Co-micronization as an efficient method for dissolution enhancement

Glibenclamide is indicated for the treatment of non-insulin-dependent diabetes. The drug belongs to Class II according to the Biopharmaceutics Classification System, with low water solubility and high permeability. Glibenclamide shows variable absorption and large variations in interindividual bioavailability and bioequivalence of the marketed products. Various methods have been described to enhance the solubility of poorly soluble drugs. Micronization, a common technique used to reduce particle size, is an established manufacturing process. The aim of the project was to use micronization process to improve dissolution of glibenclamide, but by a non-conventional approach which is the co-micronization of the drug with dissolution enhancement excipients at the same time. Nine different excipients (sodium lauryl sulfate – SLS, manitol, spray-dried lactose monohydrate – SD, lactose monohydrate 200 mesh – Lac200, hydroxypropylcellulose – HPC, hydroxypropylmethylcellulose E5 – HPMC, lutrol F68, microcrystalline cellulose 102 – MCC 102 – and polyvinylpirrolydone K30 – PVP K30) were co-micronized with glibenclamide in three different proportions (1:0.25 drug/excipient, 1:0.25:0.25 drug/excipient/SLS and 1:0.5 drug/excipient). These samples were divided in groups 1, 2 and 3, respectively. The samples were analyze by X-ray powder diffraction, infrared spectroscopy, microscopy, assay and powder dissolution. X-ray powder diffraction indicated that all samples did not show polymorphic change (samples presented characteristics peaks of the more soluble form). These results were in agreement with infrared spectroscopy. Assay evaluation showed a low variation between the theoretical and the determined values, which made it possible to calculate the mass for the dissolution tests. In general, the co-micronized samples had higher dissolution results than the raw material. The dissolution of the four samples of group 1 (glibenclamide with SLS, PVP K-30, SD lactose and lutrol F68) showed dissolution efficiency above 80%. In group 2, all samples had dissolution efficiency of more than 80%, except the one produced with lutrol F68. In group 3, only the sample with SLS had efficiency above 80%. When comparing group 2, which has an addition of SLS in the mixture, to group 1, it was possible to see an improvement in almost all the co-micronized samples. When compared to group 3, we noticed that the increase of the excipients proportion decreased the dissolution effectiveness, in general. For the next steps, we expect to use the best samples, based on dissolution results, to conduct further tests. Since almost all of the co-micronized samples had higher dissolution percentages compared to the raw material, we can confirm that reducing particles size can increase efficiency and that this process is enhanced with the presence of the dissolution enhancement excipients.

Keywords: *glibenclamide; co-micronization, dissolution.*