

New formulas for successful drug delivery

Hot-melt extrusion for enhanced solubility and bioavailability

Andreas Gryczke,
an enabler in excipients



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 **BASF**
The Chemical Company

Pioneering drug delivery methods from BASF



“The key to success for our pharmaceutical customers is innovation, speed-to-market and cost-effectiveness. With our comprehensive product portfolio and expertise in hot-melt extrusion technology, we help our customers to successfully develop even challenging drug formulations.” ...

... says Andreas Gryczke, Manager Technical Marketing. Our work in developing more effective excipients is designed to ensure the best pharmacological performance for active ingredients. Our excipients in combination with hot-melt extrusion technology help you to enhance and control the oral bioavailability of your active ingredient. Synthetic polymers are the preferred carriers for hot-melt extrusion technology due to their easily controlled and adjustable characteristics.

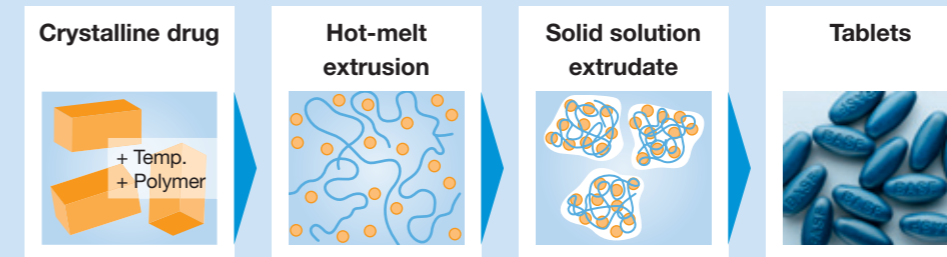


BASF leads the way in hot-melt extrusion polymers and technology

Hot-melt extrusion has been used in the plastics and food industry since the 1930s. In the 1980s, BASF was the first company to introduce the hot-melt extrusion process to pharmaceutical production. Poorly soluble actives can often be enhanced in their solubility and thereby in their bioavailability e.g. by molecularly dispersing them in a polymeric carrier. A hot-melt extrusion process always yields a solid dispersion and melt extrudates usually have a high density, which also makes the process suitable for producing controlled release formulations. The melt obtained from the extrusion process is a viscous fluid that can be directly shaped into any desired form.

As the extrusion and compounding process has been well characterized and understood in the plastics industry for decades, it is our mission to help understand and implement the technology. We help you to start using hot-melt extrusion technology and to discover its advantages, including the versatility to develop drug formulations with it. The true potential of hot-melt extrusion technology in pharmaceuticals is only just beginning to be seen and BASF research is revealing just how exciting it could be.

From poor API solubility to final formulation



- Polymer acts as protective matrix for the drug molecule to freeze the drug's current condition
- Drug can be crystalline dispersed or molecularly dispersed in the polymer, depending on desired application and given miscibility with the polymer
- Rate of dissolution will be controlled by the polymer and can be enhanced for the drug or can be delayed, depending on the chosen polymer

BASF polymers and the hot-melt extrusion process are the perfect combination for your formulation challenges

The extrusion process can deliver excellent batch-to-batch consistency. The equipment required has a small footprint at lab scale and even smaller in production scale. As a continuous process, hot-melt extrusion can deliver large batches or very small batches by flexibly adjusting process time. Production capacity can be increased by transferring the formulation to a larger-scale extruder or by installing multiple extruder units in parallel. This offers additional flexibility when producing a number of different products. Every step of the extrusion process can be monitored in detail by different analytical tools, such as FT-NIR or other spectroscopic methods. This allows permanent quality monitoring, leading to fast batch releases and avoiding longer failures in the process. BASF is currently exploring process characteristics to further develop dedicated excipients. We partner with universities and industry to strengthen your capabilities in this exciting technology.



Free hot-melt extrusion compendium

BASF's ground-breaking pharmaceutical hot-melt extrusion compendium is now available. This must-have resource includes everything you need to know to achieve your required release profiles under robust processing conditions.

