

Optimization of wet and melt granulation processes

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Wet granulation is one of the most used methods for the industrial preparation of fast or controlled release granules. Anyway, in recent years, the interest in melt granulation has increased due to the numerous advantages of this technique over traditional wet granulation. In fact the melt granulation does not require the use of organic or aqueous solvents, making the entire process less consuming in terms of time and energy as compared to wet granulation.

Our recent research focused on the study and the optimization of wet and melt granulation performed both in high-shear mixers-granulators and in fluid bed granulators, technologies widely diffused in the pharmaceutical industry, even if the interest on melt granulation of pharmaceutical powders in fluidised bed is more recently than in high shear mixer.



1. Description of the product

An advantageous wet granulation method, alternative to conventional, named “steam granulation”, has been developed. In particular, a wet granulation process in high-shear mixer was optimized in order to obtain controlled released granules using cholestyramine as resin and potassium diclofenac as model exchangeable anionic drug. The binders, hydroxypropylmethylcellulose (HPMC) and pregelatinized starch were added as a powder and the steam was introduced on to the powder mixture.

In the case of melt granulation, the binder is constituted by a low melting point material. Melt granulation can be performed using two procedures: the spray-on method involves the spraying of a molten binder onto the powders, while the in situ melt granulation employs a solid binder which is heated above its melting point by hot air (fluidised bed) or by impeller frictional forces and heating jacket (high-shear mixer). Examples of hydrophilic binders used to prepare improved-release dosage forms include polyethylene glycols and poloxamers, while hydrophobic binders such as waxes, fatty acids, fatty alcohols and glycerides can be utilized for prolonged-release formulations. Processing parameters have to be optimized according to the used equipment.

2. Innovative aspect of the product

Optimization of a wet granulation process: the goal of this work was to evaluate the suitability of steam granulation as an innovative and fast method for the preparation of granules containing a drug-resin complex (resinate). Resinate and granules were prepared directly in a high shear mixer granulator. The results indicate that enteric release granules were obtained in a fast procedure without applying any enteric coating onto the granules and thus reducing the processing time.

Optimization of melt granulation process: The main aim of this research was to compare high-shear mixers and fluidised bed processes with particular attention to the final technological, physicochemical and biopharmaceutical properties of granules. In addition, the study evaluated the suitability of melt granulation in fluidised bed for improving the dissolution rate of two drugs. Agglomerates having same composition (a non-steroidal anti-inflammatory agent, ibuprofen or ketoprofen, as model drug, PEG 6000 as hydrophilic meltable binder and lactose as diluent) were produced by in situ melt granulation using both equipment and their morphology, particle size, flowability, friability, drug loading, dissolution behaviors and physicochemical properties have been evaluated and compared.

3. Main advantages of the offer

Wet granulation: The preparation of a solid oral pharmaceutical form in a single procedure and the possibility of combining different steps into one processing unit is very interesting for pharmaceutical industry because it is less consuming in terms of time, energy and material handling compared to traditional multistep methods.

Melt granulation: In situ melt granulation of pharmaceutical powders can be successfully performed in both high-shear mixer and fluidised bed granulators. Due to the different mechanism of granule growth, the utilization of a different equipment has strong impact on the particle size distribution of the granules and on their morphology. On the contrary, the equipment effect on others technological properties is little, as all the granules possess low friability and excellent flowability. Moreover either the solid state characteristics of the products and the dissolution behaviors of ibuprofen and ketoprofen granules are found to be practically independent of the equipment and all granules show a significant increase of the drug dissolution rate in acidic conditions. This finding is very important as it indicates that in pharmaceutical industry, if necessary, it can be possible to switch from one equipment to another maintaining constant the biopharmaceutical properties of the granules.

4. Technology key words

Steam granulation –melt granulation – controlled release granules - fast dissolving granules

5. Current Stage of Development

Ongoing research

6. Intellectual Property Rights

The product is not covered by patent.

Technical and scientific publications

B. Albertini, N. Passerini, M.L. González-Rodríguez, C. Cavallari, M. Cini, L. Rodriguez. Wet granulation as innovative and fast method to prepare controlled release granules based on an ion-exchange resin. J. Pharm. Sci., 2008, 97(3), 1313-1324.

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