Improved Solubility of Hydrophobic Drugs using Hot Melt Extrusion Technology

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Abstract. It is estimated that about 40% of all new chemical entities have poor bioavailability because of low aqueous solubility. This percentage still increases due to combinatorial chemistry and the impact of lipophilic receptors[1]. Solubility is essential for the therapeutic effectiveness of the drug, independent of the route of administration. Poorly soluble drugs are often a challenging task for formulators in the industry. Conventional approaches for enhancement of solubility have limited applicability, especially when the drugs are poorly soluble simultaneously in aqueous and in non-aqueous media. Solubilisation may be affected by co-solvent water interaction, micellar solubilisation, reduction in particle size, inclusion complexes, solid dispersion, and change in polymorph[2].

Bioavailability is a measure of the extent that a therapeutically active drug reaches the systemic circulation and is available at the site of action.[3] Bioavailability is mainly controlled by the delivery of the drug as determined by its pharmaceutical formulation, the solubility, and the permeability through the gut wall. In addition, the bioavailability can be decreased through decomposition of the drug in the gastrointestinal tract, by formation of non-absorbable complexes, by metabolization, or by premature elimination. With such a high amount of potentially therapeutic drugs being rendered useless due to their low solubility and therefore inadequate drug delivery there is a pressing need to overcome this problem.

Over the past decade the use of biodegradable polymers for the administration of pharmaceuticals has increased dramatically. The most important biomedical applications of biodegradable polymers are in the areas of controlled drug delivery systems[4].

Extrusion is the process of converting a raw material into a product of uniform shape and density by forcing it through a die under controlled conditions. It represents an efficient manufacturing technology capable of dispersing drugs in a melt up to a true molecular solution of the active agent in a matrix.[1] Increasing dissolution rate and bioavailability of poorly water-soluble APIs is one of the important challenges at the development of solid dosage forms.

The high number of hot-melt extrusion patents for pharmaceutical applications issued in the last few years reflects the great international interest in the pharmaceutical application of hot-melt extrusion. This fact entails a challenge to develop new approaches in respect of formulations and processing2. With such a high percentage of newly discovered drugs never making it to market due their high hydrophobicity there is a major requirement to find ways of increasing the solubility of these drugs. The aim of this study is to improve the solubility of a hydrophobic drug and therefore increase its bioavailability in the body using polymeric materials and hot melt extrusion. Characterisation techniques such as dissolution, differential scanning calorimetry and rheometry will also be employed.

References:

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