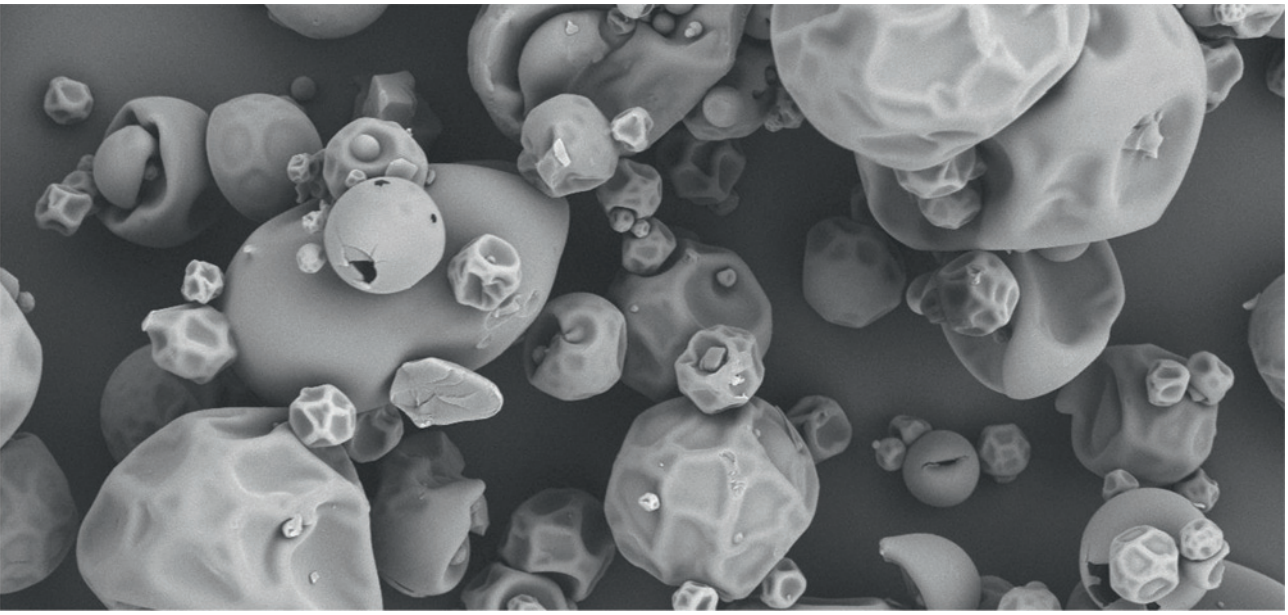
# VIVAPHARM® PVP/VA

## Copovidone, Ph.Eur. USP/NF, JPE, E 1208, FCC



### The Ultimate Tablet Binder for All Processing Technologies

- Direct Compression
- Dry Granulation
- Hot Melt Extrusion
- Wet Granulation

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## Introduction

The objective of drug formulation is to develop a product that delivers therapeutic effectiveness in terms of the correct dosage and required bioavailability, while also ensuring that the final product is robust and disintegrates according to its drug release requirement.

Given the properties of an active pharmaceutical ingredient (API), formulators are often challenged with selecting the correct excipient and the appropriate technology to achieve a powder mix that has good compactibility and flow characteristics.

Several technologies are available: the preferred direct compression, wet granulation, and dry granulation, as well as hot melt extrusion for poorly soluble drug actives with low bioavailability.

**VIVAPHARM® PVP/VA 64** is the ultimate tablet binder for all processing technologies.

**VIVAPHARM® PVP/VA 64** is a 6:4 linear random copolymer of N-vinylpyrrolidone and vinyl acetate (Figure 1).

The vinyl acetate component in **VIVAPHARM® PVP/VA 64** reduces the hydrophilicity and glass transition temperature ($T_g$) compared to Povidone homopolymers of similar molecular weight.

As a result, **VIVAPHARM® PVP/VA 64** is the ultimate tablet binder that extends its excellent adhesive property in wet granulation, as well as in dry granulation and direct compression.

Due to its spherical, hollow particle morphology (Figure 2) and high plasticity, **VIVAPHARM® PVP/VA 64** performs exceptionally well as a binder for direct compression.

