



## PHARMACOLOGICAL SIGNIFICANCE OF *WITHANIA SOMNIFERA* IN INFLAMMATION-RELATED DISORDERS

Anjlee Yadav\*, Vivek Gupta, Jitendra Kumar Malik, Gyan Singh, Yogesh Bhardwaj

Research Scholar, Faculty of Pharmacy, PK University, Thanra - 473665, Madhya Pradesh, India.



\*Corresponding Author: Anjlee Yadav

Research Scholar, Faculty of Pharmacy, PK University, Thanra - 473665, Madhya Pradesh, India.

DOI: <https://doi.org/10.5281/zenodo.19905888>

**How to cite this Article:** Anjlee Yadav\*, Vivek Gupta, Jitendra Kumar Malik, Gyan Singh, Yogesh Bhardwaj. (2026). Pharmacological Significance of Withania Somnifera In Inflammation-Related Disorders. World Journal of Pharmaceutical and Life Sciences, 12(5), 142–153.

This work is licensed under Creative Commons Attribution 4.0 International license.



Article Received on 31/03/2026

Article Revised on 21/04/2026

Article Published on 01/05/2026

### ABSTRACT

Inflammation is a multifaceted biological response that underlies the progression of numerous acute and chronic diseases, including arthritis, cardiovascular disorders, diabetes, and neurodegenerative conditions. Despite the widespread use of conventional anti-inflammatory drugs, their prolonged administration is often associated with significant adverse effects, thereby necessitating the exploration of safer, plant-based therapeutic alternatives. Medicinal plants have emerged as promising candidates due to their multi-targeted actions, biocompatibility, and long-standing use in traditional medicine systems. Among these, *Withania somnifera* (Ashwagandha) has gained remarkable attention for its potent anti-inflammatory, antioxidant, and immunomodulatory properties. The therapeutic efficacy of *Withania somnifera* is largely attributed to its rich repertoire of bioactive phytoconstituents, including withanolides (notably withaferin A), alkaloids, and sitoindosides. These compounds exert significant pharmacological effects by modulating critical inflammatory pathways, such as inhibition of nuclear factor-kappa B (NF-κB), suppression of pro-inflammatory cytokines (TNF-α, IL-6), and downregulation of cyclooxygenase-2 (COX-2). Furthermore, its strong antioxidant potential plays a pivotal role in mitigating oxidative stress, thereby interrupting inflammation-driven cellular damage and disease progression. A substantial body of evidence from in vitro and in vivo studies highlights its efficacy in attenuating inflammatory responses; while emerging clinical investigations further support its therapeutic relevance in managing inflammation-associated disorders, including arthritis and metabolic syndromes. However, challenges such as lack of extract standardization, heterogeneity in experimental designs, and limited large-scale clinical validation persist. Future research should emphasize advanced formulation strategies, molecular mechanistic studies, and robust clinical trials to unlock its full therapeutic potential, ensuring safer, effective, and evidence-based integration into modern healthcare systems globally.

**KEYWORDS:** *Withania somnifera*, Ashwagandha, Inflammation, Withanolides, Anti-inflammatory, Medicinal plant.

### 1. INTRODUCTION

Inflammation is a multifaceted and protective mechanism of the body to harmful stimuli (pathogens, toxins, tissue injury, and others). It is broadly classified into acute and chronic inflammation. Acute inflammation is a transitory reaction that is marked by redness, heat, swelling, pain and loss of function, which is an important defense mechanism to repair tissue.<sup>[1]</sup> By contrast, chronic inflammation is a dysregulated response with prolonged duration and a contribution to the development of various pathological conditions. The

chronic inflammation may result in tissue damages and is believed to be one of the major causes of most chronic illnesses.<sup>[2]</sup>

Inflammation is at the centre of development and progression of different diseases, such as rheumatoid arthritis, diabetes mellitus, cardiovascular diseases, and neurodegenerative diseases, including Alzheimer and Parkinson diseases. Under such circumstances, prolonged manufacture of inflammatory mediators, cytokines, and reactive oxygen species (ROS) leads to

cellular injuries and dysfunction of physiological functions.<sup>[3]</sup>

Despite the wide use of synthetic anti-inflammatory agents, including non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, to treat inflammatory conditions, the long-term use of these drugs is linked to adverse effects in most instances, including gastrointestinal irritation, cardiovascular risks, immunosuppression, and organ toxicity. It is this that has led to the pursuit of better and safer alternatives.<sup>[4]</sup>

