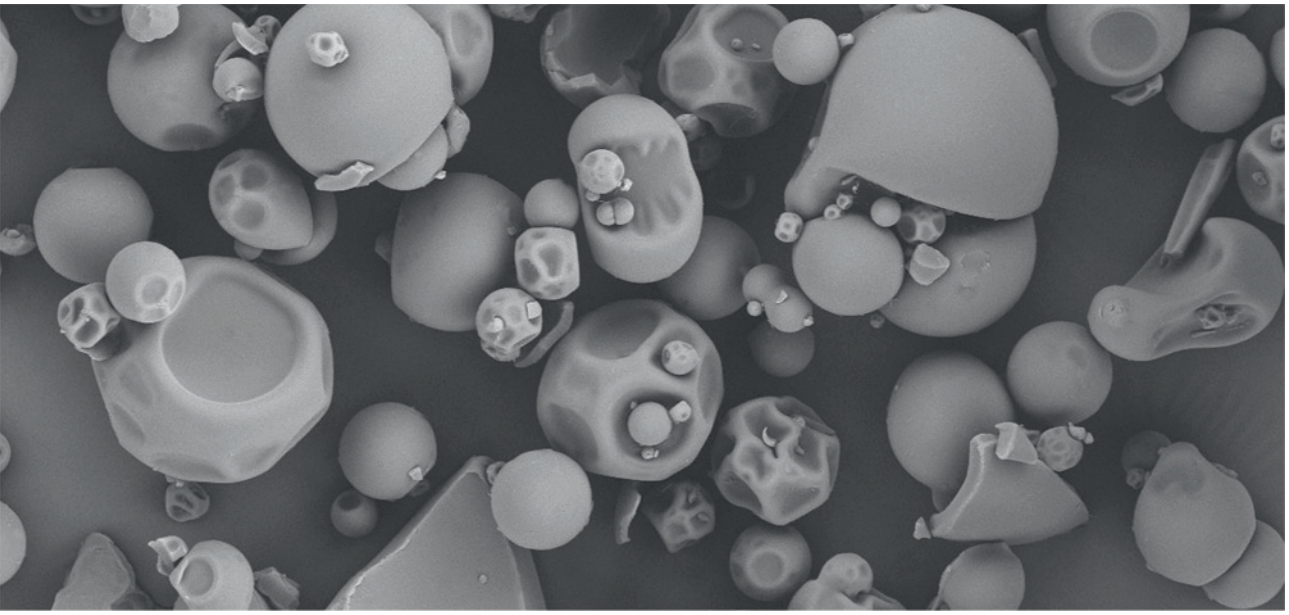
VIVAPHARM® PVP

Povidone, Ph.Eur, USP/NF, JP, E 1201, FCC



The Classic Wet Binder with Optimal Balance Between Adhesive Strength and Ease of Handling

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Introduction

Wet granulation is a process widely used in the pharmaceutical industry to obtain the required properties of a tableting mixture including: good compactibility, flowability and content uniformity. The process involves using a liquid binder to lightly agglomerate the powder mixture containing the active pharmaceutical ingredient (API) which cannot be formulated by direct compression due to one or more of the properties above. The ideal binder should be highly soluble to ensure rapid dispersibility in the solvent of choice. It should also have both a strong adhesive property and a low viscosity to ensure easy handling. **VIVAPHARM® PVP K30** is the classic wet binder with optimal balance between adhesive strength and ease of handling.

