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Potential Beneficiary Effects of Clobenpropit Injection to Heal Dementia

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Alzheimer's disease is a neurodegenerative disease characterized clinically by gradual memory loss and cognitive impairment. Neuronal degeneration in Alzheimer's disease is caused by plaque aggregation caused by excessive synthesis of $-amyloid (A$) and the formation of Neurofibrillary Tangles (NFTs) caused by tau protein phosphorylation. Understanding the specific vulnerability for cognitive deficiencies leading to dementia is difficult; nonetheless, various pathways have been identified as being responsible for memory and learning problems, including cholinergic insufficiency, oxidative stress, and neuro-inflammation. Treatment with selective cholinesterase inhibitors, which resulted in an increase in ACh levels at cholinergic synapses, is also an effective therapy for the treatment of Alzheimer's disease and dementia.

The injection of clobenpropit corrected the scopolamine-induced learning impairment in mice by activating the noradrenergic system in a step-through passive avoidance test. Furthermore, a bilateral intrahippocampal injection of clobenpropit improves spatial memory deficits in rats produced by MK-801 in an eight-arm radial maze exercise by modulating the levels of different neurotransmitters11. As a result, the goal of this investigation was to see if clobenpropit might protect mice against memory loss and cholinergic dysfunction caused by LPS.

The study was carried out at Pharmacology Research Laboratory, Department of Pharmacology and Toxicology, Qassim University, Saudi Arabia. Clobenpropit hydrobromide from Cayman Chemical (Ann Arbor, Michigan, USA) and lipopolysaccharides from Sigma-Aldrich Co (St. Louis, Missouri, USA) were obtained. Cloud-Clone Corp. in the United States provided ELISA kits for mouse acetylcholine and acetyl cholinesterase. The animal facility, Department of Pharmacology and Toxicology, College of Pharmacy, Qassim University, Saudi Arabia, provided a total of 24 adult male ICR mice ranging in age from 8-12 weeks (25-35 g). Animals were divided into four groups at random, each with six animals, and were given either vehicle or clobenpropit treatment.

The first group served as a control, simply receiving vehicle treatment for 30 days and four doses of regular saline injections. The second group (LPS) was LPS-induced and was given vehicle for 30 days before receiving four doses of lipopolysaccharides on days 22, 23, 24, and 25. The third (LPS+CLO1) and fourth (LPS+CLO3) groups received clobenpropit orally for thirty days and were injected with four doses of LPS as an LPS-induced group.

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The cognitive declines caused by LPS induction were demonstrated by a significant reduction in Transfer Latency (TL) duration in the Elevated Plus-Maze (EPM) test, a decrease in exploration time as well as discrimination ability in the Novel Object Recognition (NOR) test, and a decline in mouse novel arm performance in the Y-maze.

The current findings could support clobenpropit potential efficacy in reversing LPS-induced cognitive impairments by enhancing cholinergic transmission by antagonizing pre-synaptic histamine H3 receptors in cholinergic neurons. This was revealed in neurons after an inflammatory-related damage. As a result, the current preliminary pre-clinical findings may point to clobenpropit benefits in the prevention of neuro-inflammatory-related neuronal diseases.

Using raised plus-maze, novel object identification, and Y-maze exercises, researchers were able to improve a variety of behavioural metrics. The cholinergic activity of the LPS challenged mouse brain was enhanced by increasing acetylcholine levels and decreasing acetyl cholinesterase activity.

JOURNAL REFERENCE

Mani, V., M. Arfeen, H.M. Ali, A.M.H. Abdel-Moneim and A. Alhowail, 2022. Neuroprotective effect of clobenpropit in lipopolysaccharides-induced mice via enhancing cholinergic transmission. Int. J. Pharmacol., 18: 321-330.

KEYWORDS

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