The multi-targeted mechanisms, relatively few side effects, and natural origin have resulted in a significant level of attention given to herbal medicines. One of them is *Withania somnifera* (Ashwagandha), a commonly used Ayurvedic medicinal plant, that has been widely researched regarding its anti-inflammatory, antioxidant, and immunomodulatory effects. It is rich in a variety of bioactive compounds which make it have therapeutic potential.<sup>[5]</sup>

The current review will be the attempt to assess the pharmacological importance of *Withania somnifera* in inflammatory based disorders in detail, its phytochemical composition, action mechanisms, experimental studies, and therapeutic potential in future.<sup>[6]</sup>

## 2. Literature Search Methodology

A systematic and comprehensive literature search was conducted to collect relevant scientific information on the pharmacological significance of *Withania somnifera* in inflammation-related disorders. Multiple electronic databases, including PubMed, Scopus, Google Scholar, and ScienceDirect, were systematically searched to ensure a broad and reliable coverage of published literature. The search was limited to articles published in English.<sup>[7]</sup>

Relevant keywords and their combinations were used to retrieve appropriate studies. These included “*Withania somnifera*,” “Ashwagandha,” “inflammation,” “anti-inflammatory activity,” “withanolides,” “cytokines,” “NF- $\kappa$ B,” and “oxidative stress.” Boolean operators such as AND and OR were applied to refine the search strategy and improve the specificity of results.<sup>[8]</sup>

Inclusion criteria comprised original research articles, review papers, and experimental studies (both in vitro and in vivo) that specifically investigated the anti-inflammatory potential, phytochemistry, and pharmacological mechanisms of *Withania somnifera*. Studies involving clinical trials, molecular mechanisms, and formulation approaches were also considered. Exclusion criteria included studies lacking sufficient methodological details, non-peer-reviewed articles, duplicate publications, and studies not directly related to inflammation.<sup>[9]</sup>

The selection of studies was carried out through a stepwise screening process. Initially, titles and abstracts were reviewed to assess relevance, followed by full-text evaluation of selected articles. Reference lists of relevant papers were also manually screened to identify additional studies. The collected data were then critically analyzed and systematically organized to ensure a coherent and comprehensive review.<sup>[10]</sup>

## 3. Botanical Description and Ethnomedicinal Uses

One of the most significant medicinal plants in traditional medicines, especially Ayurveda, is *Withania somnifera*, also known as Ashwagandha or Indian ginseng. It has been broadly known to have various pharmacological effects such as anti-inflammatory, antioxidant, adaptogenic and immunomodulatory effects making it very pertinent in the treatment of disorders that are related to inflammation.<sup>[11]</sup>

### Taxonomy

*Withania somnifera* belongs to the kingdom Plantae, division Magnoliophyta, class Magnoliopsida and order Solanales. It is a family of Solanaceae that include other medicinally important plants like *Solanum* species. *Withania* genus has various species, which are characterized by biologically active compounds, especially steroidal lactones called withanolides, which are the main contributors to the pharmacological activity of the plant.<sup>[12]</sup>

### Morphology

*Withania somnifera* is a small, erect, perennial shrub morphologically, which usually reaches a height of 30150 cm. The plant has a well-developed root system with thick, fleshy, cylindrical roots, the most common part used as medicine. Their leaves are simple, dull, ovate green, and grow alternately on the stem, and possess a characteristic smooth texture. Its plant bears inconspicuous flowers, of a greenish-yellow tint, and afterwards produces small, spherical, orange-red fruits, wrapped up in a papery, inflated calyx. These morphological characteristics are fundamental in proper identification, standardization and pharmacognostic analysis of the plant material.<sup>[13]</sup>

### Distribution

*Withania somnifera* is very common in tropical and subtropical parts of the world. It is common in India, particularly in dry and semi-arid areas like Madhya Pradesh, Rajasthan, Gujarat and Uttar Pradesh. Part of the Middle East and parts of Africa also cultivate the plant. It has been found to grow well in sandy or loamy soils with good drainage and in warm climatic conditions with little to moderate rainfall. Its versatility to harsh environment conditions also leads to its wide availability and conventional use.<sup>[14]</sup>