Download your free copy at:
www.innovate-excipients.basf.com

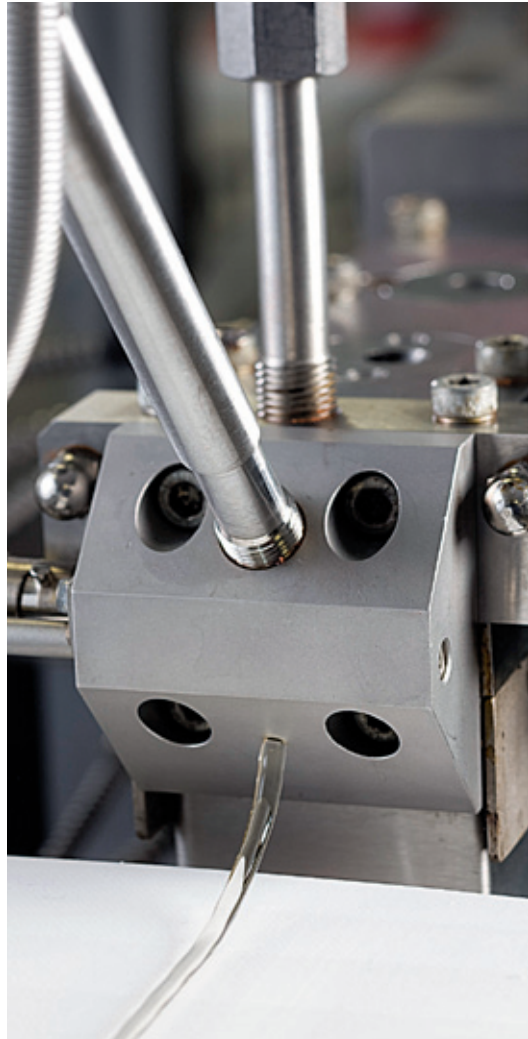
The broad range of BASF excipients with proven capabilities

Soluplus®	Solubilizing agent, dispersant, crystallisation inhibitor, immediate release matrix T _g : 70 °C, T _{Degradation} : 250 °C
Kollidon® VA 64/VA 64 fine	Solubilizing agent, dispersant, crystallisation inhibitor, immediate release matrix T _g : 101 °C, T _{Degradation} : 230 °C
Kollidon® 12 PF	Solubilizing agent, dispersant, crystallisation inhibitor, immediate release matrix T _g 90 °C, T _{Degradation} : 225 °C
Kollidon® 17 PF	Solubilizing agent, dispersant, crystallisation inhibitor, immediate release matrix T _g : 138 °C, T _{Degradation} : 175 °C
Kollidon® 30	Solubilizing agent, dispersant, crystallisation inhibitor, immediate release matrix T _g : 149 °C, T _{Degradation} : 175 °C
Kollidon® 90 F	Solubilizing agent, dispersant, crystallisation inhibitor, immediate release matrix T _g : 156 °C, T _{Degradation} : 200 °C
Kollidon® SR	controlled release matrix systems also for poorly soluble drugs T _g : 39 °C/152 °C, T _{Degradation} : 210 °C
Kollocoat® MAE 100 P	For enteric matrix, solid solutions for non-immediate release drug delivery systems T _g : 114 °C, T _{Degradation} : 150 °C
Kollocoat® IR	For immediate release matrices T _g : 45 °C, T _{Melt} : 208 °C, T _{Degradation} : 200 °C

* Former trademarks

Kollocoat® Protect	For immediate release matrices T _g : 45 °C, T _{Melt} : 205 °C, T _{Degradation} : 200 °C
Kolliphor™ P 188/P 188 micro *Lutrol® F 68	Acts as solubilizer, emulsifier and as plasticizer T _{Melt} : 55 °C, T _{Degradation} : 180 °C
Kolliphor™ P 407/P 407 micro *Lutrol® F 127	Acts as solubilizer, emulsifier and as plasticizer T _{Melt} : 55 °C, T _{Degradation} : 180 °C
Kolliphor™ RH 40 *Cremophor® RH 40	Acts as non-ionic solubilizer, emulsifier and as plasticizer T _{Degradation} : 200 °C
Kollisol™ PEG 300 *Lutrol® E 300	Acts as co-solvent and as plasticizer T _{Melt} : -15--10 °C, T _{Degradation} : >220 °C
Kollisol™ PEG 400 *Lutrol® E 400	Acts as co-solvent and as plasticizer T _{Melt} : 4-8 °C, T _{Degradation} : >220 °C
Kolliphor™ PS 80 *Polysorbate® 80 PH	Surfactant to solubilize drugs T _{Boiling} : >100 °C
Kolliphor™ SLS *Texapon® K 12 G PH	Surfactant to solubilize T _{Melt} : approx. 205 °C, T _{Degradation} : >220 °C
Kolliwax™ GMS I *Speziol® MD Pharma	Acts as plasticizer T _{Melt} : 58-59 °C, T _{Boiling} : 238-240 °C
Kolliwax™ SA *Speziol® C 18 Pharma	Acts as plasticizer T _{Melt} : 59 °C, T _{Boiling} : 210 °C
Kolliphor™ TPGS *Speziol® TPGS Pharma	Acts as antioxidant, solubilizer, stabilizer, plasticizer T _{Melt} : 40 °C, T _{Degradation} : >210 °C
Kollisol™ GTA *Speziol® GTA	Acts as plasticizer, solubilizer T _{Melt} : -77 °C, T _{Boiling} : approx 258 °C

