar
Hardness	97 N
Disintegration	1 – 2 min
Friability	0.7 %

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) + Phenprobamat Tablets (200 mg + 200 mg)

1. Formulation

Paracetamol, powder < 0.5 mm	200 g
Phenprobamat	200 g
Avicel PH 101 [5]	35 g
Kollidon VA 64 [1]	20 g
Kollidon CL [1]	10 g
Magnesium stearate [2]	5 g
Aerosil 200 [4]	q.s.

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight	465 mg
Diameter	12 mm
Form	biplanar
Hardness	54 N
Disintegration	< 1 min
Friability	0.8 %

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) Chewable Tablets (300 mg)

1. Formulation

I.	Paracetamol, milled (Hoechst)	300 g
	Sucrose, milled	600 g
	Kollidon CL-M [1]	550 g
	Orange flavour (FDO)	30 g
	Strawberry flavour (FDO)	30 g
II.	Kollidon 30 [1]	60 g
	Ethanol 96 %	about 425 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a sieve and press with medium compression force.

3. Tablet properties

Weight	1,620 mg
Diameter	20 mm
Form	biplanar
Hardness	111 N
Disintegration	27 min
Friability	1%

4. Taste on chewing of the tablets

Sweet, fruity and only very slightly bitter.

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) Effervescent Tablets (500 mg)

1. Formulation

I.	Paracetamol, powder < 300 µm	500 g
	Sodium bicarbonate	500 g
	Tartaric acid, powder	430 g
	Dextrose	200 g
	Flavouring	
II.	Kollidon 30 [1]	20 g
	Isopropanol	100 ml
III.	Polyethylene glycol 6000, powder [6]	60 g

2. Manufacturing (Wet formulation)

Granulate the mixture I with solution II, pass through a 0.8 mm sieve, add III, mix and press to tablets.

3. Tablet properties

Weight	1,700 mg
Diameter	16 mm
Form	biplanar
Hardness	150 N
Disintegration	4 min
Friability	0.7%

Paracetamol (= Acetaminophen) Instant Granules (500 mg)

1. Formulation

I.	Paracetamol, fine powder	50 g
	Sorbitol instant (Merck)	130 g
	Lutrol F 127 [1]	50 g
	Citric acid, powder	3 g
	Sodium citrate	3 g
II.	Kollidon 90 F [1]	8 g
	Ethanol 96 %	50 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II and dry.
Fill 2.44 g in sachets (= 500 mg Paracetamol).

3. Properties of the granules

The free flowing granules are very well dispersible in cold water.

4. Properties of the suspended granules

The taste of the suspension is only slightly bitter (2.44 g in a glass water). No sedimentation can be observed during some minutes.

6.7 Formulations of semi-solid drugs (Lab scale)

Paracetamol (= Acetaminophen) Suppositories (150 mg and 500 mg)

1. Formulations

		No. 1 150 mg	No. 2 500 mg
I.	Paracetamol, fine powder	15.4 g	50.0 g
	Aerosil 200 [4]	0.2 g	–
II.	Lutrol E 400 [1]	–	10.0 g
	Lutrol E 1500 [1]	129.0 g	60.0 g
	Lutrol E 4000 [1]	55.4 g	80.0 g

2. Manufacturing

Melt the mixture II and suspend the mixture I. Fill the molten mass in the moulds of suppositories.

3. Properties of the suppositories

Weight ..... 2.0 g
Solubility in water ..... easy
Colour ..... colourless

4. Physical stability (Formulation No. 1)

No crystallisation after the storage of 6 weeks at 6 °C, 20 °C or 40 °C.

5.8 Liquid Formulations (Lab scale)

Paracetamol (= Acetaminophen) Suspension (5 % = 500 mg/10 ml)

1. Formulation

Paracetamol, powder	5.0 g
Citric acid, powder	0.5 g
Sodium citrate	0.5 g
Kollidon CL-M [1]	5.0 g
Orange flavour	0.1 g
Dextrose	30.0 g
Water	58.9 g

2. Manufacturing

Prepare the solution of dextrose in water and add the other solid ingredients with stirring in the following sequence: citric acid, sodium citrate, orange flavour, Kollidon CL-M and paracetamol. A white, homogeneous suspension is obtained.

3. Properties of the suspension

Practically tasteless, stable suspension showing almost no sedimentation during 24 hours and good redispersibility (easily to homogenize by shaking twice to 3 times).

5.8 Liquid Formulations (Lab scale)

Paracetamol (= Acetaminophen) Syrup (5 % = 500 mg/10 g)

1. Formulation

Paracetamol (Merck)	5.0 g
Sorbitol, crystalline [10]	5.0 g
Cyclamate sodium	4.0 g
Strawberry flavour	0.1 g
Kollidon 25 [1]	20.0 g
Glycerol	15.0 g
1,2-Propylene glycol Pharma [1]	20.0 g
Water	31.0 g

2. Manufacturing

Dissolve first Kollidon 25 and then the other solid components in the solvent mixture of glycerol, propylene glycol and water.

3. Properties of the syrup

Clear solution of certain viscosity having only a slightly bitter taste.

4. Physical stability

The solution remained clear during more than 1 week at 6 °C and during more than 3 months at 25 °C and 40 °C.

The colour of the solution changed only a little during 3 months at 25 °C and 40 °C. To prevent of discolouration during storage 0.2 to 0.5% of cysteine could be added as antioxidant.

5. Chemical stability (HPLC)

No loss of paracetamol was found during 3 months at 40 °C.

5.8 Liquid Formulations (Lab scale)

Paracetamol (= Acetaminophen) Syrup for Children (2.5 % = 250 mg/10 ml)

1. Formulation

Paracetamol, crystalline	2.5 g
Kollidon 25 or Kollidon 30 [1]	30.0 g
Glycerol	6.0 g
Sodium cyclamate	4.0 g
Orange flavour	< 0.1 g
Raspberry flavour	0.2 g
Water	57.5 g

2. Manufacturing

Dissolve Kollidon in water, add paracetamol and cyclamate, heat to 50 °C and stir to obtain a clear solution. Dissolve the flavours and mix with glycerol.

3. Properties of the syrup

The obtained syrup is a viscous, clear sweet and only slightly bitter liquid.

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) Tablet Cores (500 mg)

1. Formulation

I.	Paracetamol, powder (RPR)	500 g
	Dicalcium phosphate [9]	30 g
	Kollidon CL [1]	12 g
	Kollidon VA 64 [1]	20 g
II.	Kollidon 90 F [1]	10 g
	Ethanol 96%	max. 70 g
III.	Kollidon CL [1]	12 g
	Polyethylene glycol, powder [6]	10 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, sieve and mix with III. Press with high compression force of 25 – 30 kN.

3. Tablet properties

Weight	587 mg
Diameter	11 mm
Form	biconvex
Hardness	157 N
Disintegration	< 1 min
Friability	< 0.1%
Dissolution, 10 min	88%
30 min	97%

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) Tablets (500 mg)

1. Formulations

	No. 1	No. 2
Paracetamol, crystalline (Synopharm)	500 g	500 g
Avicel PH 102 [5]	137 g	150 g
Kollidon VA 64 [1]	35 g	20 g
Kollidon CL [1]	21 g	15 g
Magnesium stearate [2]	3 g	–
Polyethylene glycol 6000, powder [6]	–	15 g
Aerosil 200 [4]	4 g	2 g

2. Manufacturing (Direct compression)

Pass the lubricant through a 200 µm sieve, mix all other components, pass through a 0.8 mm sieve, add the lubricant and press with high compression force of 25 – 30 kN.

3. Tablet properties

	No. 1	No. 2
Weight	699 mg	703 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	60 N	87 N
Disintegration	6 min	1 min
Friability	0.7 %	0.4 %
Dissolution, 10 min	84 %	73 %
30 min	98 %	86 %

2.9 Tablet formulations (Lab Scale)

Paracetamol (= Acetaminophen) Tablets for Children (200 mg)

1. Formulation

Paracetamol (= Acetaminophen, Merck) ....210 g
Avicel PH 101 [5] .....168 g
Kollidon VA 64 [1] .....13 g
Kollidon CL [1] .....6 g
Magnesium stearate [2] .....2 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

Weight .....401 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....65 N
Disintegration.....< 1 min
Friability.....0.4 %

Phendimetrazin Tablets (35 mg)

1. Formulation

Phendimetrazin	35 g
Ludipress [1]	281 g
Corn starch [3]	281 g
Magnesium stearate [2]	> 3 g
Aerosil 200 [4]	> 3 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

Weight	604 mg
Diameter	12 mm
Form	biplanar
Hardness	146 N
Disintegration (water)	3 – 4 min
Friability	0.2 %

4. Remark

The amount of Ludipress and/or corn starch could be reduced.

Phenindion Tablets (50 mg)

1. Formulation

Phenindion	50 g
Ludipress [1]	165 g
Magnesium stearate [2]	2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	230 mg
Diameter	8 mm
Form	biplanar
Hardness	193 N
Disintegration	15 min
Friability	0.1%

2.9 Tablet formulations (Lab Scale)

Phenolphthalein Tablet Cores (200 mg)

1. Formulation

I.	Phenolphthalein	200 g
	Dibasic calcium phosphate [9]	150 g
II.	Kollidon 30 [1]	11 g
	Isopropanol or ethanol 96 %	q. s.
III.	Kollidon CL [1]	19 g
	Magnesium stearate [2]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, mix with III, pass through a 0.8 sieve and press with low compression force.

3. Tablet properties

Weight	385 mg
Diameter	9 mm
Form	biconvex
Hardness	280 N
Disintegration (water)	< 1 min
Friability	0.2 %

5.8 Liquid Formulations (Lab scale)

Phenytoin Oral Suspension (5 %)

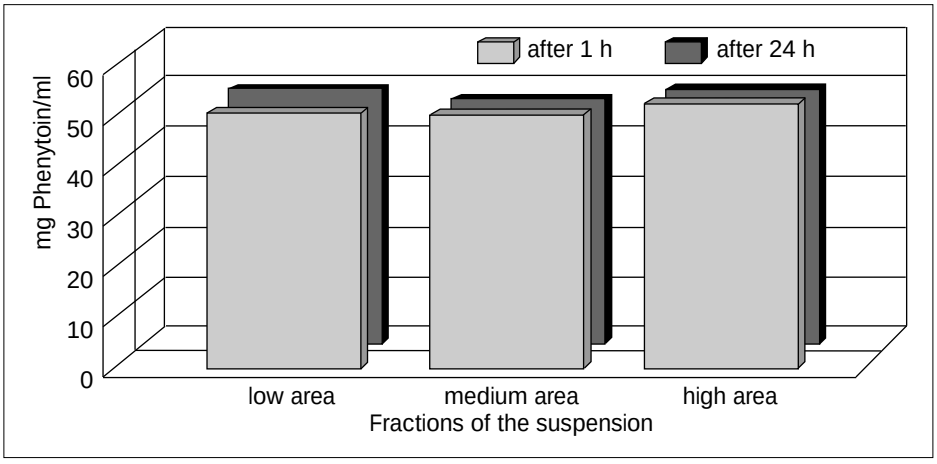
1. Formulation

Phenytoin .....5 g
Kollidon CL-M [1] .....8 g
Kollidon 90 F [1].....1 g
Preservative .....q.s.
Water.....86 g

2. Manufacturing

Dissolve the preservative and Kollidon 90 F in water and suspend Kollidon CL-M and phenytoin.

3. Content uniformity of phenytoin in the suspension



Phenytoin Sodium Tablets (100 mg), DC

1. Formulation

Phenytoin sodium (Sigma)	100 g
Ludipress [1]	235 g
Magnesium stearate [2]	10 g
Kollidon CL [1]	8 g
Aerosil 200 [4]	5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	346 mg
Diameter	12 mm
Form	biplanar
Hardness	82 N
Disintegration	9 min
Friability	0.2 %
Dissolution, 10 min	57 %
30 min	89 %

2.9 Tablet formulations (Lab Scale)

Phenytoin Sodium Tablets (100 mg), WG

1. Formulation

I.	Phenytoin sodium	100 g
	Dicalcium phosphate [9]	50 g
	Sucrose, crystalline	45 g
II.	Kollidon 25 [1]	10 g
	Isopropanol + Ethanol (1 + 1)	30 g
III.	Kollidon CL [1]	5 g
	Magnesium stearate [2]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with high compression force.

3. Tablet properties

Weight	209 mg
Diameter	8 mm
Form	biplanar
Hardness	60 N
Disintegration	3 min
Friability	0.5 %

Phenytoin Tablets (100 mg)

1. Formulation

Phenytoin base (Fluka)	100 g
Ludipress [1]	235 g
Magnesium stearate [2]	2 g
Stearic acid [7]	2 g
Kollidon CL [1]	8 g
Aerosil 200 [4]	5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	351 mg
Diameter	12 mm
Form	biplanar
Hardness	81 N
Disintegration	1 min
Friability	0.4 %

6.7 Formulations of semi-solid drugs (Lab scale)

Piroxicam + Dexpanthenol Gel (0.5 % + 5.0 %)

1. Formulation

Piroxicam (Sigma)	0.5 g
1,2-Propylene glycol Pharma [1]	25.0 g
Dexpanthenol (BASF)	5.0 g
Ethanol 96 %	5.0 g
Triethanolamine	about 0.4 g
Lutrol F 127 [1]	23.0 g
Water	46.0 g

2. Manufacturing

First mode of preparation:
Prepare the solution of piroxicam in propylene glycol and dexpanthenol at 70 – 80°C, add ethanol and Lutrol F 127. Stirr the highly viscous mixture, add 50 % of the hot water (70°C), adjust the pH with triethanolamine to about 7, add the rest of the water, cool to room temperature when the air bubbles escaped and adjust the pH to about 8.

Alternative mode of preparation:
Dissolve piroxicam in propylene glycol, dexpanthenol and triethanolamine. Cool the mixture of Lutrol F 127 and water to about 5 °C and mix with the piroxicam solution. Add the ethanol. Maintain the cool temperature until the air bubbles escaped.

3. Properties of the gel

A clear colourless gel was formed having a pH of about 8.

4. Remark

The addition of ethanol is not essential because it reduces the viscosity.

2.9 Tablet formulations (Lab Scale)

Piroxicam Water Dispersible Tablets (20 mg)

1. Formulation

Piroxicam	20 g
Corn starch [3]	150 g
Ludipress [1]	50 g
Kollidon CL [1]	8 g
Polyethylene glycol 6000 powder [6]	10 g
Aerosil 200 [4]	1 – 2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low to medium compression force.

3. Tablet properties

Weight	238 mg
Diameter	8 mm
Form	biplanar
Hardness	66 N
Disintegration (water)	57 sec
Friability	0.1%

2.9 Tablet formulations (Lab Scale)

Placebo Tablets

1. Formulation

Ludipress [1].....99.9 %
Magnesium stearate [2] .....0.1 %

2. Manufacturing (Direct compression)

Mix the components, sieve and press.

3. Influence of the compression force on the tablet properties (300 mg tablet weight)

	compression force		
Property	**7 kN**	**15 kN**	**22 kN**
Hardness	45 N	110 N	160 N
Disintegration	1 min	2 – 3 min	3 – 4 min
Friability	0.05 %	< 0.05 %	< 0.05 %

5.8 Liquid Formulations (Lab scale)

Polidocanol Wound Spray (0.5 %)

1. Formulation

I.	Polidocanol	1 g
	Kollidon VA 64 [1]	10 g
	Ethocel® 20 (Dow)	10 g
	Lutrol E 400 [1]	4 g
II.	Ethyl acetate	135 g
	Isopropanol	40 g

2. Manufacturing of the solution

Dissolve the components I in the solvent mixture II.

3. Manufacturing of the spray

Fill the solution into spray cans with the necessary quantity of propellant (e. g. propane/butane) or in a mechanical pump bottle.

6.7 Formulations of semi-solid drugs (Lab scale)

Povidone-Iodine + Lidocain Gel (10 %)

1. Formulation

I.	PVP-Iodine 30/06 (BASF)	10.0 g
	Lidocain hydrochloride	1.0 g
	Sodium chloride	1.0 g
II.	Lutrol F 127 [1]	20.0 g
III.	Sodium hydroxide solution, 1 molar	7.9 g
IV.	Water	61.1 g

2. Manufacturing

Dissolve the solids (I) in water (IV), cool to about 6 °C, dissolve Lutrol F 127 (II) and adjust the pH value with the sodium hydroxide solution (III). Maintain the cool temperature until the air bubbles escaped.

3. Properties of the gels

Viscosity (Brookfield, 23 °C)	54,000 mPa · s
pH value (20 % in water)	4.7

4. Stability (14 days, 52 °C)

Viscosity (Brookfield, 23 °C)	51,000 mPa.s
pH value (20 % in water)	2.4
Loss of available iodine	15.5 %

Povidone-Iodine Bar Soap (5 %)

1. Formulation

PVP-Iodine 30/06 (BASF).....50 g
Fragance.....10 g
Water.....75 g
Syndet base (see Remark) .....940 g

2. Manufacturing

Dissolve PVP-Iodine in water, mix the solution with the fragrance and the syndet base. Pass the blend 4 x through a three-roller mill. Give the blend 3 times through a plodder with a narrow sieve hole disk.

Pass the blended material through a wide sieve hole disk combined with a mouth hole disk. Heat the area of the 2 disks is to 50 °C by a heating collar.

Cut the bar in pieces on a Lab stamper.

3. Remark

Composition of the syndet base (sequence of concentration):

Disodium lauryl sulfosuccinate
Sodium lauryl Sulfate
Cetylstearyl alcohol
Paraffin
Glycerol stearate
Water
Titanium dioxide

6.7 Formulations of semi-solid drugs (Lab scale)

Povidone-Iodine Bar Soaps (5 %)

1. Formulations

		No. 1	No. 2
I.	PVP-Iodine 30/06 (BASF)	10.0 g	10.0 g
	Water	15.0 g	15.0 g
II.	Texapon® K 12 (Henkel)	48.3 g	48.3 g
	Setacin® F special paste (Zschimmer + Schwarz)	48.3 g	–
	Emcol® 4400.1 (Wilco)	–	48.3 g
	Cetylstearyl alcohol	29.0 g	29.0 g
	Paraffin (56 – 58 °C)	19.3 g	19.3 g
	Glycerol monostearate	45.2 g	45.2 g

2. Manufacturing

Heat mixture II to 75 – 80 °C and cool to about 50 °C well stirring. Add solution I and let cool to room temperature continuously stirring.

Pass the blend four times through a three-roller mill and let dry over night at room temperature. Cut the bar in pieces on a Lab stamper.

3. Chemical stability (40 °C during 4 weeks)

	No. 1	No. 2
Loss of available iodine	9.1 %	11.5 %

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Concentrates for Broilers and Cattles (20 %)

1. Formulations

		No. 1	No. 2
I.	PVP-Iodine 30/06 (BASF)	20.0 g	20.0 g
II.	Texapon® K 12 (Henkel)	–	5.0 g
	Cremophor NP 14 [1]	5.0 g	–
III.	Tartaric acid	7.3 g	7.3 g
	Sulfuric acid, diluted	4.3 g	4.3 g
	Ethanol 96 %	10.0 g	10.0 g
	Water	ad 100 g	ad 100 g

2. Manufacturing

Dissolve the surfactant II in solution III and add slowly PVP-Iodine I.

3. Properties of the solutions

Brown transparent liquids having a pH of about 1.

4. Administration as preventive desinfectant

Dilute about 3 ml of the concentrate with 1 l of water.

Povidone-Iodine Cream (10 %)

1. Formulation

I.	PVP-Iodine 30/06 (BASF)	10.0 g
	Citric acid solution 0.1 molar	24.1 g
	Na_2HPO_4 solution 0.2 molar	36.9 g
II.	Cremophor A 6 [1]	2.0 g
	Cremophor A 25 [1]	2.0 g
	Cetylstearyl alcohol	10.0 g
	Liquid paraffin	10.0 g
	Glycerol	5.0 g

2. Manufacturing

Prepare a basic cream from the emulsifying agents and the fatty substances (II). Stir in the PVP-iodine dissolved in the buffer solutions (I).

3. Properties of the cream

Brown cream having a pH of 4.5.

4. Chemical stability

	After production	After 14 days/52 °C
pH	4.5	4.1
Available iodine	1.09 %	0.99 %
Loss of iodine	–	9.2 %

During this stress test at 52 °C the emulsion was separated into two phases.

2.9 Tablet formulations (Lab Scale)

Povidone-Iodine Effervescent Vaginal Tablets (350 mg)

1. Formulation

I.	PVP-Iodine 30/06 M 10 (BASF)	360 mg
II.	Ludipress [1]	1,450 mg
	Tartaric acid	360 mg
	Sodium bicarbonate	265 mg
III.	Talc [10]	19 mg
	Calcium arachinate [2]	2 mg
	Aerosil 200 [4]	2 mg

2. Manufacturing (Direct compression)

Dry the mixture II for 4 hours at 60 °C, mix with I and III and press to tablets.

3. Tablet properties

Weight	2.5 g
Diameter	20 mm
Form	biplanar
Hardness	200 N
Disintegration in water	7 min
Friability	0.9 %

4. Application

The tablet is dissolved in water to obtain a vaginal douche solution.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Foam Spray (10 %)

1. Formulation

PVP-Iodine 30/06 (BASF) .....10.0 g
Cremophor A 25 [1] .....0.01 g
Water .....ad 100 g

2. Manufacturing

Dissolve PVP-Iodine in the solution of Cremophor A 25 in water.

Fill the aerosol cans with 90 parts of this solution and 10 parts of propane + butane (1+3).

3. Chemical stability (14 days, 52 °C)

The content of available iodine dropped to 98 %.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Gargle Solution Concentrate (10 %)

1. Formulation

PVP-Iodine 30/06 (BASF) .....10.0 g
Propylene glycol Pharma [1].....1.0 g
Ethanol 96 %.....9.0 g
Water.....80.0 g

2. Manufacturing

Dissolve the PVP-Iodine in the solvent mixture.

