Technical Information

Kollidon® 90 Evo

Povidone

® = Registered trademark of BASF in many countries.

BASF
We create chemistry

1. Introduction

Povidone (polyvinylpyrrolidone, PVP) is widely used as an excipient in various pharmaceutical dosage forms. Polyvinylpyrrolidone polymers were first synthetized by the chemist Walter Reppe in BASF laboratories in the 1930s.

PVP can be produced in commercial scale in a wide range of different molecular weights by radical polymerization, in either water or organic solvents, of the monomer N-vinylpyrrolidone. In the Pharmacopoeias, the Povidone grades are typically characterized by the K-value which correlates to the relative viscosity of the polymer in water and therefore, to the mean molecular weight of the polymer chains.

Kollidon® 90 Evo is a soluble, high molecular weight Povidone with a K-value of about 90 that is available as almost white, free-flowing powder. Kollidon® 90 Evo provides a strong binding effect and is used as a wet binder in the formulation of solid oral dosage forms. Additional applications include as a viscosity modifier and adhesive in transdermal patches.

Kollidon® 90 Evo replaces the former grade Kollidon® 90 F, with an improved impurity profile with lower specified limits for parameters such as 2-pyrrolidone and aldehydes.

BASF provides the full range of PVP excipients and dedicated Technical Information Sheets are available for all Kollidon® grades.

2. Chemical & Physical Properties

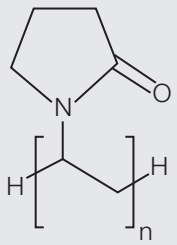
Name

povidone, PVP, polyvinylpyrrolidone, poly(1-vinyl-2-pyrrolidone), povidonum, polyvidone

Raw material and production information

Kollidon® 90 Evo is produced by radical polymerization of the monomer N-vinylpyrrolidone in water, generating a highly viscous polymer solution which is then dried using a drum dryer. The resulting polymer flakes are directly milled to provide the final product as a free flowing powder.

Chemical Structure



Kollidon® 90 Evo has very low specified impurity limits for 2-pyrrolidone, hydrazine and aldehydes. Details are provided in the product specification.

CAS number

9003-39-8

Particle Characteristics

The product parameters described in this section are considered characteristic values and are not included in the product specification.

Particle Morphology

Both, particle size and particle morphology of Kollidon® 90 Evo are controlled in the final milling step of the production process. The particles show the typical morphology of a milled powder with dense particles, irregular shape, and rough edges.

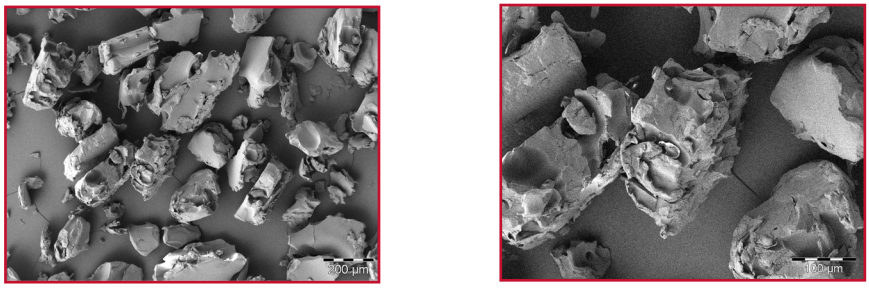


Fig. 1: Scanning Electron Microscopy (SEM) images of Kollidon® 90 Evo particles.

Particle Size Distribution

The typical range for particle size distribution of Kollidon® 90 Evo is given in Table 1. Values are obtained by means of light scattering (Fraunhofer mode) applying a dispersive air pressure of 2 bar.

Table 1:	d (0.1) [µm]	d (0.5) [µm]	d (0.9) [µm]	d (4.3) [µm]
	50 - 120	140 - 240	24 – 27	150 - 250

Table 2 shows the ranges for the particle size of Kollidon® 90 Evo as measured by air jet sieving (amplitude: 2,0 mm).

