# FORMULATION HANDBOOK


**A Guide for R+D**

JRS PHARMA

LEADING THE WORLD IN EXCIPIENTS

A Member of the JRS Group

# FORMULATION HANDBOOK

## Introduction

**Dear Customer,**

**"LEADING THE WORLD IN EXCIPIENTS"** -
summarizes our commitment to the full range of technical services and support that we provide for formulation development.

Take advantage of the experience and application know-how available from our JRS PHARMA's Technical Competence Centers in all questions relating to solid dosage forms.

This Formulation Handbook provides you with practical examples and ideas together with an understanding of, and guides for diverse applications.

Use our suggestions and examples as the first steps (creative ideas) for your own solutions.

Further technical details and product information can be found on the Internet under **www.jrspharma.com.**

Our experts will be happy to answer any questions. We look forward to a co-operative discussion with you.

JRS PHARMA
Technical Competence and Service Centers


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# FORMULATION HANDBOOK

## JRS Excipients

## Product Overview



### The High Functionality Excipient

#### PROSOLV SMCC®

**Silicified Microcrystalline Cellulose (Microcrystalline Cellulose, Ph.Eur., NF, JP & Silica, Colloidal Anhydrous, Ph.Eur. & Colloidal Silicon Dioxide NF & Light Anhydrous Silicic Acid JP)**

**PROSOLV SMCC®** is the most significant innovation in high functionality excipients today. Used with simpler Direct Compression, it emulates the outcome of alternative granulations while significantly reducing the number and quantity of excipients.

**PROSOLV SMCC®** is the high functionality ingredient that offers significant benefits in terms of tablet size, production yield and overall cost. Early use in formulation development can result in early market entry, Direct Compression formulas and smaller tablets that consumers prefer.

**PROSOLV SMCC®** 's characteristics are high compactibility, high intrinsic flow, enhanced lubrication efficiency and improved blending properties. Its benefits are proven in formulation, manufacturing, marketing and regulatory approval.

Regulatory approvals have been simplified by the recognition that **PROSOLV SMCC®** is comprised of compendial excipients. Submissions have been approved in the USA, Europe and Japan. It is listed in the Inactive Ingredients Guide (IIG) of the US Food and Drug Administration (FDA) website.

### PROSOLV® TECHNOLOGY:

A synergistic co-processing platform resulting in a co-processed API which becomes directly compressible, becomes a highly effective binder/carrier, has maximized flow and content uniformity, stabilizes hygroscopic actives. **PROSOLV SMCC®** co-processing provides the ultimate deaggregation and dispersion of the API.

### Insoluble Tablet Binders:

#### VIVAPUR® and EMCOCEL®

**Microcrystalline Cellulose, Ph.Eur., NF, JP**

These brands of MCC are preferred excipients in tablet manufacturing due to their high compactibility, inherent flow and ability to initiate disintegration. JRS Pharma has the benefit of multiple manufacturing plants for worldwide availability.

#### EMCOMPRESS®

**Calcium Hydrogen Phosphate Dihydrate, Ph.Eur., Dibasic Calcium Phosphate, Dihydrate, USP**

The First Direct Compression Excipient. Its particles are of a size, shape, and density to maximize flow in high-speed tablet production and to reduce tablet weight variation.

**ANHYDROUS EMCOMPRESS®**: In addition to excellent flow enhancement in Direct Compression. It does not contain water of crystallization and can be used with moisture sensitive actives. It is very often used in capsule formulations and to accelerate formulation development.

### Soluble Tablet Binders:

#### EMDEX®

**Dextrates, NF**

Ideal for chewable products, it is the only compendial spherical dextrate available for Direct Compression that delivers the required flow, compaction and flavor carrying capacity for consumer products.

**EMDEX®** has a great taste masking effect.

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# JRS Excipients

# Product Overview



### CANDEX®
**Dextrates**

A plant sourced tablet and capsule dextrate

### SUGARTAB®
**Compressible Sucrose**

Excellent for chewable products, particularly vitamin formulations. It offers good flow, excellent compressibility and flavor masking.

## Functional Fillers:

### ARBOCEL®
**Powdered Cellulose, Ph.Eur., NF, JP**

Plant derived unique functional filler for capsules and tablets that shows excellent synergistic effect in hardness when used in combination with lactose and starch.

### VIVAPRESS®
**Calcium Carbonate, Ph.Eur., USP**
**Precipitated Calcium Carbonate, JP**

A Direct Compressible, calcium containing filler. **VIVAPRESS®** meets Proposition 65 for lead content.

### COMPACTROL®
**Calcium Sulfate Dihydrate, NF**

A non-hygroscopic and free-flowing product that offers excellent and long-term stability. Due to its high bulk density and free-flowing characteristics, it imparts a high degree of fluidity which is essential for high-speed compaction and capsule filling.

## Disintegrants:

### EXPLOTAB®
**Sodium Starch Glycolate, Type (A) Ph.Eur., NF**
**Sodium Carboxymethyl Starch, JPE**

The First Super Disintegrant. JRS Pharma now manufactures and markets this Super Disintegrant to ensure consistent quality, availability and the premier technical support for which we are known.

### VIVASTAR®
**Sodium Starch Glycolate, Type (A) Ph.Eur., NF**
**Sodium Carboxymethyl Starch, JPE**

Super Disintegrant having great disintegration power and cost savings.

**VIVASTAR® PSF** is innovative in that it can improve stability of certain drugs by removing residual solvents.

### VIVASOL®
**Croscarmellose Sodium, Ph.Eur., NF, JPE**

Starch-free Super Disintegrant that adds excellent results at low use levels.

### EMCOSOY®
**Soy Polysaccharides**

An all natural Super Disintegrant, which does not contain starch or sugar. Being a dietary fiber, it has excellent application in nutritional products.

### SATIALGINE®
**Alginic Acid, NF**

A pharmaceutical grade alginic acid that offers rapid swelling in an aqueous medium. It can be moistened and dried without significant loss in disintegration and combines both a wicking and swelling mechanism to promote disintegration in either wet or dry granulations.

# JRS Excipients

# Product Overview



## Lubricants:

### PRUV™
**Sodium Stearyl Fumarate, Ph.Eur., NF, JPE**

**PRUV™** is a unique tablet lubricant that is more hydrophilic than traditional lubricants, less sensitive to blending and relatively inert. This results in tablets with improved disintegration and dissolution, harder tablets and better drug stability. It can be used in all tablet formulations including chewables and effervescent tablets.

### LUBRITAB®
**Hydrogenated Vegetable Oil, NF, BP**
**Hydrogenated Oil, JP**

Less chemically reactive than most common lubricants, it can also be used as an auxiliary dry binder and controlled release matrix.

## Carriers:

### NON-PAREIL SEEDS
**Sugar Spheres, NF**

Sugar Spheres are used in multiple drug units for improved content uniformity, consistent and controlled drug release and high drug stability.

## Coating and Sustained Release:

### VIVAPHARM®
**Hydroxylpropyl Methylcellulose, Hypromellose, Ph.Eur., USP**

Low viscosity types - the economical coating polymer for protecting tablets against moisture, light oxydation, and increased patients compliance.

High viscosity types - a reproducible way to produce matrix systems for sustained release applications with different dissolution profiles.

## Thickener and Stabilizer:

### VIVAPUR® MCG
**Microcrystalline Cellulose and Carboxymethylcellulose Sodium, NF**

An excellent thixotropic gelling agent to stabilize suspensions and emulsions. It is pH stable and could be used in hot and cold medium.

# FORMULATION HANDBOOK

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| | No. | ARBOCEL® Powdered Cellulose | EMCOMPRESS® Calcium Hydrogen Phosphate | EMCOSOY® Soy Polysaccharides | EMDEX® Dextrates | EXPLOTAB® Sodium Starch Glycolate | PROSOLV SMCC® Silicified Microcrystalline Cellulose | PRUV™ Sodium Stearyl Fumarate | VIVAPUR® Microcrystalline Cellulose | VIVASOL® Croscarmellose Sodium | VIVASTAR® Sodium Starch Glycolate |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Acetylsalicylic Acid | 4282-001 | | | | | | | | ● | ● | ● |
| Allopurinol | 4282-002 | | | | | | | | ● | | ● |
| Ambroxol HCl | 4282-003 | ● | | | | | | | ● | ● | |
| Boswellia Serrata | 4282-004 | | | | | | ● | ● | | | |
| Chromium Picoliante | 4282-005 | | | | | | ● | ● | | | |
| Ciprofloxacin HCl | 4282-006 | | | | | | | | ● | | |
| Enalapril | 4282-007 | | ● | | | | ● | ● | | | ● |
| Extract of Cartilage | 4282-008 | ● | ● | | | | ● | ● | | ● | |
| Ginkgo Biloba | 4282-009 | | | ● | | | ● | ● | | | |
| Glucosamine | 4282-010 | | | | | | ● | | | | |
| Guafenesin | 4282-011 | | | | | | ● | | | | |
| Ibuprofen (Direct Compression) | 4282-012 | | | | | | | | ● | | ● |
| Ibuprofen (Direct Compression) | 4282-013 | | | | | ● | ● | ● | | | |
| Ibuprofen (Wet Granulation) | 4282-014 | | | | | | ● | ● | | | |
| Metformin | 4282-015 | | | | | | ● | | | ● | |
| Metoprolol (Direct Compression) | 4282-016 | | ● | | | | | | ● | | ● |
| Metoprolol (Direct Compression) | 4282-017 | | ● | | | | | | ● | | |
| Natural Herbal Laxative Cassia Senna + Melissa off. | 4282-018 | | | | | | ● | ● | | | ● |
| Piroxicam | 4282-019 | ● | | | | | | | ● | ● | |
| Ranitidine HCl | 4282-020 | | | | | | | | ● | | ● |
| Simethicone | 4282-021 | | ● | | ● | | | | | | |

**Disclaimer:** The information provided is based on thorough research and is believed to be completely reliable. Application suggestions are given to assist our customers, but are for guidance only. Circumstances in which our material is used vary and are beyond our control. Therefore, we cannot assume any responsibility for risks or liabilities, which may result from the use of this technical advice.


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# 4282-001

**Key Words:** High Dosage, Direct Compression

**JRS Products:** VIVAPUR® 102, VIVASTAR® P, VIVASOL®

# Acetylsalicylic Acid Direct Compression



## Comments:

Acetylsalicylic Acid, also known by trade name Aspirin, is an acetyl derivative of salicylic acid which is a white, crystalline, weakly acidic substance, with melting point 137°C.
It is useful in the relief of headache and muscle and joint aches. Acetylsalicylic acid is also effective in reducing fever, inflammation, and swelling and thus has been used for treatment of rheumatoid arthritis, rheumatic fever, and mild infection.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Acetylsalicylic Acid** | 500.0 | 500.0 | 74.6 |
| **VIVAPUR® 102** (Microcrystalline Cellulose) | | 140.0 | 20.9 |
| **VIVASTAR® P** (Sodium Starch Glycolate) | | 23.4 | 3.5 |
| Magnesium Stearate | | 3.3 | 0.5 |
| Fumed Silica (Aerosil®) | | 3.3 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 670.0 mg |
| Tablet diameter: | 13 mm |
| Compaction force: | 27 - 28 kN |
| Hardness: | 79.1 N |
| Disintegration time: | 40 sec |

## Procedure

**Blending:**

Acetylsalicylic Acid, **VIVAPUR® 102** and **VIVASTAR® P** were blended to homogeneity for 15 minutes. Then a sieved mixture of Magnesium Stearate and Aerosil® were added and mixed for another 5 minutes. The powder mix is ready for Direct Compression.