3. Properties of the concentrate

Brown transparent liquid.

4. Administration

Dilute 10 ml of the concentrate with about 100 ml of water.

Povidone-Iodine Gel-Cream (10 %)

1. Formulation

I.	PVP-Iodine 30/06 (BASF)	10.0 g
II.	Citric acid solution, 0.1 molar	35.9 g
	$NA_2HPO_4 \cdot 12H_2O$ solution, 0.2 molar	18.1 g
	Lutrol E 400 [1]	5.0 g
III.	Liquid paraffin	10.0 g
IV.	Lutrol F 127	15.0 g
V.	Lutrol F 127	7.0 g

2. Manufacturing

Dissolve I in solution II, mix with III and dissolve IV at about 20 °C. Cool to 5 – 8 °C and dissolve V. Maintain cool until all air bubbles disappeared.

3. Properties

Brown turib gel.

4. Chemical stability (20–25 °C)

	0 Months	3 Months	6 Months
pH	3.4	3.1	3.1
Available iodine	1.0 %	0.99 %	0.95 %
Loss of iodine	–	1 %	5 %
Viscosity (Brookfield)	113,000 mPa · s	124,000 mPa · s	122,000 mPa · s

Povidone-Iodine Gels (10 %)

1. Formulations

		No. 1	No. 2
I.	PVP-Iodine 30/06 (BASF)	10.0 g	10.0 g
	Sodium chloride	–	1.0 g
II.	Lutrol F 127 [1]	20.0 g	20.0 g
III.	Sodium hydroxide solution, 1 molar	–	7.9 g
IV.	Water	70.0 g	61.1 g

2. Manufacturing

Dissolve the solids (I) in water (IV), cool to about 6 °C, dissolve Lutrol F 127 (II) and adjust the pH value with the sodium hydroxide solution (III). Maintain cool until all air bubbles escaped.

3. Properties of the gels

	No. 1	No. 2
Viscosity (Brookfield, 23 °C)	61,000 mPa · s	54,000 mPa · s
pH value (20 % in water)	2.2	4.6

4. Stability (14 days, 52 °C)

	No. 1	No. 2
Viscosity (Brookfield, 23 °C)	58,000 mPa · s	45,000 mPa · s
pH value (20 % in water)	1.9	2.7
Loss of available iodine	10.2 %	8.0 %

Povidone-Iodine Glucose Ointment (2.5 %)

(According to R. Dolder, M. Asanger, APV-Pharmazie in der Praxis No. 3, Febr. 1987, 5 – 7)

1. Formulation

I.	PVP-Iodine 30/06 (BASF)	2.6 g
	Ethanol 96 %	4.5 g
II.	Glucose [1]	84.9 g
	Lutrol E 4000 [1]	3.4 g
	Glycerol	0.6 g
	Water	0.6 g

2. Manufacturing

Dissolve Lutrol E 4000 in the hot mixture of glycerol and water and add the glucose warmed to 60 – 80 °C. Incorporate solution (I) in the obtained paste .

3. Properties of the ointment

Brown viscous and turbid paste.

4. Chemical stability

	After production	**After 14 days/52 °C**
Available iodine	0.291%	0.287%
Loss of iodine	–	1.4%

5. Remark

A similar formulation using sucrose instead of glucose is mentioned in the European Patent 0258761 (Kowa).

Povidone-Iodine Lipstick or After Shave Stick (10 %)

1. Formulation

I.	PVP-Iodine 30/06 M 10 (BASF)	10 g
II.	White Mineral Oil	18 g
	Sicovit Titanium dioxide [1]	6 g
III.	Luvitol EHO [1]	22 g
	Cetyl alcohol	5 g
	Bees wax	23 g
	Solid paraffin (mp. 50/55 °C)	15 g
	Cremophor RH 40 [1]	1 g

2. Manufacturing

Melt the mixture III at 60°C, stir it into the suspension II and finally add I. When a homogeneous suspension has been obtained cast the sticks in preformed moulds.

3. Properties

Brown homogeneous sticks

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Liquid Spray (10 %)

1. Formulations

	No. 1	No. 2
PVP-Iodine 30/06	10.0 g	10.0 g
Kollidon VA 64 [1]	15.0 g	15.0 g
n-Propanol	75.0 g	–
Ethanol	–	75.0 g

2. Manufacturing

Dissolve Kollidon VA 64 in the mixture of solvents and add slowly PVP-Iodine to the well stirred solution.
Fill in aerosol cans with propellants like propane+butane or with manual valves.

3. Chemical Stability

The obtained solutions showed no loss of iodine after the storage of 15 days at 60 °C.

Povidone-Iodine Lozenges (5 mg)

1. Formulation

PVP-Iodine 30/06 M 10 (BASF)	5.0 g
Sorbitol, cryst. [10]	150.0 g
Menthol, crystalline	4.0 – 5.0 g
Eucalyptol, crystalline	4.0 – 5.0 g
Aspartame, potassium	1.0 g
Saccharine, sodium	0.1 g
Aerosil 200 [4]	1.0 g
Magnesium stearate [2]	1.0 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve an d press with medium compression force.

3. Tablett properties

Weight	176 mg
Diameter	8 mm
Form	biplanar
Hardness	100 N
Disintegration in water	> 10 min
Friability	0.2 %

6.7 Formulations of semi-solid drugs (Lab scale)

Povidone-Iodine Mastitis Cream for Cattles (10 %)

1. Formulation

I.	PVP-Iodine 30/06 (BASF)	10 g
II.	Liquid paraffin	10 g
	Vaseline	10 g
	Cetylstearyl alcohol	5 – 8 g
	Cremophor A 6 [1]	2 g
	Cremophor A 25 [1]	2 g
III.	Propylene glycol Pharma [1]	5 g
	Water	53 – 56 g

2. Manufacturing

Dissolve PVP-Iodine I in the solvents III. Mix the components II by heating, stir the solution I/III in the molten mixture II and cool by stirring.

3. Stability (52 °C, 14 days)

The cream is physically stable and shows no loss of iodine.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Mouth Wash and Gargle Solution Concentrate (7.5 %)

1. Formulation

I.	PVP-Iodine 30/06 (BASF)	7.5 g
	Saccharin sodium	0.5 g
	Water	15.0 g
II.	Menthol	0.2 g
	Anise oil + eucalyptus oil, 1+1	0.1 g
	Lutrol E 400 [1]	15.0 g
	Ethanol 96 %	50.0 g

2. Manufacturing

Dissolve PVP-Iodine and saccharin in water and mix with solution II.

3. Properties of the concentrate

Brown transparent liquid having a fresh odour.

4. Chemical stability (20–25 °C)

	0 Months	6 Months	12 Months
Available iodine	0.91 %	0.89 %	0.82 %
Loss of iodine	–	2.2 %	2.2 %

5. Administration

Dilute 10 – 20 ml with a glass of water. A brown liquid is obtained having a fresh taste.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Ophthalmic Solution (0.4 %)

1. Formulation

PVP-Iodine 30/06	0.40 g
Potassium iodide	0.20 g
Potassium iodate	44.8 mg
Sodium chloride	1.74 g
Sodium hydroxide solution, 0.01 molar	0.05 g
Water	97.56 g

2. Manufacturing

Dissolve PVP-Iodine slowly in the solution of the salts.

3. Properties of the solutions

Clear, brown liquid of low viscosity.

4. Chemical stability (Stress test at 52 °C)

	Initial	After 14 days
pH	6.2	6.7
Available iodine	0.055 %	0.053 %
Loss of iodine	–	3.6 %
Free iodine	1.9 ppm	1.9 ppm

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Ophthalmic Solution (1.0 %)

1. Formulation

PVP-Iodine 30/06	1.00 g
Potassium iodide	0.50 g
Potassium iodate	0.11 g
Water	98.39 g

2. Manufacturing

Dissolve PVP-Iodine slowly in the solution of the salts.

3. Properties of the solutions

Clear, brown liquid of low viscosity.

4. Chemical stability (Stress test at 52 °C)

	Initial	After 14 days
pH	6.3	7.2
Available iodine	0.15 %	0.16 %
Loss of iodine	–	0 %
Free iodine	1.9 ppm	2.2 ppm

Povidone-Iodine Powder Spray

1. Formulation

I. PVP-Iodine 30/06 M 10 (BASF).....25.0 g
Maize PO_4 Aerosol (Hauser) .....25.0 g
II. Isopropyle myristate .....1.5 g
Dow Corning 344 Fluid (DOW).....10.0 g
Pentane .....50. g
III. Propane + butane, 1+3.....22.0 g

2. Manufacturing

Suspend PVP-Iodine and Maize-PO4-Aerosol (I) in the liquid mixture II and fill in aerosol cans with the propellants III.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Pump Spray (1%)

1. Formulation

PVP-Iodine 30/06 (BASF)	1.00 g
Water	10.00 g
Potassium iodide	0.10 g
Xylitol	10.00 g
Propylene glycol Pharma [1]	78.75 g
Menthol, crystalline	0.10 g
Peppermint oil double rect.	0.05 g

2. Manufacturing

Dissolve potassium iodide in water, warm up to 40 °C and dissolve xylitol. At room temperature dilute with propylene glycol, dissolve PVP-Iodine and add the flavours.

3. Properties of the solution

Clear brown liquid with a sweet refreshing taste.

4. Chemical stability

After storage of 15 hours at 80 °C a loss on iodine of about 7% has been determined.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Seamless Solutions (10 %)

1. Formulations

	No. 1	No. 2
PVP-Iodine 30/06 (BASF)	10.0 g	10.0 g
Natrosol® HR 250 (Hercules)	1.0 g	–
Lutrol F 127 [1]	0.2 g	–
Sodium hydroxide, 1 molar solution	3.2 g	–
Tylose® M 300 (Hoechst)	–	2.0 g
Texapon® K 12 (Henkel)	–	0.2 g
Citric acid solution 0.1 molar	–	59.5 g
Sodium biphosphate solution 0.2 molar	–	28.3 g
Water	85.6 g	–

2. Manufacturing

Formulation No. 1:
Dissolve Lutrol F 127 and than Natrosol in the water. As soon as both are dissolved add slowly the PVP-Iodine to the well stirred solution. Adjust the pH with the sodium hydroxide solution to about 3.5.

Formulation No. 2:
Dissolve Tylose M 300 in the mixture of the citric acid and sodium biphosphate solutions, add Texapon and slowly dissolve the PVP-Iodine.

3. Properties of the solutions

Brown, clear solutions having a certain viscosity and a pH of 3 – 4.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Shampoo (7.5 %)

1. Formulation

PVP-Iodine 30/06 (BASF) .....7.5 g
Neutronyx® S 60 (Onyx) .....25.0 g
Super Amide® L 9 (Onyx) .....4.0 g
Natrosol® 250 HR (Hercules) .....0.5 – 0.7 g
Water .....ad 100 g

2. Manufacturing

Dissolve Super Amide and Natrosol in hot water (about 60 °C) and then dissolve PVP-Iodine. After cooling incorporate Neutronyx.

3. Properties of the shampoo

Brown, clear solution. The viscosity can be changed by modification of the amount of Natrolsol 250 HR.

4. Chemical stability

In the stress test (14 days, 52 °C) the loss of available iodine was about 12 %.

Povidone-Iodine Soft Gel (1%)

1. Formulation

PVP-Iodine 30/06 (BASF).....1.0 g
Natrosol® HR 250 (Hercules).....2.5 g
Water.....96.5 g

2. Manufacturing

Dissolve PVP-Iodine and Natrosol HR 250 in the well stirred water.

3. Properties of the gel

Appearance.....Clear brown gel.
Viscosity (Brookfield, 23°C).....31,500 mPa · s

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Solution (10 %), I

1. Formulations

	No. 1	No. 2
PVP-Iodine 30/06 (BASF)	10.0 g	10.0 g
Lutrol F 127 [1]	–	0.3 g
Lutrol E 400 [1]	–	0.5 g
Citric acid 0.1 molar solution	43.6 g	43.2 g
$Na_2HPO_4 \cdot 12H_2O$ 0.2 molar solution	46.4 g	46.0 g

2. Manufacturing

Dissolve the PVP-Iodine (and Lutrol F 127) in the mixture of the buffer solutions (and Lutrol E 400).

3. Properties of the solutions

Brown clear solutions having a low viscosity and pH of about 4.5.

4. Chemical stability of formulation No. 1 (20–25 °C, 1 year)

	0 Month	6 Months	12 Months
Available iodine	100 %	100 %	96 %
pH	4.4	4.1	4.4

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Solution (10 %), II

1. Formulation

I.	PVP-Iodine 30/06 (BASF)	10.00 g
II.	Texapon® K 12 (Henkel)	0.03 g
III.	Sodium biphosphate (Na_2HPO_4)	0.14 g
	Sodium citrate	0.03 g
	Sodium hydroxyde solution, 1 molar	2.08 g
	Glycerol	1.00 g
	Water	86.42 g

2. Manufacturing

Dissolve Texapon K 12 (II) in solution III and add slowly PVP-Iodine to the well stirred solution.

3. Properties of the solution

Brown transparent liquid having a pH of 4.5.

4. Chemical stability

	After production	After 14 days/52 °C
pH	4.5	3.5
Available iodine	1.08 %	1.03 %
Loss of iodine	–	4.6 %

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Surgical Scrubs (7.5 %), I

1. Formulations

	No. 1	No. 2
PVP-Iodine 30/06 (BASF)	7.5 g	7.5 g
Neutronyx® S 60 (Onyx)	25.0 g	–
Lutensit® AES (BASF)	–	25.0 g
Monoamide® 150 MAW (Mono)	–	4.0 g
Super Amide® L 9 (Onyx)	4.0 g	–
Floral Bouquet	q. s.	q. s.
Water	63.5 g	63.5 g

2. Manufacturing

Dissolve Super Amide or Monoamide in hot water, cool, dissolve PVP-Iodine and add Neutronyx or Lutensit.

3. Properties of the scrub

Brown, clear viscous solution. The pH of formulation No. 1 is about 3.4

4. Chemical stability of formulation No. 1 (20–25 °C)

	0 Month	6 Months	12 Months
Available iodine	100 %	99 %	87 %
pH	3.6	4.3	4.6

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Surgical Scrubs (7.5 %), II

1. Formulations

	No. 1	No. 2	No. 3
PVP-Iodine 30/06 (BASF)	7.5 g	7.5 g	7.5 g
Texapon® K 12 (Henkel)	15.0 g	–	–
Lutensit® A-ES (BASF)	–	18.7 g	–
Fenopon® CO 436 (Rhône-Poulenc)	–	–	20.0 g
Super Amide® L 9 (Onyx)	4.0 g	4.0 g	1.2 g
Glycerol	–	–	25.0 g
Water	73.5 g	68.8 g	46.3 g

2. Manufacturing

Dissolve the surfactants in hot water (add glycerol) and incorporate the PVP-Iodine.

3. Properties of the scrubs

Brown, clear viscous solution.

4. Stability (14 days at 52 °C)

	No. 1	No. 2	No. 3
Loss of available iodine	12.2 %	13.9 %	10.8 %

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Teat-Dip Solution for Cattles (3 %)

1. Formulation

PVP-Iodine 30/06 (BASF)	3.00 g
Glycerol	8.00 g
Glacial acetic acid	0.80 g
Sodium hydroxide solution, 50 %	0.35 g
Water	ad 100.0 g

2. Manufacturing

Mix all liquid components and dissolve PVP-Iodine.

3. Properties of the solution

Brown transparent liquid having a pH of 4.3.

4. Chemical stability

After the storage at 52 °C during 14 days the loss of available iodine was 11.5 %.

Povidone-Iodine Transparent Ointment (10 %)

1. Formulation

I.	PVP-Iodine 30/06 (BASF)	10.0 g
	Lutrol E 400 [1]	60.0 g
	Sodium hydroxide, 1 molar solution	4.6 g
	Water	0.4 g
II.	Lutrol E 4000 [1]	25.0 g

2. Manufacturing

Prepare solution I, heat to about 60 °C, incorporate II stirring very well and cool to room temperature.

3. Properties

Transparent ointment like a gel having a ph of 4. Miscible and washable with water.

4. Stability (14 days, 52 °C)

The content of available iodine dropped only to 99% and the pH to 3.6.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Vaginal Douche Concentrate (10 %)

1. Formulation

PVP-Iodine 30/06 (BASF) .....10.0 g
Lutrol E 400 [1].....0.5 g
Lutrol F 127 [1].....0.3 g
Citric acid, 0.1 molar solution .....43.2 g
$Na_2HPO_4 \cdot 12H_2O$, 0.2 molar solution .....46.0 g

2. Manufacturing

Dissolve PVP-Iodine and Lutrol F 127 in the mixture of the buffer solutions with Lutrol E 400.

3. Properties of the solution

Brown, clear solution having a low viscosity and a pH of about 4.3.

6.7 Formulations of semi-solid drugs (Lab scale)

Povidone-Iodine Vaginal Ovula (5 %)

1. Formulation

PVP-Iodine 30/06 M 10 (BASF) .....5 g
Lutrol E 400 [1].....10 g
Lutrol E 4000 [1].....85 g

2. Manufacturing

Melt the Lutrol E grades by gentle heating. Stir in the micronized PVP-Iodine product in small portions into the melt.

After a uniform suspension has been obtained, pour it into polyethylene moulds.

3. Properties

Homogeneous brown coloured ovula having a weight of 2.0 g.

4. Chemical stability

In a stress test (14 days/52 °C) and at room temperature (one year) no loss of available Iodine were measured.

Povidone-Iodine Vaginal Ovula (10 %)

1. Formulation

PVP-Iodine 30/06 M 10 (BASF).....10 g
Lutrol E 400 [1] .....5 g
Lutrol E 1500 [1].....50 g
Lutrol E 4000 [1].....35 g

2. Manufacturing

Melt the Lutrol E grades by gentle heating. Stir in the micronized PVP-Iodine product in small portions into the melt.

After a uniform suspension has been obtained, pour it into polyethylene moulds.

3. Properties

Homogeneous brown coloured ovula have a weight of 2.0 g.

4. Chemical stability

In a stress test (14 days/52 °C) and at room temperature (one year) no loss of available Iodine were measured.

5.8 Liquid Formulations (Lab scale)

Povidone-Iodine Viscous Solution (1%)

1. Formulation

PVP-Iodine 30/06 (BASF).....1.0 g
Natrosol® HR 250 (Hercules).....1.5 g
(Buffer.....q.s.)
Water.....97.5 g

2. Manufacturing

Dissolve PVP-Iodine and Natrosol in the well stirred water.

3. Properties of the solution

Clear brown viscous liquid.
Viscosity (Brookfield): 7,500 mPa · s

4. Chemical and physical stability

In a stress test (15 hours at 80 °C) the loss of iodine was 13.3 % and no change of the appearance was observed.

Prazosin Tablets (5 mg)

1. Formulations

	No. 1	No. 2
Prazosin hydrochloride, anhydrous (Knoll)	5 g	–
Prazosin hydrochloride, polyhydrate (Knoll)	–	6 g
Ludipress [1]	94 g	93 g
Magnesium stearate [1]	1 g	1 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

Weight	109 mg	103 mg
Diameter	8 mm	8 mm
Form	biplanar	biplanar
Hardness	76 N	74 N
Disintegration	2 min	3 min
Friability	0.2 %	0.2 %

2.9 Tablet formulations (Lab Scale)

Prednisolone Tablets (20 mg)

1. Formulation

Prednisolone	20 g
Lactose monohydrate [8]	155 g
Kollidon VA 64 [1]	10 g
Kollidon CL [1]	8 g
Magnesium stearate [2]	5 g
Aerosil 200 [4]	2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	212 mg
Diameter	8 mm
Form	biplanar
Hardness	63 N
Disintegration	< 1 min
Friability	0.2 %

Prednisone Tablets (10 mg)

1. Formulation

Prednisone	10 g
Ludipress [1]	208 g
Magnesium stearate [2]	2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with low compression force.

3. Tablet properties

Weight	223 mg
Diameter	8 mm
Form	biplanar
Hardness	70 N
Disintegration	4 min
Friability	0.2 %
Dissolution, 15 min	78 %
30 min	82 %

2.9 Tablet formulations (Lab Scale)

Probenecid Tablets (500 mg)

1. Formulation

I.	Probenecid	500 g
	Corn starch [3]	130 g
II.	Kollidon 30 [1]	10 g
	Ethanol 96%	70 ml
III.	Kollidon CL [1]	25 g
	Aerosil 200 [4]	3 g
	Magnesium stearate [2]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, add III and press with low compression force.

3. Tablet properties

Weight	674 mg
Diameter	12 mm
Form	biplanar
Hardness	54 N
Disintegration	9 min
Friability	0.3%
Dissolution, 5 min	43%
60 min	100%

5.8 Liquid Formulations (Lab scale)

Procain Penicillin Injectable Suspension (300 mg/ml)

1. Formulation

I.	Procain Penicillin G	30.0 g
II.	Kollidon 17 PF [1]	0.4 g
	Carboxymethyl cellulose	0.15 g
	Sodium citrate	0.57 g
	Antioxidant	q.s.
	Preservative	q.s.
	Water of injectables	ad 100 ml

2. Manufacturing

Suspend procain penicillin G in the well stirred solution II.

3. Properties of the suspension

Aspect	homogeneous
Redispersibility	easy

4. Remark

To prevent of discolouration of the dissolved Kollidon during storage 0.2 to 0.5% of cysteine could be added as antioxidant.

5.8 Liquid Formulations (Lab scale)

Propanidide Injectable Solution (50 mg/ml)

1. Formulation

I.	Propanidide	5.0 g
	Cremophor EL [1]	20.0 g
II.	Preservatives	q. s.
	Water for injectables	ad 100 ml

2. Manufacturing

Mix propanidide with the warm Cremophor EL (60 °C) and add slowly the warm solution II. The sterilisation can be done by filtration or heat.

3. Properties of the solution

A clear colourless solution was obtained.

