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ARTICLE

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ASTRAZENECA





Bastian Käding

Managing Director, Romaco Innojet



High-precision fluid bed coating



Esomeprazole blocks the production of stomach acid and is therefore used, amongst other things, to treat gastric and intestinal ulcers and prevent reflux symptoms. The acid-labile proton pump inhibitor is absorbed in the intestine and either administered parenterally or taken orally as an enteric-coated preparation. The drug is accordingly available as an injection solution or in the form of tablets or capsules, for example so-called multiple unit pellet systems or MUPS for short. For these preparations, micropellets containing active ingredients are either mixed with powdery excipients and then compressed into tablets or alternatively filled into capsules.

One big advantage of MUPS tablets is that they dissolve easily, so that the pellets with the active pharmaceutical ingredients (API) pass through the stomach quickly due to their small diameter, regardless of whether or not it is full. The medication is consequently characterised by a highly controlled release profile and high bioavailability.

Since the active ingredient of MUPS tablets is distributed between a large number of pellets, the tablets can also be halved. By contrast, dividing coated sustained-release tablets in two would have negative effects for consumers: the active ingredient would be released immediately after swallowing, which would be tantamount to dose dumping. MUPS formulations, on the other hand, facilitate compliance.

Three-stage micropellet coating

Esomeprazole pellets for MUPS applications are often produced in a fluid bed coating process comprised of three stages. First of all, neutral starter pellets made from glucose are sprayed with the aqueous API suspension. A protective insulating layer is applied next, followed by the enteric sustained-release coating, which ensures controlled release of the drug in the intestinal tract.

Depending on the formulation, the diameter of the micropellets increases from approximately 300 µm (microns) to 1300

µm during the coating process. Parallel to this, their weight is roughly trebled from about 1.5 g to 4.7 g per pellet. Several days are usually scheduled for this method in the pharmaceutical industry. The fluid bed processors in Romaco Innojet's VENTILUS® series meet all the requirements of this demanding production process, which is based on the air fluid bed process technology developed by Dr. h. c. Herbert Hüttlin.

Three functional units make it possible

The interaction of three functional units – ORBITER®, ROTOJET® and SEPAJET® – in these fluid bed processors from Romaco Innojet lays the foundation for high quality and efficiency in the production of esomeprazole pellets. In this innovative process, the process air is introduced into the cylindrical product container through the ORBITER® booster, resulting in a spiral product movement. The spray liquid is applied with the central ROTOJET® nozzle by the

bottom spray method and the process air is subsequently discharged again via the SEPAJET® filter system.

The so-called ORBITER® booster plate consists of overlapping circular plates that ensure homogeneous flow inside the container. The speed of the micro-pellets and their path through the container can be precisely controlled in this way, preventing the particles from colliding and agglomerating. The risk of this happening is particularly great when spraying on the very sticky enteric suspensions. Esomeprazole coatings, on the other hand, tend to be highly abrasive, which is why gentle intermixing of the batch without any mechanical stresses is so immensely important.

Efficient injection system

Due to the controlled movement of the process air, the coating liquid can be applied very precisely with the central ROTOJET® spray nozzle. The liquid spray is directed upwards.

at the product bed (bottom spray), so that spray loss is significantly reduced. In addition, the rotating nozzle head effectively prevents blocked spray nozzles. This is especially vital when the sustained-release coating is applied to the esomeprazole pellets, because the enteric coating liquid polymerises easily. To optimise the coating process even further, the air temperature – and hence the product temperature – around the nozzle can be controlled differently than in the rest of the process container. This ensures particularly efficient drying and enables very short processes.

The particle droplet size is defined by the spray air introduced above and below the circular spraying gap, so that no over-wetting of the product occurs during the MUPS coating process, which takes several hours to complete. The pellets are built up homogeneously, which results in maximum moisture ex-



traction. This shortens the drying time by up to 25 percent and reduces the system's energy consumption dramatically.

What's more, the ROTOJET® nozzle can be easily replaced during the actual process without having to stop production and empty the product container. Far shorter batch processing times are the outcome.

Sustainable particle filter

Process air is discharged via the SEPAJET® filter system, which was specially designed so that the particles are constantly returned to the process. Conditioned process air cleans the individual filter bags continuously throughout the production cycle. This hot, conditioned cleaning air prevents condensation and helps extend the filter system's service life. At the same time, the geometry of the filters permits a compact machine design.

The space saved in the cleanroom is another advantage on the sustainability side, first and foremost because only one machine is needed to produce esomeprazole pellets. The fact that the cylindrical product container allows filling from 10 to 100 percent means there is

no need to empty the batch and divide it into sub-batches in the event of a process-inherent increase in pellet weight. This leads to a smaller carbon footprint for the process and time, money and storage capacity are saved.

Scale-ups made easy

The production-scale fluid bed processors in the VENTILUS® series are designed for batch sizes from 60 to 1600 litres. Since the geometry of both the cylindrical product container and the spray nozzle is scalable, scale-up processes are greatly simplified. Romaco Innojet's InnoTech laboratory in Steinen has lab, pilot and production scale machines available for product trials. Process parameters for new formulations can be determined quickly and easily using DoE (Design of Experiment), the lab software. For instance, once the spray rate, product temperature and process air volume are optimally matched, maximum leverage can be obtained from the fluid bed processor's capacity in terms of performance and quality – as the ideal starting point for developing new esomeprazole products.