

## **Title : Sedative-hypnotic like effect of 5-methoxyflavone in mice and investigation on possible mechanisms by in vivo and in silico methods**

### **Abstract**

Flavonoids have been shown to possess central nervous system (CNS) depressant effect mediated through the ionotropic GABA<sub>A</sub> receptors. In the present study, 5-methoxyflavone was evaluated for sedative-hypnotic like activity in mice and the mechanisms involved by employing a battery of tests including molecular docking studies. In the open field test, 5-methoxyflavone in various doses (50, 100 and 150 mg/kg, i.p) exhibited a significant and dose-dependent reduction in the spontaneous locomotor activity ( $F(5,30) = 87.17$   $P < 0.001$ ). Pretreatment with 5-methoxyflavone decreased the latency to sleep induction after pentobarbitone or ether administration and also significantly increased the duration of sleep ( $p < 0.001$ ). A significant and dose-dependent myorelaxant effect was observed with 5-methoxyflavone in the inclined plane, horizontal wire test and rota rod test. Pretreatment with picrotoxin, bicuculline, glycine, caffeine or NMDA either decreased or completely abolished the hypnotic effect of 5-methoxyflavone in mice. The above results revealed the involvement of GABA<sub>A</sub>, adenosine, glycine and NMDA receptors in the hypnotic effect of 5-methoxyflavone. The results of in silico studies indicated that, 5-methoxyflavone exhibits good binding affinity towards these receptors by H-bond interactions. In conclusion, the present study identified a novel and potential sedative-hypnotic like effect of 5-methoxyflavone involving multiple mechanisms.

**Keywords:** 5-methoxyflavone; Adenosine; Central nervous system; Docking; Gamma-amino butyric acid A; Sedative-hypnotic.

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