Interaction of Folk Medicinal Plant Extracts with Human α_2-Adrenoceptor Subtypes

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Forty-two extracts of folk medicinal plant organs from Pakistan were tested in competition binding assays for their interaction with the specific ligand recognition sites on the human α_2-adrenoceptor subtypes α_{2A}, α_{2B} and α_{2C}. Strong binding of the extracts (40 mg/ml) from *Acacia nilotica* (L.) Delile leaves (88–98% displacement of radiolabel) and *Peganum harmala* seeds (89–96% displacement) on three subtypes prompted us to extract these plant materials with 40% and 80% methanol, ethanol, and acetone. The extraction results indicated an absence of α_2-adrenoceptor binding activity in the stalk of *A. nilotica* and *A. tortils*, whereas the leaves of both plants contained activity. The extracts of *A. nilotica* leaves showed a slight, but consistent, preference for the α_{2C}-adrenoceptor, whereas the leaves of *A. tortils* were slightly more active on the α_{2B} subtype. The extract of *P. harmala* stalks was less active than that of its seeds. The binding activities of *A. nilotica* leaves and *P. harmala* seeds were mainly concentrated in the water and 30% methanol fractions and further sub-fractions. In a functional activity assay, the active fractions inhibited epinephrine-stimulated ^{35}S-GTPγS binding, thus indicating a predominantly antagonistic nature of the compounds with α_2-adrenoceptor affinity in these fractions. Among the known major alkaloids of *P. harmala* (demissidine, harmaline, harmine, 6-methoxyharmalan, and norharmane), only 6-methoxyharmalan showed moderate affinity (dissociation constant (K_i) of 530 ± 40 nM for α_{2A} subtype). This study is a first systematic attempt towards the discovery of potential drug candidates from these plant materials for treating α_2-adrenoceptor related diseases.