### Ethnomedicinal Uses

*Withania somnifera* is classified as a Rasayana, type of herb in Ayurvedic medicine and is known to extend life

and increase vitality and resistance to illness. The most commonly used part traditionally is the roots and it is used to increase physical strength, improve the thinking ability, relieve stress and anxiety, and enhance immunity. Although the leaves are less frequently used, they are also used in some cases based on their anti-inflammatory and analgesic effects. The therapeutic potential of the plant has been known since ancient times as it has been incorporated into many traditional formulations.<sup>[15]</sup>

#### Use in Inflammation-Related Disorders

Ashwagandha has been widely used ethnomedically to treat inflammatory disorders including rheumatoid

arthritis, joint pain, muscular inflammation and swelling. Its therapeutic effect has been credited to the effect it has on key inflammatory mediators, pro-inflammatory cytokines and oxidative stress. It also has immunomodulatory effect that is important in the immune homeostasis that is important in chronic inflammatory disorders. Modern scientific research has continued to back these traditional applications, with its possible role as a natural and effective agent in the treatment of inflammatory diseases coming to the fore.<sup>[16]</sup>

**Table 1: Taxonomical Classification and Ethnomedicinal Uses of *Withania somnifera*.**<sup>[17]</sup>

Parameter	Description
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Solanales
Family	Solanaceae
Genus	<i>Withania</i>
Species	<i>Withania somnifera</i> (L.) Dunal
Common Names	Ashwagandha, Indian ginseng, Winter cherry
Plant Parts Used	Roots (main), leaves, berries
Geographical Distribution	India, Middle East, Africa (tropical and subtropical regions)
Traditional System	Ayurveda (Rasayana herb)
Ethnomedicinal Uses	Anti-inflammatory, anti-arthritic, adaptogenic, immunomodulatory, treatment of joint pain, swelling, stress, and fatigue

#### 4. Phytochemical Profile

*Withania somnifera* has a rich and diverse phytochemical composition which is largely credited to the pharmacological activity of this plant. The plant is a reservoir of biologically active secondary metabolites that help it possess anti-inflammatory, antioxidant, adaptogenic, and immunomodulatory properties. The composition of these constituents (qualitatively and quantitatively) can be different according to the plant part (root, leaves, berries), geographical location, time of harvest, and methods of extraction. The roots are the most studied and most commonly used part of the plant in therapeutic uses.<sup>[18]</sup>

##### 4.1 Preliminary Phytochemical Screening

Initial phytochemical screening of *Withania somnifera* extracts, especially aqueous, ethanol, and methanol extracts have repeatedly indicated the presence of various significant groups of phytoconstituents. These are alkaloids and flavonoids, saponins as well as steroidal compounds, and the combination of all these compounds makes up its pharmacological profile.<sup>[19]</sup>

These compounds are detected by the use of standard qualitative tests. Dragendorffs and Mayer reagents are used to identify alkaloids whereas flavonoids are identified by the Shinoda test. Saponins are identified by the foam test and steroidal compounds are identified by the LiebermannBurchard reaction. Ethanol and methanol extracts are usually found to be more phytochemical-rich

among the various extraction solvents with a higher level of extraction efficiency. These are the main phytochemicals which have been reported to potentially have a great biological activity especially in alleviating inflammation and oxidative stress.<sup>[20]</sup>

##### 4.2 Major Bioactive Constituents

The therapeutic importance of *Withania somnifera* is mainly associated with its major bioactive constituents, which belong to distinct chemical classes and exhibit synergistic pharmacological effects:

- **Withanolides**

Withanolides are steroidal lactones and represent the signature compounds of *Withania somnifera*. Among them, **Withaferin A** is the most extensively studied and biologically active molecule. These compounds exhibit potent anti-inflammatory activity by inhibiting key inflammatory signaling pathways such as NF- $\kappa$ B and suppressing the production of pro-inflammatory cytokines. Additionally, withanolides contribute to antioxidant defense and cellular protection.<sup>[21]</sup>

