Olanzapine orodispersible films: the impact of preparation method on drug dissolution

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Background: Olanzapine (OLZ) can take the advantage of administration as orodispersible films (ODF) to improve adherence in psychiatric patients as ODF disintegrate quickly in the mouth without need of water. ODF can be prepared by solvent-casting or extrusion-based technologies. However, the preparation method needs to be carefully selected since water can influence the OLZ solid state and, consequently, the drug dissolution properties.

Purpose: This study aims to compare the OLZ dissolution from ODF obtained by an aqueous-based solvent casting and a novel hot-melt ram-extrusion 3D printing.

Methods: The ODF were prepared by casting and drying aqueous slurry of OLZ, maltodextrin (DE = 6), glycerine and sorbitan oleate; while the hot-melt ram-extrusion 3D ODF were obtained by printing a paste containing OLZ, maltodextrins (DE=6) plasticized with glycerine. In each case, 10 mg OLZ was loaded in 6 cm^2 ODF. ODF were characterized for thickness, loss on drying, disintegration time and *in vitro* dissolution in deionized water.

Results: ODF appeared homogeneous and easy to handle without cracks. The cast and printed ODF thicknesses were 140±4.5 μm and 278±13.2 μm respectively. Residual water content in ODF was in the 6-8% w/w range. In both cases, ODF disintegrated within 60 s, complying the Pharmacopeia specifications. For i*n vitro* dissolution, about 90% OLZ was released in ~3 min for the 3D printed films; in contrast, an erratic drug release was observed for the OLZ ODF made by casting with a concomitant formation of a yellow precipitate after 3 min, which suggest a change in the OLZ solid state.

Conclusion: The solvent-free hot melt ram extrusion 3D printing technique can be suitable for ODF preparation for drugs sensitive to solvent system.