The interaction of newly synthesized potential COX-2, 5-LOX dual inhibitors with human serum albumin in the presence of Tween 80

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Due to the very important relationship between inflammation and cancer, there is an increasing need for synthesizing new compounds with potential for activity in both processes. Therefore, new dual inhibitors of the COX-2 and 5-LOX enzymes, which inhibit the inflammation mediators, may also play a potential role in cancer therapy [1] and could be promising agents. In the development of new compounds, parameters characterizing the formation of complexes with human serum albumin (HSA) are particularly important, and electrochemical methods have been shown to be important because of their versatility, high sensitivity, and simplicity.

Differential pulse voltammetry (DPV) with GCE was used to investigate newly synthesized compounds, potential dual COX-2 and 5-LOX inhibitors (3-(4-fluoro-2-methylphenyl)-1-(2-hydroxy-4-methylphenyl)prop-2-en-1-one - H12, 3-(2--chlorophenyl)-1-(5-fluoro-2-hydroxyphenyl)prop-2-en-1-one - H13, 1-(5-fluoro-2-hydroxyphenyl)-3-(2-(trifluorome-thyl)phenyl)prop-2-en-1-one - H14, and 1-(4-aminophenyl)-3-(4-fluoro-2-methylphenyl)prop-2-en-1-one - H20)[2].

It was found that it was not possible to obtain a repeatable electrochemical signal (peak potential and peak current) when testing these compounds, probably due to the limited solubility of these compounds in the aqueous medium. A literature search revealed that possibly the application of Tween 80 could influence the enhanced dispersion and thus enable a reproducible signal [3]. For a detailed investigation compound H20 was used as it showed the highest intensity of the oxidation peak current at a concentration of 5×10^{-5} M.

The influence of different concentrations of Tween 80 (10^{-7} - 3×10^{-5} M) on the reproducibility of the signal of the compound H20 (5×10^{-5} M) in PBS pH 7.3 was investigated using DPV. Satisfactory reproducibility was achieved at a Tween 80 concentration of 2×10^{-5} M (Figure 1).

After achieving a stable H20 signal, the interaction between H20 and HSA was examined. In order to determine the binding constant, the measurements were performed at a H20 concentration of 5×10^{-6} to 6×10^{-5} M, while the HSA concentration was constant at 2×10^{-6} M. The differential peak current intensity was measured before and after the interaction of H20 with HSA and by using the log (ΔI / (ΔI_{max} - ΔI)) *vs.* log c_{H20} dependence [4] the binding constant, K was calculated, $K = 5.5\times10^4$ M^{-1}.

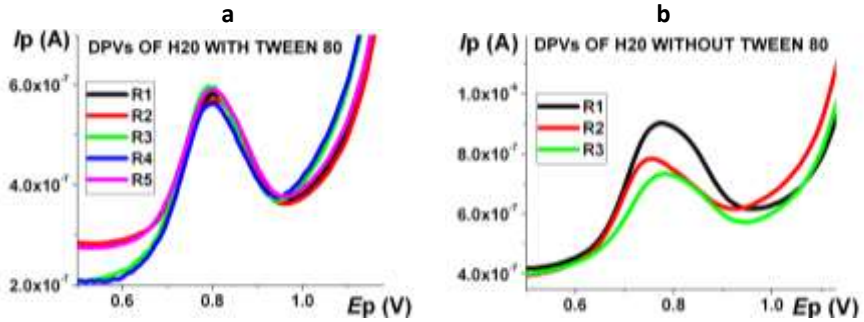

Figure 1. DPVs of a) H20, c = 5×10^{-5} M in PBS with Tween 80 (2×10^{-5} M); b) H20, c = 5×10^{-5} M in PBS without Tween 80

A simple, accurate, inexpensive, and sensitive voltametric method was developed for the investigation of redox behaviour and interaction with human serum albumin in the presence of Tween 80 of the newly synthesized compound H20 which has low solubility in aqueous solutions.

Acknowledgement: This research was supported by the Science Fund of the Republic of Serbia, 7739840, Utilization of interplay between inflammation and cancer in the development of compounds with anticancer activity—INFCANPLAY.

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