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Preparation and Evaluation of Solid Oral Lipid-Based Diazepam Preparations

N. RADOMAN, M. RADIVOJŠA, J. PETROVIĆ, S. IBRIĆ

Institute of Pharmaceutical Technology, Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia

E-mails: rad_nikola@yahoo.com (N. Radoman), maja_radivojsa@yahoo.com (M. Radivojša), jpetrovic@pharmacy.bg.ac.rs (J. Petrović)

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The study demonstrates two approaches in formulation of solid oral lipid-based diazepam preparations (BCS class II drug). The aim of the study was to formulate tablets and hard capsules, using emulsifier and adsorbent. Lipid-based preparations improve drug solubility and permeability, i. e. bioavailability. Solid silicate carriers are able to adsorb liquid lipid formulations, resulting in freely flowable and compressible powders [1].

Twelve formulations have been prepared, using emulsifier Labrafil®M2125CS (linoleoyl macrogolglycerides) to solubilize diazepam, Neusilin®UFL2 (magnesium aluminium silicate) as adsorbent, with the varying ratio of diazepam solution:adsorbent (1:1 to 4:1), and disintegrators Ac-Di-Sol® and Ludiflash® (with the ratio varying from 0–90 %). Formulations have been filled in hard capsules or compressed into tablets using excenter tablet press. Diazepam release study from prepared capsules or tablets has been conducted in rotating basket apparatus (ErwekaDT600, 0.1 M HCl, 100 rpm, 500 ml, 45 minutes).

Diazepam release studies have demonstrated that it is possible to formulate lipid-based solid oral preparations with immediate diazepam release. Capsules filled with diazepam solution adsorbed on adsorbent, with the ratio of solution:adsorbent 1:1, show the fastest diazepam release rate. Addition of 10% of disintegrator in capsule formulation enhanced diazepam release rate, but when the ratio of disintegrator is increased furthermore, diazepam release is sustained. It was observed that compression of powders in tablets also led to decrease in diazepam release rate. Addition of disintegrators further sustained diazepam release leading to conclusion that a physical interaction occurs between adsorbent and disintegrators. When adsorbent was excluded from the tablet formulations diazepam release rate was enhanced, but tableting properties of such powders were compromised.

Obtained results demonstrate the possibility to formulate diazepam immediate release formulations, with the necessity of careful selection of excipients and dosage forms.

[1] Jannin V, Musakhanian J, Marchaud D. Approaches for the development of solid and semi-solid lipid based formulations. Adv Drug Deliver Rev. 2008; 60: 734–746. doi:10.1016/j.addr.2007.09.006