In addition, a lower $T_g$ makes **VIVAPHARM® PVP/VA 64** an ideal polymer matrix for solid dispersions/solutions via hot melt extrusion, which enhances the dissolution of poorly soluble drug actives.

Due to its nonionic property, it does not bear any risk of interaction with ionic APIs.

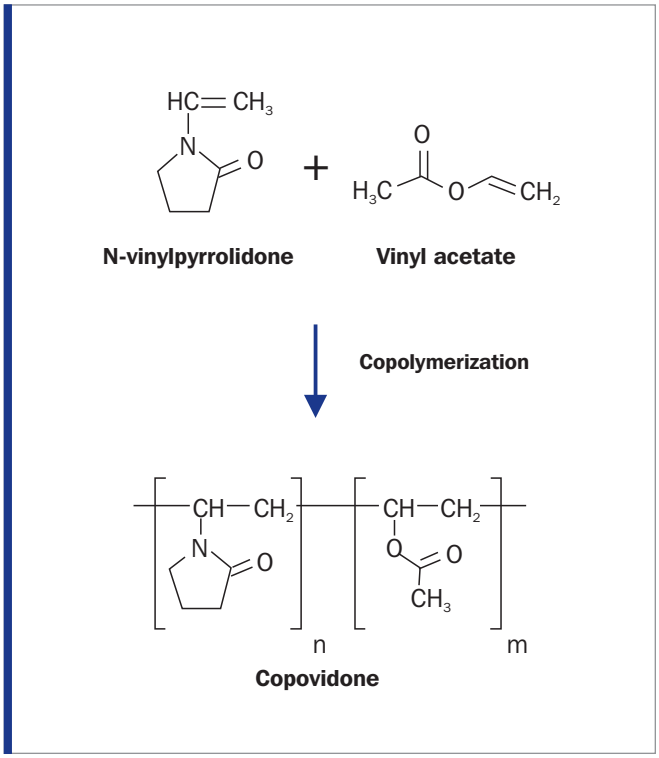


Fig. 1: Chemical Structure of **VIVAPHARM® PVP/VA 64** Copovidone from the Copolymerization of N-vinylpyrrolidone and Vinyl Acetate

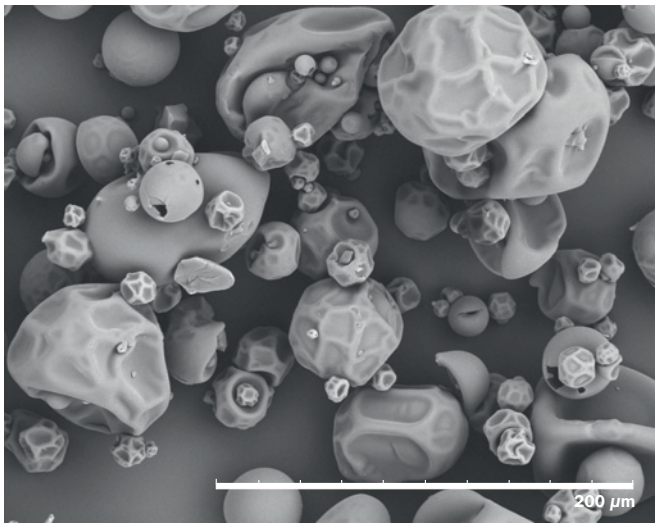


Fig. 2: Typical Scanning Electron Micrograph of **VIVAPHARM® PVP/VA 64**

## Physical Properties

- Soluble in water and a range of organic solvents
- Less hygroscopic than povidone homopolymers of similar molecular weight
- Free-flowing powder
- Plastic deformation
- Large surface area due to hollow, spherical particle morphology
- Ideal glass transition temperature ($T_g$) for hot melt extrusion
- Non-ionic copolymer

