Conference abstract PMS30

Physical Stability of Carvedilol in Solid Dispersions with Porous Silica

B. KOVAČIČ [1,2], O. PLANINŠEK [2], F. VREČER [1,2]

[1] Krka d.d., Šmarješka cesta 6, SI-8501 Novo mesto, Slovenia
[2] University of Ljubljana, Faculty of Pharmacy, Aškerčeva 7, SI-1000 Ljubljana, Slovenia

E-mail: borut.kovacic@ffa.uni-lj.si (B. Kovačič)

Sci Pharm. 2010; 78: 657 doi:10.3797/scipharm.cespt.8 PMS30

Adsorption onto silica-based high surface area carriers is a long known method of improvement drug dissolution rate, which has been described in early 1970s [1]. Porous silica has many silanol groups on its surface and can be used as pharmaceutical excipient, since it is regarded nontoxic after oral application. Due to its porous structure and large specific surface area, porous silica has a great capacity to adsorb organic compounds into its nano-sized pores and can improve physical stability of amorphous drug [2].

Solid dispersions of carvedilol in porous silica (Sylysia 350) were prepared by solvent evaporation in a vacuum evaporator which ensures efficient pore filling procedure [3]. Two sets with different concentrations of carvedilol in solid dispersions were prepared, which differ in pore filling process. Set a) was prepared by one-step filling and set b) by multiple filling of smaller portions of dissolved carvedilol into porous silica. Solid dispersions were characterized by thermal analysis (DSC), X-ray diffraction and nitrogen adsoprtion experiments. Specific surface area and porosity parameters of solid dispersion samples confirm different mechanism of drug loading within silica pores in each experimental set. Results showed that carvedilol is more efficiently "packed" inside porous matrix when multiple drug filling procedure of smaller amounts is used as suggested by absence of crystalline state of a drug and greatly reduced porosity, while at the same time physical stability of amorphous carvedilol was most improved. Due to space restriction carvedilol can not crystallize when it is entrapped in a region of pores of smaller diameters than the minimum size of crystalline nucleus. Once the amorphous form of drug is stabilized inside porous silica it remains physically stable against crystallization and water sorption, while pure amorphous drug partially crystallized and adsorbed a detectable amount of moisture.

The authors acknowledge to KRKA, d.d., Novo mesto for support in the study. Present work was partly financed by the European Union, European Social Fund.

[1] Rupprecht H, Biersack MJ, Kindl G. Freigabe schwer löslicher Substanzen von den Oberflächen partiell belegter Kieselsäuren. Colloid Polym Sci. 1974; 252: 415–416. doi:10.1007/BF01387967

[2] Takeuchi H, Nagira S, Yamamoto H, Tanimura S, Kawashima Y. Tabletting of solid dispersion particles consisting of indomethacin and porous silica particles. Int J Pharm. 2005; 293: 155–164. doi:10.1248/cpb.53.487

[3] Ohta KM, Fuji M, Takei T, Chikazawa M. Development of a simple method for the preparation of a silica gel based controlled delivery system with a high drug content. Eur J Pharm Sci. 2005; 26: 87–96. doi:10.1016/j.ejps.2005.05.002