4. Remarks

- To reduce the viscosity and the side effects, Cremophor EL could be substituted by Solutol HS 15 [1].
- In Germany Cremophor EL must be declared on the package of injectables.
- During the heat sterilisation a separation of two layers can be observed. Shaking of the ampoules during cooling gives homogeneous clear solutions.

2.9 Tablet formulations (Lab Scale)

Propranolol Hydrochloride Tablets (10 mg, 50 mg and 100 mg)

1. Formulation

	No. 1: 10 mg	No. 2: 50 mg	No. 3: 100 mg
Propranolol hydrochloride	10 g	50 g	100 g
Ludipress [1]	490 g	450 g	400 g
Magnesium stearate [2]	2.5 g	2.5 g	2.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

	No. 1	No. 2	No. 3
Weight	514 mg	496 mg	505 mg
Diameter	12 mm	12 mm	12 mm
Form	biplanar	biplanar	biplanar
Hardness	112 N	86 N	101 N
Disintegration	2 min	2 min	3 min
Friability	0.1%	0.2%	0.1%

4. Remarks

- In the case of formulation No. 1 or No. 2 the amount of Ludipress and the tablet weight could be reduced.
- These formulations can be used for tablet cores, too.

2.9 Tablet formulations (Lab Scale)

Propranolol Tablets Cores (40 mg)

1. Formulation

Propranolol	40.0 g
Ludipress [1]	108.0 g
Magnesium stearate [2]	0.3 g
Stearic acid [7]	0.4 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

Weight	150 mg
Diameter	8 mm
Form	biconvex
Hardness	75 N
Disintegration	3 min
Friability	0.2 %

3.5 Coating formulations (Lab Scale)

Protective Film Coating with Ethyl Cellulose + Kollidon VA 64

1. Formulation

I.	Kollidon VA 64 [1]	5 g
	Ethocel® 20 (Dow)	5 g
	Sicovit Titanium dioxide [1]	20 g
	Talc	13 g
	Sicovit Colour lake [1]	q. s.
	Isopropanol	98 g
	Water	59 g
II.	Isopropanol	140 g
	Water	60 g

2. Manufacturing of the suspension

Dissolve Ethocel and Kollidon VA 64 in isopropanol, add the water and suspend the colorants and the talc. Pass this mixture through a colloid mill and add solution II.

3. Coating procedure (Fludized bed)

Tablet core loading	5 kg
Inlet air temperature	40 °C
Outlet air temperature	38 °C
Inlet flap	Position 10
Outlet flap	Positon 4
Spraying pressure	3 bar
Spraying time	15 min.
Final drying	2 min.
Quantity of film forming agent/cm^2	1 mg

3.5 Coating formulations (Lab Scale)

Protective Film Coating with Hydroxypropyl Cellulose + Kollidon VA 64

1. Formulations

	No. 1	No. 2
Kollidon VA 64 [1]	20 g	20 g
Klucel® EF (Hercules)	20 g	20 g
Talc	20 g	–
Sicovit Colour lake or Pigment [1]	q. s.	q. s.
Isopropanol	–	760 g
Water	740 g	–

2. Manufacturing of the suspension

Dissolve Klucel and Kollidon VA 64 in isopropanol or water and suspend the colorants and the talc. Pass this mixture through a colloid mill.

3. Coating procedure (Sugar coating pan)

	No. 1	No. 2
Tablet core loading	2 kg	2 kg
Amount of coating suspension	800 g	800 g
Spray phase	3 s	6 s
Interval	0.5 s	0.5 s
Drying phase (warm air)	6 s	6 s
Interval	2 s	2 s
Nozzle (Walther WA XV)	0.8 mm	0.8 mm
Quantity of sprayed suspension/min	6.8 g	25 g
Quantity of solids applied on each tablet core	3.1 mg	3.2 mg
Total coating time	5 – 6 h	1 h

3.5 Coating formulations (Lab Scale)

Protective Film Coating with Hydroxypropylmethyl Cellulose + Kollidon VA 64

1. Formulation

I.	Kollidon VA 64 [1]	53 g
	Lutrol E6000 [1]	12 g
	HPMC 6 mPa · s (e. g. Pharmacoat® 606, Shin-etsu)	79 g
	Water	732 g
II.	Sicovit Titanium dioxide [1]	36 g
	Sicovit Iron oxide Red 30 [1]	18 g
	Talc [10]	54 g
	Water	216 g
		1200 g

2. Manufacturing of the suspension

Dissolve Lutrol E6000 and Kollidon VA 64 in 732 ml of water, add HPMC and stirr 45 min avoiding the formation of too much of air bubbles.
Suspend the pigments and talc in 216 ml of water and pass this mixture through a colloid mill.
To obtain the final coating suspension mix solution I with suspension II.

3. Coating procedure (Accela Cota 24″)

Tablet core loading	5.0 kg
Core size	9 mm biconvex
Amount of coating suspension applied	1.2 kg
Inlet air temperature	60 °C
Outlet air temperature	40 °C
Nozzle	1.0 mm
Rotation speed of the pan	12 rpm
Spraying pressure	2.0 bar
Spraying rate	50 g/min
Spraying time (continuously)	34 min
Final drying	2 min
Drying after spraying	5 min at 60 °C
Quantity of film former applied	3.14 mg/cm^2

3.5 Coating formulations (Lab Scale)

Protective Film Coating with Kollidon VA 64

1. Formulation

Kollidon VA 64 [1]	50 g
Lutrol E 6000 [1]	40 g
Glycerol	5 g
Sicovit Iron oxide or Lake [1]	15 g
Sicovit Titanium dioxide [1]	30 g
Talc [10]	50 g
Water	ad 1,000 g

2. Manufacturing

A 500-g sample of this suspension was passed through a disk mill and sprayed under the following conditions:

Sugar-coating pan

Spray gun	Walther WAXV with 1-mm nozzle
Spraying time	3 sec
Pause	0.5 sec
Dry air	6 sec
Pause	3 sec

Accela Cota 24″ (continuous spraying)

Spray gun	Walther WAXV with 0.8-mm nozzle
Temperature at inlet	45 °C
Temperature at outlet	38 °C
Spraying pressure	2 bar
Spraying time	≥ 50 min

3. Remark

If the film is to sticky a certain part of Kollidon VA 64 should be substituted by HPMC or sucrose.

3.5 Coating formulations (Lab Scale)

Protective Film Coating with Polyvinyl Alcohol + Kollidon VA 64

1. Formulation

I.	Kollidon VA 64 [1]	50 g
	Lutrol E6000 [1]	12 g
	Polyvinyl alcohol (Mowiol® 8,88. Hoechst)	76 g
	Water	840 g
II.	Sicovit Titanium dioxide [1]	37 g
	Sicovit Iron oxide red [1]	18 g
	Talc	56 g
	Water	168 g
		1257 g

2. Manufacturing of the suspension

Dissolve Lutrol E6000 and Kollidon VA 64 in 840 ml of water, add the polyvinyl alcohol and stirr 45 min avoiding the formation of too much of air bubbles.
Suspend the pigments and talc in 168 ml of water and pass this mixture through a colloid mill.
To obtain the final coating suspension mix solution I with suspension II.

3. Coating procedure (Accela Cota 24'')

Tablet core loading	5.0 kg
Amount of coating suspension	1.26 kg
Inlet air temperature	59 °C
Outlet air temperature	46 °C
Nozzle	1.0 mm
Rotation speed of the pan	15 rpm
Spraying pressure	2.0 bar
Spraying rate	15 g/min
Spraying time (continuously)	83 min
Final drying	5 min
Quantity of film former applied	about 3 mg/cm^2

3.5 Coating formulations (Lab Scale)

Protective Film Coating with Shellac + Kollidon 30

1. Formulation

Shellac	177 g
Kollidon 25 or 30 [1]	20 g
Sicovit Titanium dioxide [1]	185 g
Talc	65 g
Cetyl alcohol	15 g
Sorbitane trioleate	30 g
Sicovit Colour lake [1]	50 g
Isopropanol or ethanol	458 g

2. Manufacturing of the coating suspension

Dissolve shellac and sorbitane oleate in the warm solvent and then Kollidon and cetyl alcohol. Add titanium dioxide, talc and the lake and mix in the colloid mill.

3. Application of the coating suspension

About 50 g suspension were applied to 1 kg of tablet cores in a conventional coating pan or in a Accela Cota pan (1 – 2 mg film formers/cm^2)

2.9 Tablet formulations (Lab Scale)

Pseudoephedrine Tablets (60 mg)

1. Formulations

I.	(+) Pseudoephedrine hydrochloride (Knoll)	60 g
II.	Dicalcium phosphate, DI-TAB [9]	95 g
III.	Kollidon 30 [1]	5 g
	Water	q.s.
IV.	Polyethylene glycol 6000, powder [6]	20 g
	Aerosil 200 [4]	2 g

2. Manufacturing

Granulate dicalcium phosphate II with solution III, dry, pass through a 0.8 mm sieve, mix with I, add IV and press with low compression force.

3. Tablet properties

Weight	192 mg
Diameter	8 mm
Form	biplanar
Hardness	82 N
Disintegration	4 min
Friability	0.3 %

2.9 Tablet formulations (Lab Scale)

Pyrazinamide Tablets (500 mg), DC

1. Formulation

Pyrazinamide.....500.0 g
Ludipress [1] .....134.5 g
Kollidon CL [1].....12,0 g
Aerosil 200 [4].....3.5 g

2. Manufacturing (Direct compression)

Mix all components, sieve through a 0.8 mm screen and press with medium compression force.

3. Tablet properties

Weight .....652 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....96 N
Disintegration .....45 seconds
Friability.....0.36 %
Dissolution, 45 min .....89 %

2.9 Tablet formulations (Lab Scale)

Pyrazinamide Tablet (500 mg), WG

1. Formulation

I.	Pyrazinamide	500 g
	Corn starch [3]	50 g
II.	Kollidon 30 [1]	20 g
	Ethanol 96%	approx. 200 ml
III.	Kollidon CL [1]	(5-) 10 g
	Magnesium stearate [2]	6 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, mix with III and press with low compression force.

3. Tablet properties

Weight	605 mg
Diameter	12 mm
Form	biplanar
Hardness	131 N
Disintegration	3 min
Friability	0.25%
Dissolution, 15 min	78%
30 min	96%

2.9 Tablet formulations (Lab Scale)

Ranitidine Tablet Cores (150 mg)

1. Formulation

Ranitidine .....150 mg
Ludipress [1].....147 mg
Magnesium stearate [2].....3 mg

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm screen and press with low compression force.

3. Tablet properties

Weight .....305 mg
Diameter .....8 mm
Form .....biconvex
Hardness.....61 N
Disintegration .....2 – 3 min
Friability.....0.5 %

4. Remark

If the flowability of the tabletting mixture is not sufficient about 1% Aerosil 200 [4] could be added.

2.9 Tablet formulations (Lab Scale)

Ranitidine Tablet Cores (300 mg)

1. Formulation

Ranitidine	300 g
Ludipress [1]	295 g
Magnesium stearate [2]	5 g
Aerosil 200 [4]	5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm screen and press with low compression force.

3. Tablet properties

Weight	600 mg
Diameter	12 mm
Form	biconvex
Hardness	72 N
Disintegration	5 min
Friability	0.6 %
Dissolution, 45 min	95 %

2.9 Tablet formulations (Lab Scale)

Rifampicin Tablets (450 mg)

1. Formulation

I.	Rifampicin	450 g
	Corn starch [3]	58 g
II.	Kollidon 90 F [1]	9 g
	Isopropanol or ethanol 96 %	50 ml
III.	Kollidon CL [1]	15 g
	Stearic acid [7]	10 g
	Magnesium stearate [2]	2 g
	Aerosil 200 [4]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, sieve and mix with the components of III and press with low compression force to tablets.

3. Tablets properties

Weight	550 mg
Diameter	12 mm
Form	biplanar
Hardness	95 N
Disintegration	1 – 2 min
Friability	0.6 %

2.9 Tablet formulations (Lab Scale)

Saccharin Effervescent Tablets (15 mg)

1. Formulation

Saccharin sodium	15 g
Tartaric acid	10 g
Sodium bicarbonate	14 g
Kollidon VA 64 [1]	2 g
Polyethylene glycol 6000, powder [6]	2 g

2. Manufacturing (Direct compression)

Dry saccharin sodium and tartaric acid 1 hour at 100°C. Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	42 mg
Diameter	5 mm
Form	biplanar
Hardness	23 N
Disintegration (45 °C, water)	1 min
Friability	0.6 %

Saccharin Tablets (15 mg)

1. Formulations

	No. 1	No. 2
Saccharin sodium (Roth)	15.0 g	15.0 g
Ludipress [1]	31.0 g	31.0 g
Kollidon CL [1]	2.0 g	2.0 g
Magnesium stearate [2]	0.3 g	0.3 g
Polyethylene glycol 6000, powder [6]	2.0 g	–
Lutrol F 68 [1], milled < 100 µm	–	2.0 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight	51 mg	51 mg
Diameter	5 mm	5 mm
Form	biplanar	biplanar
Hardness	33 N	29 N
Disintegration (water)	< 2 min	< 2 min
Friability	0.2 %	0.2 %

Selegiline Tablets (5 mg)

1. Formulation

Selegiline (Knoll)	5 g
Ludipress [1]	94 g
Magnesium stearate [2]	1 g

2. Manufacturing (Direct compression)

Mix all components intensively, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	99 mg
Diameter	6 mm
Form	biplanar
Hardness	81 N
Disintegration	3 – 4 min
Friability	< 0.1%

Serratio Peptidase Tablets (10 mg)

1. Formulation

Serratio peptidase .....10 g
Ludipress [1] .....228 g
Magnesium stearate [2] .....2 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix intensively and press with low compactation force (6 kN).

3. Tablet properties

Weight .....238 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....80 N
Disintegration .....3 – 4 min
Friability .....< 0.2 %

Silimarin Tablets (35 mg)

1. Formulation

Silimarin.....35.5 g
Ludipress [1] .....410.5 g
Magnesium stearate [2].....4.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force (about 10 kN).

3. Tablet properties

Weight .....458 mg
Diameter .....12 mm
Form .....biplanar
Hardnes.....0.1%
Disintegration .....3 min
Friability .....< 0.1%

2.9 Tablet formulations (Lab Scale)

Simethicone Chewable Tablets (70 mg)

1. Formulation

I.	Simethicone dry powder 25 %	280.0 g
	Sucrose, powder	158.0 g
	Kollidon 90 F [1]	7.0 g
II.	Kollidon 90 F [1]	3.5 g
	Isopropanol	q.s.
III.	Aerosil 200 [4]	2.8 g
	Magnesium stearate [2]	2.8 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add mixture III, mix throroughly, and press with high compression force.

3. Tablet properties

Weight	442 mg
Diameter	12 mm
Form	biplanar
Hardness	40 N
Disintegration	> 30 min
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Simethicone Chewable Tablets (80 mg)

1. Formulation

I.	Simethicone (Wacker Siliconoil S 184)	80 g
II.	Sorbitol, crystalline [10]	400 g
	Aerosil 200 [4]	20 g
III.	Ludipress [1]	390 g
	Menthol, powder	2 g
	Magnesium stearate [2]	8 g

2. Manufacturing (Granulation)

Mix the components II with the simethicone oil I, pass through a 0.8 mm sieve, add mixture III, mix thoroughly, pass again through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

Weight	870 mg
Diameter	16 mm
Form	biplanar
Hardness	81 N
Friability	< 0.1%

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Simethicone Instant Granules (60 mg and 120 mg)

1. Formulation

I.	Simethicone (Abil® 200, Goldschmidt)	10.0 g
	Cremophor RH 40 [1]	5.0 g
II.	Kollidon VA 64 [1]	3.0 g
	Ethanol	40.0 g
III.	Sorbitol, crystalline (Merck)	50.0 g
	Fructose (Merck)	50.0 g
	Kollidon CL-M [1]	50.0 g
	Orange flavour (Dragoco)	0.5 g

2. Manufacturing

Introduce solution II into the mixture I. Granulate the powder mixture III with the well stirred mixture I/II, dry and pass through a 1 mm sieve. Fill 1 or 2 g in sachets.

3. Properties of the granules

- Free flowing white granules;
- 98 % coarser than 50 µm;
- Easily dispersible in cold water without any physical separation during 30 min.

4. Administration

Take the content of one sachet (1 g = 60 mg simethicone or 2 g = 120 mg simethicone) as powder or disperse the recommended amount (e.g. 1 to 2 g) in 100 ml of drinking water.

5.8 Liquid Formulations (Lab scale)

Sobrerol Injectable Solution (75 mg/5 ml)

1. Formulation

Sobrerol	1.5 g
Kollidon 17 PF [1]	6.0 g
Water for injectables	100.0 ml

2. Manufacturing

Dissolve sobrerol slowly in the well stirred solution of Kollidon 17 PF.

The sterilisation can be done by filtration through a 0.2 µm filter.

3. Properties

Appearance	clear
Viscosity	very low

4. Remark

Preservatives could be added if it is needed.

To prevent of discolouration of Kollidon in the solution during storage 0.1 to 0.5% of cysteine could be added as antioxidant.

2.9 Tablet formulations (Lab Scale)

Sodium Fluoride Tablets (0.5 mg)

1. Formulation

Sodium fluoride (Merck)	0.55 g
Sorbitol, crystalline [10]	56.25 g
Dicalcium phosphate, DI-TAB [9]	56.25 g
Kollidon VA 64 [1]	2.20 g
Magnesium stearate [2]	0.50 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

Weight	116 mg
Diameter	6 mm
Form	biplanar
Hardness	144 N
Disintegration	8 – 9 min
Friability	< 0.1%

4. Remark

If the content uniformity is not sufficient a premix of sodium fluoride and sorbitol or DI-TAB should be prepared separately before mixing with the rest of the excipients.

2.9 Tablet formulations (Lab Scale)

Sodium Fluoride Tablets (1.3 mg)

1. Formulation

Sodium fluoride (Merck) .....1.3 g
Ludipress [1] .....76.7 g
Magnesium stearate [2].....0.4 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight .....78 mg
Diameter .....5 mm
Form .....biplanar
Hardness.....82 N
Disintegration .....4 min
Friability .....< 0.1%

4. Remark

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

2.9 Tablet formulations (Lab Scale)

Spironolactone Tablets (25 mg)

1. Formulation

Spironolactone .....25.0 g
Ludipress [1].....175.0 g
Magnesium stearate [2].....1.5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with medium compression force.

3. Tablet properties

Weight .....197 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....153 N
Disintegration.....13 min
Friability .....< 0.1%

2.9 Tablet formulations (Lab Scale)

Spirulina Extract Chewable Tablets (250 mg)

1. Formulation

Spirulina extract, powder .....250 g
Ludipress [1] .....245 g
Polyethylene glycol 6000, powder [6].....25 g
Aerosil 200 [4].....5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight .....495 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....149 N
Disintegration (water).....not tested
Friability.....0.2 %

3.5 Coating formulations (Lab Scale)

Subcoating for Core Protection

1. Formulation

Kollidon VA 64 [1] .....100 g
Ethanol or isopropanol.....900 g

2. Manufacturing (Accela Cota)

Spray the solution onto the warm tablet cores (30 – 40 °C) for few minutes before to continue with the aqueous main coating procedure. The amount of 0.4 mg/cm^2 tablet surface is sufficient for a good subcoating protection.

3. Remark

No plastisizer is needed in this formulation due to the plasticity of Kollidon VA 64.

2.9 Tablet formulations (Lab Scale)

Sucralfate + Sodium Alginate Tablets (500 mg + 20 mg)

1. Formulation

I.	Sucralfate	500 g
	Sodium alginate	20 g
	Corn starch [3]	70 g
II.	Kollidon 30 [1]	20 g
	Ethanol 95%	80 ml
III.	Kollidon CL [1]	30 g
	Magnesium stearate [2]	3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a sieve, mix the dry granules with III and press with low compression force.

3. Tablet properties

Weight	660 mg
Diameter	12 mm
Form	biplanar
Hardness	90 N
Disintegration	3 – 4 min
Friability	0.3%

3.5 Coating formulations (Lab Scale)

Sugar Coating, automatic

(According to Nürnberg, Pharm. Ind. 28,5 (1996) 221 – 304)

1. Formulation of the coating suspension

Sucrose	760 g
Kollidon 30 [1]	80 g
Sicovit Titanium dioxide [1]	90 g
Calcium carbonate	90 g
Talc	290 g
Sicovit Colour lake [1]	q. s.
Glycerol	40 g
Water	630 g

2. Manufacturing of the coating suspension

Dissolve the sucrose in the hot water, than mix with glycerol, dissolve Kollidon 30 and suspend the other components.

3. Coating procedure

4 kg of tablet cores with a weight of 420 mg were sprayed with 2.5 kg of the above suspension in a conventional coating pan under the following conditions:

Spray phase	5 s
Interval	10 min.
Drying phase (warm air)	10 min.
Total coating time	16 h

3.5 Coating formulations (Lab Scale)

Sugar Coating, manual

1. Formulations

	No. 1 White	No. 2 Coloured
Kollidon 30 [1]	16.8 g	16.8 g
Carmelose sodium	14.6 g	14.6 g
Aerosil 200 [4]	10.7 g	10.7 g
Talc	81.0 g	81.0 g
Polysorbate or Cremophor RH 40 [1]	5.3 g	5.3 g
Sicovit Titanium dioxide [1]	70 g	115.0 g
Sicovit Colour lake or Pigment [1]	–	17.3 g
Sucrose	3,135 g	3,135 g
Water	1,650 g	1,650 g

2. Manufacturing of the coating suspensions

Dissolve Kollidon, Polysorbate or Cremophor and sucrose in the water and suspend the other components in this solution. Mix in a colloid mill.

3. Application of the coating suspension

Start with formulation No. 1 by means of the manual sugar coating procedure during some hours. After changing to formulation No. 2 continue with the same procedure until homogeneous coloured sugar coated tablets are obtained.

