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Catalysis of immobilised human flavin-containing monooxygenase

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Human flavin-containing monooxygenase isoform 3 (hFMO3) is a hepatic enzyme that catalyses the oxygenation of a large number of structurally diverse drugs and xenobiotics transforming them into benign and readily excretible products. Since the design and development of new therapeutic drugs may take advantage of these detoxifying properties, much interest has been focused on the development of novel techniques suitable for pharmacological research applied to hFMO3 catalytic properties.

With this aim, an hFMO3 electrochemical sensor, developed by modifying a glassy carbon electrode with an entrapping gel obtained by glutaraldehyde co-crosslinking of hFMO3 with bovine serum albumin, is reported in this work. Redox properties of hFMO3 sensor have been compared with those of FAD entrapped gel electrode by cyclic voltammetry, revealing for the protein bound FAD, a significant shift of redox peaks towards negative potentials and a total reversibility of the redox reaction. The redox potential measured for the entrapped protein was -411±10 mV (vs. Ag/AgCl). The responsiveness of the sensor was investigated with four different substrates, trimethylamine, ammonia, triethylamine and benzydamine (nonsteroidal anti-inflammatory drug) by calculating kinetic parameters including the apparent Michaelis-Menten constant (82.3±4.3; 94.1±6.4; 120.7±11.2 and 115.9±6.8 μM, respectively), sensitivity (39-45 $mAM^{-1}cm^{-2}$) and response linearity from 2-80 μM.

The data obtained confirm that the hFMO3 sensor has good characteristics in terms of substrate detection, reproducibility and stability, therefore can be employed for catalytic activity measurements of new chemical entities turned over by hFMO3.