

NMA/AGSM/2022/BCS/009 - Reversal and Preventive Pleiotropic Mechanisms Involved in the Antipsychotic-Like Effect of Geraniol, Acyclic Isoprenoid Monoterpene in Ketamine-Induced Psychosis in Mice

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Abstract

Background: Schizophrenia is a chronic neuropsychiatric disease characterized by neurochemical, neurotrophic, and oxido-inflammatory derangements. Geraniol is a neuroactive acyclic isoprenoid monoterpene, which has been reported to demonstrate depressant and antioxidant/anti-inflammatory activities. Herein, we investigated whether geraniol could prevent or reverse ketamine-induced schizophrenic-like behaviours and the underlying putative mechanisms in mice.

Methodology: In the preventive protocol, mice received intraperitoneal injections of geraniol (25, 50, and 100 mg/kg), risperidone (0.5 mg/kg), or saline daily for 14 consecutive days prior to ketamine (20 mg/kg/day, i.p.) from days 8-14. In the reversal protocol, the animals received ketamine or saline for 14 days prior to geraniol, risperidone, or saline treatments. Schizophrenic-like behaviors representing positive, negative, and cognitive symptoms were evaluated with open-field, social-interaction, and Y-maze tests. Thereafter, the brain levels of dopamine, serotonin, GABAergic (indexed by glutamic-acid decarboxylase), acetyl-cholinesterase, brain-derived neurotrophic factor (BDNF), oxidative/nitregic stress (glutathione, malondialdehyde, nitrite), and inflammatory (TNF- α , IL-6, NFk-B) biomarkers were measured in the striatum, prefrontal cortex, and hippocampus.

Results: Geraniol (50-100 mg/kg) prevented and reversed ketamine-induced hyperlocomotion and social and cognitive deficits. Also, geraniol (100 mg/kg) attenuated ketamine-induced dopaminergic, serotonergic, GABAergic, and cholinergic neurotransmissions in brain region-dependent manners. The increased TNF- α , IL-6, NFk-B, and nitrite levels accompanied by decreased glutathione concentrations in the striatum, prefrontal cortex, and hippocampus in ketamine-treated mice were significantly prevented and reversed by geraniol like risperidone.

Conclusion: These findings suggest that geraniol exhibits an antipsychotic-like effect via attenuation of neurochemical, neurotrophic, and oxido-inflammatory changes in mice brains.

Keywords: Schizophrenia, Oxidative stress, Neuroinflammation, Neurochemical, Antioxidants, Antipsychotics, Geraniol.

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