- **Alkaloids**

Alkaloids such as **somniferine**, withanine, anaferine, and tropine are present in various parts of the plant. These nitrogen-containing compounds are known for their neuroprotective, adaptogenic, and mild anti-inflammatory effects. They play a crucial role in

modulating stress responses and maintaining physiological balance.<sup>[22]</sup>

- **Sitoindosides**

Sitoindosides are glycowithanolides that possess significant antioxidant and immunomodulatory properties. They enhance the body's defense mechanisms by reducing oxidative stress and regulating immune responses. Their role in improving resistance to stress and inflammation further supports the therapeutic potential of *Withania somnifera*.<sup>[23]</sup>

#### 4.3 Analytical Techniques

To ensure accurate identification, characterization, and quantification of phytoconstituents, several advanced analytical techniques are employed in the study of *Withania somnifera*:

##### High-Performance Liquid Chromatography (HPLC):

HPLC is widely used for the separation and quantitative estimation of withanolides and other major compounds. It provides high accuracy, reproducibility, and sensitivity, making it a standard method for phytochemical analysis.<sup>[24]</sup>

**Liquid Chromatography–Mass Spectrometry (LC-MS):** LC-MS offers precise molecular characterization and structural identification of complex phytochemicals. It is particularly useful in detecting minor constituents and confirming compound structures.<sup>[25]</sup>

##### Gas Chromatography–Mass Spectrometry (GC-MS):

GC-MS is mainly utilized for analyzing volatile and semi-volatile compounds present in plant extracts. It provides detailed information about the chemical composition and helps in identifying bioactive molecules.<sup>[26]</sup>

##### High-Performance Thin Layer Chromatography (HPTLC):

HPTLC is an efficient and cost-effective technique for phytochemical fingerprinting and quality control of herbal formulations. It ensures consistency, standardization, and authenticity of plant extracts.<sup>[27]</sup>

These analytical techniques are essential for validating the phytochemical profile, ensuring quality assurance, and supporting the development of standardized herbal formulations of *Withania somnifera* for therapeutic use.

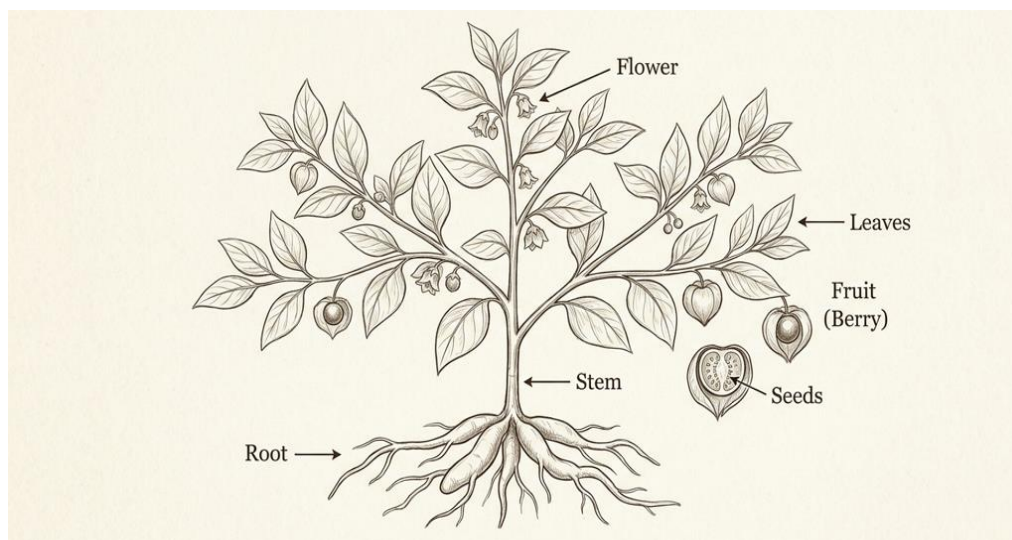


Figure 1: Morphology of *Withania somnifera*.<sup>[28]</sup>

Table 2: Major Phytochemical Constituents of *Withania somnifera*.<sup>[29]</sup>

