ABSTRACT

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Thesis title: Determination of Lipophilicity of Drugs by HPLC

In this thesis a RP-HPLC method for fast and reliable determination of lipophilicity was proposed and tested.

Stationary phase was selected by using hydrophobic substraction model. Capacity factors of the chosen substances were initially measured on Zorbax ECLIPSE XDB C18 250x4,6 mm, 5µm column, which exhibits almost identical retention characteristics as the column used for this purpose until now. Then the capacity factors of the same substances were determined by using Zorbax ECLIPSE XDB-C18 50x4,6 mm, 1,8µm column that was selected to reduce retention times significantly. A group of newly synthesised drugs based on structure of pyrazine served as samples for the measurement. The reproducibility of the capacity factor values determined using both columns was compared and the independence of the capacity factor on the mobile phase flow was confirmed.

The capacity factors of two homologous series and a group of benzimidazols were consequently determined on Zorbax ECLIPSE XDB-C18 50x4,6 mm, 1,8µm column using various compositions of mobile phases. Several various approaches of extrapolation to zero content of MeOH in the mobile phase were tested and one of them was recommended for practical use. The measured values of lipophilicity were compared to the values of ClogP calculated by computer program ChemDraw Ultra 12.0. In addition the lipophilicity values of benzimidazols were extra compared to published values of partition coefficient obtained in octanol-water system.

Key words: lipophilicity, HPLC, capacity factor, drug