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# # 4282-001

**Key Words:** High Dosage, Direct Compression

**JRS Products:** VIVAPUR® 102, VIVASTAR® P, VIVASOL®

# Acetylsalicylic Acid Direct Compression



| **Dissolution test:** | |
|---|---|
| Dissolution medium: | 900 ml 0.1 N HCl, 37°C, n=6 |
| Samples are taken after 5, 10, 20, 30, 45 and 60 minutes. The sample volume is 3 ml. | |
| The determination of the active ingredient is done by an UV-spectrophotometer at $\lambda$ = 280 nm. | |

## Equipment:

| | |
|---|---|
| Tablet press: | Korsch EK 0, instrumented |
| Turbula mixer: | Type T2A |
| Hardness tester : | Pharmatest PTB 311, n=6 |
| Friability tester: | ERWEKA TAP |
| Disintegration tester: | ERWEKA ZT 3 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Shimadzu UV-2101 PC |

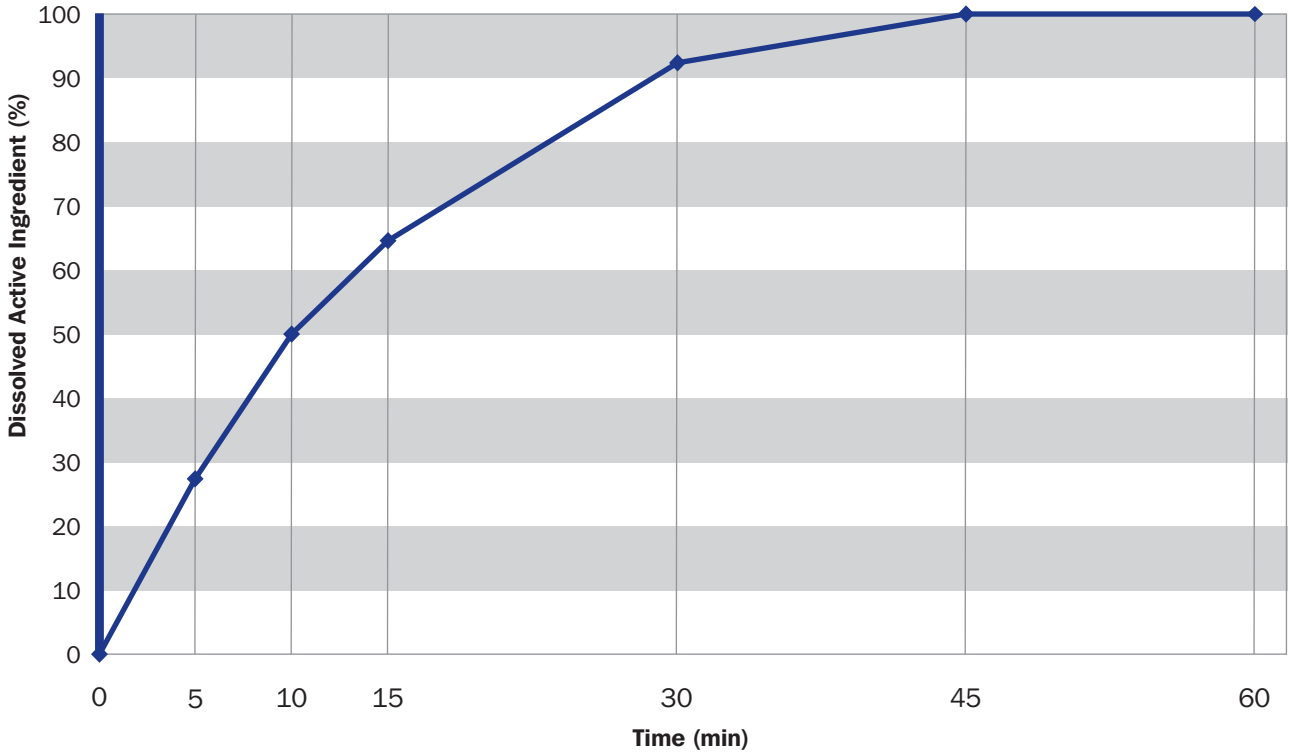


**Diagram 1:**
Typical dissolution profile diagram of an Acetylsalicylic Acid 500 mg tablet, produced according to the above given formulation.



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# FORMULATION HANDBOOK

# 4282-002

**Key Words:** Poor Flowability, Direct Compression

**JRS Products:** VIVAPUR® 102, VIVASTAR® P

# Allopurinol Direct Compression



## Comments:

Allopurinol is used to treat chronic gout (gouty arthritis). This condition is caused by too much uric acid in the blood. It is also used to prevent or treat other medical problems that may occur if too much uric acid is present in the body. These include certain kinds of kidney stones or other kidney problems.

Allopurinol can be directly compressed using **VIVAPUR®** Microcrystalline Cellulose as a binder.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Allopurinol** | 100.0 | 100.0 | 55.5 |
| **VIVAPUR® 102** (Microcrystalline Cellulose) | | 72.0 | 40.0 |
| **VIVASTAR® P** (Sodium Starch Glycolate) | | 6.2 | 3.5 |
| Magnesium Stearate | | 0.9 | 0.5 |
| Fumed Silica (Aerosil® 200) | | 0.9 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 180.0 mg |
| Tablet diameter: | 9 mm |
| Compaction force: | 24 - 25 kN |
| Hardness: | 91.3 N |
| Disintegration time: | 11 sec |

## Procedure

**Blending:**

Allopurinol, **VIVAPUR® 102** and **VIVASTAR® P** were mixed in a Turbula mixer for 15 minutes. Then a sieved mixture of Magnesium Stearate and Aerosil® were added and mixed for another 3 minutes. The powder mix was ready for Direct Compression.

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 9 mm punch,biplane |
| Turbula mixer: | Type T2A |
| Hardness tester: | Pharmatest PTB 311, n=6 |
| Friability tester: | Erweka TAP |
| Disintegration tester: | Erweka ZT 3 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Shimadzu UV-2101 PC |

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# # 4282-002

**Key Words:** Poor Flowability, Direct Compression

**JRS Products:** VIVAPUR® 102, VIVASTAR® P

## Allopurinol Direct Compression



| **Dissolution test:** | |
|---|---|
| Dissolution medium: | 900 ml 0.1 N HCl, 37°C, n=6 |
| Samples are taken after 5, 10, 20, 30, 45 and 60 minutes. The sample volume is 3 ml. Samples were diluted if necessary. The determination of the active ingredient is done by an UV-spectrophotometer at λ = 248.8 nm. | |

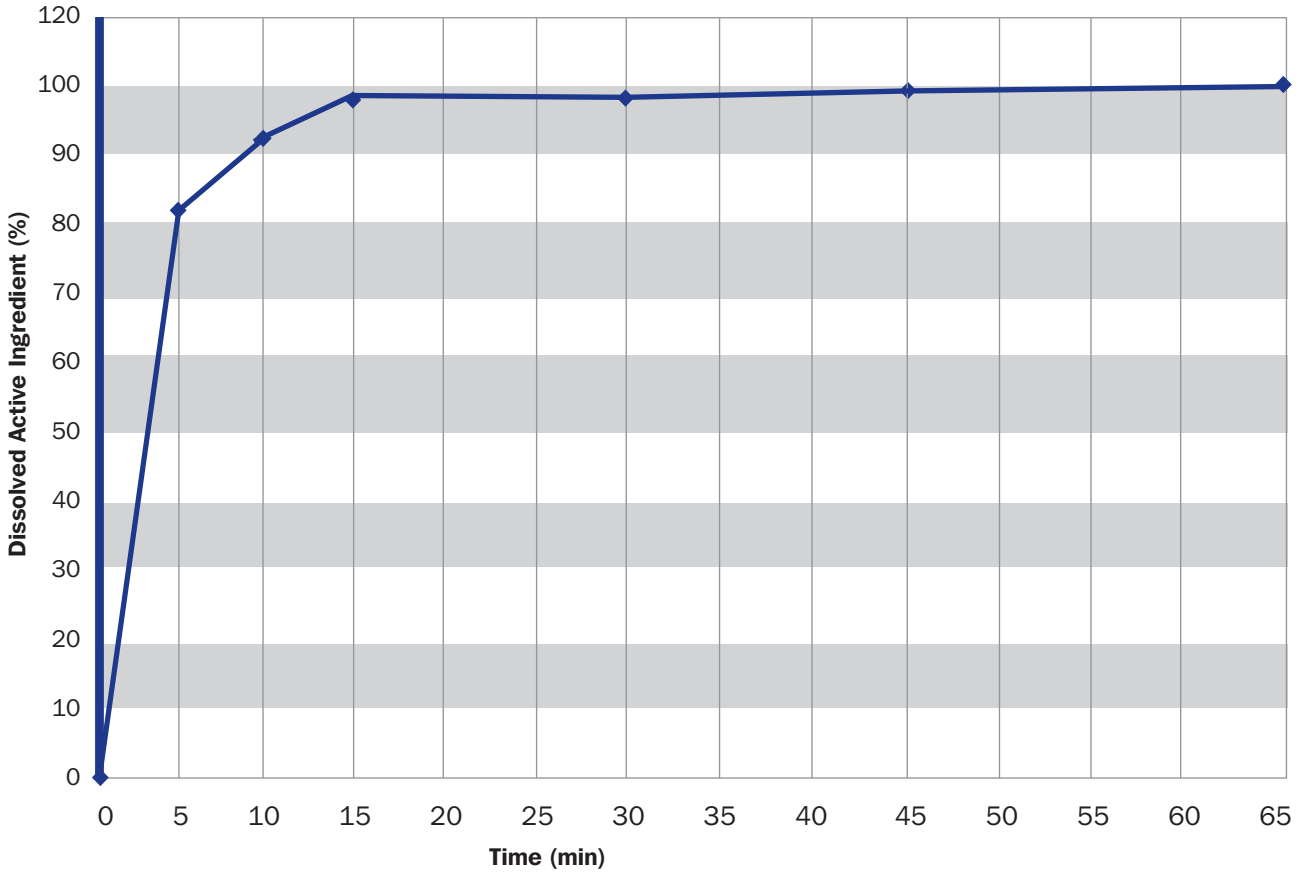


**Diagram 1:**
Typical dissolution profile diagram of a Allopurinol tablet, produced according to the above given formulation.



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# FORMULATION HANDBOOK

# # 4282-003

**Key Words:** Poorly Soluble, Low Dosage, Direct Compression
**JRS Products:** VIVAPUR® 12, ARBOCEL® A 300, VIVASOL®

# Ambroxol HCl Direct Compression



## Comments:

Ambroxol Hydrochloride is an example for a poorly soluble active substance used in low concentrations. It can be compressed directly by using **VIVAPUR®** Microcrystalline Cellulose as a dry binder and **ARBOCEL®** Powdered Cellulose as a plant-derived filler.