Plant Part	Compound	Phytochemical Class	Pharmacological Activity
Root	Withaferin A	Withanolide (steroidal lactone)	Anti-inflammatory, anticancer
Root	Withanolide D	Withanolide	Anti-inflammatory, immunomodulatory
Leaves	Withanone	Withanolide	Antioxidant, neuroprotective
Root	Somniferine	Alkaloid	Adaptogenic, mild anti-inflammatory
Root	Withanine	Alkaloid	Neuroprotective, calming effect
Whole plant	Anaferine	Alkaloid	Antispasmodic, CNS activity
Leaves	Tropine	Alkaloid	Anticholinergic activity
Root	Sitoindoside VII	Glycowithanolide	Antioxidant, anti-stress
Root	Sitoindoside VIII	Glycowithanolide	Immunomodulatory
Leaves	Flavonoids (Quercetin)	Flavonoid	Antioxidant, anti-inflammatory
Whole plant	Saponins	Saponin	Anti-inflammatory, immune boosting
Root	$\beta$ -sitosterol	Phytosterol	Anti-inflammatory, cholesterol-lowering

## 5. Pharmacological Activities Related to Inflammation

*Withania somnifera* has a wide range of pharmacological activities which are directly or indirectly linked with regulation of inflammatory processes. Its therapeutic effect is largely determined by its capacity to act on various molecular targets hence offering a multi-dimensional approach in the management of disorders related to inflammation.<sup>[30]</sup>

### 5.1 Anti-inflammatory Activity

The anti-inflammatory effect of *Withania somnifera* is one of the most important pharmacological characteristics of the plant. The mechanism of action of this effect is mainly achieved by inhibiting major inflammatory enzymes and mediators of the inflammatory cascade.<sup>[31]</sup>

Plant extracts and its active constituents especially withanolides including withaferin A have been demonstrated to suppress enzymes like cyclooxygenase-2 (COX-2) and lipoxygenase (LOX) which are involved in the production of pro-inflammatory mediators, including prostaglandins and leukotrienes. *Withania somnifera* suppresses those enzymes and thus is effectively used as a biochemical anti-inflammatory.<sup>[32]</sup>

Moreover, it dramatically decreases the synthesis of the pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-6 (IL-6). These cytokines are key contributors to chronic inflammation and autoimmune diseases. Their down regulation assists in the regulation of inflammatory processes and aids in the prevention of tissue damage.

### 5.2 Antioxidant Activity

Inflammation is closely connected with oxidative stress because an excessive generation of reactive oxygen species (ROS) can cause and maintain inflammatory reactions. *Withania somnifera* has been shown to possess great antioxidant properties and this factor contributes to its anti-inflammatory action.<sup>[33]</sup>

The bioactive substances in the plant are free radical scavengers, which counter the ROS and inhibit oxidative damage to the cellular components like lipids, proteins, and DNA. Such ROS scavenging potential is useful in disrupting the chain of oxidative stress-induced inflammation.

Moreover, *Withania somnifera* increases the activity of endogenous antioxidant defense mechanism, such as enzymes such as superoxide dismutase (SOD), catalase and glutathione peroxidase. It helps the overall homeostasis of cells, as well as prevents the damage of tissues caused by inflammation, by diminishing the oxidative stress.<sup>[34]</sup>

### 5.3 Immunomodulatory Effects

Besides its direct anti-inflammatory and antioxidant effects, *Withania somnifera* has important immunomodulatory effects. It assists in balancing the immune system by balancing the innate and adaptive immune responses.<sup>[35]</sup>

Plant adjusts the actions of immune cells, such as macrophages, lymphocytes, and natural killer (NK) cells, hence improving the immune defense system of the body without over-activating the immune system. It is also useful in ensuring immune homeostasis, which is the prevention of excessive production of inflammatory mediators.