## Benefits and Applications:

- Spherical structure leads to good flowability
- Hollow particle morphology leads to an increased surface area that enhances particle bonding and good compressibility
- Direct Compression: Excellent binder at 2 - 10 % use level. Performs synergistically with other direct compression binder-fillers such as **PROSOLV® SMCC** (silicified microcrystalline cellulose), **VIVAPUR®** (microcrystalline cellulose), **EMCOMPRESS®** (dicalcium phosphate), and many more
- Dry Granulation: Can be used as a binder in dry granulation (roller compaction)
- Wet Granulation: Enables wet granulation of moisture sensitive APIs due to low hygroscopicity
- Hot Melt Extrusion: Acts as a polymer matrix for solid dispersions/solutions via hot melt extrusion due to ideal glass transition temperature at 105 °C
- Film Coating: Ideally suited as co-film-former

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## Case Study 1: Acetylsalicylic Acid

### Formulation Characteristics

A direct compression formulation of acetylsalicylic acid, a poorly compressible API, was selected to compare the functionality of **VIVAPHARM® PVP/VA 64** against other PVP/VA 64 products on the market.

### Formulation

| Products | Amount [%] |
|---|---|
| Acetylsalicylic Acid 500 mg | 63.45 |
| **VIVAPUR® MCC 102** Microcrystalline Cellulose | 25.38 |
| Copovidone | 7.62 |
| **VIVAPHARM® PVPP XL** (Crospovidone) | 3.17 |
| **PRUV®** Sodium Stearyl Fumarate | 0.38 |
| Total | **100** |

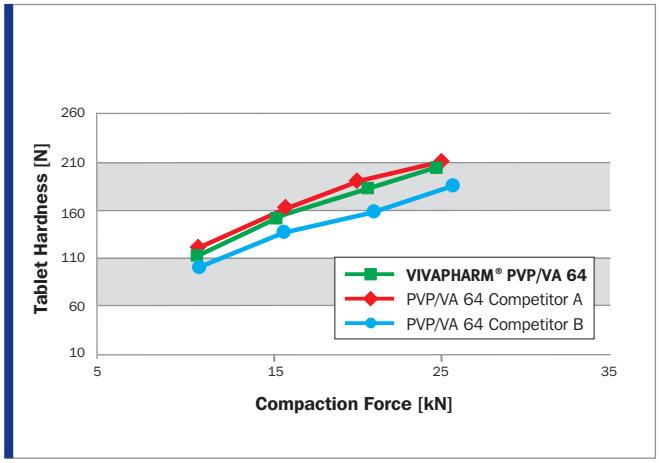
Tab. 1

### Formulation Results of Acetylsalicylic Acid

**VIVAPHARM® PVP/VA 64** and marketed products A and B all performed within the same range in terms of tablet hardness, friability, and disintegration time.

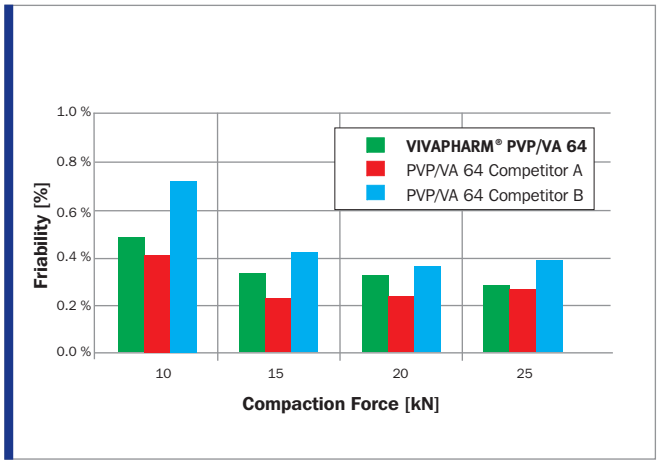
**VIVAPHARM® PVP/VA 64** facilitated 75 % acetylsalicylic acid release in 30 minutes.

