Curcumin, piperine, and capsaicin: a comparative study of spice-mediated inhibition of human cytochrome P450 isozyme activities

ABSTRACT

Inhibition of cytochrome P450 (P450) enzymes (CYP) has been shown to lower the metabolism of drugs that are P450 substrates and to consequently alter their pharmacokinetic profiles. Curcumin (CUR), piperine (PIP), and capsaicin (CAP) are spice components (SC) that inhibit the activities of a range of P450 enzymes, but the selection of which SC to be prioritized for further development as an adjuvant will depend on the ranking order of the inhibitory potential of the SCs on specific P450 isozymes. We used common human recombinant enzyme platforms to provide a comparative evaluation of the inhibitory activities of CUR, PIP, and CAP on the principal drug-metabolizing P450 enzymes. SC-mediated inhibition of CYP3A4 was found to rank in the order of CAP (IC50 1.84 ± 0.71 μM) ~ PIP (2.12 ± 0.45 μM) > CUR (11.93 ± 3.49 μM), while CYP2C9 inhibition was in the order of CAP (11.95 ± 4.24 μM) ~ CUR (14.58 ± 4.57 μM) > PIP (89.62 ± 9.17 μM). CAP and PIP were significantly more potent inhibitors of CYP1A2 (IC50 2.14 ± 0.22 μM and 14.19 ± 4.15 μM, respectively) than CUR (IC50 > 100 μM), while all three SCs exhibited weak activity toward CYP2D6 (IC50 95.42 ± 12.09 μM for CUR, 99.99 ± 5.88 μM for CAP, and 110.40 ± 3.23 μM for PIP). Of the three SCs, CAP thus has the strongest potential for further development into an inhibitor of multiple CYPs for use in the clinic. Data from this study are also useful for managing potential drug–SC interactions.