Ambroxol HCl is a mucolytic agent which is widely used in chronic bronchitis in Europe. Ambroxol HCl is very popular as an Active Pharmaceutical Ingredient for children.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Ambroxol HCl** | 30.0 | 30.00 | 20.0 |
| **VIVAPUR® 12** (Microcrystalline Cellulose) | | 69.30 | 46.2 |
| **ARBOCEL® A 300** (Powdered Cellulose) | | 46.20 | 30.8 |
| **VIVASOL®** (Croscarmellose Sodium) | | 3.00 | 2.0 |
| Magnesium Stearate | | 0.75 | 0.5 |
| Fumed Silica (Aerosil® 200) | | 0.75 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 150.0 mg |
| Tablet diameter: | 8 mm |
| Compaction force: | 12.5 kN |
| Hardness: | 64.0 N |
| Disintegration time: | 13 sec |
| Friability: | <0.1 % |

## Procedure

**Blending:**
All ingredients were mixed for 4 minutes and compressed at a compaction force of approx. 12.5 kN.

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 8 mm punch |
| Turbula mixer: | Type T2A |
| Hardness tester: | Pharmatest PTB 311 |
| Friability tester: | ERWEKA TAP |
| Disintegration tester: | ERWEKA ZT 3 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Shimadzu UV-2101 PC |

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# # 4282-003

**Key Words:** Poorly Soluble, Low Dosage, Direct Compression
**JRS Products:** VIVAPUR® 12, ARBOCEL® A 300, VIVASOL®

## Ambroxol HCl
## Direct Compression



| **Dissolution test:** | |
|---|---|
| Dissolution medium: | 900 ml 0.1 N HCl, 37°C, n=6 |
| Samples are taken after 1, 5, 10, 15, 20, 30, 45, 60, 75 and 90 minutes. The sample volume is 3 ml. Samples were diluted if necessary. The determination of the active ingredient is done by an UV-spectrophotometer at λ = 223 nm. | |

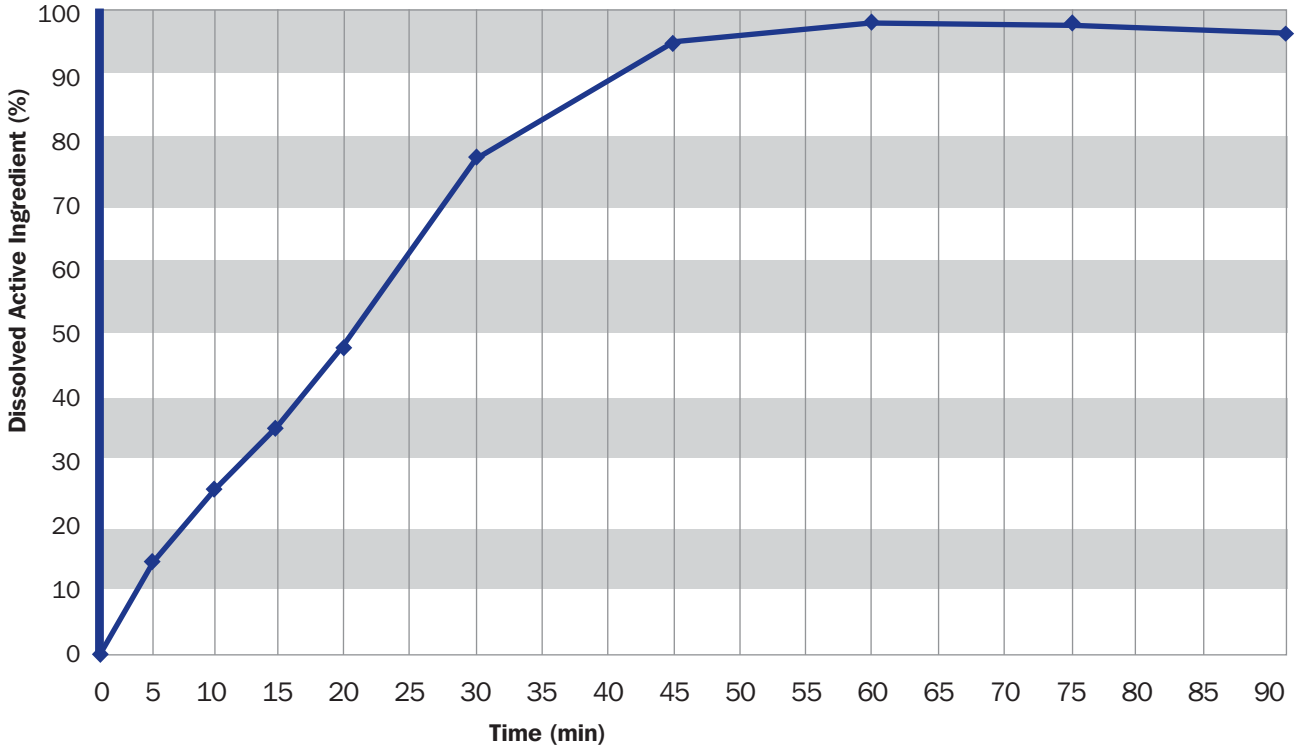


**Diagram 1:**
Typical dissolution profile diagram of a Ambroxol tablet, produced according to the above given formulation.



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# FORMULATION HANDBOOK

# # 4282-004

**Key Words:** Botanical Extract, Sticky Active, High Dosage, Direct Compression
**JRS Products:** PROSOLV® HD 90, PRUV™

# Boswellia Serrata Direct Compression



## Comments:

Boswellia has been used historically for various conditions, including arthritis and other inflammation. It is a gum resin, cohesive in nature and, consequently, poorly flowing. Since Boswellia extract is a gum resin, it is also very poorly compactable. Due to its physical characteristics, Boswellia is generally granulated prior to tablet manufacture.

Using **PROSOLV® HD 90**, Boswellia was formulated into a directly compressible tablet.
**PROSOLV® HD 90** not only provided the necessary binding properties required for direct compression tableting, but also served as the tablet disintegrant.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Boswellia extract** | 200.0 | 200.0 | 49.75 |
| **PROSOLV® HD 90** (Silicified Microcrystalline Cellulose) | | 200.0 | 49.75 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 2.0 | 0.50 |

## Tablet Characteristics

| | |
|---|---|
| Tablet mass: | 402 mg |
| Hardness: | 14.4 kp |
| Compaction force: | 15.2 kN |
| Tablet weight variation: | 2.3% |
| Tablet disintegration time: | 225 sec |

## Procedure

**Blending:**

**PROSOLV® HD 90** and **PRUV™** were dispensed to the correct masses and transferred to a Patterson-Kelly twin-shell V-blender. Boswellia was sieved through a twenty mesh and transferred into the V-blender. The powders were blended for five minutes.

| **Equipment:** | |
|---|---|
| Blender: | Patterson-Kelly twin-shell V-blender |
| Flowability apparatus: | Hanson Research Flodex™ |
| Tablet press: | Korsch PH-106 instrumented rotary tablet press |
| Hardness tester: | Erweka TBH-30 |
| Disintegration tester: | Erweka ZT-62 |
| Friability tester: | Erweka TA-3 |



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# FORMULATION HANDBOOK

# 4282-005

**Key Words :** Sticky Active, High Dosage, Direct Compression

**JRS Products:** PROSOLV SMCC®, PRUV™

## Chromium Picolinate Direct Compression



## Comments:

Chromium Picolinate is a poorly flowing, low dose biomolecule. Chromium is an essential trace element. It is reported to play an important role in blood sugar regulation and acts as a cofactor to a number of enzymes involved in energy production as well as reducing lipid levels. It can be directly compressed using a combination of **PROSOLV SMCC® 50** and **PROSOLV SMCC® 90**.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Chromium Picolinate** | 0.4 | 0.4 | 0.27 |
| **PROSOLV SMCC® 50** (Silicified Microcrystalline Cellulose) | | 15.0 | 9.95 |
| **PROSOLV SMCC® 90** (Silicified Microcrystalline Cellulose) | | 135.0 | 89.58 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 0.3 | 0.20 |

## Tablet Characteristics

| | |
|---|---|
| Tablet mass: | 151 mg |
| Hardness: | 20 kN |
| Compaction force: | 23 kp |
| Tablet disintegration time: | 158 sec |

## Procedure

**Blending:**

Chromium Picolinate, **PROSOLV SMCC® 90** and **PROSOLV SMCC® 50** added to the V-blender and blended for 30 minutes. **PRUV™** was added to the blender and blended for additional three minutes.

| **Equipment:** | |
|---|---|
| Blender: | Patterson-Kelly 2 qt. twin-shell V-blender |
| Flowability apparatus: | Hanson Research Flodex™ |
| Tablet press: | Korsch PH-106 rotary tablet press |
| Hardness tester: | Erweka TBH-30 |
| Disintegration tester: | Erweka ZT-62 |
| Friability tester: | Erweka TA-3 |



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# FORMULATION HANDBOOK

# # 4282-006

**Key Words:** Very Low Bulk Density, Dry Compaction
**JRS Products:** VIVAPUR® 12

# Ciprofloxacin HCl Dry Compaction



## Comments:

Ciprofloxacin HCl is a material of very low bulk density and has to be **precompacted**. This can be done with a dry compactor or by "re-processing".
Ciprofloxacin is an antibiotic that stops multiplication of bacteria by inhibiting the reproduction and repair of their genetic material (DNA).

Ciprofloxacin is used to treat infections of the skin, lungs, airways, bones, and joints caused by susceptible bacteria. Ciprofloxacin is also frequently used to treat urinary infections caused by bacteria such as E. Coli. Ciprofloxacin HCl is effective in treating infectious diarrheas caused by E. Coli, Ciprofloxacin campylobacter jejuni and shigella bacteria.

## Formulation

### Step 1 (Granules)

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Ciprofloxacin HCl** | 500.0 | 500.0 | 85.1 |
| **VIVAPUR® 12** (Microcrystalline Cellulose) | | 75.0 | 12.8 |
| Magnesium Stearate | | 7.5 | 1.3 |
| Fumed Silica (Aerosil® 200) | | 5.0 | 0.8 |

### Step 2 (Tablets)

| | mg/tablet | Contribution (%) |
|---|---|---|
| **Ciprofloxacin Granules** | 587.5 | 85.1 |
| **VIVAPUR® 12** (Microcrystalline Cellulose) | 93.5 | 13.6 |
| Magnesium Stearate | 5.0 | 0.7 |
| Fumed Silica (**Aerosil® 200**) | 4.0 | 0.6 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 690.0 mg |
| Tablet diameter: | 13 mm |
| Compaction force: | 8.5 kN |
| Hardness: | 109.7 N |
| Disintegration time: | 9 min |
| Friability: | 0.36 % |

## Procedure

**Blending:**
In the **first step** tablets were made of 20 mm insize and in the **second step** the tablets have been crushed by passing them through a dry granulator with a screen size of 19 mesh (800 $\mu$m). The resulting granules have been compressed to the final tablet by mixing of all ingredients for 4 minutes and compressing at a compaction force of approx. 8.5 kN.

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# # 4282-006

**Key Words:** Very Low Bulk Density, Dry Compaction
**JRS Products:** VIVAPUR® 12

## Ciprofloxacin HCl Dry Compaction



| Equipment: | |
|---|---|
| Granulator: | Erweka 20240 |
| Tablet press: | Korsch EK 0 excentric press, 13 mm punch |
| Turbula mixer: | Type T2A |
| Hardness tester: | Schleuniger Type 2 E |
| Friability tester: | Pharmatest Type PTF 1, Nr. 6453 |
| Disintegration tester: | Pharmatest Standard, Type PTZ, Nr. 6454 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Cecil Spectrophotometer, Series 1000 (CE 1021) |

| Dissolution test: | |
|---|---|
| Dissolution medium: | 900 ml 0.1 N HCl, 37°C, n=6 |
| Samples are taken after 1, 5, 10, 20, 30, 60, 90, 120, 180, 240 and 300 minutes. The determination of the active ingredient is done by an UV-spectrophotometer at $\lambda$ = 278.7 nm. | |

