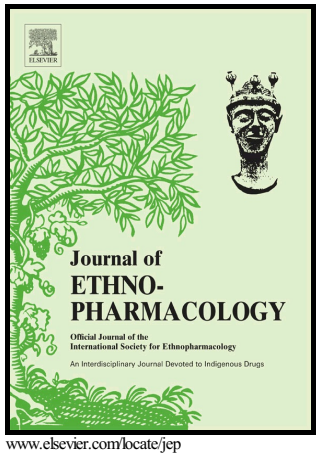

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Bush mint (*Hyptis suaveolens*) and spreading hogweed (*Boerhavia diffusa)* medicinal plant extracts differentially affect activities of CYP1A2, CYP2D6 and CYP3A4 enzymes

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Abstract

Ethno-pharmacological relevance: *Hyptis suaveolens* (L) Poit and *Boerhavia diffusa* Linn are medicinal herbal plants commonly found in the tropics and sub-tropics. They are used to treat various conditions among them boils, dyslipidaemia, eczema, malaria, jaundice and gonorrhoea. Thus, the herbal medicinal extracts are now found as part of some commercial herbal formulations. There has not been adequate characterisation of these medicinal herbs on their effects on drug metabolising enzymes.

Aim of the study: To investigate the effects of extracts of *Hyptis suaveolens* (HS) and *Boerhavia diffusa* (BD) on activity of drug metabolizing enzymes, CYP1A2, CYP2D6 and CYP3A4, as well predict their potential for herb-drug interaction. A secondary aim was to identify constituent compounds such as polyphenolics, in the crude extract preparations of *Hyptis suaveolens* and *Boerhavia diffusa* and measure them for activity.

Materials and methods: CYP450 inhibition assays using recombinant CYP450 (rCYP) and fluorescence screening employing individual isozymes (CYP1A2, CYP2D6 and CYP3A4) were used to determine reversible- and time-dependent inhibition (TDI) profiles of extracts of *Hyptis suaveolens* and *Boerhavia diffusa*. Inhibition kinetic parameters, K_i and K_{inact} were also estimated. UPLC-MS employing a Synapt G2 (ESI negative) coupled to a PDA detector was used to identify polyphenolic compounds in crude extracts of *Hyptis suaveolens* and *Boerhavia diffusa*.

Results: The inhibitory potency of *Hyptis suaveolens* and *Boerhavia diffusa* extracts varied among the different enzymes, with CYP1A2 (3.68 ± 0.10µg/mL) being the least inhibited by HS compared to CYP2D6 (1.39 ± 0.01 µg/mL) and CYP3A4 (2.36 ± 0.57 µg/mL). BD was most potent on CYP3A4 (7.36 ± 0.94 µg/mL) compared to both CYP2D6 (17.79 ± 1.02 µg/mL) and CYP1A2 (9.48 ± 0.78µg/mL). Extracts of *Hyptis suaveolens* and *Boerhavia diffusa* exhibited TDIs on all CYPs. The most prominent phenolic candidates identified in both medicinal herbs using UPLC-MS analysis included caffeic acid, rutin, quercetin, citric acid, ferulic acid and gluconic acid. These phenolic compounds are thought to potentially give HS and BD their therapeutic effects and inhibitory