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TITLE

Mitragyna Speciosa (MS) as a Medicine in Thailand and Malaysia

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Aim of the study: Mitragyna speciosa (MS) under the local name of "Kratom" or "Ketum" is traditionally used by workers in Thailand and Malaysia as a daily stimulant and sedative.

Due to these potential uses, it is necessary to study the long-term safety profile of plant active compound. In this work, we evaluated the effects of sub chronic exposure to mitragynine, the main alkaloid compound of this MS leaves in rats.

Materials and methods: MG or vehicle were administered orally at different doses of 1, 10, 100 mg/kg daily for 28 days. Relative body weight as well as general behaviour, adverse effects and mortality were checked daily before and after each animal treatment, respectively. Motor activity of each testing group was assessed in open field test once a week. Being sacrificed on day 29, relative weight of liver, spleen, kidney, lung, heart, and brain was calculated while blood samples and selected organs (liver, kidney and brain) of each animal were sent for further hematological, biochemical, and histopathological analysis.

Results: none of the doses used induced mortality or evident toxicity signs during the 28 days administration of MG. Daily oral administration of MG at the dose of 1 and 10 mg/kg resulted in an increase in the relative body weight in both male and female during 4 weeks of experiment which was statistically significant in male. The higher dose of 100 mg/kg decreased the relative body weight in both sexes which was significant especially in female at the last weeks of treatment. The relative weights of organs such as lung, heart, and spleen did not showed any significant difference versus control group while kidney (L) and brain showed significant decrease in weight at high dose of 100mg/kg in male. Liver relative weight showed a significant increase in low dose (1mg/kg) followed by a considerable decrease in weight in high dose (100mg/kg) group of female rats. On the other hand in blood analysis, the long term exposure to MG produced an increase in chol., AST, ALT, Urea and LDH in high dose group (100mg/kg) which was significantly remarkable in female group. There were some significant hematological changes in high dose (100mg/kg) group of female such as a decrease in WBC, RBC, HGB, HCT, and MCV. Significant decline in PLT for all female treated groups (1, 10, 100 mg/kg) was also noticed. The repeated exposure to MG produced an increase in the number of crossings and rearings in the open field at low dose of 1 mg/kg compared to control which was more significant in female group.

Conclusions: These results demonstrated that sub chronic oral administration of the highest dose of MG (100mg/kg), the main active compound of MS, can induce severe hepato- and nephrotoxicity with anorexia remarkably in female group after long term use. However, lowest dose of MG (1mg/kg) which is almost equal to daily intake of workers and laborers showed a stimulant effect in locomotor activity and increase in food intake. The results also confirmed the higher sensitivity of female as suitable animal sex for toxicity studies.