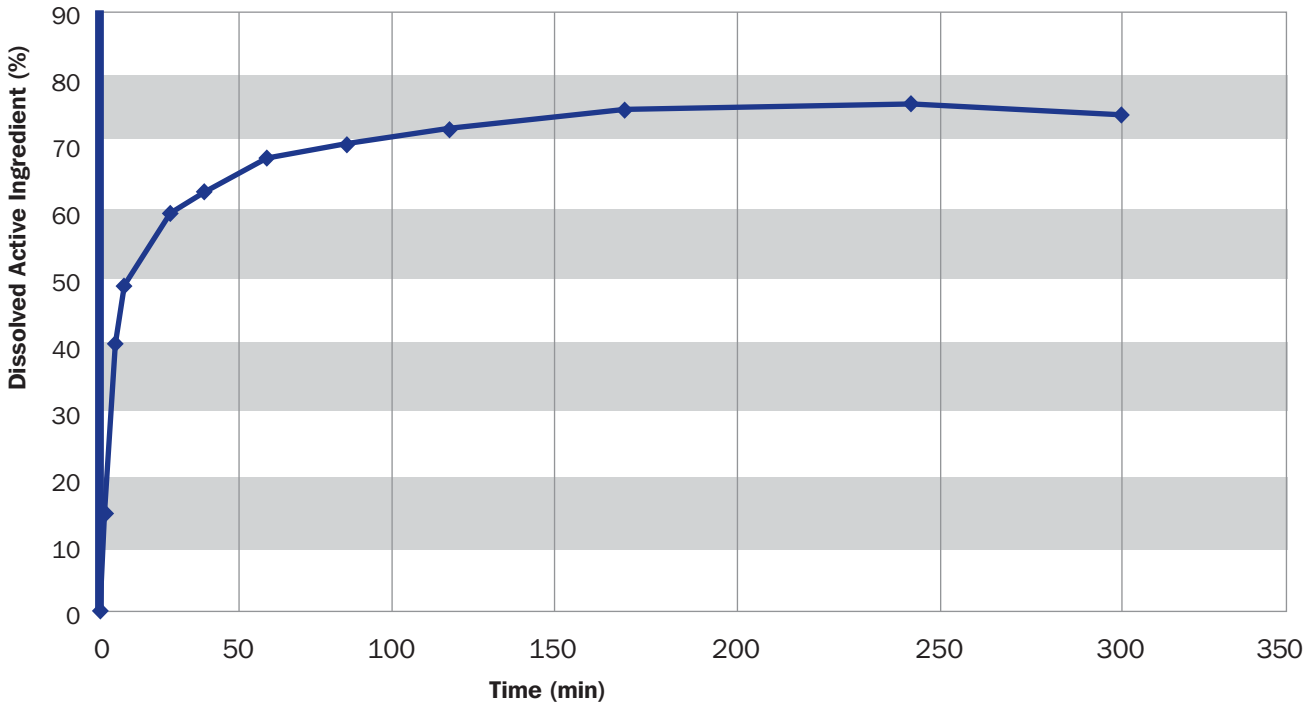


**Diagram 1:**
Typical dissolution profile diagram of a Ciprofloxacin tablet, produced according to the above given formulation.



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# FORMULATION HANDBOOK

# # 4282-007

**Key Words:** Poor Flowability, Low Dosage, Direct Compression
**JRS Products:** PROSOLV SMCC® 90, EMCOMPRESS®, VIVASTAR®, PRUV™

# Enalapril Direct Compression



## Comments:

Enalapril is in a case of drugs called Angiotensin-Converting-Enzyme Inhibitors (ACE Inhibitors). It is used to lower blood pressure and to prevent and treat heart failure.

Enalapril which is a poor flowing API can be directly compressed using **PROSOLV SMCC® 90** and **EMCOMPRESS®** as binders.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Enalapril maleate** | 10.0 | 10.0 | 5.1 |
| **PROSOLV SMCC® 90** (Silicified Microcrystalline Cellulose) | | 93.7 | 47.8 |
| **EMCOMPRESS®** (Calcium Hydrogen Phosphate) | | 85.4 | 43.6 |
| **VIVASTAR® P** (Sodium Starch Glycolate) | | 5.9 | 3.0 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 1.0 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 196.0 mg |
| Tablet diameter: | 8 mm |
| Angle of repose: | 43° |
| Bulk density: | 0.52 g/ml |
| Compaction force: | 17 - 18 kN |
| Hardness: | 10.8 kp |
| Friability: | 0.03 % |
| Disintegration time: | 14 sec |

## Procedure

**Blending:**

Enalapril maleate, **PROSOLV SMCC® 90, EMCOMPRESS®** and **VIVASTAR® P** were blended to homogeneity for 10 minutes. Then **PRUV™** was added and mixed for another 3 minutes. The powder-mix was ready for direct compression.

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 8 mm punch |
| Hardness tester: | Schleuniger 2E |
| Friability tester: | Pharmatest PFT |
| Disintegration tester: | Pharmatest Standard PTZ |



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# FORMULATION HANDBOOK

# # 4282-008

**Key Words:** Very Hygroscopic, Sticky, Direct Compression
**JRS Products:** PROSOLV SMCC® 90, EMCOMPRESS®, ARBOCEL® P 290, VIVASOL®, PRUV™

# Extract of Cartilage Direct Compression



## Comments:

Extract of Cartilage is a hygroscopic substance with a very high water content. The substance is very sticky. The extract is a product made from the cartilage of the common dogfish shark. There are several diseases which can affect the cartilage, for example arthritis.
It was possible to develop a simple formulation with **PROSOLV SMCC®** Silicified Microcrystaline Cellulose in Direct Compression.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Extract of Cartilage** | 186.9 | 186.9 | 35.6 |
| Ascorbic Acid crystalline | | 43.5 | 8.3 |
| **PROSOLV SMCC® 90** (Silicified Microcrystalline Cellulose) | | 199.0 | 37.9 |
| **EMCOMPRESS®** (Calcium Hydrogen Phosphate) | | 70.3 | 13.4 |
| **ARBOCEL® P 290** (Powdered Cellulose) | | 5.25 | 1.0 |
| Talcum | | 9.45 | 1.8 |
| **VIVASOL®** (Croscarmellose Sodium) | | 8.0 | 1.5 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 2.6 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 525.0 mg |
| Tablet diameter: | 13 mm |
| Angle of repose: | 44° |
| Bulk density: | 0.49 g/ml |
| Compaction force: | 9.1 kN / 18.4 KN / 22 KN |
| Hardness: | 2.5 kp / 7.3 kp / 9.7 kp |
| Friability: | 0.26 % |
| Disintegration time: | 25 min |

## Procedure

**Blending:**

Extract of Cartilage, Ascorbic Acid, **PROSOLV SMCC® 90** and **EMCOMPRESS®** were blended for 15 minutes. **ARBOCEL® P 290**, Talcum and **VIVASOL®** were added and blended for another 10 minutes. After that **PRUV™** was added and mixed for 3 minutes.

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 13 mm punch |
| Hardness tester: | Schleuniger 2E |
| Disintegration tester: | Pharmatest Standard PTZ |
| Friability tester: | Pharmatest PTF |



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# FORMULATION HANDBOOK

# # 4282-009

**Key Words:** Sticky Active, High Dosage, Direct Compression
**JRS Products:** PROSOLV SMCC® 90, EMCOSOY®, PRUV™

# Ginkgo Biloba Direct Compression



## Comments:

Ginkgo Biloba extract is a poorly flowing, poorly compressible herbal extract used as a short-term memory enhancing natural herbal remedy. It can be directly compressed using **PROSOLV SMCC® 90** due to its enhanced flow, compaction, and excellent active loading properties. Tablet disintegration is achieved using **EMCOSOY®**, a naturally derived soy polysaccharide disintegrant.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Ginkgo Biloba extract** | 60.0 | 60.0 | 46.2 |
| **PROSOLV SMCC® 90** (Silicified Microcrystalline Cellulose) | | 60.6 | 46.6 |
| **EMCOSOY®** (Soy Polysaccharides) | | 6.0 | 4.6 |
| Talcum | | 3.0 | 2.3 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 0.4 | 0.3 |

## Tablet Characteristics

| | |
|---|---|
| Tablet mass: | 130 mg |
| Hardness: | 19.65 kp |
| Compaction force: | 12.0 kN |
| Tablet disintegration time: | 180 sec |

## Procedure

**Blending:**

Add Ginkgo Biloba extract and **PROSOLV SMCC® 90** to the blender and mix for 10 minutes. Add **EMCOSOY®** and Talcum to the blender and blend for 10 minutes. Add **PRUV™** to the blender and mix for additional five minutes.

| **Equipment:** | |
|---|---|
| Blender: | Patterson-Kelly 2 qt. twin-shell V-blender |
| Tablet press: | Korsch PH-106 rotary tablet press |
| Hardness tester: | Erweka TBH-30 |
| Disintegration tester: | Erweka ZT-62 |



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# FORMULATION HANDBOOK

# # 4282-010

**Key Words:** Very Hygroscopic, Sticky, Direct Compression
**JRS Products:** PROSOLV SMCC® 90

# Glucosamine Direct Compression



## Comments:

Glucosamine is a very hygroscopic and sticky substance. It is found naturally in the body and it´s a form of amino sugar that is believed to play a role in cartilage formation and repair. Glucosamine is extracted from animal tissue (carb, lobster or shrimp shells) and is promoted as a treatment of arthritis. It was possible to develop a simple formulation with **PROSOLV SMCC®** in Direct Compression.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Glucosamine** | 250.0 | 250.0 | 65.0 |
| **PROSOLV SMCC® 90** (Silicified Microcrystalline Cellulose) | | 130.9 | 34.0 |
| Magnesium Stearate | | 4.1 | 1.0 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 385.0 mg |
| Tablet diameter: | 20 mm |
| Angle of repose: | 42° |
| Bulk density: | 0.52 g/ml |
| Compaction force: | 25 - 27 kN |
| Hardness: | 7.8 kp |
| Disintegration time: | 1 min 20 sec |

## Procedure

**Blending:**

Glucosamine and **PROSOLV SMCC® 90** were blended to homogeneity for 15 minutes. Then Magnesium Stearate was added and mixed for another 3 minutes. The powder mix was ready for direct compression.

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 20 mm punch |
| Hardness tester: | Schleuniger 2E |
| Disintegration tester: | Pharmatest Standard PTZ |



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# FORMULATION HANDBOOK

# 4282-011

**Key Words:** Sticky Active, High Dosage, Direct Compression
**JRS Products:** PROSOLV® HD 90

# Guafenesin Direct Compression



## Comments:

Guafenesin is a flocculated, low melting point expectorant. It is poorly flowing and poorly compressible and is typically granulated prior to solid dosage form manufacture.
**PROSOLV® HD 90** delivered a directly compressible, disintegrating tablet with excellent formulation and tableting characteristics. By comparison, **PROSOLV® HD 90** provided harder, smaller tablets at lower compaction forces than comparable high density microcrystalline cellulose formulations.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Guafenesin** | 200.0 | 200.0 | 40.0 |
| **PROSOLV® HD 90** (Silicified Microcrystalline Cellulose) | | 295.0 | 59.0 |
| Talcum | | 5.0 | 1.0 |

## Tablet Characteristics

| | |
|---|---|
| Tablet mass: | 500 mg |
| Hardness: | 12 kp |
| Compaction force: | 8.5 kN |
| Tablet thickness: | 5.1 mm |
| Tablet disintegration time: | 5 sec |

## Procedure

**Blending:**

**PROSOLV® HD 90** and Talcum were dispensed to the correct masses and transferred to a Patterson-Kelly twin-shell V-blender. Guafenesin was sieved through a twenty sieve and transferred into the V-blender. The powders were blended for five minutes.

| **Equipment:** | |
|---|---|
| Blender: | Patterson-Kelly twin-shell V-blender |
| Flowability apparatus: | Hanson Research Flodex™ |
| Tablet press: | Riva Piccola instrumented rotary tablet press |
| Hardness tester: | Key HT-500 |
| Disintegration tester: | GlobePharma ED-2L |
| Friability tester: | GlobePharma FT-400 |