### Tablet Hardness



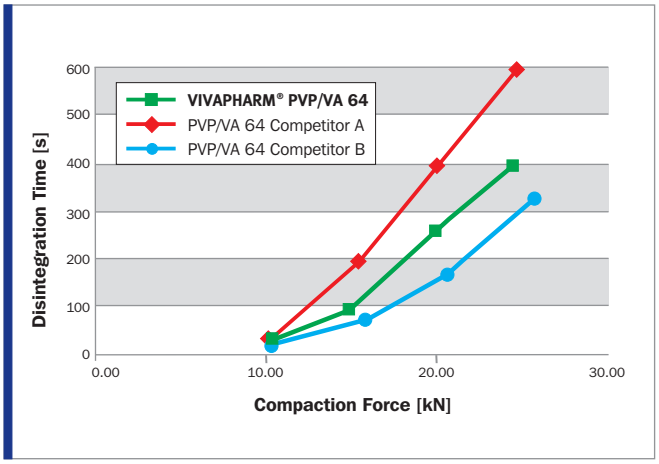

Graph 1: Compression Force Profile of Acetylsalicylic Acid Tablets

### Friability



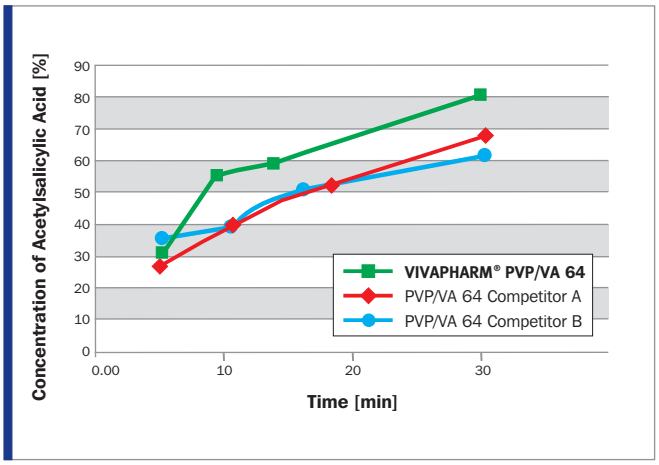

Graph 2: Friability of Acetylsalicylic Acid Tablets

## Disintegration Time




Graph 3: Disintegration Profile of Acetylsalicylic Acid Tablets

## Dissolution Profile




Graph 4: Average (n=6) % Acetylsalicylic Acid Dissolved

## Summary

A direct compression formulation of acetylsalicylic acid was achieved with **VIVAPHARM® PVP/VA 64** and **VIVAPUR® MCC 102**.

Although acetylsalicylic acid is known to be poorly compressible, the formulation resulted in robust tablets with low friability at all compaction forces, as well as good disintegration times.

**VIVAPHARM® PVP/VA 64** facilitated 75 % acetylsalicylic acid release in 30 minutes.

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## Case Study 2: Acetaminophen

### Formulation Characteristics

Acetaminophen was chosen as a model API in order to demonstrate the synergistic benefit of using **VIVAPHARM® PVP/VA 64** in combination with our high functionality excipient, **PROSOLV®SMCC 90**. Acetaminophen is generally known to have poor compressibility, and as a result, it is typically wet granulated. It can only be tableted via direct compression by using high levels of excipients of at least 60 %, which means 500 mg acetaminophen would result in a final tablet weight of 1,200 mg. The goal of this formulation was to achieve a tablet weight of 700 mg with a 500 mg acetaminophen load via direct compression.

| Products | Amount [g] |
|---|---|
| Acetaminophen 500 mg | 500 |
| **PROSOLV® SMCC 90** Silicified Microcrystalline Cellulose | 140 |
| Copovidone | 36 |
| **VIVAPHARM® PVPP XL** (Crospovidone) | 21 |
| **PRUV®** Sodium Stearyl Fumarate | 3 |
| Total | **700** |

Tab. 2

### Formulation Results of Acetaminophen

| Parameter | VIVAPHARM® PVP/VA 64 | PVP/VA 64 Competitor A | PVP/VA 64 Competitor B |
|---|---|---|---|
| Tablet Weight | 700 mg | 700 mg | 700 mg |
| Compaction Force | 25 kN | 25 kN | 25 kN |
| Tablet Hardness | 55 N | 59 N | 55 N |
| Tensile Strength | 0.62 Mpa | 0.67 Mpa | 0.62 Mpa |
| Disintegration Time | < 45 s | < 45 s | < 45 s |
| Dissolution $t_{75\,\%}$ | < 10 min | < 10 min | < 10 min |
| API Content Uniformity | 3.32 % | 3.48 % | 3.52 % |

Tab. 3

## Summary

This case study presents a high-dose, poorly compressible API that is typically wet granulated. The combination of **VIVAPHARM® PVP/VA 64** and **PROSOLV® SMCC 90** in the formulation achieved the target total tablet weight of 700 mg via direct compression. This formulation not only eliminates the wet granulation step, but also maximizes drug loading and reduces the amount of excipients required.