4. Remark

The polishing can be done by means of a solution of beeswax or polyethylene glycol 6000.

3.5 Coating formulations (Lab Scale)

Sugar Film Coating

1. Formulation of the coating suspension

Sucrose	200 g
Kollidon VA 64 [1]	50 g
Sicovit Titanium dioxide [1]	30 g
Sicovit Colour lake [1]	15 g
Lutrol E 4000 [1]	40 g
Talc	50 g
Water	ad 1200 g

2. Manufacturing of the coating suspension

Dissolve the sucrose, Kollidon VA 64 and Lutrol E 4000 in the water and suspend the other components. Pass through a colloid mill.

3. Coating procedure (Accela Cota 24″)

Tablet core loading	5.0 kg
Amount of coating suspension	1.2 kg
Inlet air temperature	45 °C
Outlet air temperature	35 °C
Nozzle	0.8 mm
Rotation speed of the pan	15 rpm
Spraying pressure	2.0 bar
Spraying time (continuously)	50 min
Quantity of film former applied	4 mg/cm^2

5.8 Liquid Formulations (Lab scale)

Sulfadiazine + Trimethoprim Veterinary Concentrated Oral Suspension (40 % + 8 %)

1. Formulation

Sulphadiazine.....40 g
Trimethoprim.....8 g
Sodium hydroxide .....6 g
Kollidon CL-M [1] .....2 g
Water.....44 g

2. Manufacturing

Dissolve sodium hydroxide in water and suspend the active ingredients and Kollidon CL-M.

3. Properties of the suspension

A homogeneous white suspension was obtained. It showed some sedimentation after 7 days but the redispersibility was very easy. The pH was 12.

2.9 Tablet formulations (Lab Scale)

Sulfadiazine Tablets (450 mg)

1. Formulation

I.	Sulfadiazin	465.0 g
	Lactose monohydrate D 20 [8]	93.0 g
II.	Kollidon 30 [1]	14.0 g
	Water	200.0 g
III.	Kollidon CL [1]	23.4 g
	Talc [10]	1.8 g
	Aerosil 200 [4]	0.2 g
	Calcium arachinate [2]	0.2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add mixture III and press with low compression force.

3. Tablet properties

Weight	602 mg
Diameter	12 mm
Form	biplanar
Hardness	152 N
Disintegration	3 min
Friability	< 0.1%
Dissolution, 10 min	77%
20 min	87%
30 min	89%

5.8 Liquid Formulations (Lab scale)

Sulfadimethoxine Veterinary Injectable Solution (2.5 % = 250 mg/10 ml)

1. Formulation

I.	Sulfadimethoxine	5 g
	Ethanol 96 %	40 ml
	Propylene glycol Pharma [1]	40 ml
II.	Kollidon 12 PF [1]	70 g
	Antioxidant	q. s.
	Water for injectables	q. s. ad 200 ml

2. Manufacturing

Mix solution I slowly with solution II at 60 °C and cool.

3. Properties of the solution

Appearance	clear
pH	7
Viscosity	very low

4. Physical stability (20–25 °C)

No recrystallisation after some weeks.

5. Remark

To prevent of discolouration of Kollidon in the solution during storage 0.2 to 0.5 % of cysteine could be added as antioxidant.

2.9 Tablet formulations (Lab Scale)

Sulfadimidine Tablets (500 mg)

1. Formulation

I.	Sulfadimidine (Cilag)	500.0 g
	Lactose monohydrate [8]	100.0 g
II.	Kollidon 30 [1]	15.0 g
	Water	200.0 g
III.	Kollidon CL [1]	25.0 g
	Talc [10]	2.4 g
	Aerosil 200 [4]	0.3 g
	Calcium arachinate [2]	0.3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press.

3. Tablet properties

Weight	610 mg
Diameter	12 mm
Form	biplanar
Hardness	120 N
Disintegration	2 – 3 min
Friability	0.7 %

5.8 Liquid Formulations (Lab scale)

Sulfadoxine + Trimethoprim Veterinary Injectable Solution (1000 mg + 200 mg/10 ml)

1. Formulation

Sulfadoxine	2.0 g
Trimethoprim	10.0 g
Soluphor P [1]	56.0 g
Water for injectables	29.0 g
Sodium hydroxide	q. s.

2. Manufacturing

Disolve sulfadoxine and trimethoprim in Soluphor P, add the water, and set to pH 8.5 with sodium hydroxide.

3. Properties of the solution

Appearance	clear, colourless
pH	8.5

5.8 Liquid Formulations (Lab scale)

Sulfadoxine Solution (2 % = 20 mg/ml)

1. Formulation

I.	Sulfadoxine	2.0 g
	Lutrol E 400 [1]	68.0 g
II.	Preservative	q. s.
	Water	30.0 g

2. Manufacturing

Prepare solution I at 60 °C. Heat the solution II to the same temperature and mix slowly with solution I.

3. Properties of the solution

A clear, colourless solution of low viscosity was obtained.

4. Physical stability

No change of the clarity after 2 weeks stored at 6 °C and at 20 – 25 °C.

2.9 Tablet formulations (Lab Scale)

Sulfamethoxazole + Trimethoprim Tablets (400 mg + 80 mg)

1. Formulation

I.	Sulfamethoxazole	400 g
	Trimethoprim	80 g
II.	Kollidon 30 [1]	15 g
	Isopropanol	q.s.
III.	Kollidon CL [1]	24 g
	Talc [10]	2 g
	Magnesium stearate [2]	8 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.8 mm sieve, dry, add III and press with low compression force.

3. Tablet properties

Weight	546 mg
Diameter	12 mm
Form	biplanar
Hardness	115 N
Disintegration	9 min
Friability	0.6 %

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Sulfamethoxazol + Trimethoprim Dry Syrup (400 mg + 80 g/10 ml)

1. Formulation

Sulfamethoxazol	4.0 g
Trimethoprim	0.8 g
Sorbitol, crystalline [10]	30.0 g
Sodium citrate	5.0 g
Sodium gluconate	5.0 g
Kollidon CL-M [1]	10.0 g
Vanillin	0.1 g
Saccharin sodium	0.1 g
Chocolate flavour	0.1 g
Sodium benzoate	0.1 g

2. Manufacturing

Mix all components and sieve for administration. Fill 55 g of the mixture in a 100 ml flask.

3. Preparation of the administration form

Shake 55 g of the powder with 100 ml of water until a homogeneous suspension is obtained.

4. Properties of the obtained suspension

No sedimentation during more than 24 hours.

The redispersibility is very easy after 2 weeks.

5.8 Liquid Formulations (Lab scale)

Sulfamethoxazole + Trimethoprim Oral Suspension (400 mg + 80 mg/5 ml)

1. Formulations

		No. 1	No. 2
I.	Sulfamethoxazole	8.0 g	8.0 g
	Trimethoprim	1.6 g	1.6 g
	Kollidon CL-M [1]	3.0 g	–
II.	Sucrose	10.0 g	5.0 g
	Lutrol F 127 or Lutrol F 68 [1]	–	3.0 g
	Water	77.0 g	82.4 g
III.	Vanillin	0.2 g	q.s.
	Chocolate flavour	0.2 g	q.s.

2. Manufacturing

Sieve the components I, suspend in solution II and add the flavours III.

3. Properties of the suspensions

	No. 1	No. 2
Colour:	beige	beige
Viscosity:	very low	very low
Sedimentation after 2 weeks:	not observed	very few
Redispersibility after 2 months:	very easy	easy

5.8 Liquid Formulations (Lab scale)

Sulfamoxole + Trimethoprim Veterinary Injectable Solution (400 mg + 80 mg/10 ml)

1. Formulation

Sulfamoxole	4.0 g
Trimethoprim	0.8 g
Kollidon 12 PF [1]	30.0 g
Parabene	0.2 g
Sodium sulfite or cysteine	0.4 g
Propylene glycol Pharma [1]	10.0 g
Water for injectables	44.6 g
Ethanol	10.0 g

2. Manufacturing

Dissolve Kollidon, parabene, sodium sulfite (or cysteine) in the mixture of water und propylene glycol, heat, add the active ingredients and stir until they are dissolved. Add ethanol, cool and sterilize.

3. Properties of the solution

A clear solution was obtained.

4. Remark

The use of sodium sulfite in injectables is not allowed in all countries.

2.9 Tablet formulations (Lab Scale)

Sulfathiazole Tablets (250 mg)

1. Formulations

		No. 1	No. 2
I.	Sulfathiazole	250 g	250 g
	Lactose monohydrate [8]	237 g	–
	Dicalcium phosphate [9]	–	237 g
	Kollidon 30 [1]	12 g	12 g
II.	Water	q.s.	q.s.
III.	Kollidon CL [1]	12 g	12 g
	Magnesium stearate [2]	2 – 3 g	2 – 3 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solvent II, pass through a 0.8 mm sieve, dry, add III and press with low compression force.

3. Tablet properties

Weight	504 mg	512 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	115 N	154 N
Disintegration	1 min	< 1 min
Friability	0.2 %	0.2 %
Dissolution, 10 min	80 %	69 %
20 min	96 %	90 %

Sulfathiazole Veterinary Injectable Solution (8 mg/ml)

1. Formulation

Sulfathiazole	0.8 g
Kollidon 12 PF or Kollidon 17 PF [1]	12.5 g
Sodium sulfite	< 0.1 g
Water for injectables	100.0 g

2. Manufacturing

Dissolve Kollidon and sulfathiazole at 70 °C in water and cool slowly to room temperature.

Sterilisation can be done by filtration through a 0.2 filter.

3. Properties of the solution

Appearance	clear
Viscosity	very low

4. Remarks

A preservative can be added if needed.

To prevent of discolouration of Kollidon in the solution during storage 0.2 to 0.5% of cysteine could be added as antioxidant instead of sodium sulfite.

5.8 Liquid Formulations (Lab scale)

Sulfathiazole Veterinary Oral Solution (8 mg/ml)

1. Formulation

Sulfathiazole	0.8 g
Kollidon 25 [1]	22.5 g
Preservative	q.s.
Water	100.0 ml

2. Manufacturing

Dissolve Kollidon 25 and Sulfathiazole at 70 °C in water and cool slowly to room temperature.

3. Properties of the solution

Appearance	clear
Viscosity	low

4. Remark

An antioxidant to stabilize the colour of solution could be added (0.02% sodium bisulfite or 0.5% cysteine).

2.9 Tablet formulations (Lab Scale)

Tannin-Crospovidone Complex Tablets (55 mg + 230 mg)

1. Formulation

I.	Tannic acid	55.0 g
	Water	230.0 g
II.	Kollidon CL [1]	230.0 g
III.	Avicel PH 101 [5]	33.0 g
	Talc [10]	2.6 g
	Aerosil 200 [4]	0.3 g
	Calcium arachinate [2]	0.3 g

2. Manufacturing

Prepare solution I, suspend II and filtrate the formed insoluble tannin-crospovidone complex. Wash with water until the water is clear, pass the solids through a 0.8 mm sieve and dry. Add the components III and press with low compression force.

3. Tablet properties

Weight	323 mg
Diameter	12 mm
Form	biplanar
Hardness	40 N
Disintegration	< 1 min
Friability	0.8 %

2.9 Tablet formulations (Lab Scale)

Terazosin Tablets (1 mg and 5 mg)

1. Formulations

	1 mg	5 mg
Terazosin hydrochloride (Knoll)	1.1 g	5.5 g
Ludipress [1]	98.0 g	94.0 g
Magnesium stearate [2]	1.0 g	1.0 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix intensively and press with low compression force (10 kN).

3. Tablet properties

Weight	98.1 mg	97.6 mg
Diameter	6 mm	6 mm
Hardness	94 N	105 N
Disintegration	5 min	5 min
Friability	0.1%	< 0.1%
Dissolution, 5 min	59%	41%
10 min	97%	97%
20 min	100%	100%

4. Remark

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

5.8 Liquid Formulations (Lab scale)

Terfenadine Suspension (60 mg/5 ml = 1.2 %)

1. Formulation

Terfenadine	1.2 g
Lutrol F 127 [1]	3.0 g
Cremophor RH 40 [1]	3.6 g
Preservative	q.s.
Water	92.2 g

2. Manufacturing

Dissolve Lutrol F 127 and Cremophor RH 40 in water at 40 °C. Whilst stirring slowly add the terfenadine.

3. Properties of the suspension

A tasteless milky suspension was obtained.

4. Physical stability

After 7 days of storage at room temperature almost no sedimentation of the terfenadine was observed but the redispersibility by shaking (2 times) was very easy.

2.9 Tablet formulations (Lab Scale)

Terfenadine Tablets (60 mg)

1. Formulation

Terfenadine .....60 mg
Ludipress [1] .....235 mg
Kollidon CL [1].....6 mg
Magnesium stearate [2].....1 mg

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with very low compressive force.

3. Tablet properties

Weight .....301 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....183 N
Disintegration .....5 min
Friability .....< 0.1%

Tetracycline Tablets (125 mg)

1. Formulation

Tetracycline hydrochloride (Welding)	125 g
Ludipress [1]	100 g
Avicel PH 101 [5]	42 g
Magnesium stearate [2]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with very low compression force.

3. Tablet properties

Weight	278 mg
Diameter	8 mm
Form	biplanar
Hardness	64 N
Disintegration	1 – 2 min
Friability	< 0.1%

4. Physical stability (12 months, 20–25 °C)

Weight	278 mg
Diameter	8 mm
Form	biplanar
Hardness	63 N
Disintegration	1 – 2 min
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Tetracycline Tablets (250 mg)

1. Formulation

I.	Tetracycline hydrochloride	250.0 g
	Lactose monohydrate D 20 [8]	175.0 g
	Kollidon 30 [1]	15.0 g
	Kollidon CL [1]	25.0 g
II.	Talc [10]	28.0 g
	Aerosil 200 [4]	3.5 g
	Calcium arachinate [2]	3.5 g

2. Manufacturing (Direct compression)

Pass the components I through a 0.5 mm sieve, add the mixture II and press with low compression force.

3. Tablet properties

Weight	505 mg
Diameter	12 mm
Form	biplanar
Hardness	62 N
Disintegration	3 min
Friability	0.5 %

Tetrazepam Tablets (50 mg)

1. Formulation

Tetrazepam	50 g
Avicel PH 101 [5]	113 g
Starch 1500 (Colorcon)	30 g
Kollidon VA 64 [1]	5 g
Magnesium stearate [2]	2 g

2. Manufacturing (Direct compression)

Pass the components through a 0.5 mm sieve and press with low compression force.

3. Tablet properties

Weight	208 mg
Diameter	8 mm
Form	biplanar
Hardness	106 N
Disintegration	1 – 2 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Theophylline + Ephedrine Tablets (130 mg + 15 mg)

1. Formulation

Theophylline 0.1/0.4 mm (Knoll).....130 g
Ephedrine hydrochloride (Knoll) .....15 g
Ludipress [1] .....150 g
Aerosil 200 [4].....2 g
Magnesium stearate [2] .....2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with very low compression force.

3. Tablet properties

Weight .....302 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....141 N
Disintegration .....9 min
Friability.....0.1%
Dissolution of Theophylline 15 min 45%
30 min 85%
60 min 97%

2.9 Tablet formulations (Lab Scale)

Theophylline Tablets (100 mg)

1. Formulation

Theophylline 0.1/0.4 mm (Knoll).....100 g
Ludipress [1] .....147 g
Magnesium stearate [2] .....3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with low compression force.

3. Tablet properties

Weight .....247 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....83 N
Disintegration .....2 min
Friability .....0.15 %

5.8 Liquid Formulations (Lab scale)

Theophylline Injectable Solution (200 mg/5 ml)

1. Formulation

Theophylline (Knoll) .....2 g
Kollidon 12 PF [1] .....15 g
Propylene glycol Pharma [1] .....10 g
Preservative .....q.s.
Antioxidant.....q.s.
Water for injectables .....ad 50 g

2. Manufacturing

Dissolve Kollidon 12 PF and the preservative/antioxidant in water and add theophylline to the well stirred solution

3. Properties of the solution

The obtained clear and somewhat yellowish solution had got the pH value 5.2 and did not recrystallize in a short term test.

4. Remarks

To prevent of discolouration of Kollidon in the solution during storage 0.2 to 0.5% of cysteine could be added as antioxidant.

6.7 Formulations of semi-solid drugs (Lab scale)

Tretinoin + Alpha Bisabolol Gel (50 mg + 100 mg/100 g)

1. Formulation

I.	Tretinoin (BASF)	0.05 g
	Lutrol E 400 [1]	5.0 g
	Cremophor RH 40 [1]	6.0 g
	Butylhydroytoluene	0.04 g
	(-)alpha-Bisabolol, natural (BASF)	0.1 g
II.	Water	70.3 g
	Preservatives	q.s.
III.	Lutrol F 127 [1]	18.5 g

2. Manufacturing

Add solution II slowly to the clear solution I at about 40 °C. Heat to about 50 °C and dissolve about 14 g of III in the combined solution I/II. Cool to about 6 °C and dissolve the rest of III. Maintain cool until the air bubbles escaped.

3. Properties of the gel

A clear yellowish gel was obtained.

4. Chemical stability (20–25 °C, dark)

	0 Months	6 Months	12 Months
Tretinoin content	100 %	100 %	96 %

There was no loss of alpha bisabolol during these 12 months.

5. Remark

It is important to protect this formulation against light to avoid the isomerization and degradation of tretinoin.

6.7 Formulations of semi-solid drugs (Lab scale)

Tretinoin + Dexpanthenol Gel (50 mg + 2,500 mg/100 g)

1. Formulation

I.	Tretinoin (BASF)	50.0 mg
	Lutrol E 400 [1]	5.0 g
	Cremophor RH 40 [1]	6.0 g
	Butylhydroytoluene	40 mg
II.	Water	68.4 g
	Dexpanthenol (BASF)	2.5 g
III.	Lutrol F 127 [1]	18.0 g

2. Manufacturing

Add II slowly to the clear solution I at about 40 °C. Heat to about 50 °C and dissolve about 4 g of III in I/II. Cool to about 6 °C and dissolve the rest of III. Maintain cool until the air bubbles escaped.

3. Properties of the gel

A clear yellowish gel was obtained.

4. Chemical stability (12 months, 23 °C, dark)

Tretinoin	96 %
Dexpanthenol	100 %

5. Remark

It is important to protect the gel against light to avoid the isomerization and degradation of tretinoin.

6.7 Formulations of semi-solid drugs (Lab scale)

Tretinoin Cream (50 mg/100 g)

1. Formulation

I.	Tretinoin (BASF)	0.05 g
	Luvitol EHO [1]	8.0 g
II.	Cremophor A 6 [1]	3.0 g
	Cremophor A 25 [1]	1.5 g
	Glycerol monostearate	3.0 g
	Cetyl alcohol	3.0 g
	Tegiloxan® 100 (Goldschmidt)	0.5 g
III.	Butylhydroxytoluene	0.04 g
	Propylene glycol Pharma [1]	4.0 g
	Preservatives	0.5 g
	Perfumes	0.2 g
	Water	76.2 g

2. Manufacturing

Separately prepare solution I and mixture II by heating to about 75 °C. Heat mixture III until a clear solution is formed. To the warm mixture II add solution I, then mixture III and cool by stirring.

3. Chemical stability (20–25 °C, dark)

Months	Tretinoin content	Loss of tretinoin
0	0.046 %	
3	0.047 %	0 %
6	0.046 %	0 %
9	0.047 %	0 %
12	0.047 %	0 %

Analytical method: Spectrophotometric at 358 nm in chloroform + 2-propanol 1+1 (E 1%/1 cm = 1,480)

4. Remark

It is important to protect the gel against light to avoid the isomerizatio-nand degradation of tretinoin.

Tretinoin Gel (50 mg/100 g)

1. Formulation

I.	Tretinoin (BASF)	0.05 g
	Ethanol	15.0 g
	Cremophor RH 40 [1]	1.0 g
	Perfume	q.s.
	Butylhydroxytoluene	0.04 g
II.	Carbopol® 940 (Goodrich)	0.5 g
	Water	76.0 g
III.	Triethanolamine	0.7 g
	Water	6.6 g

2. Manufacturing

Prepare suspension II and add solution III to the well stirred suspension. When a clear mixture is formed add solution I.

3. Properties

A clear yellowish gel was obtained.

4. Chemical stability (20–25 °C, dark)

No loss of tretinoin was measured after 1 year.

5. Remark

It is important to protect the gel against light to avoid the isomerization and degradation of tretinoin.

5.8 Liquid Formulations (Lab scale)

Tretinoin Solution (50 mg/100 g)

1. Formulation

I. Tretinoin (BASF).....0.05 g
Cremophor RH 40 [1].....14.0 g
Propylene glycol Pharma [1] .....15,0 g
Butylhydroxytoluene .....0.05 g
Alpha Bisabolol nat. (BASF).....0.1 g
II. Water.....70.0 g
Parabenes/sorbic acid .....q.s.

2. Manufacturing

Heat mixture I to 40 – 50 °C to obtain a clear solution. Introduce this warm solution slowly in solution II. It forms a clear yellow solution.

3. Properties of the solution

Clear yellow liquid.

4. Chemical stability (20–25 °C, protected from light)

Months	Tretinoin content
0	0.046 % = 100 %
3	0.046 %
6	0.044 %
9	0.045 %
12	0.044 % = 96 %

5. Remark

It is very important to protect this formulation from light to avoid the isomerization and degradation of tretinoin.

2.9 Tablet formulations (Lab Scale)

Triamcinolone Tablets (4 mg)

1. Formulation

Triamcinolone	4 g
Ludipress [1]	191 g
Kollidon CL [1]	2 g
Magnesium stearate [2]	2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with low compression force.