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# # 4282-011

**Key Words:** Sticky Active, High Dosage, Direct Compression
**JRS Products:** PROSOLV® HD 90

## Guafenesin Direct Compression



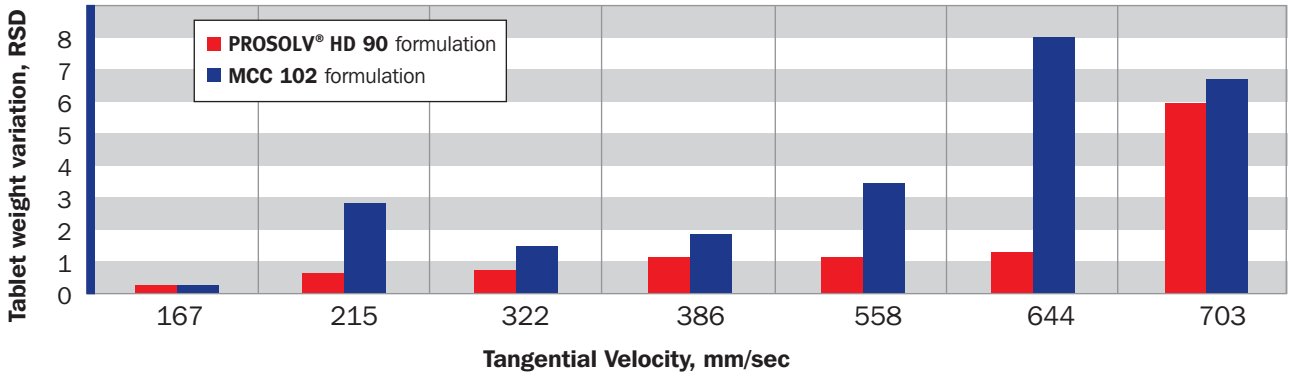


**Diagram 1:**
Tablet Weight Variation as a Function of Die Table Tangential

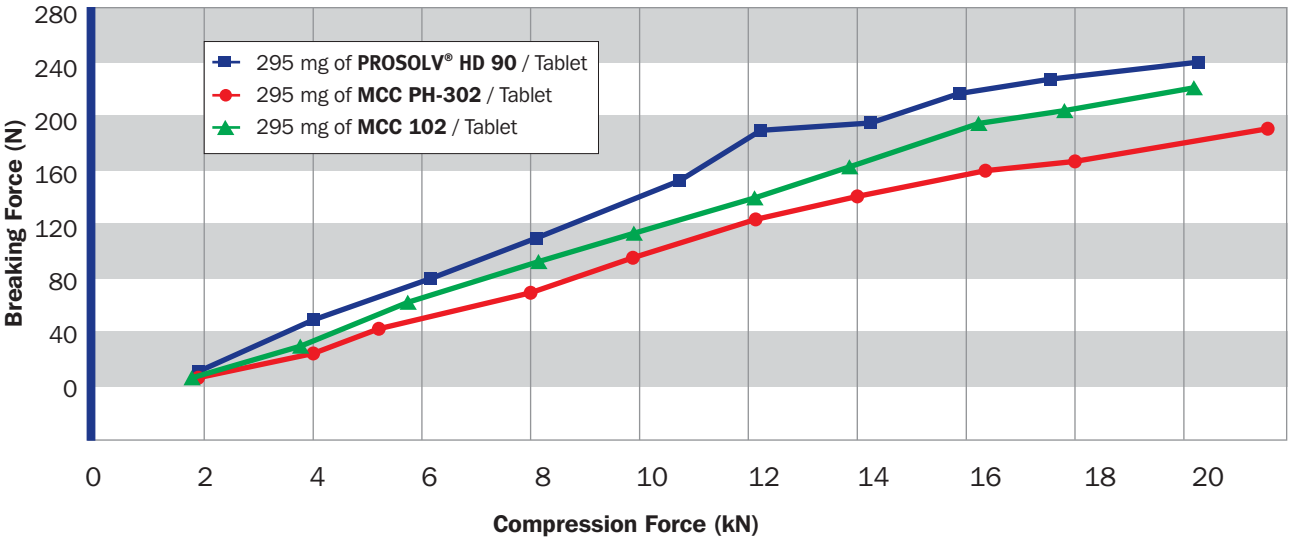


**Diagram 2:**
Tablet Hardness as a Function of Compaction Force

200 mg Guafenesin Tablet Formulation Compaction Profiles

| | | |
|---|---|---|
| High density Microcrystalline Cellulose formulation |  | **PROSOLV® HD 90** formulation |

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# FORMULATION HANDBOOK

# 4282-012

**Key Words:** Sticky Active, High Dosage, Direct Compression
**JRS Products:** VIVAPUR® 102, VIVASTAR® P

# Ibuprofen Direct Compression



## Comments:

Ibuprofen is a poorly flowing, poorly compacting, low melting point, waxy API used to relieve minor pain, tenderness and inflammation. Ibuprofen belongs to the group Non-Steroidal Anti-Inflammatory Drug (NSAIDs). Because of its relatively low anti-inflammatory properties it is often used in high dosage. Ibuprofen can be directly compressed using **VIVAPUR®** Microcrystalline Cellulose as a binder and as disintegrant.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Ibuprofen** | 200.7 | 200.7 | 47.5 |
| **VIVAPUR® 102** (Microcrystalline Cellulose) | | 200.7 | 47.5 |
| **VIVASTAR® P** (Sodium Starch Glycolate) | | 16.9 | 4.0 |
| Magnesium Stearate | | 2.1 | 0.5 |
| Fumed Silica (Aerosil®) | | 2.1 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 422.5 mg |
| Tablet diameter: | 7 mm |
| Compaction force: | 23 - 24 kN |
| Hardness: | 83.6 N |
| Disintegration time: | 9 sec |

## Procedure

**Blending:**

Ibuprofen, **VIVAPUR® 102** and **VIVASTAR® P** were blended to homogeneity for 15 minutes. Then a sieved mixture of Magnesium Stearate and Aerosil® were added and mixed for another 5 minutes. The powder mix is ready for Direct Compression.

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# # 4282-012

**Key Words:** Sticky Active, High Dosage, Direct Compression
**JRS Products:** VIVAPUR® 102, VIVASTAR® P

## Ibuprofen Direct Compression



| **Dissolution test:** | |
|---|---|
| Dissolution medium: | 900 ml buffer pH 7.4, 37°C, n=6 |
| Samples are taken after 5, 10, 20, 30, 45 and 60 minutes. The sample volume is 3 ml. The determination of the active ingredient is done by an UV-spectrophotometer at λ = 222 nm (diluted 1:9). | |

## Equipment:

| | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 7 mm punch, biplane |
| Turbula mixer: | Type T2A |
| Hardness tester : | Pharmatest PTB 311, n=6 |
| Friability tester: | ERWEKA TAP |
| Disintegration tester: | ERWEKA ZT 3 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Shimadzu UV-2101 PC |

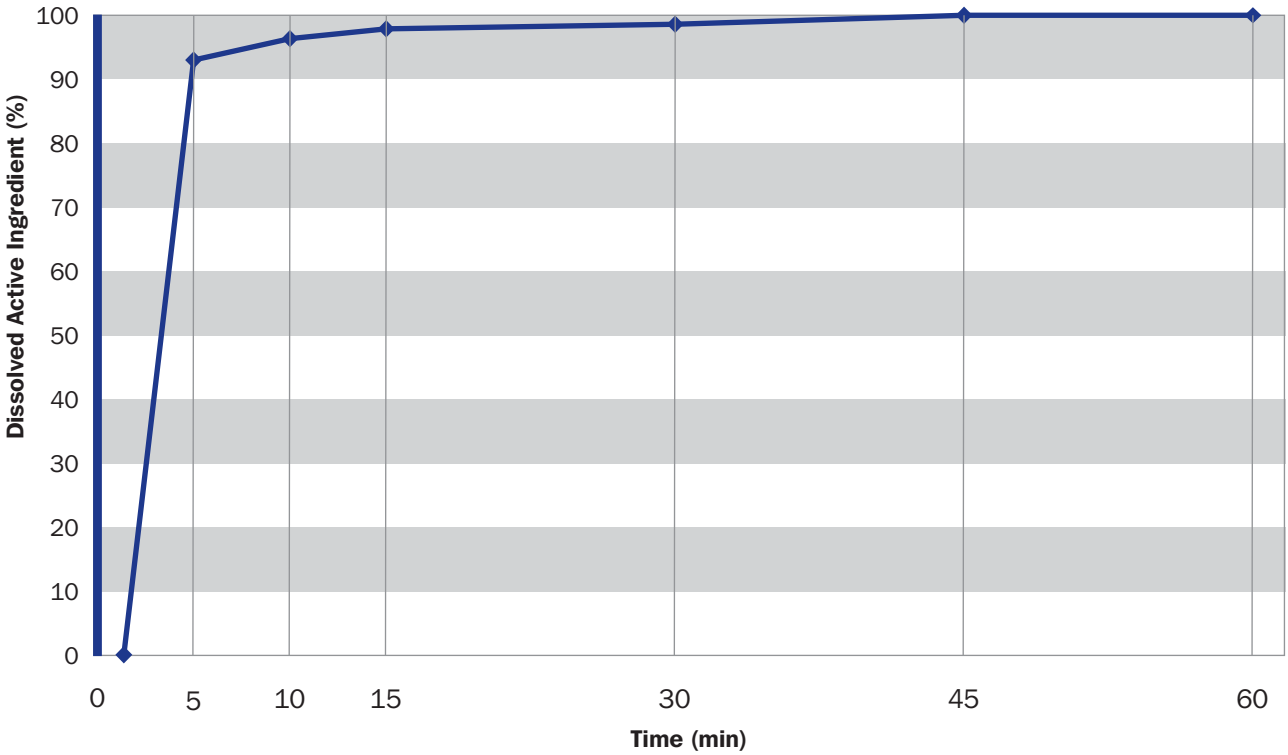


**Diagram 1:**
Typical dissolution profile diagram of a Ibuprofen 200 mg tablet, produced according to the above given formulation.



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# FORMULATION HANDBOOK

# # 4282-013

**Key Words:** Sticky Active, High Dosage, Direct Compression
**JRS Products:** PROSOLV SMCC® 90, EXPLOTAB®, PRUV™

# Ibuprofen Direct Compression



## Comments:

Ibuprofen is a poorly flowing, poorly compacting, low melting point, waxy API used to relieve minor pain, tenderness and inflammation. **PROSOLV SMCC® 90**, due to its excellent rheological properties and high inherent compactibility, provided a directly compressible tablet with improved mechanical characteristics, where other conventional tableting ingredients failed in Direct Compression applications.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Ibuprofen** | 200.0 | 200.0 | 55.5 |
| **PROSOLV SMCC® 90** (Silicified Microcrystalline Cellulose) | | 148.0 | 41.2 |
| **EXPLOTAB®** (Sodium Starch Glycolate) | | 6.0 | 1.6 |
| Talcum | | 4.0 | 1.1 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 2.0 | 0.6 |

## Tablet Characteristics

| | |
|---|---|
| Tablet mass: | 360 mg |
| Flow rate: | 14.3 g/sec |
| Angle of repose: | 26° |
| Hardness: | 4.8 kp |
| Compaction force: | 12.0 kN |
| Friability: | 0.47 % |

## Procedure

**Blending:**

Each ingredient, excluding the lubricant, was dispensed to the correct mass and transferred to the V-blender and mixed for 10 minutes. **PRUV™** was dispensed to the correct mass, transferred to the V-blender and mixed for additional five minutes.

| **Equipment:** | |
|---|---|
| Blender: | Twin-shell V-blender |
| Flowability: | Ph. Eur. Method 2.9.16 |
| Tablet press: | Korsch instrumented tablet press |



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# FORMULATION HANDBOOK

# # 4282-015

**Key Words:** Sticky Active, High Dosage, Direct Compression
**JRS Products:** PROSOLV SMCC® 90, VIVASOL®, PRUV™

# Metformin Direct Compression



## Comments:

Metformin is a very popular pharmaceutical active ingredient. Because of the high dosages of this active, metformin normally is wet granulated. This formulation is for Direct Compression with **PROSOLV SMCC®**.

Metformin is used to regulate blood glucose (sugar) levels. It is mainly to treat non-insulin-dependent diabetes mellitus (Type II diabetes).

