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Development and in-vitro evaluation of matrix based CR pellets for Diltiazem HCl using extrusion and spheronization

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The objective of the present study was to develop a matrix based CR pellet formulation by incorporating hydrophobic materials into a basic formulation for pellets. A basic pellet formulation consisting of drug and microcrystalline cellulose was used and magnesium stearate was incorporated as hydrophobic release modifier. The feasibility of using a plastic material, such as HPMC, as a binder and release modifier was also tested using aqueous and non-aqueous granulation procedures. Extrusion-spheronization technique, employing the rotating roller extruder (Model 10, Caleva, U.K.) with standard 1 mm screen and spheronizer (Model 120, Caleva, U.K.) with 120 mm diameter 3 x 3 mm squared pitch 1 mm depth, was used to prepare the pellets. A theoretical CR formulation was developed based on the pharmacokinetic characteristics of the drug and desired target blood concentrations (Ritschel, 1989). The developed CR formulations were compared with theoretical and marketed CR product. The critical process parameters were identified to be moisture content of the extrudate, spheronization speed, spheronization time, drying time and drying temperature. The prepared formulations were evaluated for product yield, average pellet size and size distribution, flow properties and drug release profile. The drug release profile from the formulation DLTZ-2 was found to be more sustained when compared to the release profile of a marketed product consisting of coated pellets and was more close to the desired theoretically calculated release profile (Figure-1). Owing to its plastic nature, formulations containing HPMC were difficult to spheronize and cylindrical extrudate was obtained as the final product. However, the promising results in terms of the sustained release profile of the formulations were obtained in the study which suggest that the current approach holds a good potential and can be exploited for obtaining matrix based CR pellets which would offer all the advantages of a multiparticulate drug delivery system with an added advantage of reduced processing time and cost by bypassing the release controlling polymer membrane coating step and thus enhancing the pharmacoeconomics of the dosage form.

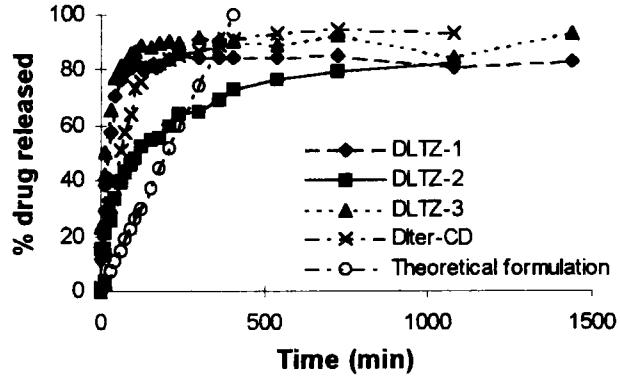

Figure 1: Drug release profile of different formulations in pH 7.4 phosphate buffer.

Ritschel, W.A., (1989) Drug Dev. Ind. Pharm., 15: 1073-1103.