Table 2:	Fraction of particles < 50 µm [g/100g]	Fraction of particles > 250 µm [g/100g]
	0 – 10	5-27

Powder Density

Table 3 shows bulk and tap density values for Kollidon® 90 Evo, as tested according to DIN EN ISO 60.

Table 3:	Bulk Density [g/l]	Tap Density [g/l]
	390 – 500	450-600

Powder Rheology: Compressibility test

Compressibility values (percent reduction in volume with applied force) obtained with an FT4 powder rheometer using the standard test configuration are presented in Table 4.

Table 4:	Conditional bulk density [g/l]	Compressibility @ 15 kPa [%]
	400 – 500	7-8

Angle of Repose and Flow Through an Orifice

Angle of repose and flowability obtained with a GTB granulate flow tester (orifice diameter 6 mm) are reported in Table 5.

Table 5:	Angle of repose [°]	Flow rate, 100 g [g/s]
	37-40	1-2

Polymer Characterization

The product parameters described in this section are considered characteristic values and are not included in the product specification.

Molecular Weight Distribution

As inherent to polymers, Kollidon® 90 Evo is composed of a distribution of polymer chains of different lengths and thus described by molecular weight distribution. The molecular weight can be expressed in different forms, as weight average molecular weight, as number average molecular weight, and as viscosity average molecular weight.

The viscosity average molecular weight finds application in the Pharmacopoeias with the K-value of aqueous Povidone solutions as indirect measurement of the molecular weight of the polymers.

The weight average molecular weight (Mw) can be determined by means of Size Exclusion Chromatography (SEC) in combination with a detection system based on multi angle light scattering (MALLS).

Table 6 shows that all tests confirm the high molecular weight of Kollidon® 90 Evo.

Table 6:	Nominal K-Value	K-Value Range	Mw by SEC-MALLS [g/mol]
	90	81.0 - 97.2	900 000 – 1 200 000

Solubility

Kollidon® 90 Evo shows a solvent dependent solubility. Due to its high polarity, it is soluble in water and polar organic solvents, and insoluble in hydrocarbons.

In Table 7 below, “soluble” signifies that a solution of at least 10% can be prepared, and “insoluble” signifies that the solubility is less than 1%.

Table 7: Solubility of Kollidon® 90 Evo	
Soluble in (min. 10 g/l):	
chloroform	n-butanol
cyclohexanol	n-propanol
ethanol abs.	polyethylene glycol 300
glycerol	polyethylene glycol 400
isopropanol	propylene glycol
methanol	triethanolamine
methylene chloride	water
Insoluble in (max. 1 g/l):	
cyclohexane	pentane
diethyl ether	carbon tetrachloride
ethyl acetate	toluene
liquid paraffin	xylene

Glass transition temperature Tg_2

Kollidon® 90 Evo Tg_2 ~ 176 °C

The glass transition temperature Tg_2 is determined by means of differential scanning calorimetry (DSC).

To ensure that water is not influencing the result by acting as a plasticizer, two heating cycles are conducted for the measurement. The first heating cycle ensures that water is eliminated from the sample. After cooling the dried polymer to room temperature, the Tg_2 is then determined in a second cycle.

Solution Viscosity

Kollidon® 90 Evo aqueous solutions are highly viscous, thereby showing the typical behavior of high molecular weight PVP. Figure 2 shows the shear viscosity of a Kollidon® 90 Evo aqueous solution with 12.5% solid content.

Figure 3 shows the zero-shear viscosity of aqueous solutions of Kollidon® 90 Evo in dependency of their respective concentration.