* Former trademarks





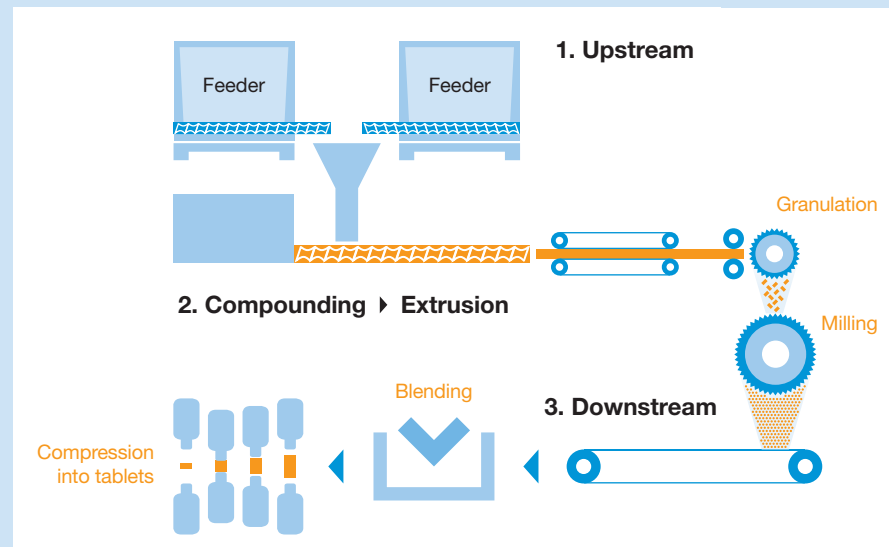
Award-winning Soluplus® provides a new dimension in solubility and bioavailability

Our innovative Soluplus® product was the world's first polymeric excipient designed especially for the hot-melt extrusion process. It shows outstanding solubilization properties, high flowability and excellent extrudability, even at relatively low temperatures. The addition of a plasticizer is not required and the low extrusion temperature makes it possible to extrude active ingredients that are thermally sensitive.

Soluplus® was developed to form glassy solid solutions with many drug molecules. Its chemical structure allows binding the drug via hydrogen bonding to immobilize the drug over its shelf-life. During dissolution, Soluplus® encapsulates the dissolved drug molecules in polymeric micelles, allowing oversaturated drug solutions and avoiding drug precipitation. Because Soluplus® has been developed for high-content matrix systems, we have proven its toxicological safety in comprehensive studies, enabling you to quickly start developing stable and safe solid dispersions. As with other BASF excipients suitable for hot-melt extrusion, Soluplus® shows superior processing characteristics and yields for long-term stable solid dispersions.



The Melt Extrusion Process at a glance



Hot-melt extrusion is a quality-by-design friendly technology that allows the execution of design-of-experiments to characterize process and formulation fingerprints with continuous data acquisition to gain the required knowledge for the development of required control space. BASF polymers can be extruded at a wider temperature range and are not sensitive to different shear stresses, allowing an optimum processing range to be identified for your active pharmaceutical ingredient.

Depending on desired formulation characteristics, you can choose the right base polymer from our broad polymer and excipient portfolio.

Radically enhanced bioavailability

Poor solubility in drugs can lead to low or significantly reduced bioavailability. In two in-vivo studies, itraconazole and fenofibrate showed that Soluplus® delivered a major increase in bioavailability.

Soluplus® has already proved its worth in the industry. In 2010, it was awarded a silver medal in the CPhI Innovation Awards.

Soluplus®: a winning solution

- Soluplus® acts as solubilizer for poorly soluble active pharmaceutical ingredients
- Soluplus® forms stable glassy solid solutions
- Soluplus® shows superior extrudability and processability in subsequent process steps compared to other pharmaceutical polymers



Outstanding range. Uncompromising quality.

- Hot-melt extrusion allows innovative and cost-effective drug delivery formulation
- Enhanced bioavailability and controlled release via hot-melt extrusion
- BASF provides you with customer-specific solutions and global support

The hot-melt extrusion process is robust, consistent and can be used in any pharmaceutical manufacturing plant. Innovative products like Soluplus® demonstrate how active ingredients can be formulated within a reliable matrix and hence can show highly improved bioavailability.

Contact us to find out how Andreas Gryczke and his colleagues can use hot-melt extrusion technology to help you produce high-quality, high-performance pharmaceutical products.

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