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Metformin** (Biesterfeld) | 850.0 | 850.0 | 70.8 |
| **PROSOLV SMCC® 90** (Silicified Microcrystalline Cellulose) | | 319.0 | 26.6 |
| **VIVASOL®** (Croscarmellose Sodium) | | 25.0 | 2.1 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 6.0 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| **Powder Mix:** | |
| Angle of repose: | 37° |
| Bulk density: | 0.59 g/ml |
| **Tablet:** | |
| Tablet weight: | 1200 mg |
| Diameter of tablet: | 16 mm |
| Compaction force: | 18 - 20 kN |
| Hardness: | 5.2 - 5.5 kp |
| Disintegration time: | 17 sec |

## Procedure

**Blending:**
Metformin, **PROSOLV SMCC® 90** and **VIVASOL®** were blended to homogeneity. Then **PRUV™** was added and mixed for another 3 minutes. The powder-mix was ready for Direct Compression.

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0, instrumented |
| Hardness tester: | Schleuniger 2E |
| Disintegration tester: | Pharmatest Standard PTZ |
| Dissolution tester: | Pharmatest PTW 2 |
| Spectrophotometer: | Cecil Spektralphotometer, Series 1000 |

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# # 4282-015

**Key Words:** Sticky Active, High Dosage, Direct Compression
**JRS Products:** PROSOLV SMCC® 90, VIVASOL®, PRUV™

## Metformin Direct Compression



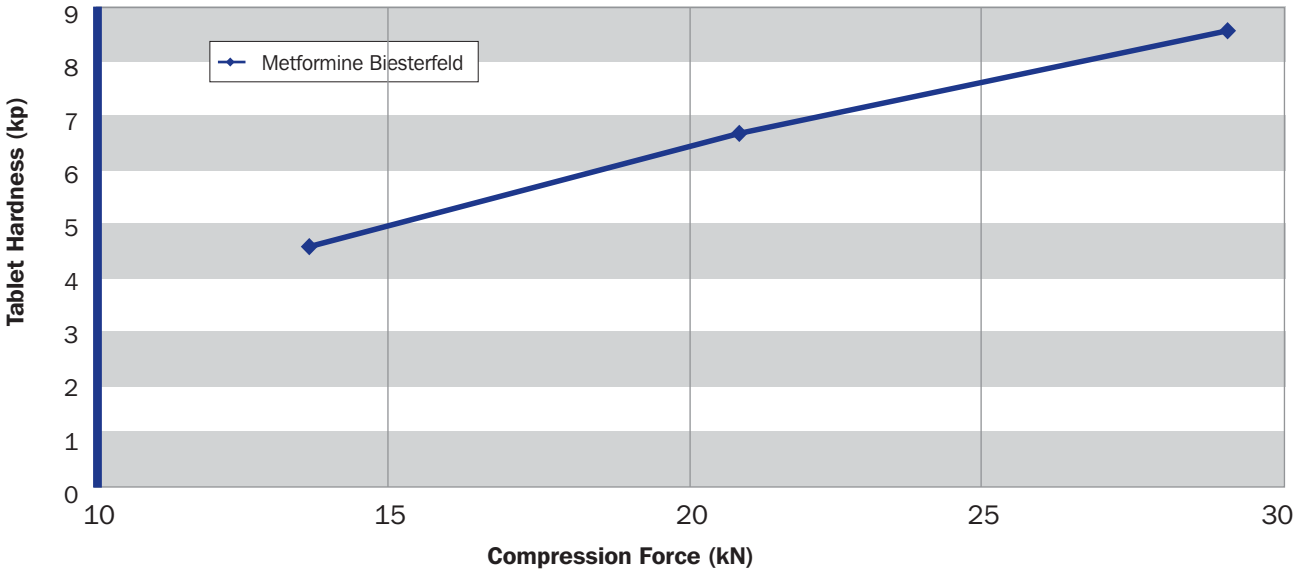


**Diagram 1:**
Typical compression diagram of a Metformin tablet, produced according to the above given formulation.

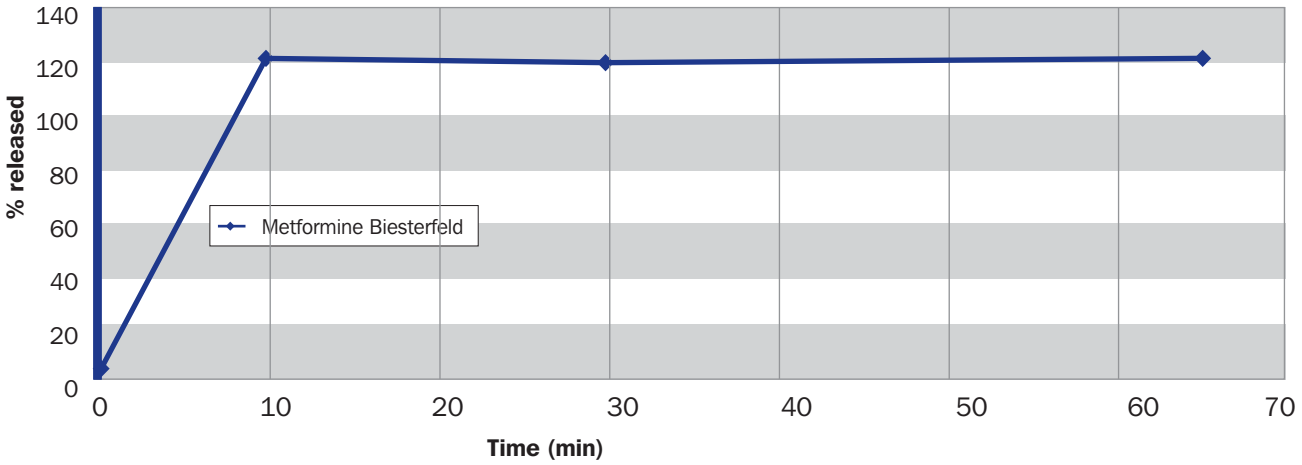


**Diagram 2:**
Typical dissolution profile diagram of a Metformin tablet, produced according to the above given formulation.



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# 4282-016

**Key Words:** Highly Soluble, Medium Concentration, Direct Compression
**JRS Products:** VIVAPUR® 12, VIVASTAR® P, EMCOMPRESS®

# Metoprolol Direct Compression



## Comments:

Metoprolol tartrate is an example for a highly soluble active used in medium concentrations.
Metoprolol is a selective $\beta_1$-adrenoreceptor blocking agent to treat hypertension and to prevent angina pectoris.

It can be directly compressed using **VIVAPUR®** Microcrystalline Cellulose and **EMCOMPRESS®** Calcium Hydrogen Phospate as a combination of binders.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Metoprolol tartrate** | 50.88 | 50.88 | 27.5 |
| **EMCOMPRESS®** (Calcium Hydrogen Phosphate) | | 50.88 | 27.5 |
| **VIVAPUR® 12** (Microcrystalline Cellulose) | | 74.00 | 40.0 |
| **VIVASTAR® P** (Sodium Starch Glycolate) | | 7.40 | 4.0 |
| Magnesium Stearate | | 0.93 | 0.5 |
| Fumed Silica (**Aerosil® 200**) | | 0.93 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 185.0 mg |
| Tablet diameter: | 8 mm |
| Compaction force: | 32 - 33 kN |
| Hardness: | 81.9 N |
| Disintegration time: | 9 min 38 sec |

## Procedure

**Blending:**

Metoprolol tartrate, **EMCOMPRESS®**, **VIVAPUR® 12** and **VIVASTAR® P** were mixed in a Turbula mixer for 15 minutes. Then a sieved mixture of Magnesium Stearate and Aerosil® was added and mixed for another 3 minutes. The powder mix was ready for Direct Compression.

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 8 mm punch, biplane |
| Turbula mixer: | Type T2A |
| Hardness tester: | Pharmatest PTB 311, n=6 |
| Friability tester: | Erweka TAP |
| Disintegration tester: | Erweka ZT 3 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Shimadzu UV-2101 PC |

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# # 4282-016

**Key Words:** Highly Soluble, Medium Concentration, Direct Compression
**JRS Products:** VIVAPUR® 12, VIVASTAR® P, EMCOMPRESS®

## Metoprolol Direct Compression



| **Dissolution test:** | |
|---|---|
| Dissolution medium: | 900 ml 0.1 N HCl, 37°C, n=6 |
| Samples are taken after 5, 10, 20, 30, 45 and 60 minutes. The sample volume is 3 ml. Samples were diluted if necessary. The determination of the active ingredient is done by an UV-spectrophotometer at λ = 222 nm. | |

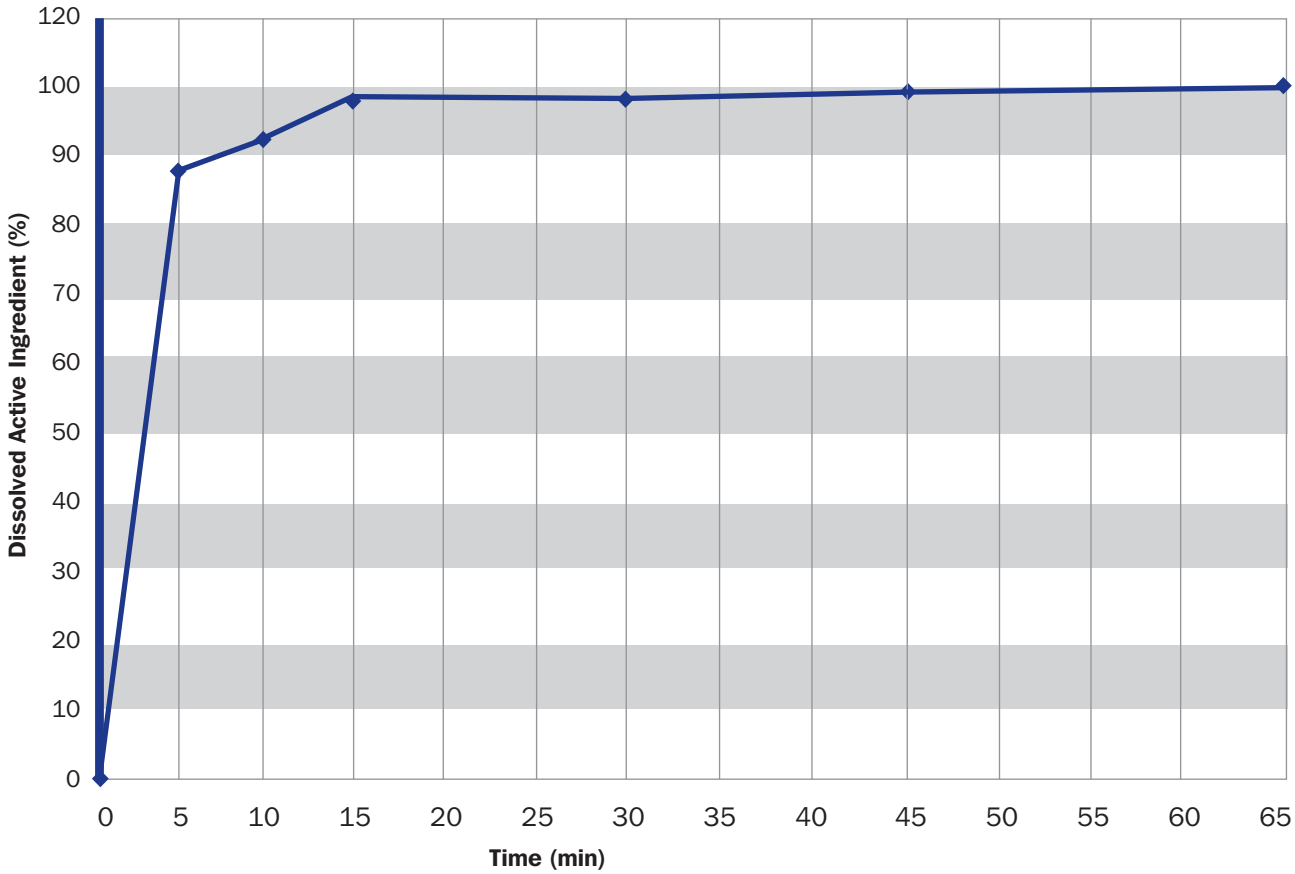


**Diagram 1:**
Typical dissolution profile diagram of a Metoprolol tartrate tablet, produced according to the above given formulation.