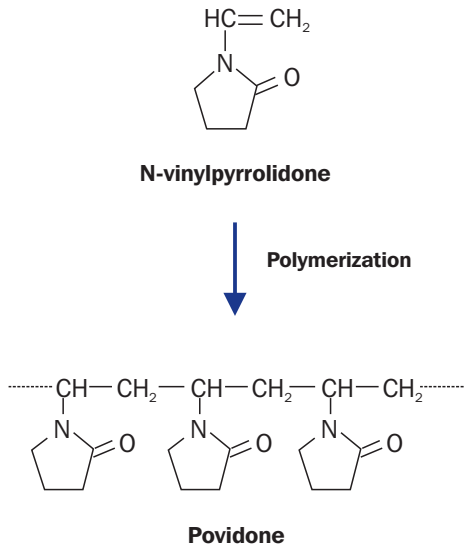

Fig. 1: Chemical Structure of **VIVAPHARM® PVP K30** Povidone from the Polymerization of N-vinylpyrrolidone

VIVAPHARM® PVP K30 is a synthetic water-soluble homopolymer consisting of N-vinylpyrrolidone (Figure 1).

Based on the polymerization process, povidones are available in different molecular weights. The K-value denotes the intrinsic viscosity of the polymer related to the molecular weight, and is derived from the relative viscosity of the aqueous solution measured at 25 °C.

The direct correlation between the molecular weight and properties enables the appropriate grade to be used in each formulation in the appropriate concentration in order to achieve the optimum effect.

VIVAPHARM® PVP K30 is highly adhesive at low viscosity, thus offering the optimal balance between adhesive strength and ease of handling at a low use level of 2 - 5 %. **VIVAPHARM® PVP K30** has excellent solubility in water and a range of organic solvents, and is supplied as a free-flowing powder with spherical particle morphology (Figure 2). This ensures rapid dispersibility and ultimate flexibility in the solvent of choice. Due to its non-ionic property, it does not bear any risk of interaction with ionic APIs.

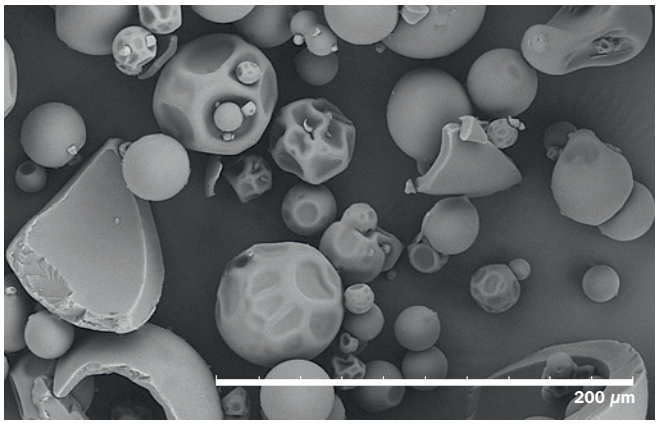

Fig. 2: Typical Scanning Electron Micrograph of **VIVAPHARM® PVP K30**

Physical Properties

- Excellent solubility in water and a range of organic solvents
- Free-flowing powder – rapid dispersibility in solvent of choice
- Highly adhesive at low viscosity
- pH stable
- Non-ionic polymer
- Non-toxic

Principles of Wet Granulation

Wet granulation involves using a liquid binder to lightly agglomerate the powder mixture containing the active pharmaceutical ingredient (API) which cannot be formulated by direct compression due to certain characteristics. The formation of liquid bridges is strongly influenced by the viscosity of the wet binder (Figure 3). Typically, the lower the viscosity, the shorter the process time. The higher the viscosity, the greater the adhesive power. However, high viscosity may also cause problems during the granulation process.

There are three main wet granulation techniques:

- Low shear wet granulation processes use low speed planetary mixers, take a considerable amount of time to achieve a uniformly mixed state, and have an even longer drying time.
- High shear wet granulation processes use equipment with low speed impellers in combination with high speed chopper blades that mix the powder and liquid at a very fast rate. High shear processes typically result in greater densification of particles, thus less porosity, and more reproducible granulation.
- Fluid bed granulation is a multiple-step wet granulation process performed within a single unit to preheat, granulate, and dry the powders. Generally this process results in porous, less dense granules which may benefit the compaction and dissolution properties of the granules. The viscosity of the binder may also impact the granulation process due to practical limitations on the dispensation of high viscosity binder solution through the spray nozzle.

