

Double whammy

In collaboration with Ghent University, **Labo Smeets** has developed a new technology that enables the continuous production of water-soluble granules. Managing director Jef Verplaetse explains how twin screw extruders can improve the bioavailability of medicines that are not easily soluble in water.



The advantages of the Twin Screw Granulator are a continuous process, limited upscaling problems and the absence of solvents.

Poorly soluble drugs present a challenge: no matter how potent the active ingredient, there are problems of incomplete absorption and low bioavailability. The recipients are thus unlikely to benefit from the full clinical effect. This is particularly the case for medicines belonging to class II (poorly soluble, highly permeable) and class IV (poorly soluble, poorly permeable) of the biological classification system. Where such drugs are administered via drinking water, only a small proportion of the active ingredient is released: tests have shown figures as low as 15%.

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In response to this situation, Labo Smeets has pioneered its latest technology. In collaboration with Ghent University, the Belgian pharmaceutical powders company has developed a granulation technique for converting poorly soluble drugs into highly soluble granules.

“If a drug is to be administered via drinking water, dissolving it is key,” says managing director Jef Verplaetse. “Our granules guarantee dissolution of 100%.”

The benefits are obvious: high solubility leads to a swift release of the active pharmaceutical ingredient (API), which in turn increases bioavailability. This minimises wastage, because less API is needed to produce the same effect.

Twin-screw technology

Although the Twin Screw Granulator used for this purpose did not become operational until January 2011, the technology was first envisioned decades ago.

“The concept of using twin screw extruders for the granulation of drug preparations started in the mid-1980s,” says Verplaetse. “However, granules were not homogeneous and required a great deal of optimisation.”

A drug load of up to 60% can be achieved for drugs of class II and class IV of the BCS system.

The technology now ensures a very intense and effective blending under strictly controllable conditions, which helps ensure the stability of APIs. Moreover, the continuous granulation process, as distinct from batch production, is speedy and straightforward.

“The main problem of batch production is the scale-up from laboratory to industrial production capacity,” explains Verplaetse. “Such problems can be avoided with a

Why use a twin screw extruder?

The pharmaceutical industry is becoming ever more interested in continuous process technologies. Such technologies present many benefits, not least the fact they enable a larger production capacity, reduce time and costs, and avoid scale-up problems.

Twin screw extruders have been used for continuous production processes for many years. Particularly prominent in the plastics industry, in which polymers are mixed with additives to give plastic compounds, they facilitate a very intense and effective blending under strictly controllable temperature conditions.

Generally, twin screw extruders are preferred to single screw extruders because they give better mixing at lower melt temperatures, and benefit from greater flexibility in terms of their design.

Despite the long pedigree of this technology, only now is the pharmaceutical industry starting to reap its benefits. With recent developments focusing on the optimisation of the screw profiles and the choice of materials used, twin screw extruders may now be used for producing homogeneous granules for drug preparations.

The Twin Screw Granulator (Pharma TSG 24) used by Labo Smeets is supplied by Thermo Scientific, an important player in the production of twin screw granulators and extruders. It has been operational since January 2011 and, in its production of water soluble granules, has been put to the most pioneering of purposes.

continuous granulation technology, in which the only parameter that needs to be changed is production time.”

Finally, the low temperatures at which the blending process occurs offers interesting perspectives for temperature-sensitive APIs.

Solubility needs

At present, Labo Smeets' focus is the veterinary market. While mixing drugs with animal feed is arguably simpler than dissolving them in water, it is difficult to control the concentration level in feed granules or to estimate batch sizes with any accuracy. Highly soluble drugs are therefore a pressing need. Applications in the human drugs market may also be on their way. Labo Smeets has, for example, successfully developed a paracetamol suitable both for animals and people.

“Bioavailability is going to become ever more important for human medicines,” says Verplaetse. “APIs that are taken orally should be available for the body and not simply wasted. Improved bioavailability also means that the effect of the drug as a function of the given doses can be better understood.”

New horizons

Twin screw granulation has many possible applications, which are yet to be explored. While Labo Smeets has concentrated mainly on melt granulation with a

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hydrophilic matrix, the same technology can be used with a lipophilic matrix. This should bode especially well for the manufacture of tablets.

“Another field we are looking into is wet granulation,” says Verplaetse. “The excellent blending properties of the twin screw extruders can make a high-quality granulate. Finally, we are considering polymer granulation applications for controlled release, using ethyl cellulose or polyethylene oxides as carriers.”

The new patented technology offers new opportunities for the lifecycle management of drugs. The major advantage of the technology is that, as well as improving solubility and bioavailability, it enables the creation of new lifecycle opportunities for old molecules. In a time when patents are expiring, new creative ideas are needed to ensure the continued value of those products: Labo Smeets' twin screw granulation process is one such innovation. ■

Further information

Laboratoria Smeets
www.labosmeets.be



New: Twin Screw extrusion for improving the water solubility of APIs.



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