

EXTRACTS AND KAVALACTONES OF *PIPER METHYSTICUM* G. FORST (KAVA-KAVA) INHIBIT P-GLYCOPROTEIN IN VITRO

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Abstract

Root extracts from kava-kava (*Piper methysticum* G. Forst) are clinically used for the treatment of anxiety and restlessness. Due to reported cases of liver toxicity, kava-kava extracts were withdrawn from the market in several countries in 2002. Because the efflux transporter P-glycoprotein (P-gp) is involved in the absorption, distribution, and excretion of many drugs and often participates in drug-drug interactions, we studied the effect of a crude kava extract and the main kavalactones kavain, dihydrokavain, methysticin, dihydromethysticin, yangonin, and desmethoxyyangonin on the P-gp-mediated efflux of calcein-acetoxymethylester in the P-gp-overexpressing cell line P388/dx and the corresponding cell line P388. The crude extract and the kavalactones showed a moderate to potent inhibitory activity with f_2 (concentration needed to double baseline fluorescence) values of 170 $\mu\text{g/ml}$ and 17 to 90 μM , respectively. The f_2 value of yangonin could not be determined due to its higher lipophilicity. In conclusion, our results for the first time demonstrate P-gp-inhibitory activity of kava-kava and its components in vitro.