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News & Comments

Ciproxifan's Potential to Prevent Neuroinflammatory-Related Neuronal Diseases

Fawaz Abdelrazak

The pathogenesis of major chronic neurodegenerative disorders such as Alzheimer's Disease (AD) and Parkinson's Disease is assumed to be linked to brain inflammation (PD). It triggers excessive production of pro-inflammatory chemicals by stimulating microglia and resident immune cells in the brain, resulting in neurodegeneration. When it comes to neurodegenerative disorders, the prevalence of Alzheimer's disease-related dementia is now estimated to be at 40-50 M instances, with that figure expected to climb to 74.7 M by 2030. Aside from cytokines, other important variables in the brain inflammatory process include prostaglandin E2, oxidative stress, and reactive nitrogen species. Activated immune-inflammatory pathways, oxidative and nitrosative stress and metabolic abnormalities in the brain are all linked to mitochondrial dysfunction.

HH3R antagonists inhibit the release of histamine and other neurotransmitters before they reach the synaptic level, making them a prospective target for CNS illnesses like narcolepsy, cognitive deficits, ADHD, and pain. The goal of the current study was to see how Ciproxifan's pre-treatment for 30 days affected LPS-induced neuroinflammation and mitochondrial dysfunction in a mouse model.

Sigma-Aldrich Co (St. Louis, MO, USA) provided fine chemicals such as Ciproxifan's maleate and lipopolysaccharides isolated from Escherichia coli. ELISA kits for mouse IL-6, TNF-", IL-10, TGF-$1 and COX-2 were procured from Cloud-Clone Corp., Texas, USA. A total of 24 male ICR mice of adult age (between 8-12 weeks, body weight between 25-35 g) were procured from the animal house maintained by the Department of Pharmacology and Toxicology, College of Pharmacy, Qassim University, KSA for the current study. The mice were placed into four groups, each with six mice, and three animals were kept in a cage for the duration of the experiment. Each of the animals was slaughtered and brain tissue was extracted from the skull after 30 days of therapy. MyBioSource Inc. provided the MRCC-I, MRCC-II, and MRCC-IV mouse ELISA kits. The results were shown as Mean Standard Error (SEM). One-way ANOVA was used.

Ciproxifan's effects on COX-2 activity in LPS-challenged mouse brains are shown. In the LPS-challenged brain, the effect of Ciproxifan's therapy on MRCC-I, II, and IV activity is displayed.

Mitochondrial dysfunctions are linked to a reduction in MRCC activity.

Activities with the treatment of Ciproxifan's 1 and 3 mg kg^{-1} in LPS-induction were identical to control

animals on the level of brain MRCC-I, II, and IV.

The bulk of studies confirmed Ciproxifan's neuroprotective effects via lowering neuroinflammation and mitochondrial toxicity, as demonstrated by lower levels of Cyclooxygenase-2 (COX-2) and proinflammatory cytokines while enhancing anti-inflammatory responses.

Considering the importance of neuroinflammation in nervous system disorders, as well as oxidative stress, which also plays a role in memory and learning impairments in AD.As a result, anti-inflammatory drugs appear to have some benefits.

The findings potentially support Ciproxifan's neuroprotective efficacy in correcting LPS-induced inflammatory damages in the brain by antagonizing pre-synaptic HH3Rs. Furthermore, the effects of Ciproxifan's on neuroinflammation-induced mitochondrial dysfunction were investigated. The existing preclinical evidence suggests that Ciproxifan's can prevent neuroinflammatory-related neuronal disorders. Ciproxifan's anti-inflammatory potential was demonstrated by its ability to reduce LPS-induced increases in COX-2 enzyme activity and pro-inflammatory cytokines (TNF-"and IL-6) levels in the brain. It also boosted the quantities of anti-inflammatory cytokines (TGF-$1 and IL-10) in the body.

JOURNAL REFERENCE

Mani, V., M. Arfeen, A.M.H. Abdel-Moneim and H.M. Ali, 2022. Ciproxifan attenuates lipopolysaccharide-induced neuroinflammation and mitochondrial dysfunctions in mouse brain. Int. J. Pharmacol., 18: 407-414.

KEYWORDS

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