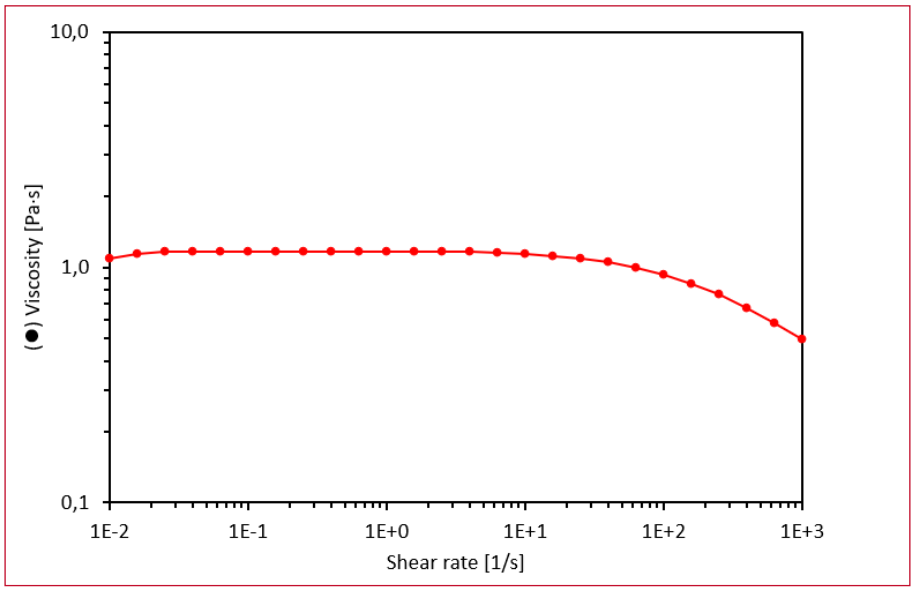


Fig. 2: Shear viscosity of Kollidon® 90 Evo aqueous solution [12.5 weight%] in rotation rheometer, 25 °C

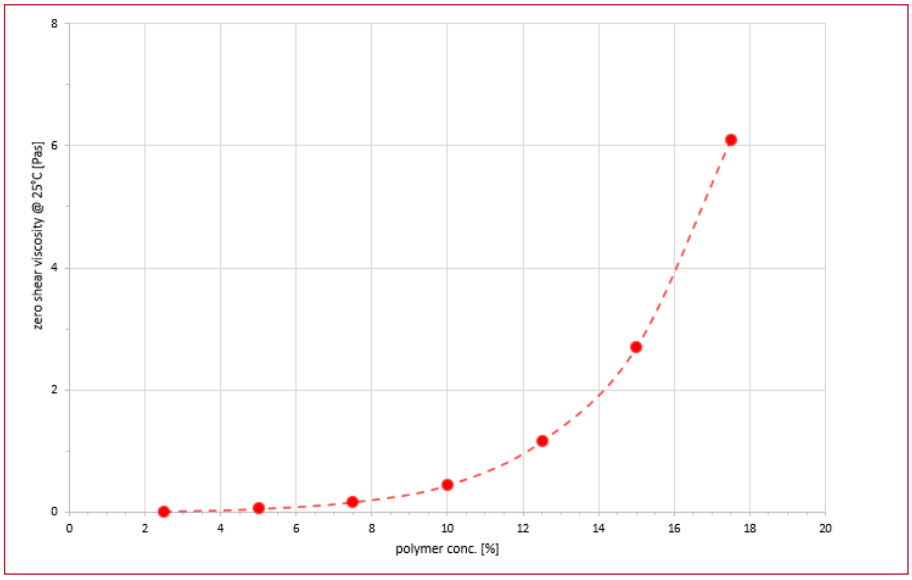


Fig. 3: Zero-shear viscosity of Kollidon® 90 Evo aqueous solutions in dependence of their solid content (rotation rheometer, 25 °C)

3. Handling & safety instructions

Kollidon® 90 Evo is packaged in PeroXeal® to minimize peroxide formation by eliminating, as far as possible, oxygen in the packaging. BASF´s PeroXeal® concept includes filling the product powder under inert conditions and using a liner with oxygen barrier properties. The liner is then vacuumized and heat-sealed for proper closure.

