Conference abstract PPAT12

**Application of Experimental Design for Screening Study of Dissolution Test Conditions: Levothyroxine Sodium Immediate-Release Tablets**

**I. KOCIC, I. HOMSEK, M. DACEVIC**

R&D Institute, Galenika ad, Belgrade, Serbia

E-mail: ivana_kocic@yahoo.com (I. Kocic)


The aim of the study was to present an example of experimental design application to set up the dissolution test conditions for the two immediate-release products of levothyroxine sodium (L-Na) with proven bioequivalence: the generic product A and the reference product B [1, 2]. The description of the dissolution profiles by using model-independent methods included the calculation of mean dissolution time (MDT) from the *in vitro* data for both formulations. MDT for the products were compared one to each other as well as with mean absorption time (MAT), calculated from the *in vivo* data [3]. The experimental factorial design $2^3$ was applied with following independent variables: concentration of surfactant used ($X_1$), volume of dissolution medium ($X_2$), and paddle stirring speed ($X_3$). Dependent variables were set up as a difference between the MDT observed under various experimental conditions for the investigated products ($Y_1$), as well as the difference between MDT and MAT for each product ($Y_2 = \text{MDT}_{\text{prod. A}} - \text{MAT}_{\text{prod. A}}; Y_3 = \text{MDT}_{\text{prod. B}} - \text{MAT}_{\text{prod. B}}$). The obtained results showed that the paddle rotation speed was the most significant drug release factor. The medium volume had very small effect on responses $Y_1$ and $Y_2$ but its impact could not be regarded as negligible in the case of response $Y_3$. The surfactant used for dissolution testing showed significant effect on the tested parameters, but the observed effects were contradictory and general conclusion could not be made. This study showed the limited applicability of experimental design in the optimization of the dissolution conditions for two different L-Na formulations. The significant differences among *in vitro* release profiles were obtained and there was not unique dissolution test model applicable to both investigated products.


Presented at the 8th Central European Symposium on Pharmaceutical Technology, September 16th–18th 2010, Graz, Austria.