VIVAPHARM® PVP K30 is the ideal binder in all wet granulation processes by any of the methods below:

- Wet addition: As granulation solution (binder + solvent)
- Dry addition: Dry mixture of API and binder; Solvent is added to the dry mix
- Combination: Some binder is mixed with the API, and the rest is dissolved in the granulation solution → the preferred choice if the amount of solvent is restricted

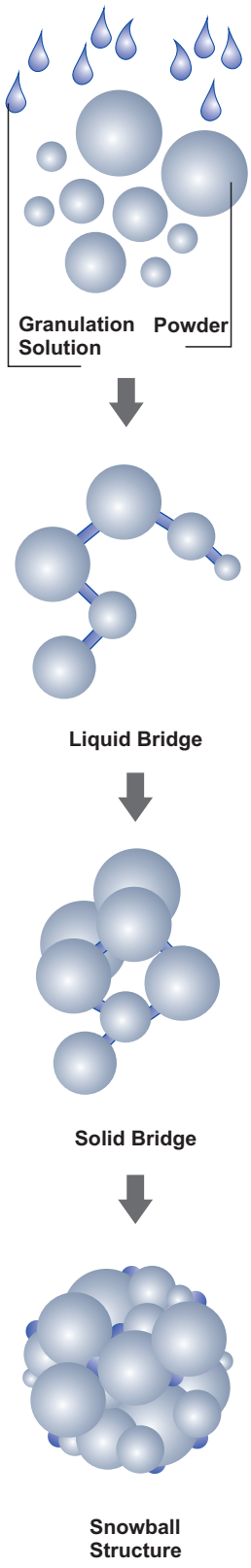

Fig. 3: Wet Granulation Process

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Criteria of a Wet Binder	Performance Impact
Solubility in a Wide Range of Organic Solvents	Fast dispersibility in solvents (including water). Aqueous solutions are preferred to solvent-based systems but may not be suitable for drugs which are degraded by hydrolysis. Hence solubility in a range of organic solvents is favorable.
Low Viscosity Solution	Ease of handling → high viscosity binder solution may cause clogging of spray nozzle.
High Binding Efficiency	Lower use levels required to produce tablets with higher breaking force and lower friability at potentially lower compaction force.
High Water Solubility	No impact on drug dissolution at high use levels.

Tab. 1: Criteria of a Wet Binder and the Impact on Performance

VIVAPHARM® PVP K30 is the classic wet binder with optimal balance between adhesive strength and ease of handling.

Benefits

- High binding capacity – the classic binder for wet granulation at low concentrations (2 - 5 %)
- Excellent solubility in water, as well as a range of organic solvents for ultimate flexibility in processing options with respect to API solubility profile
- Low viscosity grade ensures ease of handling
- Dissolution and bioavailability enhancement of poorly soluble APIs
- Inhibits crystallization of APIs – stabilizes amorphous drugs in solid dispersions/solutions in combination with **VIVAPHARM® PVP/VA 64**
- Non-ionic polymer – does not bear any risk of interaction with ionic APIs

Case Study: Naproxen

Formulation Characteristics

Naproxen, a BCS* class II drug whose bioavailability is rate-limited due to its poor solubility, was chosen as a model API. It is typically wet granulated because of its poor compactibility. In many cases, the addition of other binder-fillers before tableting is necessary in order to achieve suitable tablet hardness with low friability. In this case study, wet granulation of Naproxen was performed with 5 % of Povidone K30 as a binder solution. **VIVAPHARM® PVP XL** and magnesium stearate were added as extragranular superdisintegrant and lubricant; respectively. The goal of this formulation was to achieve good tablet hardness with low friability, rapid disintegration and good dissolution of the API. The performance of **VIVAPHARM® PVP K30** against other similar products on the market was compared.