3. Tablet properties

Weight	206 mg
Diameter	8 mm
Form	biplanar
Hardness	45 N
Disintegration	2 min
Friability	0.2 %

4. Remark

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

Trifluoperazine Tablets (5 mg)

1. Formulation

Trifluoperazine hydrochloride.....5 g
Ludipress [1] .....194 g
Magnesium stearate [2] .....1 g

2. Manufacturing (Direct compression)

Mix all components, pass through a sieve and press with very low compression force.

3. Tablet properties

Weight .....204 mg
Diameter .....8 mm
Form .....biplanar
Hardness.....65 N
Disintegration .....3 min
Friability .....0.15 %

4. Remark

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

6.7 Formulations of semi-solid drugs (Lab scale)

Ultrasonic Adhesive Gel

1. Formulation

I.	Preservative (e.g. Parabenes)	0.5 g
	Water	75.4 g
II.	Carbopol® 940 (Goodrich)	0.6 g
III.	Sodium hydroxide solution 10 %	2.0 g
IV.	Kollidon 30 [1]	1.5 g
	Water	20.0 g

2. Manufacturing

Prepare solution I by heating and add II slowly to obtain a homogeneous suspension. Add the solutions III and IV.

3. Properties of the gel

A clear colourless adhesive gel was obtained.

4. Remark

The addition of salts like sodium chloride would be possible but the consistency could be changed by such modification.

2.9 Tablet formulations (Lab Scale)

Valeriana Extract + Passiflora Extract Tablet Cores (44 mg + 30 mg)

1. Formulation

Valeriana extract, powder	44.0 g
Passiflora extract, powder	36.0 g
Avicel PH 101 [5]	120.0 g
Kollidon CL [1]	11.0 g
Aerosil 200 [4]	3.6 g
Magnesium stearate [2]	7.3 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight	231 mg
Diameter	9 mm
Form	biconvex
Hardness	49 N
Disintegration	10 min
Friability	0.3 %

2.9 Tablet formulations (Lab Scale)

Valproate Sodium Tablets (500 mg)

1. Formulation

I.	Valproate sodium	500 g
	Corn starch [3]	80 g
II.	Kollidon 30 [1]	20 g
	Isopropanol	60 ml
III.	Kollidon CL [1]	5 g
	Magnesium stearate [2]	5 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a sieve, mix the dry granules with III and press with low compression force.

3. Tablet properties

Weight	607 mg
Diameter	12 mm
Form	biplanar
Hardness	162 N
Disintegration	7 min
Friability	0.1%

4. Remark

The powder mixture was electrostatic.

2.9 Tablet formulations (Lab Scale)

Verapamil Tablets (120 mg)

1. Formulation

Verapamil hydrochloride	120 g
Ludipress [1]	270 g
Magnesium stearate [2]	3 g
Aerosil 200 [4]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight	374 mg
Diameter	12 mm
Form	biplanar
Hardness	108 N
Disintegration	5 – 6 min
Friability	0.4 %

4. Remark

The tablet weight should be increased to about 400 mg.

2.9 Tablet formulations (Lab Scale)

Vitamin A + Vitamin B_6 + Vitamin E Tablets (40,000 i.u. + 40 mg + 35 mg)

1. Formulation

Vitamin A acetate dry powder 500,000 i.u./g (BASF)	80 g
Pyridoxine hydrochloride (BASF)	40 g
Vitamin E acetate dry powder SD 50 (BASF)	75 g
Ludipress [1]	395 g
Magnesium stearate [2]	4 g
Aerosil 200 [4]	5 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight	583 mg
Diameter	12 mm
Form	biplanar
Hardness	89 N
Disintegration	13 min
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin A + Vitamin C + Vitamin D_3 Chewable Tablets for Children (2,000 i.u. + 30 mg + 200 i.u.)

1. Formulation

Vitamin A + D_3 dry powder 500,000 + 50,000 i.u./g (BASF)	4.0 g
Ascorbic acid, powder (BASF)	33.0 g
Sucrose, crystalline	300.0 g
Sorbitol, crystalline [10]	300.0 g
Mannitol	300.0 g
Ludipress [1]	300.0 g
Stearic acid [7]	5.0 g
Saccharin sodium	0.1 g
Cyclamate sodium	30.0 g
Flavour mixture (Firmenich)	30.0 g
Polyethylene glycol 6000, powder [6]	20.0 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight	1,290 mg
Diameter	16 mm
Form	biplanar
Hardness	107 N
Disintegration	7 min
Friability	0.4 %

2.9 Tablet formulations (Lab Scale)

Vitamin A + Vitamin C + Vitamin E Tablets (1,200 i.u. + 60 mg + 30 mg)

1. Formulations

	No. 1	No. 2
Vitamin A acetate dry powder 500,000 i.u./g (BASF)	2.4 g	2.4 g
Ascorbic acid, powder (BASF)	60.0 g	60.0 g
Vitamin E acetate dry powder 50%	60.0 g	60.0 g
Mannitol	–	100.0 g
Lactose monohydrate [8]	105,0 g	–
Avicel PH 101 [5]	30.0 g	30.0 g
Kollidon 25 [1]	20.0 g	–
Kollidon VA 64 [1]	–	20.0 g
Kollidon CL [1]	–	5.0 g
Talc [10]	5.0 g	5.0 g
Aerosil 200 [4]	1.0 g	1.0 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	285 mg	279 mg
Diameter	8 mm	8 mm
Form	biplanar	biplanar
Hardness	53 N	67 N
Disintegration	15 min	6 min
Friability	< 0.1%	< 0.1%

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 + Calcium + Magnesium Injectable Solution (33,000 i.u. + 6,000 i. u. + 100 mg + 200 mg/g i.u.)

1. Formulation

I.	Vitamin A palmitate 1.7 Mio i. u./g (BASF)	2.0 g
	Vitamin D_3 (Cholecalciferol) 40 Mio. i. u./g	15 mg
	Solutol HS 15 [1]	13.0 g
II.	Water for injectables	85.0 g
III.	Calcium gluconate	1.1 g
	Magnesium sulfate	1.0 g

2. Manufacturing

Heat mixture I and the water (II) separated to about 65 °C. Add the water very slowly to the well stirred mixture I. Cool to room temperature and dissolve the components III.
After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occurred. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the solutions

A clear yellow solution was obtained.

4. Physical stability (20–25 °C, protected from light)

No change of the clarity after some days.

5. Remark

Perhaps it would be recommendable to use an other magnesium salt instead of the sulfate to avoid any precipitation of calcium sulfate during storage.

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 + Vitamin E + Beta Carotene Veterinary Injectable Solution (100,000 i.u. + 20,000 i.u. + 10 mg + 8 mg/g)

1. Formulation

I.	Vitamin A propionate 2.5 Mio i.u./g (BASF)	4.4 g
	Vitamin D_3 40 Mio i.u./g	0.05 g
	Benzyl alcohol	1.0 g
	Cremophor EL [1]	9.0 g
II.	Water for injectables	72.3 g
III.	Vitamin E acetate	1.0 g
	Butylhydroxytoluene	0.4 g
	Cremophor EL [1]	< 9.0 g
IV.	Beta-Carotene crystalline (BASF)	0.8 g

2. Manufacturing

Heat mixture I to 65 °C. Heat the water II to 65 °C and add it slowly to the heated mixture I. A clear solution is formed (= Mixture I/II).
Heat the mixture III to 180 °C. When the temperature is reached add the beta-carotene IV, hold for 3 min at this temperature and then add Mixture I/II slowly during the next 4 minutes. Let cool under continuous stirring of about 30 minutes. A clear solution is formed.
After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occurred. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the solution

Dark red-brown, clear solution.

4. Remark

In Germany Cremophor EL must be declared on the package of injectables.

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 + Vitamin E Aqueous Injectable Emulsion for Cattles (500,000 i.u. + 75,000 i.u. + 50 mg/ml with Solutol HS 15)

1. Formulation

Vitamin A propionate (2.5 Mio i. u./g (BASF)	22.0 g
Vitamin D3 40 Mio. i. u./g	0.2 g
Vitamin E acetate (BASF)	5.5 g
Butylhydroxytoluene	0.5 g
Solutol HS 15 [1]	15.0 g
Benzyl alcohol	1.0 g
Water for injectables	ad 100 ml

2. Manufacturing

Mix the vitamins, Solutol HS 15, butylhydroxytoluene and benzyl alcohol at approx. 60 °C, and then add the water (60 °C) slowly and with vigorous stirring. – After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occurred. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the emulsion

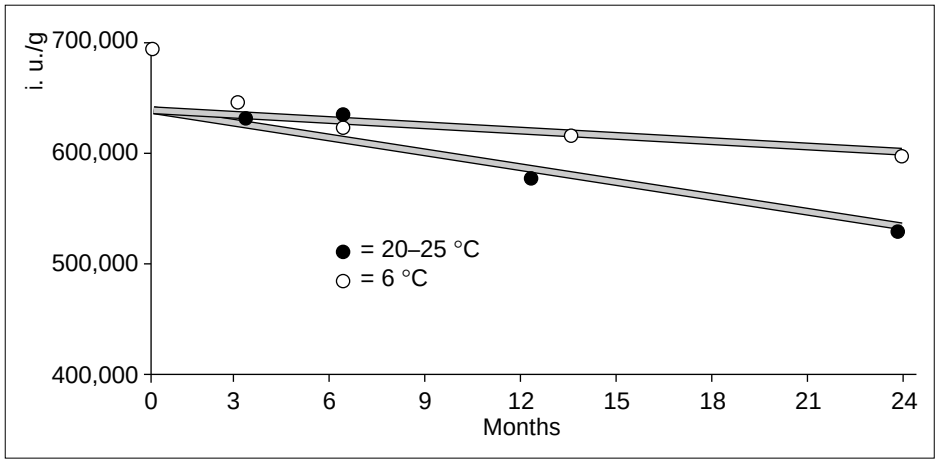
Aspect: Milky, pale yellow emulsion.
Viscosity: Less than 20 mPa · s

4. Physical stability (20–25 °C, protected from light)

No change of the appearance during 2 years.

5. Chemical stability of vitamin A (2 years, protected from light)

Room temperature: 9 % loss after 1 year, 16 % loss after 2 years.



5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 + Vitamin E Aqueous Injectable Emulsion for Cattles (500,000 i.u. + 75,000 i.u. + 50 mg/ml with Cremophor EL)

1. Formulation

Vitamin A propionate .....22.0 g
2.5 Mio i. u./g (BASF)
Vitamin D_3 (Cholecalciferol) .....0.2 g
Vitamin E acetate (BASF) .....5.0 g
Cremophor EL [1] .....10.0 g
Butylhydroxytoluene .....0.5 g
Benzyl alcohol.....1.0 g
Water for injectables.....ad 100 ml

2. Manufacturing

The vitamins, Cremophor EL, butylhydroxytoluene and benzyl alcohol are mixed together at around 60 °C, and water at 60 °C is slowly incorporated with vigorous stirring.
After the ampoules have been sterilized, they should be briefly shaken whilst they are still hot, to eliminate any separation of the phases.

3. Properties of the emulsion

Pale yellow milky, stable emulsion with a viscosity of less than 30 mPa · s.

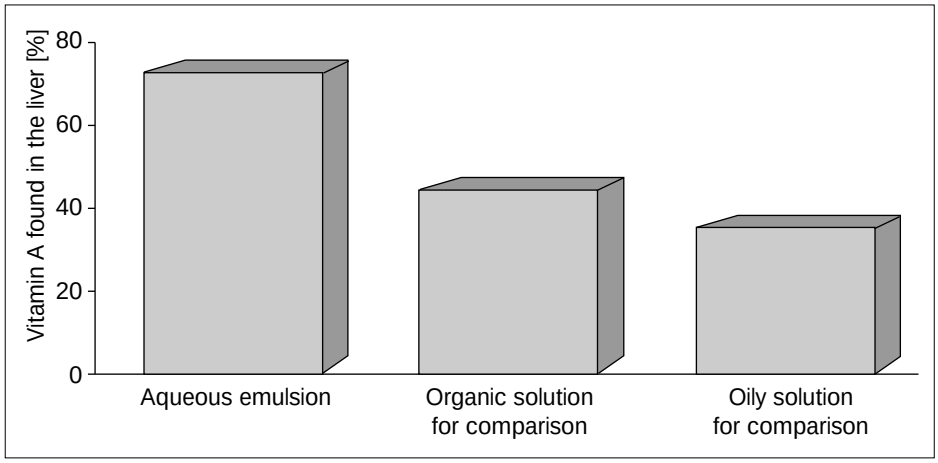
4. Chemical stability of vitamin A (Stress test at 40°C)

	1 Month	2 Months	3 Months
Vitamin A content	92%	86%	81%

5. Remark

In Germany Cremophor EL must be declared on the package of injectables.

6. Bioavailability of vitamin A in broilers after 7 days (intramuscular application)



5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 + Vitamin E Concentrates, Water-miscible (120,000 i.u. + 60,000 i.u. + 40 mg/ml)

1. Formulations

		No. 1	No. 2
I.	Vitamin A palmitate 1.7 Mio. i. u./g (BASF)	7.10 g	–
	Vitamin A propionate 2.5 Mio i. u./g (BASF)	–	4.80 g
	Vitamin D_3 40 Mio i.u./g	0.15 g	0.15 g
	Vitamin E acetate (BASF)	4.20 g	4.20 g
	Butylhydroxytoluene	0.06 g	0.06 g
	Cremophor EL [1]	30.0 g	29.0 g
II.	Glycerol	6.50 g	6.50 g
	Preservative	q.s.	q.s.
	Water	ad 100 ml	ad 100 ml

2. Manufacturing

Heat mixture I to about 65 °C, stir well and add very slowly the warm solution II (65 °C).

3. Properties of the solutions

Yellow, clear viscous liquids, miscible with water.

Clarity:	Formulation No. 1:	28 FTU
	Formulation No. 2:	32 FTU

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 + Vitamin E Injectable Solution in Organic Solvents for Cattles (500,000 i.u. + 75,000 i.u. + 50 mg/ml)

1. Formulation

Vitamin A palmitate 1.7 Mio i.u./g (BASF)	35.0 g
Vitamin D_3 2.0 Mio i.u./g in arachis oil	4.5 g
Vitamin E acetate (BASF)	5.5 g
DL-alpha Tocopherol (BASF)	0.5 g
Butylhydroxyanisole	1.5 g
Cremophor EL [1]	2.5 g
Miglyol® 812 (Dynamit-Nobel)	10.7 g
Benzyl alcohol	2.0 g
Benzyl benzoate	37.8 g

2. Manufacturing

Mix all components at about 60 °C and cool.

3. Properties of the solution

Yellow clear liquid.

4. Chemical stability (stress test at 40 °C)

3 – 4 % loss of vitamin A per month.

5. Remark

In Germany Cremophor EL must be declared on the package of injectables.

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 + Vitamin E Veterinary Injectable Solution (100,000 i.u. + 20,000 i.u. + 10 mg/g)

1. Formulation

I	Vitamin A propionate 2.5 Mio i.u./g (BASF)	4.4 g
	Vitamin D3 40 Mio i.u./g	0.05 g
	Vitamin E acetate	1.0 g
	Cremophor EL [1]	< 15.0 g
	Butylhydroxytoluene	0.4 g
	Benzyl alcohol	1.0 g
II.	Water for injectables	78.1 g

2. Manufacturing

Mix the components I and heat to 65 °C. Heat the water II to 65 °C separately and add it very slowly to the well stirred mixture I. If the obtained yellow solution is not completely clear heat for some minutes more at 65 °C.

After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occurred. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the solution

Clear, yellow liquid of low viscosity.

4. Remark

In Germany Cremophor EL must be declared on the package of injectables.

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 Concentrate, Water-miscible (100,000 i. u./A + 20,000 i. u./D_3/ml)

1. Formulation

Vitamin A palmitate 1.7 Mio. i. u./g (BASF)	6.5 g
Vitamin D_3 40 Mio. i. u./g	55 mg
Butylhydroxytoluene	0.3 g
Cremophor RH 40 [1]	26.0 g
Preservative	q.s.
Water	67.2 g

2. Manufacturing

Mix the vitamins and the antioxidant with Cremophor RH 40 at 65 °C. Add very slowly the solution of the preservative in water, also heated to 65°C, with vigorous stirring.

3. Properties of the concentrate

Clarity:	Clear (27 FTU)
Density (25°C):	1.014 g/ml
Viscosity (25°C):	25 mPa · s

The concentrate is miscible with water and can be processed further to liquid pharmaceuticals.

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 Concentrate, Water-miscible (120,000 i. u. A + 12,000 i.u. D/g)

1. Formulation

I. Vitamin A palmitate .....7.10 g
1.7 Mio i.u./g (BASF)
Vitamin D_3 40 Mio i.u./g .....0.03 g
Butylhydroxytoluene.....0.15 g
Cremophor RH 40 [1].....25.0 g
II. Preservative .....q.s.
Water .....ad 100.0 g

2. Manufacturing

Heat the mixture I to about 65 °C, stir well and add very slowly the warm solution II (65 °C).

3. Properties of the solution

Slightly opalescent, yellow liquid, miscible with water (Clarity: 34 FTU).

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 Drops (30,000 i.u. + 3,000 i.u./g)

1. Formulation

.	Vitamin A palmitate 1.7 Mio i. u./g (BASF)	1.9 g
	Vitamin D_3 40 Mio. i. u./g	7.5 mg
	Cremophor RH 40 [1]	12.0 g
	Butylhydroxytoluene	0.3 g
	Lutrol E 400 [1]	10.0 g
II.	Parabene	0.8 g
	Sorbic acid	0.2 g
	Water	74.8 g

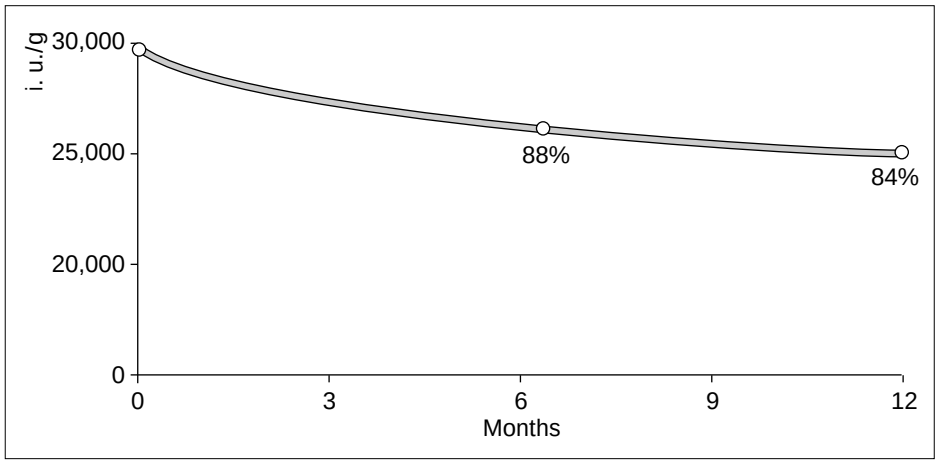
2. Manufacturing

Heat mixture I and solution II to about 65 °C and add II slowly to the well stirred mixture I.

3. Properties of the solution

Yellow clear or slightly opalescent liquid.

4. Chemical stability of vitamin A (about 23 °C)



5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 Injectable Solutions (30,000 i.u. A + 5,000 or 10,000 i.u. D_3/ml)

1. Formulation

	30,000 i.u. A + 5,000 i.u. D_3	30,000 i.u. A + 10,000 i.u. D_3
Vitamin A palmitate 1.7 Mio i.u./g (BASF)	1.9 g	1.9 g
Vitamin D_3 40 Mio i.u./g	0.013 g	0.026 g
Butylhydroxytoluene	0.1 g	0.1 g
Solutol HS 15 [1]	9.0 – 10.0 g	10.0 g
Preservative	q.s.	q.s.
Water for injectables	ad 100 ml	ad 100 ml

2. Manufacturing

Heat the mixture of the vitamins with butylhydroxytoluene and Solutol HS 15 to about 65 °C. Heat the solution of the preservative in water to the same temperature and add it slowly to the well stirred vitamin mixture.

After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occured. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the solutions

Clear yellow solutions where obtained.

4. Physical stability (20–25 °C, protected from light)

No change was observed during 1 year.

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 Oral Solution for Children (1,000 i.u. + 100 i.u. /ml)

1. Formulation

I.	Vitamin A palmitate 1.7 Mio i.u./g (BASF)	60.0 mg
	Vitamin D_3 40 Mio i.u./g	0.3 mg
	Butylhydroxytoluene	0.2 mg
	Cremophor EL or Cremophor RH 40 [1]	3.0 g
II.	Preservative	q.s.
	Flavour	q.s.
	Water	ad 100 ml

2. Manufacturing

Heat mixture I to about 65 °C, stir well and add slowly the hot solution II (65 °C).

3. Properties of the solution

Clear, yellow liquid.

4. Physical stability (20–25 °C)

No change of appearance after 2 weeks.

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin D_3 Syrup (30,000 i.u. + 10,000 i.u. /ml)

1. Formulation

I. Vitamin A palmitate.....1.9 g
1.7 Mio i.u./g (BASF)
Vitamin D_3 40 Mio i.u./g .....25 mg
Cremophor RH 40 .....7.0 g
II. Sugar syrup 50 % .....ad 100 ml

2. Manufacturing

Heat mixture I to about 45 °C, stir well and add slowly the syrup II.

3. Properties of the syrup

Clear, yellow liquid. pH 6.2.

