A comparison of preparation methods on the in vitro performances of olanzapine orodispersible films

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Abstract

Introduction: Olanzapine (OLZ) is a poorly water-soluble drug with an intricate polymorphism (1), available on the market as orodispersible tablets to improve the patient's adherence in the treatment of schizophrenia. Orodispersible films (ODF) represents a valid alternative which allow to eliminate the fear of choking. Unfortunately, production methods of ODF require the preparation of an aqueous dispersion of the drug or the melting of the components (2). Both processes can cause unintended drug phase transformations which directly affect its dissolution rate and, therefore, biopharmaceutical performances. This work focused on the influence of two different preparation methods, namely solvent casting and hot melt printing, on the *in vitro* performances of OLZ ODF aiming to evaluate the possible loading of drug substances with a significant physical instability.
Methods: An amount of 10 mg OLZ was loaded into 2×3 cm ODF prepared by solvent-casting and hot-melt ram-extrusion printing using maltodextrin DE 6 and glycerol as film forming material and plasticizer, respectively. X-ray diffraction and DSC were carried out to study the OLZ solid state. ODF were characterized in terms of thickness, stickiness, loss on drying. Moreover, disintegration time and the in vitro dissolution profiles were also evaluated.
Results: The adopted experimental conditions permitted to obtain ODF without visual defects, easy to handle with a thickness around 140 µm and 278 µm for cast and printing, respectively. Residual water content in ODF was in the 6-8% w/w range. All ODF disintegrated within 80 s, complying the Pharmacopeia specifications. Regarding the in vitro dissolution, about 90% OLZ was released within 3 min from the printed films; in contrast, an erratic drug release was observed for cast ODF with the concomitant formation of a yellow precipitate after 3 min. The X-ray diffraction patterns of OLZ loaded into ODF suggested that the casting process caused a variation in the drug form, which could be responsible of this anomalous behavior.
Conclusion: This study highlighted the potential of hot-melt printing as a method to load drugs which can undergo to solid state modification after exposure to water.

References: (1) GI Polla, DR Vega, H Lanza, DG Tombari, R Baggio, AP Pedro, AJM Filho, DFG Leyva, G Dartayet, Int J Pharm 301 (1–2)2005: 33-40. (2) UM Musazzi, GM Khalid, F Selmin, P Minghetti, Int J Pharm 576(2020) 118963.

Presenter biography: Garba M. Khalid is a third-year PhD student at Università degli studi di Milano. He carries out research in the field of orodispersible dosage forms intended for patient-focused therapy.

Learning Objectives

Compare the strengths and weaknesses of different methods available to prepare ODF
Understand the influence of preparation methods on the solid state of drugs loaded into ODF
Evaluate the feasibility of hot-melt ram extrusion printing to load physically instable drugs on ODF