Please note the protection provided by PeroXeal® is only intact until the first opening of the original sealed packaging. For sensitive applications, BASF recommends proper reclosure, fast consumption, and/or peroxide monitoring.

Please refer to the individual material safety data sheet (MSDS) for instructions on safe and proper handling and disposal. Material safety data sheets are sent with every consignment.

4. Example Application(s)

Among the range of available Kollidon® grades, Kollidon® 90 Evo is the Povidone with the highest molecular weight and solution viscosity, providing Kollidon® 90 Evo with an extraordinary high wet binding capacity, unique thickening, and adhesive properties.

Kollidon® 90 Evo therefore finds application in the formulation of various oral dosage forms such as tablets, granules, solutions, and suspensions, but also in topical dosage forms, such as transdermal patches, creams, and lotions. The main applications of Kollidon® 90 Evo are summarized in Table 8.

Table 8:	Main applications of Kollidon® 90 Evo
Wet Binder	Tablets, capsules, granules, and pellets
Film former, pore former	Oral and topical films, modified release formulations, coated tablets
Solubilizer	Oral and topical formulations
Viscosity modifier	Oral, topical and ophthalmic solutions and/or suspensions
Adhesive	Transdermal systems, adhesive gels

Wet Binding

Among the various applications listed, Kollidon® 90 Evo is particularly suitable as a strong binder in wet granulation technologies. For wet binding, it is recommended to apply a solution of Kollidon® 90 Evo to the remaining dry ingredients instead of wetting all the dry powders with water. Reason is that the dense Kollidon® 90 Evo particles need to be dissolved completely for it to display the binding properties.

In wet binding, the long Kollidon® 90 Evo polymer chains deliver a stronger performance than the respective lower molecular weight polymers Kollidon® 30 and Kollidon® 25. However, its application window might be limited, due to higher solution viscosity in comparison to those Povidone grades.

The optimal balance of high binding capacity vs. viscosity allows successful formulations with relatively low amounts of 1% - 5% Kollidon® 90 Evo.

Binder in high shear wet granulation

In this section two exemplary placebo formulations are described to highlight the versatility of Kollidon® 90 Evo in high shear granulation. Aqueous polymer solutions with 1% - 12% w/w concentration of polymer are recommended to obtain solution of suitable viscosity for the granulation process.

Table 9: Placebo granulations (Diosna-Pharma P1/6)	MCC Granulation	DiCaPhos Granulation
MCC [g]	243	-
DiCaPhos [g]	-	490
Kollidon® 90 Evo solution: Concentration [w/w] Amount [g]	 1.9 % 220	 12% 105

Table 10: granules composition (dry)	MCC Granulation	DiCaPhos Granulation
MCC [g/100 g]	93.5	-
DiCaPhos [g /100 g]	-	96.5
Kollidon® 90 Evo [g/100 g]	1.5	2.5
LOD [g/100 g]]	5	1

Kollidon® 90 Evo can be applied in low concentration and low amounts in combination with a binding filler like microcrystalline cellulose (MCC), to obtain very strong granules.

In combination with a non-binding filler like dicalcium phosphate (DiCaPhos), Kollidon® 90 Evo is added in higher concentration and higher amounts to obtain granules of desired strength.

The resulting granules (Figure 4) in both cases have acceptable friability and low fines and are free-flowing.

