Title : Anxiolytic-like activity of 5-methoxyflavone in mice with involvement of GABAergic and serotonergic systems - in vivo and in silico evidences

Abstract

Anxiety disorders are common worldwide and novel compounds are investigated for anxiolytic effect. A few studies have demonstrated the anxiolytic-like activity of natural and synthetic flavonoids. 5-methoxyflavone, a synthetic flavone derivative, has been reported to exhibit central nervous system depressant (sedative-hypnotic) effect in an earlier study. The present study was designed to investigate whether 5-methoxyflavone possesses anxiolytic-like activity in mice by employing two unconditioned models of anxiety such as elevated plus maze and light-dark box test. The possible role played by GABAergic ($GABA_A$) and serotonergic ($5HT_{1A}$) systems in the anxiolytic-like effect of 5-methoxyflavone was also investigated in the elevated plus maze test. Molecular docking studies were performed to ascertain the interaction of 5-methoxyflavone with $GABA_A$ (α_2 subunit-containing) and $5HT_{1A}$ receptors. 5-methoxyflavone treatment in mice (10, 20 or 40 mg/kg, i.p) increased the number of entries and time spent in the open arms in an elevated plus maze ($p < 0.001$). In the light-dark box test a significant increase in the time spent in light compartment ($p < 0.001$) and prolonged latency to enter the dark compartment ($p < 0.01$) were also observed. Pretreatment of mice with $5HT_{1A}$ antagonist pindolol (10 mg/kg, i.p) or $GABA_A$ antagonist bicuculline (2 mg/kg, i.p) significantly attenuated the effect of 5-methoxyflavone in the elevated plus maze test. In silico studies provided evidences for good binding affinity of 5-methoxyflavone towards $GABA_A$ (α_2 subunit-containing) and serotonergic ($5HT_{1A}$) receptors by H-bond interactions. In conclusion, the present study identified a novel anxiolytic-like effect of 5-methoxyflavone involving GABAergic and serotonergic mechanisms.

Keywords: 5-methoxyflavone; Anxiolytic-like activity; Docking; GABA(A) (α(2) subunit-containing) receptor; Serotonergic (5-HT(1A)) receptor.

For more details : https://pubmed.ncbi.nlm.nih.gov/32534819/