

Drug-drug and drug-food interactions of immobilised cytochrome P4503A4

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The adverse effects of drug-drug interactions are costly both in terms of human life and investment (withdrawal of drugs from the market). Inhibition of cytochrome P450-mediated drug metabolism by a concomitantly administered second drug is one of the major causes of drug–drug interactions in humans and can lead to serious adverse reactions or toxic side effects. Although less publicised, drug-food interactions can also cause an increase or decrease in the oral drug bioavailability when co-administered, the most well-known case being that of grapefruit juice and the short-acting calcium channel blocker, nifedipine, which resulted in death.

One major limitation of these types of studies is the lack of fast and reliable tests for measuring such phenomena. Here we report the first *in vitro* characterisation of drug-drug and drug-food interactions of cytochrome P450 3A4 enzyme using an electrochemical platform devised in our group. The enzyme is immobilised on a glassy carbon electrode in the presence of a cationic polyelectrolyte, PDDA (poly(diallyldimethylammonium chloride)), and the electrons required for its catalysis provided by the electrode therefore obviating the need for the reductase and NADPH. The use of *in vitro* data to predict the inhibition of P450 enzymes by a co-administered drug/food is attractive because of the rapid and simple experimental procedures involved. In terms of drug-drug and drug-food interactions, data will be presented on P450 3A4 inhibition by both strong and weak inhibitors of this enzyme; ketoconazole (anti-fungal), cimetidine (histamine H₂-receptor antagonist), grapefruit juice, curcumin (curry spice turmeric) and resveratrol (present in red wine).