Effect of NMDA receptor antagonist and 5-HT₁₆ receptor agonist on behavioral parameters in serotonin depletion mice model

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The hypothesis of the present study is that N-methyl D-aspartate (NMDA) receptor antagonist and 5-hydroxy tryptamine (5-HT₁₆) agonist will restore brain serotonin levels and can have role in the treatment of depression. Depression hypothesis is majorly based on neurochemical alteration. The neurotransmitters like serotonin, norepinephrine, dopamine and glutamate have a strong interlink. The mice were divided into 7 groups consisting of 6 animals each. Depression was induced with P-chlorophenylalanine (PCPA). On first day 300 mg/kg and on alternative days 100 mg/kg was administered to all the groups. The drug treatment memantine, 8-OH DPAT and their combination was continued for 14 days. Fluoxetine was used as a positive control. Behavioral screening, neurotransmitters and neurochemical were measured in different regions of control and serotonin depleted mice brain to assess the anti-depressant property of the drugs. The histopathological examination was also carried out. The results have shown that, depletion of brain serotonin level with PCPA treatment and resulted in reduced locomotion, anxiety behavior and ambulation with no alteration in rearing and grooming behaviors. The NMDA antagonist memantine, 5-HT₁₆ agonist 8-OH DPAT and their combination have shown no significant change in locomotion. Whereas memantine 40 mg/kg have shown increased anxiolytic activity. The mice treated with memantine and its combination with 8-OH DPAT has shown significant change in force swim test. In neurotransmitters, the memantine and 8-OH DPAT group exhibited significant reduction in glutamate and aspartate levels, whereas GABA levels were increased. Histopathological report shows focal areas of degeneration in cerebrum region with PCPA treatment and drug treatments restored the morphology of the brain. Hence, it can be concluded that, memantine, 8-OH DPAT and their combination have better result in improving the depressive symptoms induced with PCPA than the positive control fluoxetine.

Biography
Abdul Khayum Khadar Bhatcha has received his Master of Pharmacy in Pharmacology from PSG College of Pharmacy, Coimbatore during the period 2012-2014. Currently, he is working as an Assistant Professor in Department of Pharmacology, Faculty of Pharmacy, Karpagam University, India. His research interest includes neuroischemia, ischemic stroke models and animal behavior studies.

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