4. Chemical stability of vitamin A (20-25 °C)

	After production	3 Months	6 Months
Vitamin content	100 %	99 %	97 %

2.9 Tablet formulations (Lab Scale)

Vitamin A + Vitamin E Chewable Tablets (30,000 i.u. + 35 mg)

1. Formulation

Vitamin A acetate dry powder .....66 g
500,000 i.u./g (BASF)
Vitamin E acetate dry powder.....70 g
SD 50 (BASF)
Sorbitol, crystalline [10].....425 g
Orange flavour.....15 g
Cyclamate sodium (Merck).....9 g
Polyethylene glycol 6000, powder [6].....15 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight .....602 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....204 N
Disintegration (water) .....> 15 min
Friability .....< 0.1%

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin E Drops (25,000 i. u. + 50 mg/ml)

1. Formulations

		No. 1	No. 2
I.	Vitamin A palmitate 1.7 Mio. i. u./g 1.7 Mio i.u./g (BASF)	1.5 g	1.5 g
	Vitamin E acetate (BASF)	5.0 g	5.0 g
	Cremophor RH 40 [1]	21.0 g	20.0 g
	DL-alpha-Tocopherol (BASF)	1.0 g	–
II.	Preservative	q.s.	q.s.
	Water	71.5 g	72.5 g

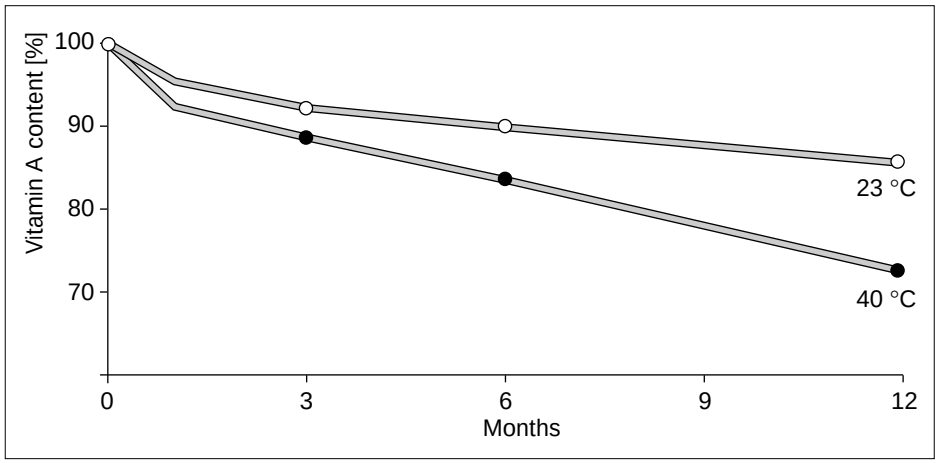
2. Manufacturing

Mix the vitamins with Cremophor RH 40 (and DL-alpha-tocopherol) at 60 °C and then add solution II (at 37 °C) slowly, with stirring.

3. Properties of the solutions

Clear, yellow, viscous liquids.

4. Chemical stability of vitamin A in Formulation No. 2



5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin E Drops (5,000 i.u. + 50 mg/ml)

1. Formulation

I.	Vitamin A palmitate 1.7 Mio i.u./g (BASF)	0.33 g
	Vitamin E acetate (BASF)	6.00 g
	Cremophor RH 40 [1]	15.00 g
II.	Ethanol 96 %	15.00 g
	Water	ad 100 ml

2. Manufacturing

Heat mixture I to about 65 °C, stir well and add slowly the mixture II.

3. Properties of the solution

Colour: yellow
Clarity: clear (turbity units: 25 FTU)

4. Remarks

It must be tested if the ethanol concentration has a sufficient preservative efficiency.

The addition of butylhydroxytoluene as antioxidant would be recommendable.

5.8 Liquid Formulations (Lab scale)

Vitamin A + Vitamin E Injectable Solution for Sheeps (250,000 i.u. + 25 mg/ml)

1. Formulation

I.	Vitamin A propionate	10.0 g
	2.5 Mio i.u./g (BASF)	
	Vitamin E acetate (BASF)	2.5 g
	Butylhydroxytoluene	0.2 g
	Solutol HS 15 [1]	30.0 g
II.	Preservative (e.g. benzyl alcohol)	q.s.
	Water for injectables	57.3 g

2. Manufacturing

Heat mixture I to 70 °C, stir well and add slowly the warm solution II.

After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occured. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the solution

Clarity:	clear to slightly opalescent
pH:	6.3
Colour:	yellow
Viscosity:	45 mPa · s

2.9 Tablet formulations (Lab Scale)

Vitamin A + Vitamin E Tablets (33,000 i.u. + 70 mg)

1. Formulation

Vitamin A acetate dry powder .....69 g
500,000 i.u./g (BASF)
Vitamin E acetate dry powder.....70 g
SD 50 (BASF)
Mannitol, granulated with 10% .....146 g
of Kollidon 30
Kollidon CL [1].....17 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

Weight .....300 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....38 N
Disintegration.....14 min
Friability .....< 0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin A Chewable Tablets (100,000 i. u.)

1. Formulation

Vitamin A acetate dry powder 325,000 i. u./g (BASF)	350 g
Mannitol	350 g
Kollidon VA 64 [1]	25 g
Magnesium stearate (Merck)	5 g
Aerosil 200 [4]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with medium compression force.

3. Tablet properties

Weight	750 mg
Diameter	12 mm
Form	biplanar
Hardness	111 N
Disintegration	24 min
Friability	< 0.1%

5.8 Liquid Formulations (Lab scale)

Vitamin A Concentrate, Water-miscible (100,000 i. u./ml)

1. Formulation

I. Vitamin A palmitate 1.7 Mio i.u./g (BASF)...6.5 g
Butylhydroxytoluene .....0.2 g
Cremophor RH 40 [1].....21.0 g
II. Preservative .....q.s.
Water.....ad 100 ml

2. Manufacturing

Heat the mixture I to about 65 °C, stir well and add very slowly the warm solution II (65 °C).

3. Properties of the solution

Clear, yellow liquid, miscible with water.

4. Physical stability (20–25 °C)

No change of appearance after 3 months.

5.8 Liquid Formulations (Lab scale)

Vitamin A Drops (50,000 i. u./ml)

1. Formulations

		No. 1	No. 2
I.	Vitamin A palmitate 1.7 Mio. i. u./g (BASF)	3.0 g	3.0 g
	Cremophor RH 40 [1]	11.0 g	10.0 g
	Lutrol E 400 [1]	–	5.0 g
	Butylhydoxytoluene (BHT)	0.1 g	0.1 g
II.	Water	85.9 g	81.9 g

2. Manufacturing

Heat the mixture I to about 65 °C, stir very well and add slowly the hot water (65 °C).

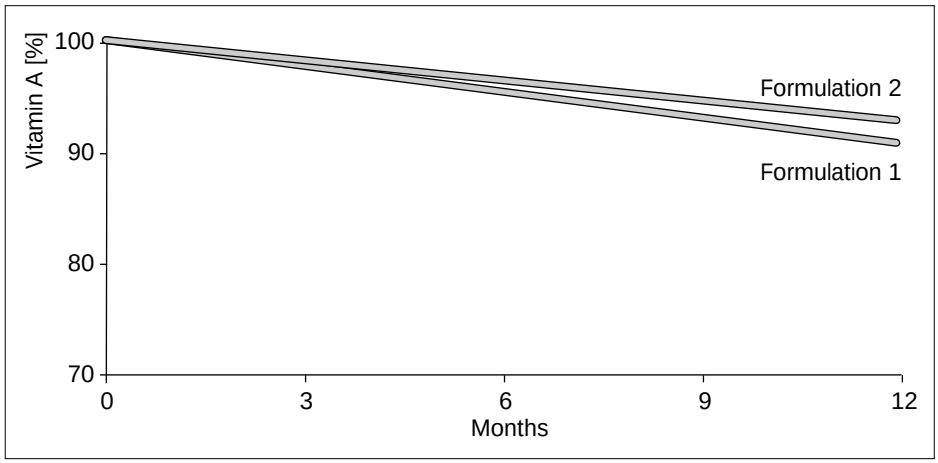
3. Properties of the solutions

Yellow clear or slightly opalescent solutions of low viscosity.

4. Physical stability (20–25 °C, protected from light)

No change of clarity and colour after 1 year.

5. Chemical stability (20–25 °C, protected from light)



5.8 Liquid Formulations (Lab scale)

Vitamin A Ethanolic Veterinary Injectable Solution (500,000 i.u./ml)

1. Formulation

I.	Vitamin A propionate	22.0 g
	Cremophor EL (or Cremophor RH 40) [1]	20.0 g
II.	Benzylalcohol	5.0 g
	Water for injectables	5.0 g
	Ethanol 96%	ad 100 ml

2. Manufacturing

Heat mixture I to about 60 °C, stir well and add slowly the warm solution II.

After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occurred. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the solution

Appearance:	Clear, yellow
Density (25 °C):	0.917 g/ml
Viscosity (25 °C):	12 mPa · s

4. Remark

In Germany Cremophor EL must be declared on the package of injectables.

Vitamin A Suppositories (150,000 i.u.)

1. Formulation

Vitamin A palmitate 1.7 Mio i.u./g (BASF).....9 g
Butylhydroxytoluene .....1 g
Cremophor RH 40 [1] .....40 g
Lutrol E 1500 [1].....80 g
Lutrol E 4000 [1].....50 g

2. Manufacturing

Dissolve butylhydroxytoluene in the warm vitamin A, add Cremophor and mix with the molten Lutrol E grades.

Fill into moulds of suppositories to obtain the weight of 2 g.

3. Properties of the suppositories

Weight: .....2.0 g
Colour: .....Homogeneously yellow
Drop point:.....54 °C
Disintegration in water:.....22 min (emulsion)

2.9 Tablet formulations (Lab Scale)

Vitamin A Tablet Cores (50,000 i. u.)

1. Formulation

Vitamin A acetate dry powder .....110 g
500,000 i. u./g (BASF)
Avicel PH 102 [5] .....100 g
Kollidon VA 64 [1] .....10 g
Kollidon CL [1] .....5 g
Aerosil 200 [4].....1 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight .....231 mg
Diameter .....9 mm
Form .....biconvex
Hardness.....64 N
Disintegration .....2 min
Friability .....< 0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin A Tablets (25,000 i. u.)

1. Formulation

Vitamin A acetate dry powder.....55.0 g
500,000 i. u./g (BASF)
Dicalcium phosphate, DI-TAB [9], ...572.0 g
granulated with 3% of Kollidon 30 [1]
Polyethylene glycol, powder [6] .....28.0 g
Kollidon CL [1].....19.4 g
Aerosil 200 [4].....5.6 g

2. Manufacturing

Granulate the dicalcium phosphate with Kollidon 30, dissolved in isopropanol or water and pass through a 0.5 mm screen. Mix the obtained dried granules with the other components, sieve and press with high compression force using a vibrating hopper.

3. Tablet properties

Weight .....680 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....40 N
Disintegration .....2 min
Friability.....0.4%

2.9 Tablet formulations (Lab Scale)

Vitamin A Tablets (50,000 i. u.)

1. Formulation

	No. 1	No. 2	No. 3
Vitamin A acetate dry powder 500,000 i. u./g (BASF)	110 g	120 g	110 g
Ludipress[1]	189 g	120 g	–
Avicel PH 101 [5]	–	10 g	154 g
Kollidon VA 64 [1]	–	–	10 g
Kollidon CL [1]	–	–	4 g
Magnesium stearate (Merck)	1 g	1 g	–
Aerosil 200 [4]	–	1 g	1 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

	No. 1	No. 2	No. 3
Weight	306 mg	250 mg	277 mg
Diameter	8 mm	8 mm	8 mm
Form	biplanar	biplanar	biplanar
Hardness	51 N	106 N	119 N
Disintegration	3 min	7 min	< 1 min
Friability	< 0.1%	0.1%	< 0.1%

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Vitamin B Complex + Amino Acids + Magnesium Effervescent Granules (Sugar-free)

(1 RDA of Vitamins + 500 mg carnitine + 20 mg glutamine)

1. Formulation

I.	Thiamin hydrochloride (BASF)	2 g
	Pyridoxine hydrochloride (BASF)	2 g
	Cyanocobalamin dry powder 0.1% (BASF)	5 g
	L-Glutamine	20 g
	Inositol	10 g
	Potassium L-aspartate	10 g
II.	DL-Carnitine hydrochloride	500 g
	Magnesium L-aspartate	350 g
	Citric acid, anhydrous	600 g
	Sodium bicarbonate (Merck)	500 g
	Flavours	q. s.
	Kollidon VA 64 [1]	50 g
III.	Isdopropanol	80 g

2. Manufacturing

Mix the components I, add the mixture II, granulate mixture I + II with the liquid III, pass through a 0.8 mm sieve, dry well and mix with III.
Fill 2.1 g of the granules in sachets.

3. Properties of the granules

Colour:	Yellow granules
Flowability:	Very good
Dispersibility:	2.1 g disperse homogeneously in 100 ml of water in about 60 seconds.

4. Administration

2.1 g of the granules correspond to about 1 RDA of the vitamins and 500 g of carnitin and 20 mg of glutamin.

2.9 Tablet formulations (Lab Scale)

Vitamin B Complex + Carnitine Tablet Cores

1. Formulation

I.	Thiamine mononitrate (BASF)	95.0 g
	Riboflavin (BASF)	20.0 g
	Nicotinamide (Degussa)	100.0 g
	Calcium D-pantothenate (BASF)	50.0 g
	Folic acid (Knoll)	2.0 g
	Biotin	0.2 g
	Cyanocobalamin, gelatin coated 1% (BASF)	0.5 g
	Carnitine hydrochloride	50.0 g
	Inositol	100.0 g
	Adenosine phosphate	2.0 g
II.	Kollidon 30 [1]	15.7 g
	Isopropanol	70.0 g
III.	Kollidon CL [1]	26.0 g
	Lactose monohydrate [8]	122.0 g
	Polyethylene glycol 6000, powder [6]	14.0 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with low compression force.

3. Tablet properties

Weight	708 mg
Diameter	13 mm
Form	biconvex
Hardness	88 N
Disintegration	1 – 2 min
Friability	0.1%

5.8 Liquid Formulations (Lab scale)

Vitamin B Complex + Minerals + Linoleic/Linolenic Acid Syrup

1. Formulation

I.	Evening primrose oil (see Remark)	5.0 ml
	Cremophor RH 40 [1]	20.0 g
II.	Water	41.0 g
III.	Ferric citrate	60 mg
	Manganese phosphate	300 µg
	Thiamine hydrochloride (BASF)	3 mg
	Riboflavin (BASF)	4 mg
	Cyanocobalamin, crystalline	10 µg
	Nicotinamide	50 mg
	Kollidon CL-M [1]	5.0 g
	Sucrose	25.0 g
	Citric acid	0.5 g
	Vanilla-flavour (Gunther)	0.2 g
	Cyclamate sodium	1.0 g
	Saccharin sodium	20 mg
IV.	Kollidon 90 F [1]	2.5 g

2. Manufacturing

Mix the primrose oil with Cremophor RH 40 heat to 60 °C and add slowly the warm water II. Add the components III to the well stirred solubilisate I/II. Finally add Kollidon 90 F to the obtained suspension portionwise with stirring.

3. Properties

Appearance:	Viscous yellow suspension (syrup)
pH:	3.3
Viscosity (25 °C):	16,000 – 17,000 mPa · s
Rel. sediment volume:	85 % after 1 week
Redispersibility:	easy

4. Remark

5 ml of Evening Primrose oil (Epopure,, Prima Rosa, South Africa) contain 3.5 g linoleic acid + 0.45 g gamma linolenic acid

2.9 Tablet formulations (Lab Scale)

Vitamin B Complex + Vitamin C + Calcium Effervescent Tablets

1. Formulation

I.	Thiamine mononitrate (BASF)	7 g
	Riboflavin (BASF)	5 g
	Nicotinamide	25 g
	Pyridoxine hydrochloride (BASF)	20 g
	Calcium D-pantothenate (BASF)	12 g
	Calcium carbonate	75 g
	Calcium glycerophosphate	164 g
	Sodium bicarbonate	400 g
	Tartaric acid, powder	300 g
	Sucrose, crystalline	400 g
	Sucrose, powder	350 g
	Kollidon 30 [1]	50 g
II.	Kollidon 30 [1]	10 g
	Isopropanol	q.s.
III.	Ascorbic acid, powder (BASF)	550 g
	Riboflavin (BASF)	2 g
	Cyanocobalamin gelatin coated 0.1% (BASF)	5 g
	Polyethylene glycol 6000, powder [6]	40 g
	Kollidon CL [1]	50 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry at 60 °C with vacuum, mix with III and press with medium to high compression force.

3. Tablet properties

Weight	2,500 mg
Diameter	20 mm
Form	biplanar
Hardness	150 N
Disintegration	2 min
Friability	0.9 %

2.9 Tablet formulations (Lab Scale)

Vitamin B Complex + Vitamin C + Ferrous Sulfate Tablets

1. Formulation

I.	Ferrous sulfate (1H20)	300 g
	Kollidon 30 [1]	15 g
II.	Kollidon 30 [1]	6 g
	2-Propanol	q.s.
III.	Thiamine mononitrate (BASF)	45 g
	Riboflavin (BASF)	10 g
	Pyridoxine hydrochloride (BASF)	82 g
	Nicotinamide	69 g
	Ascorbic acid, powder (BASF)	470 g
	Ludipress [1]	690 g
	Polyethylene glycol 6000, powder [6]	50 g
	Aerosil 200 [4]	9 g

2. Manufacturing (Wet granulation)

Granulate the mixture I with solution II, pass through a 0.8 mm sieve, mix with III and press with high compression force (25 – 30 kN).

3. Tablet properties

Weight	1,750 mg
Diameter	20 mm
Form	biplanar
Hardness	120 N
Disintegration	6 min
Friability	0.9 %

2.9 Tablet formulations (Lab Scale)

Vitamin B Complex + Vitamin C Effervescent Tablets

1. Formulation

I.	Thiamine mononitrate (BASF)	33 g
	Riboflavin (BASF)	4 g
	Pyridoxine hydrochloride (BASF)	10 g
	Nicotinamide	66 g
	Calcium D-pantothenate (BASF)	17 g
	Tartaric acid, powder	350 g
	Sodium bicarbonate	450 g
	Sucrose, crystalline	750 g
	Kollidon 30 [1]	30 g
II.	Isopropanol	q.s.
III.	Ascorbic acid, crystalline (BASF)	500 g
	Riboflavin	3 g
	Cyanocobalamin gelatin coated 0.1%	10 g
	Orange flavour	10 g
	Saccharin sodium	2 g
	Cyclamate sodium	5 g
	Polyethylene glycol 6000, powder [6]	50 g

2. Manufacturing (Wet granulation)

Granulate mixture I with the solvent II, dry, pass through a 0.8 mm sieve, mix with II and press with high compression force at maximum 30% of relative atmospheric humidity.

3. Tablet properties

Weight	2,315 mg
Diameter	20 mm
Form	biplanar
Hardness	141 N
Disintegration	2 min
Friability	0.9%

4.4 Formulation of granules, dry syrups and lyophylisates (Lab scale)

Vitamin B Complex + Vitamin C Instant Granules (2 RDA of Vitamins)

1. Formulation

I. Thiamine hydrochloride (BASF).....1.2 g
Riboflavin phosphate sodium .....1.9 g
Nicotinamide (Degussa) .....15.0 g
Pyridoxine hydrochloride (BASF).....1.5 g
Cyanocobalamin, gelatin.....5.0 g
coated 0.1% (BASF)
Ascorbic acid, powder (BASF).....50.0 g
Sucrose .....241.0 g

II. Kollidon 30 [1] .....17.0 g
Ethanol .....60 ml

2. Manufacturing

Mix the components I, granulate with soluiton II, dry and pass through a 0.8 mm sieve.

Fill 1 g of the granules in sachets, (or 10 g in 100 ml flaks as dry syrup).

3. Properties of the granules

Yellow homogeneous granules dispersible in cold water.

4. Administration

About 1 g of the granules (= 1 sachet) correspond to two daily vitamin B and vitamin C requirements of adults.

5. Chemical stability of the granules (20–25 °C)

Vitamin	After production	4 Months	6 Months
B_1	100 %	100 %	93 %
B_2	100 %	93 %	80 %
B_3	100 %	100 %	98 %
B_6	100 %	100 %	97 %
B_{12}	100 %	100 %	100 %
C	100 %	100 %	97 %

6. Remark

Due to the high loss of riboflavin phosphate sodium it should be substituted by riboflavin.

5.8 Liquid Formulations (Lab scale)

Vitamin B Complex + Vitamin C Syrup, I (2 – 3 RDA/10 g)

1. Formulation

I.	Thiamine hydrochloride (BASF)	60 mg
	Riboflavin phosphate sodium	55 mg
	Nicotinamide	250 mg
	Dexpanthenol (BASF)	120 mg
	Pyridoxine hydrochloride (BASF)	55 mg
	Ascorbic acid, crystalline (BASF)	900 mg
	Orange flavour	25 mg
	EDTA sodium	5 mg
	Propyl gallate	50 mg
	Sorbic acid	200 mg
	Kollidon 25 [1]	5 g
	Sorbitol, crystalline [10]	10 g
	Glycerol	9 g
	1,2-Propylenglycol Pharma [1]	10 g
	Water	5 g
II.	Sugar syrup DAB (sucrose + water, 64 g + 36 g)	60 g
	Total amount	100 g

2. Manufacturing

Mix solution I with sugar syrup II. Adjust the clear solution to about pH 4,2. Use nitrogen as an inert gas in the final packaging.

3. Chemical stability (20–25 °C, dark)

The following vitamin contents were determined by HPLC.

Vitamin	0 Months	6 Months	9 Months	12 Months
B_1	100 %	95 %	87 %	82 %
B_2	100 %	100 %	90 %	92 %
Nicotinamide	100 %	92 %	96 %	92 %
Dexpanthenol	100 %	95 %	88 %	90 %
B_6	100 %	100 %	100 %	88 %
C	100 %	94 %	90 %	not determined

5.8 Liquid Formulations (Lab scale)

Vitamin B Complex + Vitamin C Syrup, II

1. Formulation

I.	Thiamine hydrochloride (BASF)	27 mg
	Riboflavin phosphate sodium	27 mg
	Nicotinamide	125 mg
	Dexpanthenol (BASF)	55 mg
	Pyridoxine hydrochloride (BASF)	27 mg
	Ascorbic acid, crystalline (BASF)	400 mg
	Orange aroma	50 mg
	EDTA sodium	10 mg
II.	Propylene glycol Pharma [1]	30 g
	+ water (2 + 1)	
III.	Parabene	250 mg
	Sorbitol, crystalline [10]	15 g
	Sucrose, crystalline	100 g
	Water	70 g
	Total amount	216 g

2. Manufacturing

Dissolve the components I in mixture II. Prepare solution III by heating, cool and mix with solution I/II. Adjust to pH 4,2 – 4,5. Use nitrogen as inert gas during packaging.

