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BOOK OF ABSTRACTS



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Estimation of lipophilicity of newly synthesized potential COX-2 and 5-LOX inhibitors using RP-HPLC analysis

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The chronic inflammatory process is associated with the development and progression of many diseases such as cancer, arthritis, autoimmune diseases, etc. Dual COX-2 and 5-LOX inhibitors have been developed to provide more potent anti-inflammatory agents with a better safety profile [1].

Nineteen newly synthesised potential dual COX-2 and 5-LOX inhibitors [2] were selected and their retention properties were tested in different RP-HPLC systems. RP-HPLC analysis was performed using a C18, a cyano and an amino column. The mobile phases were binary combinations of acetonitrile and phosphate buffer (pH 5.5 and pH 7.4) as well as methanol and phosphate buffer (pH 5.5 and pH 7.4) in different ratios. The amino column proved to be inadequate as the tested compounds were not retained on it. According to preliminary results, methanol was not suitable as an organic modifier in the mobile phase as the retention time of the compounds was increased several times compared to acetonitrile. Acetonitrile was chosen as the organic modifier. The logarithmic values of the retention factors ($\log k$) were calculated for each sample and plotted with the percentage of organic modifier in the mobile phase. The chromatography parameters $\log k_w$, a and ϕ_0 were determined according to equation (1) and equation (2) (S -percentage of organic modifier in the mobile phase).

$$\log k = \log k_w + aS \quad (1)$$

$$\phi_0 = -\log k_w/a \quad (2)$$

On C18 and cyano columns, seven compounds (1A, 1G, 1ME, 1PE, and 2D) had no retention properties, which is consistent with their very low $\log D$ values, while three (1F, 1H, and QSAR17) compounds were outliers. Systems consisting of C18 and cyano columns (on both pH 5.5 and 7.4) showed good correlation coefficients between the chromatography parameters $\log k_w$, a , and ϕ_0 and the $\log D$ values determined with MarvinSketch. The most suitable system consisted of a C18 column, acetonitrile, and phosphate buffer pH 7.4, as it had the highest correlation coefficient between the chromatography parameter $\log k_w$ and the $\log D$ value ($R^2=0.9023$) (3 compounds were discarded).

[1] P, J. J.; Manju, S. L.; Ethiraj, K. R.; Elias, G. Safer Anti-Inflammatory Therapy through Dual COX-2/5-LOX Inhibitors: A Structure-Based Approach. *European Journal of Pharmaceutical Sciences* **2018**, 121, 356–381.

[2] Bošković, J.; Dobričić, V.; Mihajlović, M.; Kotur-Stevuljević, J.; Čudina, O. Synthesis, Evaluation of Enzyme Inhibition and Redox Properties of Potential Dual COX-2 and 5-LOX Inhibitors. *Pharmaceuticals* **2023**, 16 (4), 549.