The performance of **VIVAPHARM® PVP/VA 64** is comparable to other PVP/VA 64 products on the market in all aspects. At 25 kN compaction force, sufficient tablet hardness with short disintegration time was achieved. In addition, 75 % acetaminophen was released in less than 10 minutes – significantly faster than the required compendial limit of 45 minutes. This demonstrates the effectiveness of **VIVAPHARM® PVP/VA 64** in combination with **PROSOLV® SMCC 90** as binder for an immediate release oral dosage form.

## Regulatory Information

- Conforms to the current Ph. Eur., USP/NF and JP/JPE
- Certificate of Suitability (CEP) by the European Directorate for the Quality of Medicines & HealthCare (EDQM)
- DMFs are filed with the US Food and Drug Administration (FDA)
- Halal and Kosher compliant
- Listed in the Inactive Ingredient Database (IID) on the FDA website as an approved ingredient in New Drug Applications (NDA)
- **VIVAPHARM® PVP/VA 64** is listed by the European authorities (E 1208) and in the Food Chemicals Codex (FCC) by the FDA for its application in certain nutraceutical applications
- Regulatory approvals in all major markets including: USA, Europe, Japan, Mexico, Australia, India, China, and many more

## Packaging, Samples, and Storage

**Storage:**
Store in original container. Protect from excessive heat and moisture. Opened containers should be reclosed and stored in a manner which minimizes exposure to oxygen.

**Packaging:**
All Povidone, Copovidone, and Crospovidone products are known to form peroxides upon prolonged exposure to oxygen. As part of our commitment to ensuring the quality and stability of our products, **VIVAPHARM® PVP/VA 64** is packaged in 25 kg drums with multifoil LDPE/EVOH inliners under tightly controlled packaging conditions. EVOH has been carefully selected due to its outstanding gas barrier properties. Minimizing the entry of oxygen into the primary packaging minimizes the potential of peroxide formation. LDPE remains as the product contact layer. The choice of packaging has a significant impact of prolonging the shelf-life and guaranteeing the stability of **VIVAPHARM® PVP/VA 64**.

**Sample Size:**
400 g

**Case Studies**
Case studies and formulation examples are available upon request. Please contact your sales rep for more information or visit *www.jrspharma.com.*

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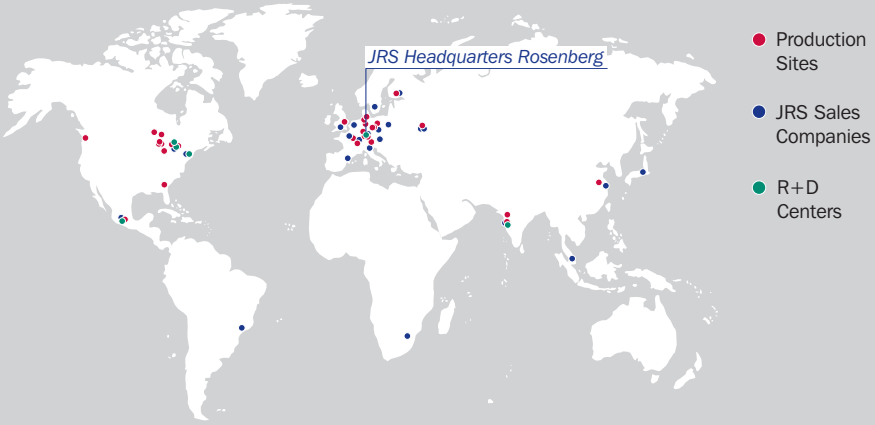


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