

Withania Somnifera as a Potential Anxiolytic and Anti-inflammatory Candidate Against Systemic Lipopolysaccharide-Induced Neuroinflammation

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Abstract

Reactive gliosis, microgliosis, and subsequent secretion of various inflammatory mediators like cytokines, proteases, reactive oxygen, and nitrogen species are the suggested key players associated with systemic inflammation-driven neuroinflammation and cognitive impairments in various neurological disorders. Conventionally, non-steroidal anti-inflammatory drugs are prescribed to suppress inflammation but due to their adverse effects, their usage is not well accepted. Natural products are emerging better therapeutic agents due to their affordability and inherent pleiotropic biological activities. In Ayurveda, Ashwagandha (*Withania somnifera*) is well known for its immunomodulatory properties. The current study is an extension of our previous report on in vitro model system and was aimed to investigate anti-neuroinflammatory potential of water extract from the Ashwagandha leaves (ASH-WEX) against systemic LPS-induced neuroinflammation and associated behavioral impairments using in vivo rat model system. Oral feeding of ASH-WEX for 8 weeks significantly ameliorated the anxiety-like behavior as evident from Elevated plus maze test. Suppression of reactive gliosis, inflammatory cytokines production like TNF- α , IL-1 β , IL-6, and expression of nitro-oxidative stress enzymes like iNOS, COX2, NOX2 etc were observed in ASH-WEX-treated animals. NF κ B, P38, and JNK MAPKs pathways analysis showed their involvement in inflammation suppression which was further confirmed by inhibitor studies. The current study provides first ever preclinical evidence and scientific validation that ASH-WEX exhibits the anti-neuroinflammatory potential against systemic LPS-induced neuroinflammation and ameliorates associated behavioral abnormalities. Aqueous extract from Ashwagandha leaves and its active phytochemicals may prove to be promising candidates to prevent neuroinflammation associated with various neuropathologies.

Keywords: Anxiety-like behavior; Ashwagandha; Inflammatory cytokines; Lipopolysaccharide; Neuroinflammation; Reactive gliosis.

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