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# 4282-017

**Key Words:** Highly Soluble, Medium Concentration, Direct Compression
**JRS Products:** VIVAPUR® 12, ARBOCEL® P 290

# Metoprolol Direct Compression



## Comments:

Metoprolol is an example for a highly soluble active used in medium concentrations. It can be compressed directly by using **VIVAPUR®** Microcrystalline Cellulose as a dry binder and **ARBOCEL®** Powdered Cellulose as a plant-derived filler. Metoprolol is a selective $\beta_1$-adrenoreceptor blocking agent to treat hypertension and to prevent angina pectoris.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Metoprolol tartrate** | 50.0 | 50.0 | 33.3 |
| **VIVAPUR® 12** (Microcrystalline Cellulose) | | 57.3 | 38.2 |
| **ARBOCEL® P 290** (Powdered Cellulose) | | 38.2 | 25.5 |
| **VIVASOL®** (Croscaramellose Sodium) | | 3.00 | 2.0 |
| Magnesium Stearate | | 0.75 | 0.5 |
| Fumed Silica (Aerosil® 200) | | 0.75 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 150.0 mg |
| Tablet diameter: | 8 mm |
| Compaction force: | 14 kN |
| Hardness: | 66.0 N |
| Disintegration time: | 11 min 56 sec |
| Friability: | <0.10 % |

## Procedure

| **Blending:** |
|---|
| All ingredients were mixed for 4 minutes and compressed at a compaction force of approx. 14 kN. |

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 8 mm punch,biplane |
| Turbula mixer: | Type T2A |
| Hardness tester: | Pharmatest PTB 311 |
| Friability tester: | Erweka TAP |
| Disintegration tester: | Erweka ZT 3 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Shimadzu UV-2101 PC |

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# # 4282-017

**Key Words:** Highly Soluble, Medium Concentration, Direct Compression
**JRS Products:** VIVAPUR® 12, ARBOCEL® P 290

# Metoprolol Direct Compression



| **Dissolution test:** | |
|---|---|
| Dissolution medium: | 900 ml 0.1 N HCl, 37°C, n=6 |
| Samples are taken after 1, 5, 10, 15, 20, 30, 45, 60, 75 and 90 minutes. The sample volume is 3 ml. Samples were diluted if necessary. The determination of the active ingredient is done by an UV-spectrophotometer at λ = 215 nm. | |

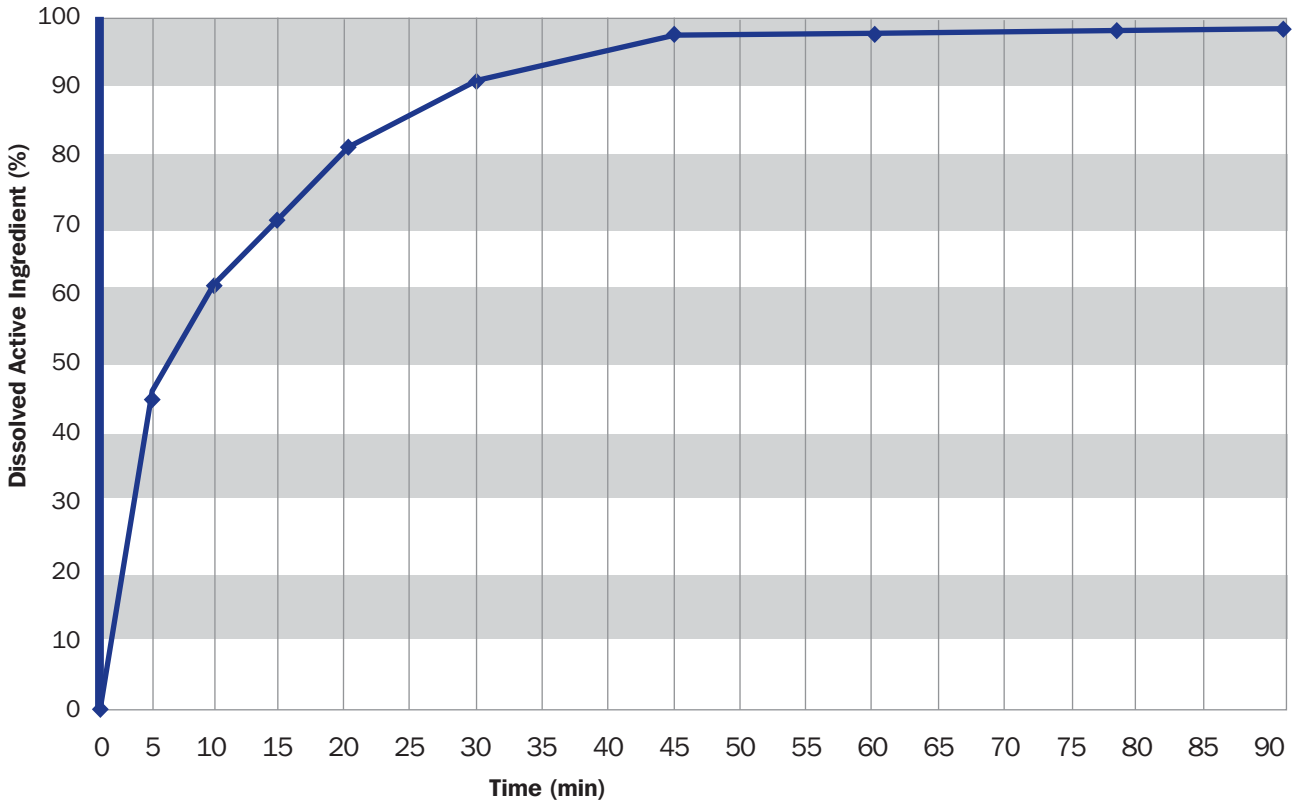


**Diagram 1:**
Typical dissolution profile diagram of a Metoprolol tartrate tablet, produced according to the above given formulation.



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# 4282-018

**Key Words:** Sticky Actives, High Dosage, Direct Compression
**JRS Products:** PROSOLV SMCC® 90, EMCOSOY®, PRUV™

# Cassia Senna & Melissa officinalis Direct Compression



## Comments:

Cassia Senna and Melissa officinalis are poorly flowing, poorly compressible herbal extracts used as natural laxative herbal remedy. It can be directly compressed easily in **PROSOLV SMCC®** due to its enhanced flow and compaction properties. Tablet disintegration is achieved using **EMCOSOY®**, naturally derived soy polysaccharide.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Senna extract** | 75.0 | 75.0 | 37.5 |
| **Melissa leaf extract** | 50.0 | 50.0 | 25.0 |
| **PROSOLV SMCC® 90** (Silicified Microcrystalline Cellulose) | | 60.0 | 30.0 |
| **EMCOSOY®** (Soy Polysaccharides) | | 8.0 | 4.0 |
| Talcum | | 6.0 | 3.0 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 1.0 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet mass: | 200 mg |
| Flow (Bridging aperture): | 14 mm |
| Hardness: | 7.2 kp |
| Compaction force: | 18.0 kN |

## Procedure

**Blending:**

Blend the Senna extract and Melissa officinalis extract together for 10 minutes. Add **PROSOLV SMCC® 90** and blend for 10 minutes. Add **EMCOSOY®** to the blender and blend for another 10 minutes. Next add Talcum to the blend and blend for five more minutes. Finally, add **PRUV™** to the blend and blend for additional five minutes.

| **Equipment:** | |
|---|---|
| Blender: | Patterson-Kelly 2 qt. Twin-shell V-blender |
| Flowability apparatus: | Hanson Research Flodex® |
| Tablet press: | Korsch PH-106 rotary tablet press |
| Hardness tester: | Erweka TBH-30 |

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# 4282-018

**Key Words:** Sticky Actives, High Dosage, Direct Compression
**JRS Products:** PROSOLV SMCC® 90, EMCOSOY®, PRUV™

## Cassia Senna & Melissa officinalis Direct Compression



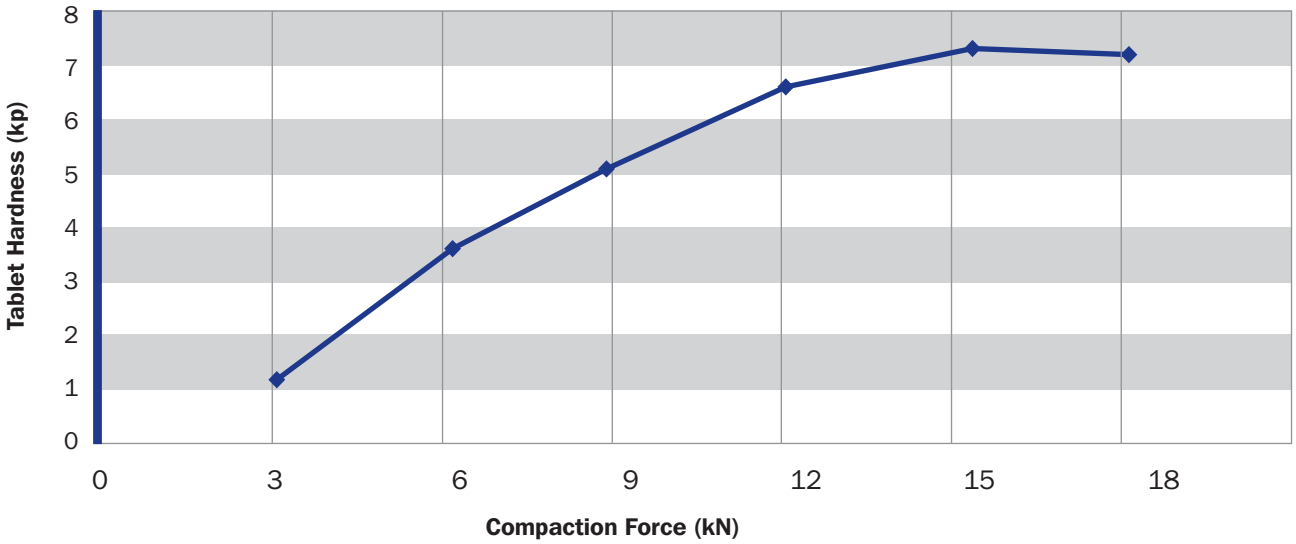


**Diagram 1:**
Tablet Hardness as a Function of Compaction Force



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# FORMULATION HANDBOOK

# # 4282-019

**Key Words:** Very Poorly Soluble, Low Dosage, Wet Granulation
**JRS Products:** VIVAPUR® 101, ARBOCEL® P 290, VIVASOL®

# Piroxicam Wet Granulation



## Comments:

Piroxicam is an example for a very poorly soluble active substance used in low concentrations.
Piroxicam is in a class of drugs called Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Piroxicam works by reducing hormones that cause inflammation and pain in the body.
It is used to reduce pain, inflammation and stiffness caused by rheumatoid arthritis and osteoarthritis.
Tablets can be produced by wet granulation using **VIVAPUR® 101** as a binder and **ARBOCEL® P 290** as a filler.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Piroxicam** | 10.0 | 10.00 | 6.7 |
| **VIVAPUR® 101** (Microcrystalline Cellulose) | | 76.80 | 51.2 |
| **ARBOCEL® P 290** (Powdered Cellulose) | | 51.20 | 34.1 |
| **VIVASOL®** (Croscarmellose Sodium) | | 3.00 | 2.0 |
| Polyviniylpyrrolidon (Kollidon® 25) | | 7.50 | 5.0 |
| Magnesium Stearate | | 0.75 | 0.5 |
| Fumed Silica (Aerosil® 200) | | 0.75 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 150.0 mg |
| Tablet diameter: | 8 mm |
| Compaction force: | 17.5 kN |
| Hardness: | 58.0 N |
| Disintegration time: | 39 sec |
| Friability: | <0.1 % |

## Procedure

**Blending:**

Piroxicam, **VIVAPUR® 101** and **ARBOCEL® P 290** were granulated with an ethanol solution of Kollidon® 25. The mass was dried and sieved through a 100 $\mu$m sieve.
For the outer phase **VIVASOL®** , Aerosil® and Magnesium Stearate were added and mixed for 5 minutes. The mixture was compressed at a compaction force of approx. 17.5 kN.

