Drug oxidation by iron porphyrins immobilized on hollow spheres

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Cytochrome P450 enzymes superfamily are responsible for metabolizing several compounds in biological media. Metalloporphyrins (MePs) has been employed as cytochrome P450 synthetic models due to their ability of mimic stereo- and enantioselective reactions of xenobiotics as pesticides, drugs and natural products under mild conditions.[1] The use of MePs as biomimetic catalysts has contributed for the elucidation of biotransformation processes and can be an alternative method to produce metabolites in large-scale, providing suitable samples for structure characterization and toxicological essays.[2] MeP immobilization on mesoporous materials can be able to increase the turnovers of the oxidation reactions, which motivated the search for new MeP-based heterogeneous systems. In this sense, we prepared a biomimetic catalyst based on iron porphyrins (FeTPFPP) immobilized on hollow spheres previously modified with aminopropil moieties, namely FeP-APHS. The catalyst was characterized by XRD, TEM, dynamic light scattering, diffuse reflectance spectroscopy, N_2 adsorption-desorption isotherms. The catalytic potential was evaluated in (Z)-cyclooctene oxidation tests, showing a turnover number (TON) around 1300 using PhIO as oxygen donor. In addition, we explored the mirtazapine (MTR) oxidation by the biomimetic catalyst, using GC-MS in identification of potential phase I metabolites *in vivo*. This antidepressant drug has 8-hydroxymirtazapine (OHM), *N*-desmethylmirtazapine (DMM), and mirtazapine-*N*-oxide (MNO) as main metabolites identified in biotransformation essays.[3] The catalytic essays of the MTR using FeP-APHS and PhIO as oxygen donor showed the formation of OHM and DMM metabolites, which are produced *in vivo*. We detected two other metabolites that are not formed *in vivo*, which have not yet been identified. The production of new metabolites from Cytochrome P450 models can thereby be useful to predict idiosyncratic drug interactions.[2]

Reference

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