POLYMER MODIFICATIONS FOR PHARMACEUTICAL EXTRUSION

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The **pharma-extrusion** shows similarities to biopolymer processing, but the peculiarities, required by the drugs, need special attention. Structure-property design and in line control is required aiming mainly to control the polymorphism/amorphization of the drug embedded and thus its dissolution. A complex approach is called "process analytical technology (PAT) technology. The continuous pharmaceutical processing, involved by this approach, is most straightforward in the case of extrusion. Stability is, however, a critical aspect to be considered. Plasticising methods and their role in stabilization efficiency are more important for pharmaceuticals than for conventional polymer systems, while the choice of relevant additives is limited by the authorities. In order to perform gentle processing and still achieve efficient amorphization **supercritical extrusion** was used. Supercritical technique, using supercritical CO_2 (sc-CO_2), is well known in the (nano)pharmaceutical technology, but the most productive way is the sc-extrusion. The amorphization can be well controlled this way because drugs of poor water solubility can be dissolved, at least partially, in CO_2. Than it can be mixed with the polymer matrix in the extruder and the expansion of the bubbles enhance the surface available by the dissolution medium. The results of such as process in the case of Carvedilol can be seen in **Figure 1**.

The drug dissolves from the extrudate very rapidly comparing to the reference.

Porous extrudate can be formed also utilizing the internal pressure of some residual water as proposed by a recent patent (1). Depending on their size and wall thickness, which limit the size of growing crystalline particles, the morphology of drug in the polymer matrix (above T_g) can be affected. An example is the extrusion of spironolactone in presence of hydroxypropyl cyclodextrine (HPβCD).

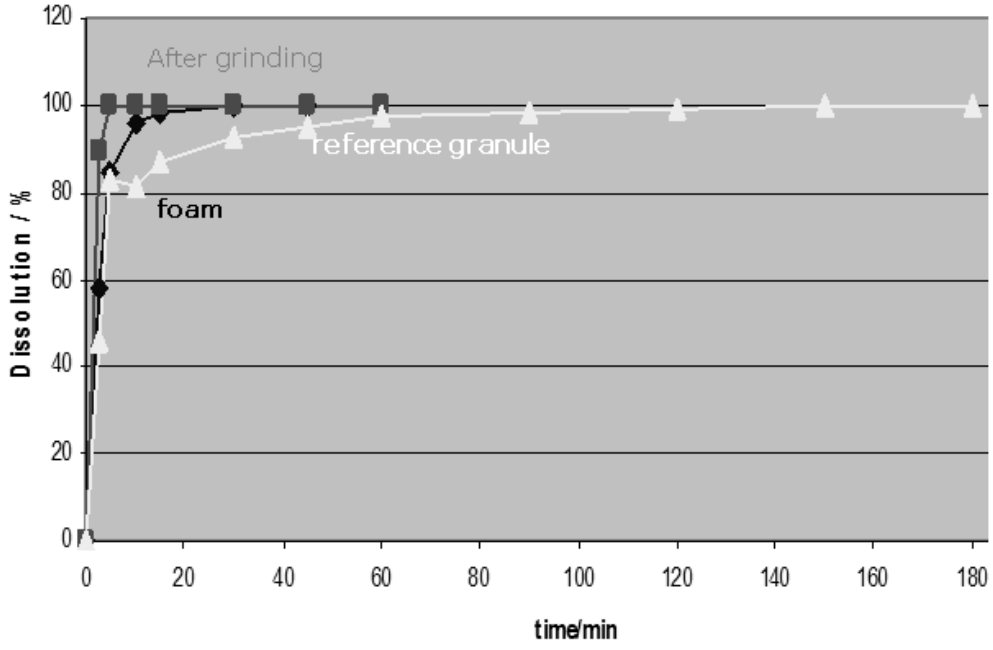

Figure 1 Dissolution of Carvedilol drug from sc-extrudate (♦), from sc-extrudate after grinding (■) and from reference (non-sc-ex) granule (Δ)

Another continuous method for amorphization is the formation of nanofibres by means of **electrospinning**. This method was introduced into the pharmaceutical technology recently. Polyvinyl pyrrolidone (PVP) and Carvedilol drug of poor water solubility were dissolved in methanol for performing electrostatic spinning. All measurements, including XRD, SEM, micro-Raman and DSC, confirmed that the drug is in amorphous state. With PVP K30 the sample dissolved immediately. This is a huge improvement compared to the crystalline Carvedilol dissolution, which took 2 hours.

Methods for forming nanostructured extrudates have a big prospect for pharmaceuticals. Their advantages include the good balance between stability and rapid dissolution.

References

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2. Z. K. Nagy, A. Balogh, I. Wagner, P. Sóti, H. Pataki, K. Molnár, G. Marosi, Nanofibrous drug delivery systems for enhanced dissolution prepared by electrospinning European Journal of Pharmaceutical Sciences 44S (2011) 152-153.