This immunomodulatory effect is especially useful in chronic inflammatory and autoimmune diseases, the dysregulation of the immune system is a major factor. *Withania somnifera* not only decreases inflammation by restoring immune balance but also enhances the overall disease resistance.<sup>[36]</sup>

## 6. Mechanism of Anti-inflammatory Action

*Withania Somnifera* has a multi-targeted and complex mechanism of action in its anti-inflammatory properties by modifying major signaling pathways and inflammatory mediators. The bioactive components especially withanolides like withaferin A are key players in the regulation of molecular pathways related to inflammation.<sup>[37]</sup>

### NF- $\kappa$ B Pathway Inhibition

NF- $\kappa$ B (NF-KB) pathway is among the most important regulators of inflammation. During inflammatory states, NF-KB will be translocated to the nucleus and activate the expression of several pro-inflammatory genes. *Withania somnifera* is demonstrated to block activation of NF- $\kappa$ B through inhibition of nuclear translocation and DNA binding capacity of NF-KB.<sup>[38]</sup>

Such inhibition results in reduced production of inflammatory mediators, such as cytokines, chemokines, and enzymes like COX-2 and inducible nitric oxide synthase (iNOS). *Withania somnifera* can effectively inhibit the process of inflammation through this central pathway by inhibiting its onset and progression.<sup>[39]</sup>

### Cytokine Suppression

Tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-1 beta (IL-1), and interleukin-6 (IL-6) are pro-inflammatory cytokines that are important in enhancing the response to inflammation. The active constituents of *Withania somnifera* have a significant effect in inhibiting the synthesis and release of these cytokines.

This cytokine inhibition assists in regulating exorbitant immune reactions and averts chronic inflammation. It is also used to help suppress tissue damage and enhance

healing in inflammatory diseases like arthritis and metabolic diseases.<sup>[40]</sup>

### COX-2 Inhibition

Cyclooxygenase-2 (COX-2) is an inducible enzyme that produces prostaglandins, important mediators of pain and inflammation. Inflammatory diseases are usually characterized by the overexpression of COX-2.

*Withania somnifera* suppresses the production and action of COX-2 thus, decreasing the production of prostaglandins. This effect resembles the effects of non-steroidal anti-inflammatory drugs (NSAIDs), except that it has fewer side effects, rendering it a safer option in the long-term.<sup>[41]</sup>

### MAPK Pathway Modulation

The cellular responses to stress and inflammation are regulated by mitogen-activated protein kinase (MAPK) signaling, such as ERK, JNK, and p38 MAPK. These pathways, through activation, result in the release of inflammatory mediators and cytokines.

*Withania somnifera* is capable of regulating MAPK signaling, by suppressing the phosphorylation and activation of the kinases. It leads to lowering of the expression of inflammatory genes and low cellular response to inflammatory stimuli. The plant continues to enhance its anti-inflammatory effect on the molecular scale by acting on the MAPK pathways.<sup>[42]</sup>