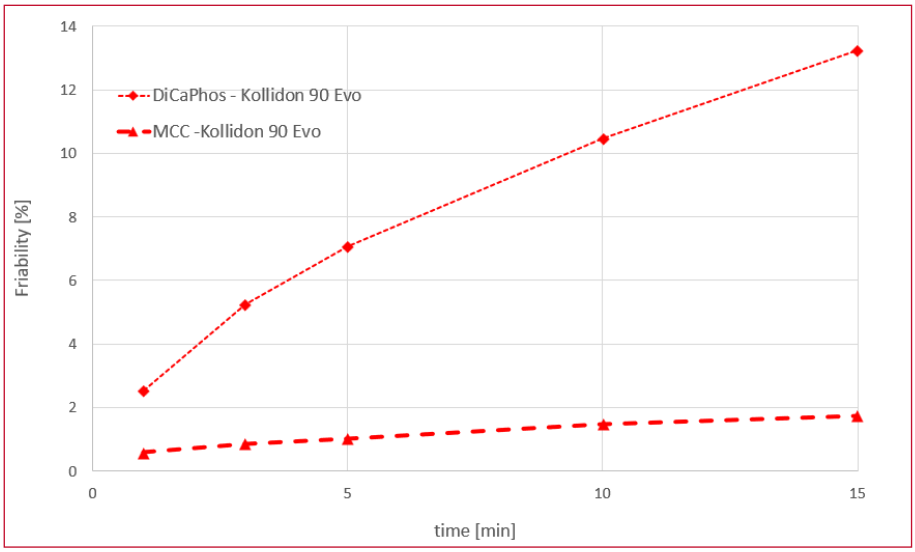


Fig. 4: Friability of MCC- Kollidon® 90 Evo (1.5%) and DiCaPhos- Kollidon® 90 Evo (2.5%) granules tested with air jet sieve LPS 200 (air volume rate 60 m3/h).

Figure 5 shows example tabletability and compressibility plots for the tablets obtained from MCC based granules. The results confirm that the binding property of this filler is enhanced in combination with Kollidon® 90 Evo used intra-granule at very low dosage, generating strong tablets even at low compression pressure.

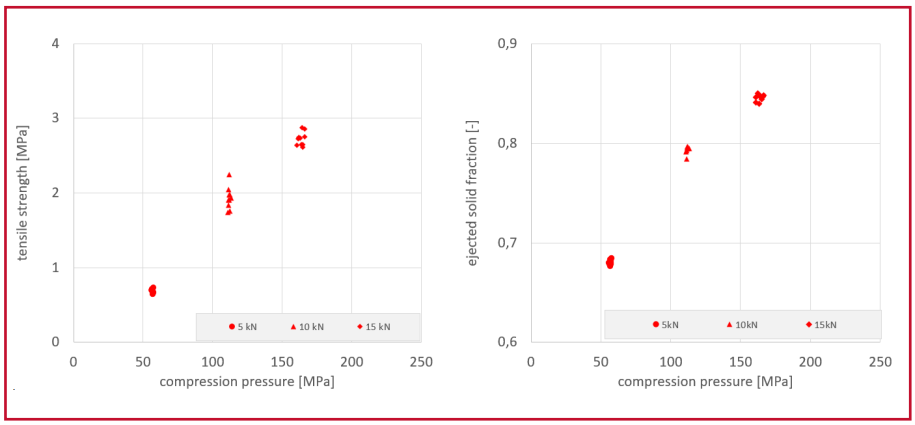


Fig. 5: Tabletability and compressibility plots for MCC - Kollidon® 90 Evo tablets (300 mg, round shaped, 1.5% Kollidon® 90 Evo intra-granule)

Figure 6 shows example tabletability and compressibility plots for the tablets obtained with dicalcium phosphate-based granules. As this filler has no own binding contribution, higher Kollidon® 90 Evo ratios and higher compression forces are applied to obtain tablets of comparable strength to the previous example.