Formulation

Products	Amount [%]
Naproxen 450 mg	92.47
Povidone K30	5.00
VIVAPHARM® PVPP XL (Crospovidone)	2.02
Magnesium Stearate	0.51
Total	**100**

Tab. 2

Formulation Results of Naproxen

VIVAPHARM® PVP K30 and other povidone products achieved the target tablet crushing strength of 100 N at similar compaction forces. All products performed within the same range in terms of friability and disintegration time, facilitating 75 % Naproxen release in 10 minutes.

Parameter	VIVAPHARM® PVP K30	PVP K30 Competitor A	PVP K30 Competitor B
Tablet Weight	500 mg	500 mg	500 mg
Tablet Hardness	100 N	100 N	100 N
Compression Force	6.4 kN	6.5 kN	7.7 kN
Tensile Strength	0.45 MPa	0.43 MPa	0.43 MPa
Friability	0.0 %	0.0 %	0.0 %
Disintegration Time	2 min 52 s	3 min 5 s	3 min 34 s

Tab. 3

* Biopharmaceutics Classification System

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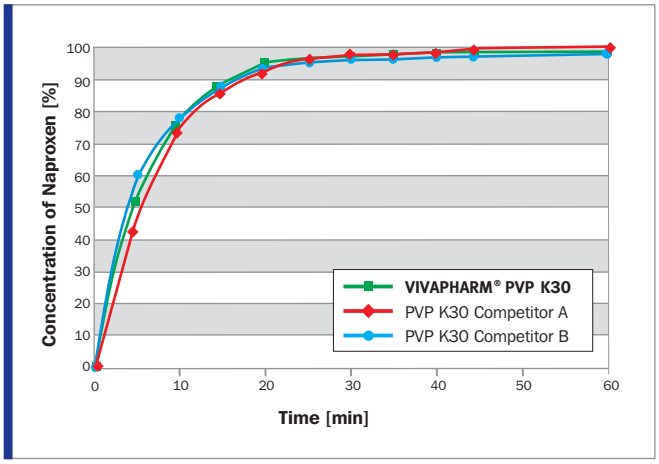
Dissolution Profile



Graph 1: Average (n=6) % Naproxen Dissolved.

Summary

At low compression force (6.4 kN), good tablet hardness with 0 % friability and a short disintegration time of 3 minutes was achieved. In addition, more than 75 % of Naproxen was released in less than 10 minutes.
This demonstrates the effectiveness of **VIVAPHARM® PVP K30** not only as wet binder but also as a dissolution enhancer for an immediate release oral tablet. The formulation eliminates the need for other binder-fillers, leading to a reduction in tablet size, better patient compliance, and marketing benefits.

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 K30** is listed by the European authorities (E 1201) and in the Food Chemicals Codex (FCC) by the FDA for its application in nutraceutical tablets such as vitamins, herbal extracts, sweeteners, etc.
- 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 K30** 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 K30**.

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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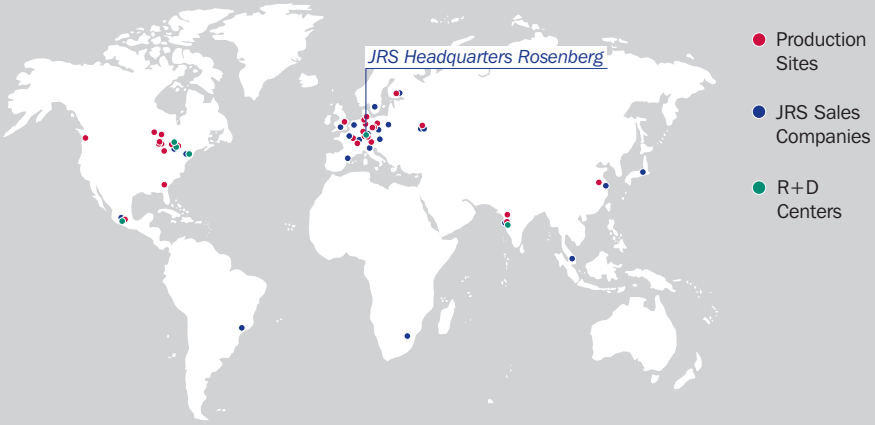

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