19th International Symposium on MICROENCAPSULATION
Pamplona (Spain). September 09-11, 2013

Celecoxib loaded microparticles obtained by VarioSol® technology

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VarioSol® is an innovative spray-cooling, solvent-free, near critical fluid-based technology proposed for the production of fine powders or microspheres; this process employs carbon dioxide as spraying and cooling agent. Drug and excipients can be melted, dispersed or dissolved in a feeding vessel and subsequently atomized through a nozzle, under controlled pressure and temperature, into a spraying tower where the melted mixture comes in contact with expanding near-critical CO_2. The expanding fluid atomises the sprayed product into microscopic particles, while simultaneously cooling it.
Drug solubilisation enhancement improves drug bioavailability, reduces absorption variability, potentially allows the lowering of administered dose, and reduces the undesirable effects of the drug. Starting from this premise, the aim of this work was to produce, using VarioSol® technology, celecoxib loaded lipid microparticles able to improve drug solubilisation and to modulate drug release. Six formulations were prepared selecting binary or ternary excipient mixtures based on glyceryl behenate (Compritol 888ATO) as main component and containing fractions of other solid and liquid excipients suitable to solubilise celecoxib, to enhance its dissolution rate in the gastrointestinal fluids increasing its wettability and to form systems having adequate characteristics to be submitted to the VarioSol® process.
All the VarioSol® products were powders composed of regular in shape and very small microparticles (diameter under 50µm). DSC profiles evidenced no peak in correspondence to the drug melting temperature but only the presence of a well evident signal with an onset temperature in the range of 65-70 °C attributable to the main excipient (Compritol 888ATO) melting. These results suggested that microparticulate systems were solid solutions in which celecoxib was uniformly and molecularly dispersed in the carrier. Microparticles showed different drug release performances according to their composition: the formulation containing Compritol and other solid excipients guaranteed a faster drug release compared to formulations in which the mixture Compritol/liquid excipient was used. In the case of solid excipients/Compritol-based formulation, the release process ended in about two hours, while for liquid excipient/Compritol systems, microparticles required about six hours to deliver completely the loaded drug. This behaviour had to be ascribed to the highest amount of drug in the these microparticulate systems. The high quantity of celecoxib was responsible for a growth of the hydrophobic characteristics of microparticles and for the changing of their drug release behaviour.

This research work was partially funded by Regione Piemonte, Polo BioPMed.