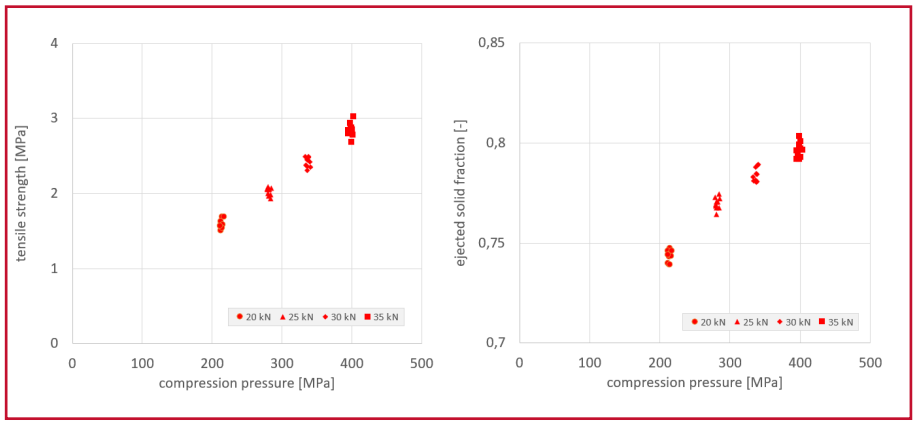


Fig. 6: Tabletability and compressibility plots for dicalcium phosphate -Kollidon® 90 Evo tablets. (500 mg, round shaped, 2.5% Kollidon® 90 Evo intra-granule)

Binder in fluid bed granulation: Metformin tablets

Kollidon® 90 Evo´s outstanding binding properties can be used to formulate dosage forms with high drug load and eventually no filler by employing fluid bed granulation. For processing APIs in fluid bed granulation, an optimal distribution of the binder solution is key to ensure that the APIs gets evenly wetted by the binder. For this purpose, low viscous solutions of Kollidon® 90 Evo (typically below 7% solid content) are ideally employed.

Metformin tablets are a typical example of such high drug load formulations, and several commercially available metformin's formulations include Povidone K90.

As Metformin is an API prone to nitrosamine formation, nitrite levels in excipients used to formulate metformin have become relevant. Kollidon® 90 Evo has been tested for nitrites and so far, no nitrites could be detected with a detection limit (LOD) of 0,7 ppm. The current version of the nitrosamines risk assessment for Kollidon® 90 Evo is available in RegXcellence®.

Kollidon® 90 Evo is therefore for both reasons a suitable binder for metformin formulations.

An example formulation is obtained by spraying Kollidon® 90 Evo aqueous solution on metformin HCl utilizing an Innojet Ventilus 1.

Table 11: Ingredients of Metformin Granules	Amount [g]	Ratio [g/100g]
Metformin HCl	248.75	97
Kollidon® 90 Evo*	125	2.5
Silicon dioxide (Aerosil 200**)	1.25	0.5

**Added as 5% aqueous solution* ***Aerosil added extragranular*

Table 12: Metformin Fluid Bed Granulation Process Settings	
solution spray rate	5g/min
nozzle diameter	1 mm
air pressure	0.8 bar
flow rate of process gas	40 - 55 m^3/h
inlet temperature	50°C

The resulting granules have low friability and fines. After blending with Aerosil they are compressed into round shaped tablets employing a Style`One Compaction simulator.

The resulting tabletability plot underlies the strong binding performance of Kollidon® 90 Evo as only 2.5% binder and no further fillers or binders are applied.

