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Sub-chronic oral administration of crude khat extract (*Catha edulis forsk*) induces schizophrenic-like symptoms in mice

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Background: Chewing fresh leaves of the khat plant (*Catha edulis forsk*) is a deep rooted and widespread habit in East Africa and the Middle East. Although a body of knowledge exists about the adverse effects of khat on health, data are sparse with regard to the consequences of long-term khat chewing in resulting schizophrenic like symptoms.

Methods: A crude extract of khat at different doses (100 mg/kg (K (khat)100), 200 mg/kg (K200) and 400 mg/kg (K400)) were administered for experimental group of mice whereas standard (ketamine (KT) 10 mg/kg- positive controls (KT10)) and vehicle (2% v/v Tween-80 in distilled water – negative control groups (CON)) were administered for control groups of mice daily for two months to evaluate sub-chronic oral administration of crude khat extract to induce schizophrenic-like symptoms in mice. Mice were subjected to a battery of behavioral tests and parameters like locomotor activity, total time spent in social interaction and level of cognition among different groups of mice were measured and analyzed.

Results: Khat at all doses significantly increased ($p < 0.001$) the mean locomotor activity score of mice compared to CON. However, the mean locomotor activity score of mice treated with khat was significantly lower ($p < 0.001$) compared to the mean locomotor activity score of KT10 mice ($p < 0.001$). The mean total time score (in seconds) spent in social interaction, mean total time score (in seconds) spent in sniffing and following the partner was significantly higher ($p < 0.001$) in CON groups of mice compared to khat and ketamine treated groups. Moreover, in spatial memory task, the mean latency score (in seconds) to find the platform of khat and ketamine treated mice was significantly higher ($p < 0.05$) when compared to CON.

Conclusions: Sub-chronic oral administration of khat showed an enhanced locomotor activity, reduced social interaction and impaired cognitive function, which demonstrated that long-term use of khat is associated with schizophrenic-like symptoms.

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The binding regions of Luteolin with its potential target ribosomal protein S5

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Liver fibrosis, a repairing response for the chronic liver injury from various pathogenesis, leads to the cirrhosis of liver. Many Chinese traditional drugs, such as matrine and luteolin, have therapeutic efficacy on the liver fibrosis but the therapeutic mechanism is unknown. The activation of hepatic stellate cells (HSCs) is a critical course in the fibrosis and the ribosomal protein S5 (RPS5), a direct target of the anti-fibrotic agent MASM, could prevent HSC activation via the reduction of Akt phosphorylation. Our early study found that RPS5 could also be the target of luteolin. Here, we simulate the combination of RPS5 and luteolin by using the Discoverystudio4.0 to predict the binding sites of RPS5 with luteolin. The simulation shows that RPS5 has four binding regions with luteolin: the first region consists of Phe97 residue; the second region consists of Asn83, Lys85, and Arg159 residues; the third region consists of Arg127, Arg145, and Lys192 residues; and the fourth region consists of Trp152, Arg159, and Glu160 residues. Mutation of these residues indicates that the Asn83 and Lys85 residues may be the major binding sites of RPS5 with luteolin. These results could provide a clue to the research on the anti-fibrotic mechanism of luteolin and the design of new drugs to inhibit the liver fibrosis.

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