Conference abstract PDD23

Release of Theophylline from Sustained Release Cylindrical Dosage Forms

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The holt-melt extrusion technique has proven to be an advantageous method for preparation of solid dosage forms. The aim of this work was to evaluate the release profiles of sustained release cylinders produced by hot-melt extrusion. The cylinders were composed of inner and outer part, both containing theophylline [1]. Cylinders were 0.5cm or 1cm long. The two parts were extruded separately, cut into pieces and joined manually. Dissolution testing was performed on USP 2 apparatus at rotation speed 50, 100 and 150 rpm. Artificial gastric and intestinal media were used consecutively.

Due to their hydrophilic / lipophilic properties inner part of cylinder releases the drug fast while outer part represents extended release component. No influence of stirring rate on theophyline release was observed for 1cm cylinders while for 0.5cm cylinders the amount of released drug slightly increased with increase of stirring rate (Fig. 1). However, due to high variability of release results significant differences could not be proven. This high variability of release results was beside other factors (poor wettability due to lipophilic components etc.) at least partly ascribed to manual preparation of the dosage forms. Manual joining of the inner and outer part of the cylinder caused void spaces between both parts as shown on the stereomicrographs (Olympus SZX12) (Fig. 2). The consequence of void spaces is additional free surface available for dissolution which can not be controlled and thus increases the variability of release results. Thus, the automatic simultaneous co-extrusion would be better choice when preparing co-extrudates as void spaces between two parts of cylinders could be avoided and variability at least partly reduced.

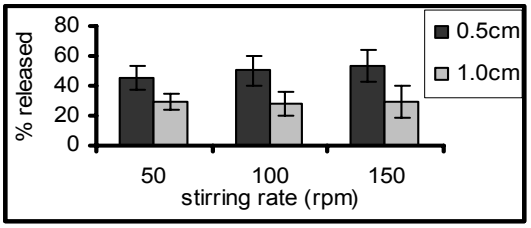

Fig. 1. Percentage of released drug after 7h of release in dependence on stirring rate

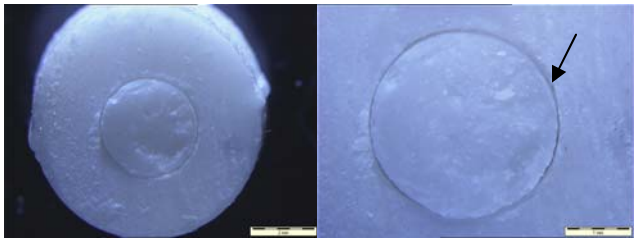

Fig. 2. Stereomicroscopic view of co-extrudates. Arrow shows void space between two parts of cylinder.

[1] Quintavalle U, Voinovich D, Perissutti B, Serdoz F, Grassi G, Dal Col A, Grassi M. Preparation of sustained release co-extrudates by holt-melt extrusion and mathematical modelling of in vitro/in vivo drug release profiles. Eur J Pharm Sci. 2008; 33: 282–293. doi:10.1016/j.ejps.2007.12.008