Mitragyna speciosa Leaf Extract Exhibits Antipsychotic-Like Effect with the Potential to Alleviate Positive and Negative Symptoms of Psychosis in Mice

Kamini Vijeeapallam*, Vijayapandi Pandy, Thubasi Kunessegaran, Dhamani D. Munugan and Murali Naidu

1 Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; 2 Department of Anatomy, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

In this study, we investigated the antipsychotic-like effect of methanol extract of Mitragyna speciosa leaf (MMS) using in vivo and ex vivo studies. In vivo studies comprised of apomorphine-induced climbing behavior, haloperidol-induced catalepsy, and ketamine-induced social withdrawal tests in mice whereas the ex vivo study was conducted utilizing isolated rat vas deferens preparation. Acute oral administration of MMS (50–500 mg/kg) showed an inverted bell-shaped dose-response in apomorphine-induced cage climbing behavior in mice. The effective inhibitory doses of MMS (75 and 100 mg/kg, p.o.) obtained from the apomorphine study was further tested on haloperidol (subcataleptic dose; 0.1 mg/kg, i.p.)-induced catalepsy in the mouse bar test. MMS (75 and 100 mg/kg, p.o.) significantly potentiated the haloperidol-induced catalepsy in mice. Interestingly, MMS at the same effective doses (75 and 100 mg/kg, p.o.) significantly facilitated the social interaction in ketamine-induced social withdrawal mice. Furthermore, MMS inhibited the dopamine-induced contractile response dose-dependently in the isolated rat vas deferens preparations. In conclusion, this investigation provides first evidence that MMS exhibits antipsychotic-like activity with potential to alleviate positive as well as negative symptoms of psychosis in mice. This study also suggests the antidopaminergic activity of MMS that could be responsible for alleviating positive symptoms of psychosis.

Keywords: apomorphine, bar test, climbing behavior, haloperidol, ketamine, Mitragyna speciosa, social withdrawal, vas deferens

INTRODUCTION

Psychosis is a devastating mental illness with a high economic burden for many countries. The molecular mechanisms involved in the pathogenesis of psychosis has been extensively studied and reported in the literature (Saigh et al., 2008). In an attempt to reduce the severity of this disease worldwide, many pharmacological treatment options have been constantly developed. Currently available antipsychotics are mainly classified into two categories: typical antipsychotics (e.g., chlorpromazine, haloperidol etc.) and atypical antipsychotics (e.g., clozapine, risperidone etc.). The former class of drugs are effective to treat only the positive symptoms such as delusion,