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INHIBITION OF MAJOR HUMAN CYTOCHROME P450 ENZYME ACTIVITIES: A COMPARISON OF CURCUMIN, PIPERINE AND CAPSAICIN

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ABSTRACT

Emerging evidence indicates that culinary spices can influence drug bioavailability and biodistribution. Spice component (SC) like curcumin is known to affect the pharmacokinetic parameters of drugs (1), which is of concern as it can lead to adverse drug interactions. The cytochrome P450 (CYP) enzyme system, in particular, CYP1A2, CYP2C9, CYP2D6 and CYP3A4, may play a mediating role as they are responsible for many significant drug-drug interactions. Studies have separately evaluated the potential of curcumin, piperine and capsaicin, the respective active components of turmeric, pepper and chilli, in inhibiting CYP enzymes. It is, however, difficult to compare their relative inhibitory potential because different enzyme sources and substrates have been applied in the studies. This paper aims to systematically compare the inhibitory activities of the SC using common recombinant human CYP enzyme systems. Piperine and capsaicin were found equally effective at inhibiting CYP3A4 (IC_{50} 4.0 µM) compared to curcumin (IC_{50} 7.5 ± 1.2 µM), while the inhibition of CYP2C9 ranked in the order of capsaicin > curcumin > piperine. Piperine was a significantly more potent inhibitor of CYP1A2 (IC_{50} 18.8 ± 7.5 µM) compared to curcumin (IC_{50} > 100 µM), whereas all 3 SC exhibited weak action towards CYP2D6, with only 60% inhibition observed at the highest concentration (120 µM) of SC used. Our results demonstrate that curcumin, piperine and capsaicin are inhibitors of CYP-mediated drug metabolism, but their inhibitory potencies varied for different CYPs, with no definitive indication of one SC being a consistently more potent CYP inhibitor than the others.