3. Properties of the solution

Yellow clear taste full solution having a density of 1.23 g/ml (25 °C).

4. Chemical stability (20–25 °C, dark)

The following vitamin contents were determined by HPLC.

Vitamin	0 Months	6 Months	9 Months	12 Months
B_1	100 %	85 %	85 %	–
B_2	100 %	91 %	91 %	87 %
Nicotinamide	100 %	100 %	100 %	100 %
Dexpanthenol	100 %	88 %	86 %	86 %
B_6	100 %	100 %	96 %	96 %
C	100 %	89 %	–	88 %

2.9 Tablet formulations (Lab Scale)

Vitamin B Complex + Vitamin C Tablets

1. Formulations

	No. 1	No. 2
Thiamine mononitrate (BASF)	5.0 g	–
Thiamine hydrochloride (BASF)	–	15.0 g
Ribolfavin (BASF)	5.0 g	2.0 g
Pyridoxine hydrochloride (BASF)	5.0 g	5.0 g
Folic acid	0.5 g	–
Choline bitartrate	–	25.0 g
Niacin	30.0 g	–
Nicotinamide	–	10.0 g
Biotin (Merck)	0.1 g	–
Calcium D-pantothenate (BASF)	10.0 g	–
Ascorbic acid, crystalline/powder (BASF)	150.0 g	100.0 g
Ludipress [1]	172.4 g	220.0 g
Kollidon VA 64 [1]	20.0 g	–
Magnesium stearate [2]	2.0 g	–
Stearic acid [7]	–	8.0 g

2. Manufacturing (Direct compression)

Weigh all ingredients in, pass through a 0.8 mm-sieve and mix. Press the mixture with medium/low compression force.

3. Tablet properties

	No. 1	No. 2
Weight	400 mg	411 mg
Diameter	10 mm	12 mm
Form	biplanar	biplanar
Hardness	95 N	69 N
Disintegration	3 – 4 min	5 min
Friability	0.1%	0.3%

4. Remark

For stability reasons it would be better to substitute thiamine hydrochloride by thiamine mononitrate in formulation No. 2.

5.8 Liquid Formulations (Lab scale)

Vitamin B Complex Injectable Solution

1. Formulation

I.	Thiamine hydrochloride (BASF)	1,100 mg
	Riboflavin phosphate sodium	660 mg
	Nicotinamide	4,400 mg
	Pyridoxine hydrochloride (BASF)	440 mg
	Cyanocobalamin	880 µg
	EDTA, disodium salt	20 mg
	Propyl gallate	50 mg
	Kollidon 17 PF [1]	10 g
II.	Parabenes	160 mg
	Citric acid	2,270 mg
	Sodium hydroxide solution 1 molar	21.6 ml
	Hydrochloric acid 0.1 molar	72.0 ml
	Propylene glycol Pharma [1]	20.0 ml
	Water for injectables	86.4 ml
	Total amount	about 200 ml

2. Manufacturing

Dissolve the mixture I in the buffer solution II, keep it during 5 min under nitrogen bubbles, filter through a 0.2 µm membrane and fill the clear yellow solution in ampoules of 2 ml under nitrogen. The pH-value is about 4.

3. Stability (20-25 °C, dark)

The following vitamin contents were determined by HPLC.

Vitamin	9 Months	12 Months
B_1	8 %	11 %
B_2	6 %	10 %
Nicotinamide	0 %	0 %
B_6	9 %	9 %
B_{12}	13 %	not tested

5.8 Liquid Formulations (Lab scale)

Vitamin B Complex Syrup

1. Formulation

Thiamine hydrochloride (BASF)	60.0 mg
Riboflavin 5-phosphate sodium	55.0 mg
Nicotinamide	250.0 mg
Dexpanthenol (BASF)	120.0 mg
Pyridoxine hydrochloride (BASF)	55.0 mg
Sorbic acid	200.0 mg
EDTA sodium	5.0 mg
Vanilline	225.0 mg
Sucrose	46.5 g
Kollidon 25 [1]	2.5 g
Glycerol	9.0 g
Propylene glycol Pharma [1]	10.0 g
Water	31.0 g

2. Manufacturing

Dissolve the sucrose in the heat mixture of glycerol, propylene glycol and water, cool to room temperature and dissolve the other components to obtain a clear solution.

3. Stability (room temperature, HPLC)

Vitamin	Content after 1 year
B_1	80 %
B_2	75 %
B_6	97 %
Nicotinamide	97 %
Dexpanthenol	92 %

2.9 Tablet formulations (Lab Scale)

Vitamin B Complex Tablets, I

1. Formulations

	No. 1	No. 2
Thiamine mononitrate (BASF)	25 g	—
Thiamine hydrochloride (BASF)	—	25 g
Riboflavin (BASF)	25 g	25 g
Nicotinamide	80 g	80 g
Calcium D-pantothenate (BASF)	40 g	40 g
Pyridoxine hydrochloride (BASF)	16 g	16 g
Cyanocobalamin gelatin coated 0.1 % (BASF)	16 g	16 g
Avicel PH 101 [5]	282 g	282 g
Kollidon 30 [1]	16 g	16 g
Aerosil 200 [4]	3 g	3 g

2. Manufacturing (Direct compression)

Pass all component through a 0.8 mm sieve, mix and press with medium to high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	513 mg	504 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	73N	68 N
Disintegration	< 1 min	< 1 min
Friability	0.4 %	0.8 %

4. Chemical stability of vitamin B1 (40°C, closed)

	0 Month	6 Months	12 Months
Formulation No. 1	100%	83%	72%
Formulation No. 2	100%	32%	11%

Result: Thiamine hydrochloride is not suitable in this formulations.

2.9 Tablet formulations (Lab Scale)

Vitamin B Complex Tablets, II

1. Formulation

Thiamine mononitrate (BASF)	2.3 g
Riboflavin (BASF)	2.6 g
Nicotinamide	2.3 g
Calcium D-pantothenate (BASF)	2.2 g
Pyridoxine hydrochloride (BASF)	2.7 g
Cyanocobalamin gelatin coated 0.1% (BASF)	2.4 g
Ludipress [1]	280.0 g
Flavour (Firmenich)	14.0 g
Saccharin sodium	0.05 g
Cyclamate sodium	4.0 g
Magnesium stearate [1]	5.0 g

2. Manufacturing (Direct compression)

Pass all component through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight	314 mg
Diameter	8 mm
Form	biplanar
Hardness	76 N
Disintegration	6 min
Friability	0.1%

4. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 + Caffeine Tablets (500 mg + 100 mg)

1. Formulation

I.	Thiamine hydrochloride (BASF)	500 g
	Caffeine (Knoll)	100 g
	Corn starch [3]	30 g
	Kollidon VA 64 [1]	20 g
II.	Kollidon VA 64 [1]	15 g
	Ethanol 96 %	q.s.
III.	Polyethylene glycol 6000, powder [6]	35 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, sieve, mix with III and press with low compression force.

3. Tablet properties

Weight	698 mg
Diameter	16 mm
Form	biplanar
Hardness	101 N
Disintegration	2 min
Friability	0.5 %

5.8 Liquid Formulations (Lab scale)

Vitamin B_1 + Vitamin B_2 + Vitamin B_3 + Vitamin B_6 Injectable Solution (100 mg + 6 mg + 40 mg + 4 mg/2 ml)

1. Formulation

I.	Thiamine hydrochloride (BASF)	11.0 g
	Riboflavin-5'-phosphate, sodium	6.6 g
	Nicotinamide	44.0 g
	Pyridoxine hydrochloride (BASF)	4.4 g
II.	Parabene	1.8 g
	Citric acid	25.2 g
	Sodium hydroxide solution, 1 molar	240 ml
	Hydrochloric acid, 0.1 molar	800 ml
	Water for injectables	960 ml

2. Manufacturing

Prepare solution II by heating and allow to cool before dissolving the components of I in it. Flush 5–10 min. with nitrogen, filter through a 0.22 µm membrane and fill into 2-ml ampoules under nitrogen.

3. Properties of the solution

A clear yellow solution was obtained having a pH of a about 4.0.

4. Chemical stability (20–25°C)

Vitamin	Content after 1 year (HPLC)
B_1	93%
B_2	90%
B_3	100%
B_6	97%

Vitamin B_{12} was not stable in this formulation

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 + Vitamin B_6 + Vitamin B_{12} Tablets (100 mg + 10 mg + 100 µg)

1. Formulation

Thiamine hydrochloride (BASF).....100 g
Pyridoxine hydrochloride (BASF).....10 g
Cyanocobalamin, gelatin coated 1% (BASF) ....10 g
Ludipress [1].....277 g
Magnesium stearate [2] .....3 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight .....394 mg
Diameter .....12 mm
Form .....biplanar
Hardness .....63 N
Disintegration .....4 min
Friability 0.3%

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 + Vitamin B_6 + Vitamin B_{12} Tablets (100 mg + 200 mg + 100 µg)

1. Formulation

Thiamine mononitrate (BASF)	100 g
Pyridoxine hydrochloride (BASF)	200 g
Cyanocobalamin gelatin coated 1% (BASF)	10 g
Ludipress [1]	250 g
Polyethylene glycol 6000, powder [6]	45 g
Aerosil 200 [4]	5 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	609 mg
Diameter	12 mm
Form	biplanar
Hardness	102 N
Disintegration	5 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 + Vitamin B_6 + Vitamin B_{12} Tablets (250 mg + 250 mg + 1 mg)

1. Formulation

I.	Thiamine mononitrate (BASF)	250 g
	Pyridoxine hydrochloride (BASF)	250 g
	Lactose monohydrate [8]	75 g
II.	Kollidon 30 [1]	25 g
	Isopropanol	q.s.
III.	Cyanocobalamin, gelatin coated 1% (BASF)	100 g
	Kollidon CL [1]	25 g
	Magnesium stearate [2]	2 g
	Talc [10]	5 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with low compression force applying a vibrating hopper.

3. Tablet properties

Weight	730 mg
Diameter	12 mm
Form	biplanar
Hardness	95 N
Disintegration	9 –10 min
Friability	0.4 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 (Thiamine) Tablets (50 mg), I

1. Formulation

	No. 1	No. 2
Thiamine hydrochloride (BASF)	50 g	–
Thiamine mononitrate (BASF)	–	50 g
Ludipress [1]	293 g	293 g
Magnesium stearate [2]	5 g	5 g
Aerosil 200 [4]	2 g	2 g

2. Manufacturing (Direct compression)

Pass all components through 0.5 mm sieve, mix and press with medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	357 mg	347 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	110 N	108 N
Disintegration	2 – 3 min	7 min
Friability	0.1%	< 0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 (Thiamine) Tablets (50 mg), II

1. Formulation

	No. 1	No. 2
Thiamine hydrochloride (BASF)	50 g	-
Thiamine mononitrate (BASF)	–	50 g
Lactose monohydrate [8]	150 g	150 g
Avicel PH 101 [5]	150 g	150 g
Kollidon CL [1]	15 g	15 g
Aerosil 200 [4]	2 g	2 g

2. Manufacturing (Direct compression)

Pass all components through 0.5 mm sieve, mix and press with high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	344 mg	373 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	150 N	150 N
Disintegration	2 min	< 1 min
Friability	0.1%	< 0.1%

4. Chemical stability of thiamine (40 °C, closed)

	0 Months	3 Months	6 Months	12 Months
Formulation No. 1	100 %	98 %	90 %	97 %
Formulation No. 2	100 %	100 %	96 %	97 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 (Thiamine) Tablets (100 mg), DC

1. Formulations

	No. 1	No. 2
Thiamine hydrochloride (BASF)	110 g	–
Thiamine mononitrate (BASF)	–	100 g
Ludipress [1]	190 g	–
Lactose monohydrate [8]	–	100 g
Avicel PH 101 [5]	–	100 g
Kollidon CL [1]	–	9 g
Aerosil 200 [4]	3 g	1 g
Magnesium stearate [2]	2 g	–

2. Manufacturing (Direct compression)

Pass all components through 0.5 mm sieve, mix and press with medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	302 mg	320 mg
Diameter	8 mm	8 mm
Form	biplanar	biplanar
Hardness	114 N	150 N
Disintegration	2 min	< 1 min
Friability	0.2 %	0.2 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 (Thiamine) Tablets (100 mg), WG

1. Formulation

I.	Thiamine hydrochloride (BASF)	100 g
	Lactose monohydrate [8]	200 g
II.	Kollidon 30 [1]	10 g
	Isopropanol	60 g
III.	Kollidon CL [1]	10 g
	Magnesium stearate [2]	2 g
	Aerosil 200 [4]	1 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry and sieve through a 0.8 mm screen, mix with III and press to tablets.

3. Tablet properties

Weight	330 mg
Diameter	8 mm
Form	biplanar
Hardness	174 N
Disintegration	7 min
Friability	0.9 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_1 (Thiamine) Tablets (300 mg)

1. Formulation

I.	Thiamine mononitrate (BASF)	300 g
	Dicalcium phosphate, DI-TAB [9]	100 g
II.	Kollidon 30 [1]	15 g
	Isopropanol	about 50 g
III.	Kollidon CL [1]	10 g
	Magnesium stearate [2]	4 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry and sieve through a 0.8 mm screen, mix with III and press to tablets.

3. Tablet properties

Weight	430 mg
Diameter	12 mm
Form	biplanar
Hardness	70 N
Disintegration	3 – 4 min
Friability	0.7 %

4. Chemical stability (30°C, 70% relative humidity)

	0 Month	3 Months	6 Months
Vitamin B1 content	298 mg	298 mg	295 mg = 99 %

Vitamin B_{12} (Cyanocobalamin) Tablets, Coloured (50 µg)

1. Formulation

I.	Cyanocobalamin gelatin coated 0.1% (BASF)	50.0 g
	Ludipress [1]	150.0 g
II.	Magnesium stearate [2]	1.5 g
	Sicovit quinoline yellow lake [1]	2.0 g
	Sicovit yellow orange lake [1]	3.0 g

2. Manufacturing (Direct compression)

Prepare the premix II, add to mixture I, pass through a 0.5 mm sieve and press with low compression force.

3. Tablet properties

Weight	209 mg
Diameter	8 mm
Form	biplanar
Hardness	80 N
Disintegration	10 min
Friability	< 0.1%
Colour	homogeneous, orange

2.9 Tablet formulations (Lab Scale)

Vitamin B_2 (Riboflavin) Tablets (3 mg)

1. Formulation

Ribolfavin C (BASF) .....3 g
Ludipress [1] .....195 g
Magnesium stearate [2] .....2 g
Aerosil 200 [4].....1 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with very low compression force (4 kN).

3. Tablet properties

Weight .....202 mg
Diameter .....8 mm
Form .....biplanar
Hardness .....97 N
Disintegration .....3 – 4 min
Friability.....0.1%
Content uniformity: meets the requirements of DAB

4. Remarks

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

If the content uniformity does not meet the requirements it would be recommended to prepare a premix of the active ingredient with a small part of the Ludipress or with lactose monohydrate before mixing with the other components of the formulation.

2.9 Tablet formulations (Lab Scale)

Vitamin B_2 (Riboflavin) Tablets (10 mg)

1. Formulation

I.	Riboflavin (BASF)	10.0 g
	Lactose monohydrate [8]	75.0 g
	Corn starch [3]	20.0 g
	Avicel PH 101 [5]	15.0 g
II.	Kollidon 30 [1]	5 g
	Water	25 g
III.	Aerosil 200 [4]	0.8 g
	Talc [10]	2.5 g
	Hydrogenated castor oil (Henkel)	1.7 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with II and press with low compression force.

3. Tablet properties

Weight	134 mg
Diameter	8 mm
Form	biplanar
Hardness	82 N
Disintegration	1 – 2 min
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin B_2 (Riboflavin) Tablets (75 mg)

1. Formulation

Riboflavin (BASF)	75 g
Sorbitol, crystalline [10]	375 g
Kollidon VA 64 [1]	23 g
Magnesium stearate [2]	4 g
Aerosil 200 [4]	12 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight	493 mg
Diameter	12 mm
Form	biplanar
Hardness	100 N
Disintegration	10 min
Friability	0.5 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_2 (Riboflavin) Tablets (100 mg)

1. Formulation

Riboflavin	100 g
Sorbitol, crystalline [10]	250 g
Kollidon VA 64 [1]	19 g
Magnesium stearate [2]	5 g
Aerosil 200 [4]	10 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

Weight	384 mg
Diameter	12 mm
Form	biplanar
Hardness	53 N
Disintegration	7 min
Friability	0.3 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_2 (Riboflavin) Tablets (150 mg)

1. Formulation

Ribolfavin (BASF)	156 g
Ludipress [1]	150 g
Magnesium stearate [2]	4 g
Aerosil 200 [4]	2 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with low compression force.

3. Tablet properties

Weight	308 mg
Diameter	8 mm
Form	biplanar
Hardness	66 N
Disintegration	2 min
Friability	0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin B_3 (Nicotinamide) Tablets (300 mg)

1. Formulation

Nicotinamide (Degussa)	320 g
Avicel PH 101 [5]	160 g
Kollidon VA 64 [1]	16 g
Magnesium stearate [2]	3 g
Aerosil 200 [4]	3 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

Weight	506 mg
Diameter	12 mm
Form	biplanar
Hardness	89 N
Disintegration	< 1 min
Friability	0.2 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_5 (Calcium D-Pantothenate) Chewable Tablets (600 mg)

1. Formulation

Calcium D-Pantothenate (BASF)	610 g
Sorbitol, crystalline [10]	150 g
Avicel PH 101 [5]	140 g
Kollidon CL [1]	30 g
Polyethylene glycol 6000, powder [6]	50 g
Flavours	q.s.

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with low compression force.

3. Tablet properties

Weight	987 mg
Diameter	12 mm
Form	biplanar
Hardness	> 150 N
Disintegration (water)	19 min
Friability	< 0.3 %

4. Remark

Perhaps the addition of Kollidon CL is not needed.

2.9 Tablet formulations (Lab Scale)

Vitamin B_5 (Calcium D-Pantothenate) Tablets (100 mg)

1. Formulation

Calcium D-Pantothenate (BASF)	100 g
Ludipress [1]	150 g
Kollidon CL [1]	10 g
Magnesium stearate [2]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with medium compression force.

3. Tablet properties

Weight	252 mg
Diameter	8 mm
Form	biplanar
Hardness	196 N
Disintegration	6 min
Friability	< 0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin B_5 (Calcium D-Pantothenate) Tablets (280 mg)

1. Formulation

Calcium D-Pantothenate (BASF)	285 g
Avicel PH 101 [5]	50 g
Dibasic calcium phosphate DI-TAB [9]	150 g
Kollidon CL [1]	20 g
Stearic acid [7]	3 g
Magnesium stearate [2]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with medium compression force.

3. Tablet properties

Weight	518 mg
Diameter	12 mm
Form	biplanar
Hardness	100 N
Disintegration	11 min
Friability	< 0.2 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_5 (Calcium D-Pantothenate) Tablets (300 mg)

1. Formulations

	No. 1	No. 2
Calcium D-Pantothenate (BASF)	300 g	305 g
Lactose Monohydrate [8]	60 g	–
Corn starch [3]	50 g	–
Sorbitol, crystalline [10]	–	75 g
Avicel PH 101 [5]	100 g	70 g
Kollidon VA 64 [1]	12 g	–
Kollidon CL [1]	25 g	15 g
Talc [10]	52 g	–
Calcium arachinate [2]	6 g	–
Aerosil 200 [4]	6 g	–
Polyethylene glycol 6000, powder [6]	–	25 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with medium/low compression force.

3. Tablet properties

	No. 1	No. 2
Weight	604 mg	488 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	62 N	135 N
Disintegration	11 min	5 min
Friability	0.8%	< 0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin B_6 (Pyridoxine) Tablets (40 mg), DC

1. Formulations

	No. 1	No. 2
Pyridoxine hydrochloride (BASF)	40 g	40 g
Lactose monohydrate [8]	150 g	150 g
Avicel PH 101 [5]	150 g	150 g
Kollidon VA 64 [1]	15 g	–
Kollidon CL [1]	10 g	–
Magnesium stearate [2]	1 g	1 g
Aerosil 200 [4]	1 g	1 g

2. Manufacturing (Wet granulation)

Pass all components through a 0.5 mm sieve, mix and press with high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	361 mg	340 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	140 N	81 N
Disintegration	2 min	2 min
Friability	< 0.1%	0.2

4. Chemical stability of Formulation No. 1 (40°C, closed)

	0 Months	3 Months	6 Months
Vitamin B_6	100%	100%	100%

2.9 Tablet formulations (Lab Scale)

Vitamin B_6 (Pyridoxine) Tablets (40 mg), WG

1. Formulation

I.	Pyridoxine hydrochloride (BASF)	40 g
	Corn starch [3]	300 g
II.	Kollidon 30 [1]	15 g
	Water + Isopropanol (1+1)	80 g
III.	Magnesium stearate [2]	1 g
	Aerosil 200 [4]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, mix with III and press with high compression force.

