

Potential Role of *Withania somnifera* in Inflammatory Arthritis: Evidence Based Research †

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Abstract: *Withania somnifera* (Ashwagandha) is an evergreen shrub with immunomodulatory potential found in dry areas of India. Its usage in traditional Indian medicine is well documented in the management of painful arthritic conditions. Proinflammatory cytokines such as TNF- α , IL-1, and IL-6 play a vital role in rheumatoid arthritis. In general, anti-arthritic drugs are used to manage inflammatory joint disease. There are few clinical studies available on the usage of the herb in arthritis that are published; however, evidence on the interactions of both the herb and anti-arthritic drugs when given together are not available. The study explored the clinical evidence, herb-drug interaction, and anti-inflammatory properties of the herb in arthritis. Published clinical studies on the anti-arthritic activities were systematically reviewed. For anti-inflammatory activity and herb-drug interaction, methanolic and hydroalcoholic extracts of both the aerial and root part of the herb, anti-arthritic drugs such as methotrexate, sulfasalazine, leflunomide, hydroxychloroquine, diclofenac, and prednisolone were used in the study. *In-vitro* assay to estimate the cytokines TNF alpha, IL-1 beta, and Interleukin-6 for the anti-inflammatory study were performed using Human Enzyme-Linked Immunosorbent Assay kits. Cytochrome P450 3A4 and 2D6 isoenzyme inhibition assay were performed for herb-drug interactions. The absorbance was noted in Multimode Microplate reader. *Withania* extracts, when mixed with the drugs, showed significantly less inhibition potential with a higher IC50 value against the CYP enzymes compared with positive control. The aerial extracts inhibited cytokines TNF-alpha and Interleukin 6 more than their respective roots, and both root extracts were better than aerial extract for interleukin beta inhibition assay. The study established evidence-based research for its potential role as anti-inflammatory and safe use with anti-rheumatic drugs.

Keywords: *Withania somnifera*; Ashwagandha; herb-drug interaction; anti-inflammatory; anti-arthritis, CYP inhibition

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Conflicts of Interest

The authors declare no conflict of interest.