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Nanosuspension with improved dissolution of cilostazol and effect of solidification on stability

Isamedin A Ali Aghrbi, Viktor Fülöp, Géza Jakab, Nikolett Kállai, Emese Balogh and István Antal
Semmelweis University, Hungary

The purpose of this study was to prepare a nanosuspension of a poorly water soluble drug by wet surfactant assisted media milling process to achieve superior solubility and in vitro dissolution rate values. Our aim was to optimize the process parameters of the wet milling technique using cilostazol (CLZ) as an active pharmaceutical agent in the predispersion. We basically investigated the influence of formulation aspects (emulsifier type; drug loading) on the grinding efficiency in predispersion. Solid state characterization of solids were also within the scope of our work along with dissolution and thermodynamic solubility comparison studies.

Cilostazol has anti-platelet aggregation, vasodilatory with minimal cardiac effects, recently indicated to reduce the degree of neuronal cell death after transient cerebral ischemia. It belongs to the Biopharmaceutical Classification System (BCS) Class II. drugs and has pH dependent poor solubility and high permeability.

The nanosuspension of CLZ was prepared using wet ball milling technique (BMT) utilizing type PM 100 ball mill, (Retsch GmbH., Germany) with $d=0.3$ mm zirconia beads. The wet milled and unmilled suspensions have undergone solidification by wet granulation, then matrix pellets were prepared by extrusion and spheronization method.

Milled CLZ particle size distribution before and after solidification was analysed by PCS (Photo Correlation Spectroscopy), zeta-potential values with Electrostatic Light Scattering (ELS) approaches.

Results: Optimized formula had Z-Average, PDI and Zeta-potential values of $336.90 \text{ nm} \pm 3.907$, 0.22 ± 0.022 and -53.20 ± 1.360 respectively. Thermodynamic solubility and dissolution rate values improved significantly due to particle size reduction and application of emulsifiers.

Biography

Isameddin A Ali Aghrbi has completed his Bachelors in pharmaceutical sciences at Tripoli University and Master degree in pharmaceutical sciences at Cairo University, his thesis topic was about biopharmaceutical study of anti-epileptic drugs. After Bachelor he worked as demonstrator at the Faculty of Pharmacy Tripoli University and after master degree he worked as assistant lecturer at Faculty of Pharmacy Tripoli University. Recently, he is a PhD student at Semmelweis University Faculty of Pharmacy, Department of Pharmaceutics. He is interested in pharmaceutical nanotechnology, formulation development and optimization fields. He presented his posters in four international conferences.

aessameddin@yahoo.com

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