3. Tablet properties

Weight	354 mg
Diameter	12 mm
Form	biplanar
Hardness	70 N
Disintegration	3 min
Friability	0.1%

4. Chemical stability (40°C, closed)

	0 Months	3 Months	6 Months
Vitamin B_6	100%	100%	100%

2.9 Tablet formulations (Lab Scale)

Vitamin B_6 (Pyridoxine) Tablets (100 mg)

1. Formulations

	No. 1	No. 2
Pyridoxine hydrochloride	100 g	100 g
Tabletlose [8]	200 g	–
Lactose monohydrate [8]	–	150 g
Avicel PH 101 [5]	–	83 g
Kollidon VA 64 [1]	10 g	10 g
Kollidon CL [1]	3 g	3 g
Magnesium stearate [2]	1 g	1 g
Aerosil 200 [4]	1 g	1 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

	No. 1	No. 2
Weight	363 mg	360 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	74 N	61 N
Disintegration	< 1 min	< 1 min
Friability	0.2 %	< 0.1 %

2.9 Tablet formulations (Lab Scale)

Vitamin B_6 (Pyridoxine) Tablets (250 mg)

1. Formulation

Pyridoxine hydrochloride (BASF).....250 g
Avicel PH 101 [5].....100 g
Kollidon VA 64 [1].....12 g
Magnesium stearate [2].....5 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight.....361 mg
Diameter.....12 mm
Form.....biplanar
Hardness.....53 N
Disintegration.....2 – 3 min
Friability.....< 0.1%

2.9 Tablet formulations (Lab Scale)

Vitamin B_6 (Pyridoxine) Tablets (300 mg)

1. Formulation

I.	Pyridoxine hydrochloride (BASF)	300 g
	Lactose monohydrate D 20 [8]	100 g
II.	Kollidon 30 [1]	20 g
	Isopropanol + water (1+1)	60 g
III.	Kollidon CL [1]	10 g
	Aerosil 200 [4]	2 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry and sieve through a 0.8 mm screen. Press with medium compression force.

3. Tablet properties

Weight	440 mg
Diameter	12 mm
Form	biplanar
Hardness	110 N
Disintegration	8 min
Friability	0.1%

4. Chemical stability (40 °C, closed)

No loss of vitamin B_6 after 3 and 6 months.

2.9 Tablet formulations (Lab Scale)

Vitamin C + Calcium Carbonate Effervescent Tablets (500 mg + 300 mg)

1. Formulation

I.	Calcium carbonate	315 g
	Sodium bicarbonate	450 g
	Tartaric acid, powder	600 g
	Kollidon 30 [1]	35 g
II.	Kollidon 30 [1]	10 g
	Isopropanol	200 g
III.	Sucrose crystalline	400 g
IV.	Ascorbic acid, crystalline (BASF)	550 g
	Kollidon CL [1]	120 g
	Polyethylene glycol 6000, powder [6]	60 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, mix with III and dry. Add IV and press with a high compression force at maximum 30 % of relative atmospheric humidity.

3. Tablet properties

Weight	2,500 mg
Diameter	20 mm
Form	biplanar
Hardness	100 N
Disintegration	2 min
Friability	2 %

2.9 Tablet formulations (Lab Scale)

Vitamin C + Vitamin E Lozenges (100 mg + 50 mg)

1. Formulation

I.	Ascorbic acid, crystalline (BASF)	100 g
	Vitamin E acetate dry powder SD 50 (BASF)	100 g
	Dextrose	400 g
	Kollidon 90 F [1]	4 g
II.	Isopropanol	25 g
III.	Polyethylene glycol 6000, powder [6]	6 g

2. Manufacturing (Wet granulation)

Granulate mixture I with isopropanol, dry, pass through a 0.8 mm sieve, mix with III and press with high compression force.

3. Tablet properties

Weight	600 mg
Diameter	12 mm
Form	biplanar
Hardness	61 N
Friability	< 0.1%

4. Stability of appearance

No change of the tablet colour during 3 months at 30 °C and 70% relative humidity.

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic acid) Chewable Tablets (100 mg, 500 mg, 1,000 mg)

1. Formulation

Ascorbic acid, powder (BASF)	42.2 %
Microcristalline cellulose, e.g. Avicel PH 101 [5]	28.3 %
Sucrose, powder	13.0 %
Sucrose, crystalline	8.0 %
Kollidon VA 64 [1]	2.4 %
Cyclamate sodium	2.4 %
Polyethylene glycol 6000, powder [6]	2.0 %
Orange flavour + strawberry flavour (2+1)	1.2 %
Aerosil 200 [4]	0.2 %
Saccharin sodium	0.1 %

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press to tablets with medium to high compression force.

3. Tablet properties

	Vitamin C content / Tablet		
	100 mg	**500 mg**	**1000 mg**
Weight	250 mg	1250 mg	2500 mg
Diameter	8 mm	15 mm	20 mm
Form	biplanar	biplanar	biplanar
Hardness	157 N	> 100 N	> 150 N
Disintegration (water)	15 min	> 15 min	14 min
Friability	< 0.1 %	0.8 %	0.6 %

4. Remark

This formulation also is mentioned in “Standardzulassungen für Fertigarzneimittel”, Deutscher Apothekerverlag, 1988.

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic Acid + Ascorbate) Chewable Tablets (500 mg)

1. Formulations

	No. 1	No. 2
Ascorbic acid, crystalline (BASF)	500 g	100 g
Sodium ascorbate, crystalline (BASF)	–	450 g
Sorbitol, crystalline [10]	1,100 g	264 g
Sucrose, crystalline	–	200 g
Sucrose, powder	–	200 g
Dextrose	300 g	–
Polyethylene glycol 6000, powder [6]	100 g	60 g
Magnesium stearate [2]	10 g	3 g
Aerosil 200 [4]	10 g	4 g
Saccharin sodium	–	1 g
Cyclamate sodium	10 g	–
Orange flavour	30 g	20 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium to high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	2,080 mg	1,295 mg
Diameter	20 mm	16 mm
Form	biplanar	biplanar
Hardness	> 150 N	126 N
Friability	0.7%	0.7%

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic acid) Chewable Tablets with Dextrose (100 mg)

1. Formulations

		No. 1	No. 2
I.	Ascorbic acid, crystalline	105 g	—
	Ascorbic acid, EC coated 97.5% (Merck)	–	110 g
	Dextrose	500 g	500 g
II.	Kollidon 90 F [1]	4 g	4 g
	Water and/or isopropanol	30 – 50 g	30 – 50 g
III.	Polyethylene glycol 6000, powder [6]	6 g	6 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II (in a fluidized bed), sieve, add III and press with high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	620 mg	620 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	150 N	> 100 N
Disintegration	10 min	not tested
Friability	< 0.1%	0.1%

4. Chemical stability (40 °C, closed)

	0 Months	3 Months	6 Months
Formulation No. 1	100 %	100 %	100 %
Formulation No. 2	100 %	92 %	93 %

5. Remarks

1. If no fluidized bed is available water should be avoided as granulation solvent.
2. The use of coated ascorbic acid does not increase the stability.

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic Acid) Chewable Tablets with Fructose (120 mg)

1. Formulation

Ascorbic acid, powder (BASF)	120 g
Fructose	500 g
Ludipress [1]	200 g
Avicel PH 101 [5]	100 g
Kollidon VA 64 [1]	15 g
Aerosil 200 [4]	4 g
Polyethylene glycol 6000, powder [6]	35 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight	970 mg
Diameter	12 mm
Form	biplanar
Hardness	222 N
Disintegration (water)	9 min
Friability	0 %

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic acid) Chewable Tablets with Sucrose (500 mg)

1. Formulation

Ascorbic acid (BASF)	500 g
Sucrose, crystalline	850 g
Avicel PH 101 [5]	575 g
Kollidon VA 64 [1]	60 g
Magnesium stearate [2]	15 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with medium compression force.

3. Tablet properties

Weight	2,000 mg
Diameter	20 mm
Form	biplanar
Hardness	130 N
Disintegration	> 20 min
Friability	0.5 %

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic acid) Effervescent Tablets (100 mg and 1000 mg)

1. Formulation

	No. 1 100 mg	No. 2 1000 mg
Ascorbic acid, powder (BASF)	112 g	–
Ascorbic acid, crystalline (BASF)	–	1000 g
Sorbitol, crystalline [10]	–	800 g
Sorbitol Instant (Merck)	200 g	–
Citric acid, anhydrous	1000 g	150 g
Sodium bicarbonate	587 g	660 g
Polyethylene glycol 6000, powder [6]	65 g	80 g
Lemon flavour	10 g	q.s.
Cyclamate sodium	25 g	q.s.
Saccharin sodium	1 g	q.s.

2. Manufacturing (Direct compression)

Dry the sodium bicarbonate during 1 hour at 100 °C, mix with the other components, pass all through a 0.8 mm sieve and press with high compression force at maximum 30 % of relative atmospheric humidity.

3. Tablet properties

	No. 1	No. 2
Weight	2050 mg	2,690 mg
Diameter	20 mm	20 mm
Form	biplanar	biplanar
Hardness	150 N	174 N
Disintegration (water)	2 – 3 min	2 – 3 min
Friability	< 0.1 %	0.8 %

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic Acid) Effervescent Tablets (500 mg)

1. Formulation

I.	Sodium hydrogen carbonate	500 g
	Tartaric acid	430 g
II.	Kollidon 25 [1]	8 g
	2-Propanol	200 ml
III.	Ascorbic acid, crystalline (BASF)	550 g
	Sucrose (<0.5 mm)	660 g
IV.	Polyethylene glycol 6000, powder [6]	67 g
	Dextrose, powder	67 g
	Orange flavour	10 g
	Saccharin sodium	1 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, pass through a 0.5 mm-sieve, and dry at 60 °C. Dry mixture III also at 60 °C and mix together with I/II and IV. At maximum 30% relative atmospheric humidity, press to effervescent tablets.

3. Tablet properties

Weight	2,300 mg
Diameter	20 mm
Form	biplanar
Hardness	100 N
Disintegration (water)	2 min

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic Acid) Tablets (100 mg)

1. Formulation

Ascorbic acid, powder (BASF).....100 g
Ludipress [1].....232 g
Magnesium stearate [2].....1 g

2. Manufacturing (Direct compression)

Mix all components, sieve and press to tablets of 335 mg weight.

3. Influence of the compression force on the tablet properties

	compression force		
Property	**7 kN**	**15 kN**	**22 kN**
Hardness	20 N	55 N	83 N
Disintegration	1 min	1 – 2 min	2 – 3 min
Friability	0.06 %	< 0.05 %	< 0.05 %

4. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic Acid) Tablets (200 mg)

1. Formulation

Ascorbic acid, powder (BASF)	200.0 g
Ludipress [1]	231.0 – 256.0 g
Kollidon VA 64 [1]	25.0 g
Kollidon CL [1]	15.0 g
Aerosil 200 [4]	1.2 g
Magnesium stearate [2]	2.5 g

2. Manufacturing (Direct compression)

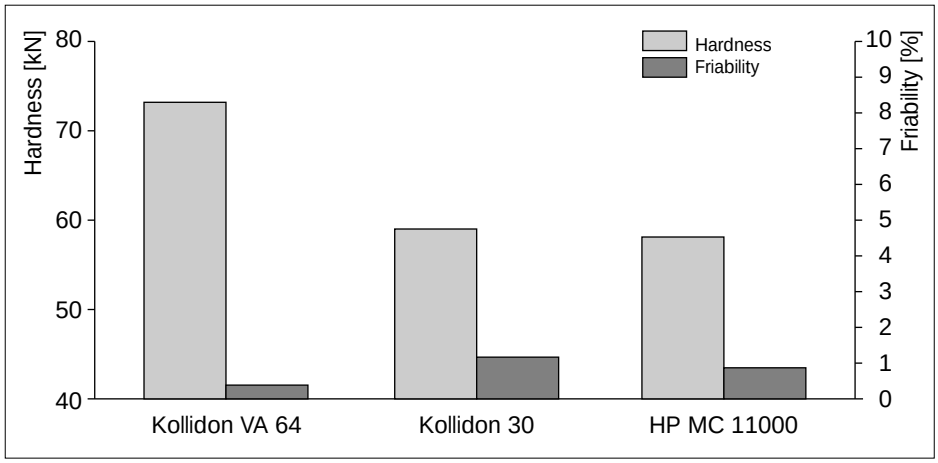
Mix all components, pass through a 0.8 mm screen and press with medium compression force (18 kN).

3. Tablet properties

Weight	499 mg
Diameter	12 mm
Form	biplanar
Hardness	73 N
Disintegration	2 min
Friability	0.4 %
Dissolution, 30 min	> 90 %

2.9 Tablet formulations (Lab Scale)

4. Substitution of Kollidon VA 64 by other dry binders



2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic Acid + Ascorbate) Tablets (250 mg)

1. Formulation

Ascorbic acid, powder (BASF)	70 g
Sodium ascorbate	208 g
Ludipress [1]	196 g
Stearic acid [7]	14 g
Orange flavour	6 g
Saccharin sodium	3 g
Aerosil 200 [4]	3 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

Weight	500 mg
Diameter	12 mm
Form	biplanar
Hardness	106 N
Disintegration	6 min
Friability	0.3 %

4. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Vitamin C (Ascorbic Acid) Tablets (400 mg)

1. Formulation

I.	Ascorbic acid, crystalline (BASF)	440.0 g
	Kollidon CL [1]	4.5 g
II.	Kollidon VA 64 [1]	13.5 g
	Isopropanol	q.s.
III.	Avicel PH 101 [5]	75.0 g
	Polyethylene glycol 6000, powder [6]	37.5 g

2. Manufacturing (Wet granulation)

Granulate mixture I with solution II, dry, pass through a 0.8 mm sieve, add III and press with medium to high compression force.

3. Tablet properties

Weight	593 mg
Diameter	12 mm
Form	biplanar
Hardness	110 N
Disintegration	4 – 5 min
Friability	0.3 %

4. Stability of appearance

No change of the tablet colour during 3 months at 30 °C and 70 % relative humidity.

5.8 Liquid Formulations (Lab scale)

Vitamin E + Benzocaine Solution (5 % + 2 %)

1. Formulation

Vitamin E acetate	5.0 g
Benzocaine	2.0 g
Lutrol F 127 [1]	5.0 g
Cremophor RH 40 [1]	25.0 g
Sorbic acid	0.2 g
Water	62.8 g

2. Manufacturing

Dissolve sorbic acid and benzocain in water at 60 °C, add slowly the heated mixture of Vitamin E acetate and Cremophor RH 40 (60 – 65 °C). Cool the clear solution to about 5 °C and dissolve Lutrol F 127.

3. Properties of the solution

Clear colourless, viscous liquid.

4. Physical stability (22 °C and 40 °C)

No change was observed after 2 months.

5.8 Liquid Formulations (Lab scale)

Vitamin E + Selenium Veterinary Injectable Solution (60 mg E + 3 mg Se/ml)

1. Formulation

I.	Vitamin E acetate (BASF)	6.0 g
	Cremophor EL or Solutol HS 15 [1]	22.0 g
II.	Preservative	q.s.
	Sodium selenite	0.33 g
	Water for injectables	ad 100 ml

2. Manufacturing

Heat mixture I to about 60 °C, stir well and add very slowly the hot solution II (60 °C).

After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occurred. Sterilization can also be performed by membrane filtration under pressure.

3. Properties of the solution

Clear or slightly opalescent, colourless liquid.

4. Remark

In Germany Cremophor EL must be declared on the package of injectables.

2.9 Tablet formulations (Lab Scale)

Vitamin E Chewable Tablets (100 mg)

1. Formulations

	No. 1	No. 2	No. 3
Vitamin E acetate SD 50 (BASF)	200 g	200 g	200 g
Ludipress [1]	–	493 g	–
Sorbitol, crystalline [10]	390 g	–	–
Mannitol	100 g	–	–
Dicalcium phosphate [9], granulated with 5% Kollidon 30	–	–	400 g
Aerosil 200 [4]	7 g	7 g	4 g
Magnesium stearate [2]	3 g	–	–

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm screen and press with high compression force.

3. Tablet properties

	No. 1	No. 2	No. 3
Weight	711 mg	727 mg	624 mg
Diameter	12 mm	12 mm	12 mm
Form	biplanar	biplanar	biplanar
Hardness	106 N	102 N	68 N
Disintegration	12 min	15 min	17 min
Friability	0%	0%	0%

4. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Vitamin E Chewable Tablets (150 mg)

1. Formulation

Vitamin E acetate dry powder SD 50 (BASF)	300.0 g
Sorbitol [10]	300.0 g
Aerosil 200 [4]	6.0 g
Saccharin sodium	0.2 g
Magnesium stearate [2]	6.0 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight	620 mg
Diameter	12 mm
Form	biplanar
Hardness	80 N
Disintegration (water)	> 30 min
Friability	< 0.1%

4. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Vitamin E Chewable Tablets (200 mg)

1. Formulation

Vitamin E acetate dry powder.....400.0 g
SD 50 (BASF)
Ludipress [1] .....200.0 g
Aerosil 200 [4] .....10.0 g
Saccharin sodium.....0.1 g

2. Manufacturing (Direct compression)

Mix all components, pass through a 0.8 mm sieve and press with high compression force.

3. Tablet properties

Weight .....610 mg
Diameter .....12 mm
Form .....biplanar
Hardness.....67 N
Disintegration (water).....> 30 min
Friability .....0 %

4. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

2.9 Tablet formulations (Lab Scale)

Vitamin E Chewable Tablets (400 mg)

1. Formulation

Vitamin E acetate dry powder.....800 g
SD 50 (BASF)
Ludipress [1].....790 g
Aerosil 200 [4].....20 g
Flavours.....q.s.

2. Manufacturing (Direct compression)

Pass all components through a 0.5 mm sieve, mix and press with high compression force.

3. Tablet properties

Weight .....1,665 mg
Diameter .....20 mm
Form .....biplanar
Hardness.....108 N
Disintegration (water) .....> 30 min
Friability .....0 %

4. Remark

These tablets could be commercialized in Europe as dietary food because all components are allowed for this application.

5.8 Liquid Formulations (Lab scale)

Vitamin E Concentrate, Water-miscible (10 % = 100 mg/ml)

1. Formulation

I. Vitamin E acetate (BASF).....10.5 g
Cremophor RH 40 [1].....25.0 g
II. Preservative .....q. s.
Water.....ad 100 ml

2. Manufacturing

Heat the mixture I and solution II separately to about 65 °C and add mixture I slowly to the well stirred solution II (or solution II slowly to mixture I).

3. Properties of the solution

Clear colourless liquid, miscible with water.

4. Physical stability (20–25 °C)

No change of appearance after 3 months.

5.8 Liquid Formulations (Lab scale)

Vitamin E Drops (50 mg/ml)

1. Formulation

I.	Vitamin E acetate (BASF)	5.0 g
	Cremophor RH 40 [1]	16.0 g
II.	Preservative	q. s.
	Water	79.0 ml

2. Manufacturing

Heat mixture I and solution II to about 65 °C and add solution II slowly to mixture I.

3. Properties of the solution

Clear or lightly opalescent, colourless liquid.

6.7 Formulations of semi-solid drugs (Lab scale)

Vitamin E Gel-Cream (10 %)

1. Formulation

Vitamin E acetate (BASF) .....10 g
Propylene glycol Pharma [1].....15 g
Lutrol F 127 [1].....20 g
Water.....55 g

2. Manufacturing

Mix vitamin E acetate with propylene glycol and add the water. After cooling to about 6 °C dissolve slowly Lutrol F 127 in the well stirred mixture. Maintain cool until the air bubbles escaped.

3. Properties of the gel-cream

Turbid white gel at temperatures between 20 – 50 °C.
Viscosity at 25 °C about 120,000 mPa · s.

4. Physical stability

After 2 weeks at 40 °C no changes of aspect or viscosity were observed.

5.8 Liquid Formulations (Lab scale)

Vitamin E Solution with Ethanol (0.01% = 1 mg/10 ml)

1. Formulation

I.	Vitamin E acetate (BASF)	10 mg
	Cremophor EL [1]	4.0 – 5.0 g
II.	Water	57.0 g
	Ethanol 96%	38.0 g

2. Manufacturing

Heat mixture I to about 60 °C, stir well and add slowly the warm solvent mixture II.

3. Properties of the solution

Clear, colourless liquid of low viscosity.

2.9 Tablet formulations (Lab Scale)

Vitamin E Tablets (50 mg)

1. Formulations

	No. 1	No. 2
Vitamin E acetate dry powder SD 50 (BASF)	100 g	100 g
Sorbitol, crystalline (Merck)	–	300 g
Mannitol	140 g	–
Tablettose [8]	140 g	–
Kollidon VA 64 [1]	15 g	–
Magnesium stearate [2]	2 g	3 g
Aerosil 200 [4]	10 g	3 g

2. Manufacturing (Direct compression)

Pass all components through a 0.8 mm sieve, mix and press with high compression force.

3. Tablet properties

	No. 1	No. 2
Weight	410 mg	413 mg
Diameter	12 mm	12 mm
Form	biplanar	biplanar
Hardness	34 N	70 N
Desintegration	9 min	11 min
Friability	< 0.1%	< 0.1%

5.8 Liquid Formulations (Lab scale)

Vitamin K1 (= Phytomenadion) Injectable Solution (10 mg and 20 mg/ ml)

1. Formulation

	No. 1	No. 2
Phytomenadion	1.0 g	2.0 g
Solutol HS 15 or Cremophor EL [1]	6.5 g	11.0g
Preservatives	q.s.	q.s.
Water for injectables	93.0 g	87.0 g

2. Manufacturing

Dissolve phytomenadion in Solutol HS 15 heated to about 60 °C and add slowly the warm water. The sterilisation can be done by heat at 120 °C or by filtration. After the ampoules have been heat-sterilized, they should be shaken for a short time, while they are still hot, to eliminate any separation of the phases that may have occurred.

3. Properties of the solution

A clear colourless solution of low viscosity was obtained.

4. Physical stability (Formulation No. 1)

Stored at 40 °C and protected from light the heat sterilized solution did not show any change of the clarity and colour after 12 weeks.

Stored at 20 – 25°C in the day light the heat sterilized solution did not show any change of the clarity and colour after 12 weeks.

5. Remark

In Germany Cremophor EL must be declared on the package of injectables.