Interaction of Folk Medicinal Plant Extracts with Human α₂-Adrenoceptor Subtypes

Ammar Saleem*a,*, Mia Engströmb, Siegfried Wursterb, Juha-Matti Savolab and Kalevi Pihlaja a

a Department of Chemistry, University of Turku, FIN-20014 Turku, Finland.
Fax: +3582333 67 00. E-mail: amsale@utu.fi
b Juvantia Pharma Ltd., Lemminkäisenkatu 5, PharmaCity, FIN-20520 Turku, Finland
* Author for correspondence and reprint requests

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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 α₂-adrenoceptor subtypes α₂A, α₂B and α₂C. 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 α₂-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 α₂C-adrenoceptor, whereas the leaves of A. tortils were slightly more active on the α₂B 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 35S-GTPγS binding, thus indicating a predominantly antagonistic nature of the compounds with α₂-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 (Kᵢ) of 530 ± 40 nM for α₂A subtype). This study is a first systematic attempt towards the discovery of potential drug candidates from these plant materials for treating α₂-adrenoceptor related diseases.