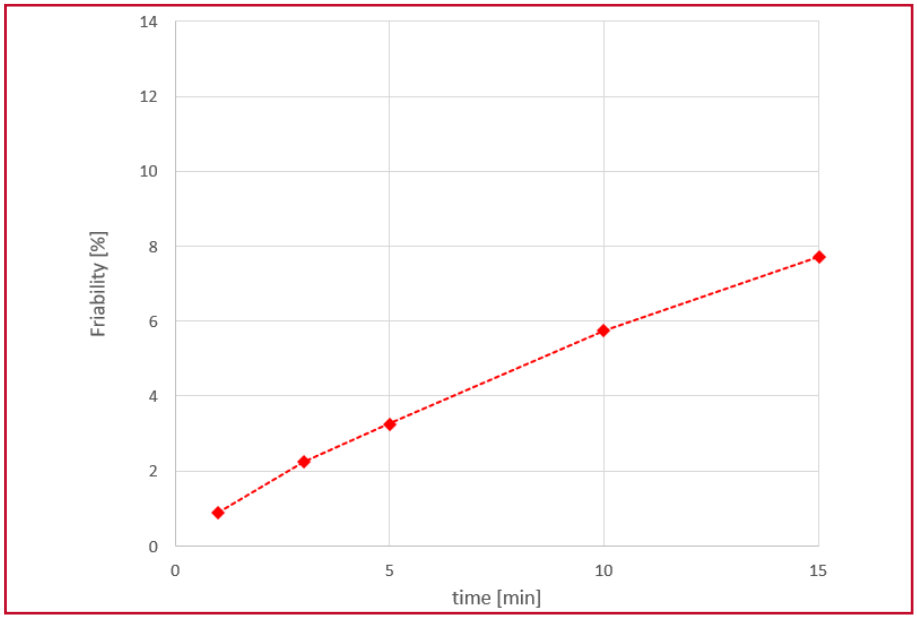


Fig. 7: Friability of metformin - Kollidon® 90 Evo granules tested with air jet sieve LPS 200 (air volume rate 60 m^3/h)

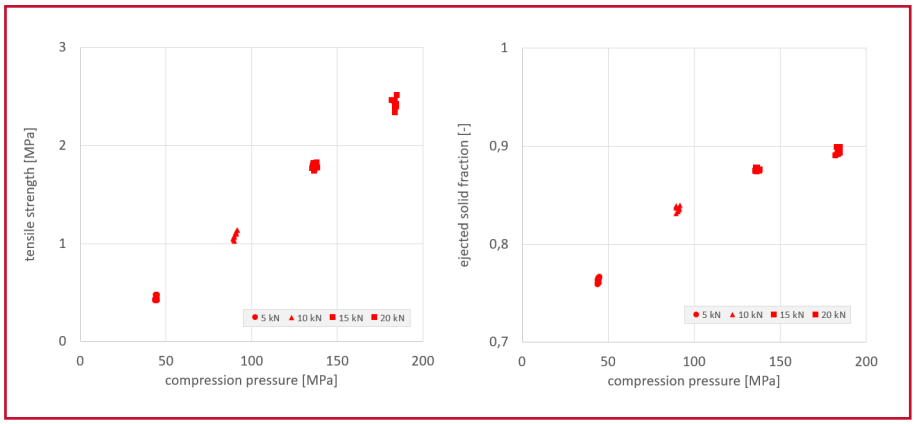


Fig. 8: Tabletability and compressibility profiles of metformin tablets (515 mg, round shaped, 2.5% Kollidon® 90 Evo intra-granule)

5. Stability & Safety

The product is stable for 36 months (3 years) after date of production, provided storage under recommended conditions. The actual retest period and storage conditions can be found in the document "Quality & Regulatory Product Summary" in RegXcellence®.

The actual version of the safety data sheet is accessible via MyProductWorld and sent with every consignment.

6. Articles and Packaging

PRD-No.*	Product name	Article numbers	Packaging Type and Size
30768117	Kollidon® 90 Evo	50810372	EVOH laminated liner in squared fiber drum, 50 kg
		50712043	EVOH laminated liner in plastic pail, 0.5 kg (non-GMP sample)

* BASF's commercial product number.

7.Documents, Quality & Regulatory Information

Visit our BASF website to learn about the benefits of Kollidon® 90 Evo:
https://pharma.basf.com/products/kollidon-90-evo

Access product documentation anytime via the BASF Virtual Pharma assistants:
Virtual Pharma Assistants

Meet your Virtual Pharma Assistants!
MyProductWorld, RegXcellence® and ZoomLab™

www.virtualpharmaassistants.com

MyProductWorld: article numbers, sample order, safety data sheet, sustainability information

RegXcellence: specification, compliance documents, regulatory product summary

ZoomLab: formulation assistance to predict starting formulations and expedite drug formulations.

Disclaimer