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**Key Words:** Very Poorly Soluble, Low Dosage, Wet Granulation

**JRS Products:** VIVAPUR® 101, ARBOCEL® P 290, VIVASOL®

# Piroxicam Wet Granulation



| Equipment: | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 8 mm punch |
| Turbula mixer: | Type T2A |
| Hardness tester: | Pharmatest PTB 311 |
| Friability tester: | ERWEKA TAP |
| Disintegration tester: | ERWEKA ZT 3 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Shimadzu UV-2101 PC |

| Dissolution test: | |
|---|---|
| Dissolution medium: | 900 ml 0.1 N HCl, 37°C, n=6 |
| Samples are taken after 5, 10, 15, 20, 30, 45, 60, 75 and 90 minutes. The sample volume is 3 ml. Samples were diluted if necessary. The determination of the active ingredient is done by an UV-spectrophotometer at $\lambda$ = 334.7 nm. | |

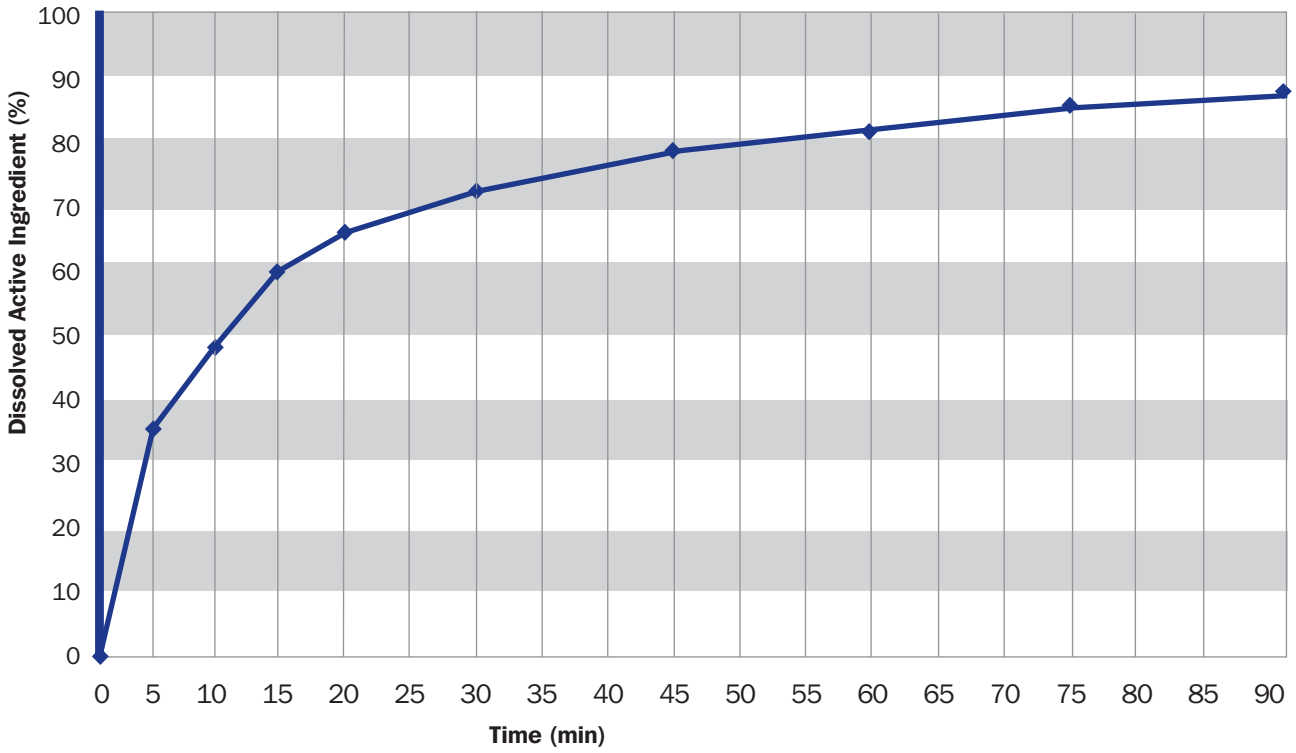


**Diagram 1:**
Typical dissolution profile diagram of a Piroxicam tablet, produced according to the above given formulation.



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# FORMULATION HANDBOOK

# 4282-020

**Key Words:** High Dosage, Direct Compression

**JRS Products:** VIVAPUR® 102, VIVASTAR® P

# Ranitidine HCl Direct Compression



## Comments:

Formulation for Direct Compression with an active content of more than 50 % of the tablet mass can be developed by using **VIVAPUR® 102** in order to get a good hardness and **VIVASTAR® P** for a short disintegration time.
The following study gives an example and shows the dissolution results of the active ingredient.

Ranitidine HCl is a histamine receptor antagonist which decreases the amount of acid the stomach produces. It is used to treat and prevent ulcers in the stomach and intestines. Ranitidine is also used to treat conditions which the stomach produces too much acid and conditions in which acid comes up into the esophagus and causes heartburn.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Ranitidine HCl** | 167.4 | 167.4 | 69.75 |
| **VIVAPUR® 102** (Microcrystalline Cellulose) | | 60.0 | 25 |
| **VIVASTAR® P** (Sodium Starch Glycolate) | | 10.2 | 4.25 |
| Magnesium Stearate | | 1.2 | 0.5 |
| Fumed Silica (Aerosil®) | | 1.2 | 0.5 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 240.0 mg |
| Tablet diameter: | 9 mm |
| Angle of repose | 32° |
| Compaction force: | 28 - 29 kN |
| Hardness: | 106.5 N |
| Disintegration time: | 5 min 12 sec |
| Friability: | 0.9 % |

## Procedure

**Blending:**

Ranitidine HCl, **VIVAPUR® 102** and **VIVASTAR® P** were blended to homogeneity for 15 minutes. Then a sieved mixture of Magnesium Stearate and Aerosil® were added and mixed for another 5 minutes. The powder mix is ready for Direct Compression.

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**Key Words:** High Dosage, Direct Compression

**JRS Products:** VIVAPUR® 102, VIVASTAR® P

# Ranitidine HCl Direct Compression



| **Dissolution test:** | |
|---|---|
| Dissolution medium: | 900 ml 0.1 N HCl, 37°C, n=6 |
| Samples are taken after 5, 10, 20, and 30 minutes. The sample volume is 3 ml. | |
| The determination of the active ingredient is done by an UV-spectrophotometer at λ = 313 nm. | |

## Equipment:

| | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 9 mm punch, biplane |
| Turbula mixer: | Type T2A |
| Hardness tester : | Pharmatest PTB 311 |
| Friability tester: | ERWEKA TAP |
| Disintegration tester: | ERWEKA ZT 3 |
| Dissolution tester: | Pharmatest PTW II, with 6 vessels, flat blade paddle |
| Spectrophotometer: | Shimadzu UV-2101 PC |

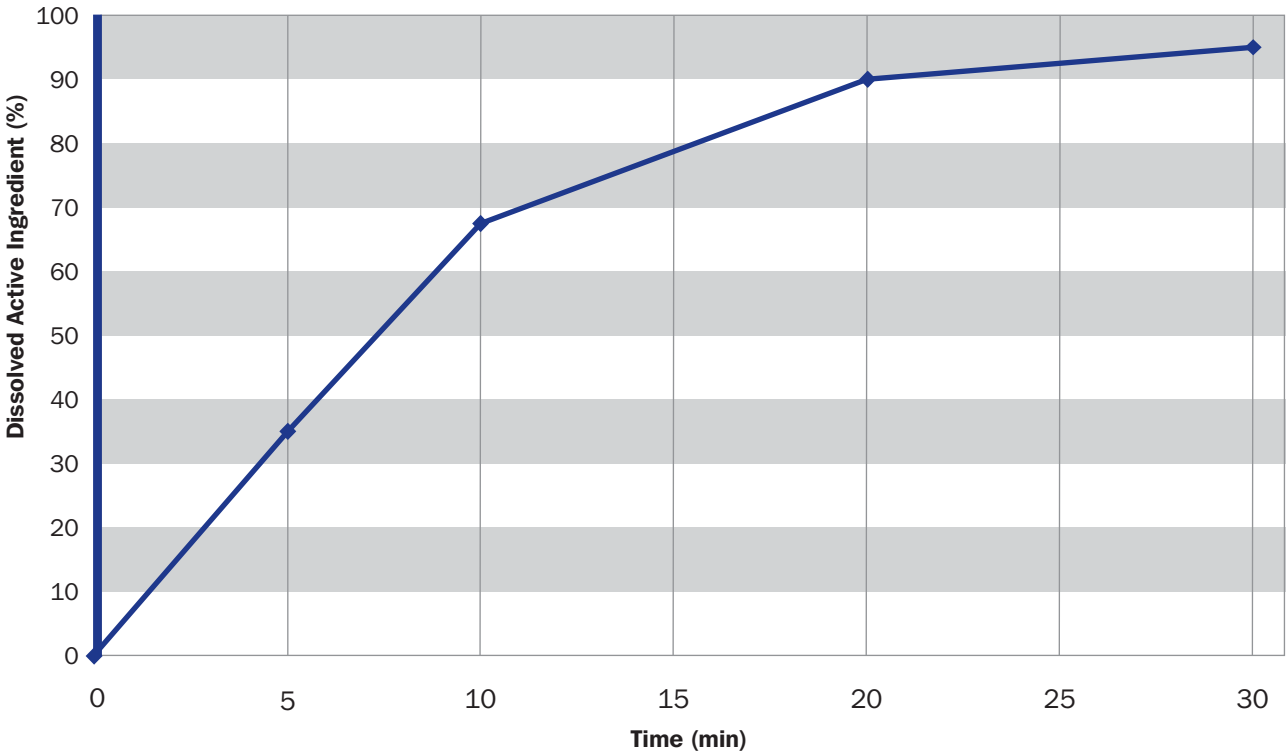


**Diagram 1:**
Typical dissolution profile diagram of a Ranitidine tablet, produced according to the above given formulation.



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# FORMULATION HANDBOOK

# # 4282-021

**Key Words:** Liquid Active, Poor Flowability, Direct Compression, Chewable Tablets
**JRS Products:** EMDEX®, EMCOMPRESS®, PRUV™

# Simethicone Direct Compression



## Comments:

Simethicone is used to treat the symptoms of gas such as uncomfortable or painful pressure, fullness, and bloating.

It can be directly compressed using **EMDEX®** and **EMCOMPRESS®** as binders. **EMDEX®** is a watersoluble binder for chewable tablets.

## Formulation

| | Active content (mg) | mg/tablet | Contribution (%) |
|---|---|---|---|
| **Simethicone** | 50.0 | 50.0 | 10.0 |
| **EMDEX®** (Dextrates) | | 150.0 | 30.0 |
| **EMCOMPRESS®** (Calcium Hydrogen Phosphate) | | 295.0 | 59.0 |
| **PRUV™** (Sodium Stearyl Fumarate) | | 5.0 | 1.0 |

## Tablet Characteristics

| | |
|---|---|
| Tablet weight: | 500.0 mg |
| Tablet diameter: | 13 mm |
| Compaction force: | 26 kN |
| Hardness: | 5.8 kp |

## Procedure

**Blending:**

Simethicone was dispersed in **EMDEX®** and blended for 10 minutes. Then **EMCOMPRESS®** was added and blended again for 5 minutes. After that **PRUV™** Sodium Stearyl Fumarate was added and blended for 3 minutes.

| **Equipment:** | |
|---|---|
| Tablet press: | Korsch EK 0 excentric press, 13 mm punch |
| Hardness tester: | Schleuniger 2E |



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