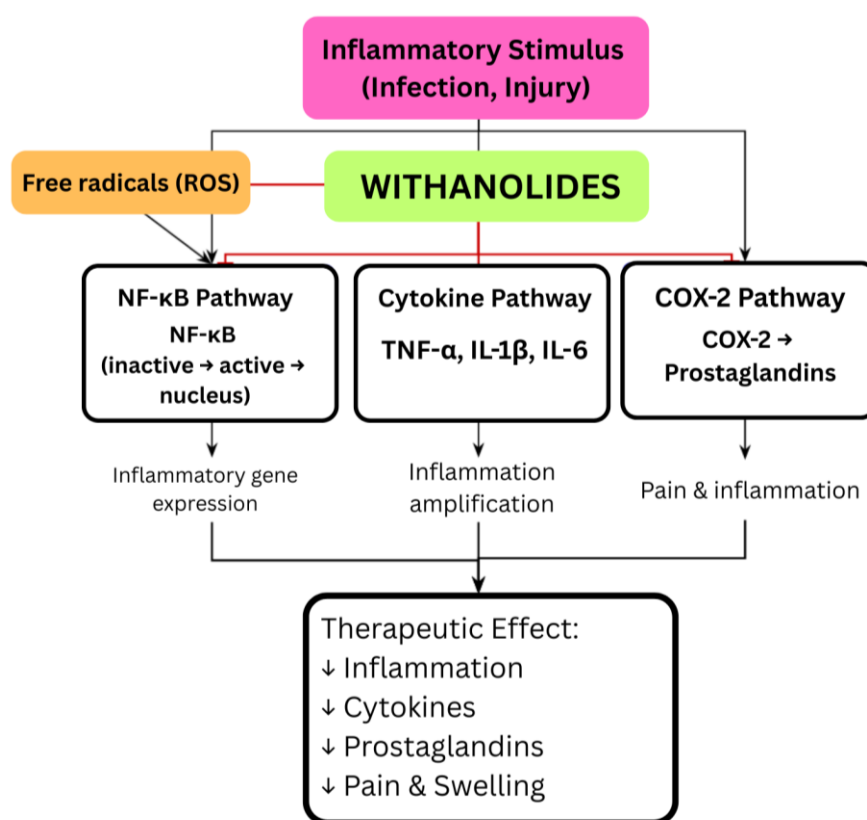


Figure 2: Mechanism of Anti-inflammatory Action of Withanolides.<sup>[43]</sup>

## 7. In Vitro and In Vivo Studies

*Withania somnifera* has a long history of anti-inflammatory research which has been conducted in vitro and in vivo experimental models. These studies have solid scientific evidence on why it is traditionally used in the management of inflammation-related disorders.<sup>[44]</sup>

### 7.1 In Vitro Studies

In vitro research is essential in comprehending cellular and molecular processes behind the anti-inflammatory effect of *Withania somnifera*. Its pharmacological effects have been extensively studied using various cell line models, especially macrophages and fibroblasts.

The line of macrophage cells (e.g., RAW 264.7 cells) are typically used to understand the process of inflammation. The *Withania somnifera* extracts or specific compounds such as withaferin A have been found to substantially inhibit the synthesis of pro-inflammatory mediators such as nitric oxide (NO), prostaglandins and cytokines such as TNF- $\alpha$  and IL-6. The key signaling pathways such as NF- $\kappa$ B and MAPK are heavily suppressed in mediation of these effects.<sup>[45]</sup>

Cellular proliferation and inflammatory responses are also determined using fibroblast cell lines. Research has shown that *Withania somnifera* improves fibroblast

viability and inflammatory stress, thus promoting tissue repair. Also, it has antioxidant properties and this helps to protect cells against oxidative damage, further enhancing its anti-inflammatory effect.

Altogether, *in vitro* researches underscore the potential of *Withania somnifera* to regulate cellular signal transduction, suppress the production of inflammatory mediators, and facilitate cell survival in the presence of inflammation.<sup>[46]</sup>

## 7.2 In Vivo Studies

Animal models are used to offer *in vivo* studies that give a detailed insight into the physiological relevance and therapeutic efficacy of *Withania somnifera* in inflammation.

Its anti-inflammatory effects have been extensively tested in different experimental models including carrageenan induced paw edema, formalin induced

inflammation, and collagen induced arthritis in rats. The models when administered *Withania somnifera* extracts have demonstrated a considerable decrease in edema, inflammation and tissue damage.<sup>[47]</sup>

The plant extract has been reported to lower the swelling of the joints, and reduce inflammatory cell invasion, and enhance mobility in arthritis models. These outcomes are connected with a decrease in the levels of pro-inflammatory cytokines and oxidative stress markers. Moreover, histopathological investigations have shown the presence of better tissue structure and less evidence of tissue inflammation in treated groups.<sup>[48]</sup>

The anti-inflammatory properties in *in vivo* systems are usually similar to the standard anti-inflammatory drugs, and have an improved safety profile. The results also corroborate the possibility of *Withania somnifera* as a natural source of therapeutic agent in the treatment of chronic inflammatory conditions.<sup>[49]</sup>

**Table 3: Summary of Pharmacological Studies on *Withania somnifera*.**<sup>[50]</sup>

Study Type	Model Used	Plant Part / Extract	Key Findings
In vitro	RAW 264.7 macrophages	Ethanollic root extract	↓ TNF- $\alpha$ and IL-6 production
In vitro	LPS-stimulated macrophages	Withaferin A	Inhibition of NF- $\kappa$ B pathway
In vitro	Human fibroblast cells	Methanollic leaf extract	Enhanced cell viability, ↓ inflammation
In vitro	Microglial cells	Withanolide extract	Neuroprotective and anti-inflammatory effect
In vitro	Keratinocyte cells	Aqueous extract	Reduced oxidative stress and cytokine levels
In vivo	Carrageenan-induced paw edema (rats)	Root extract	Significant reduction in edema
In vivo	Formalin-induced inflammation (rats)	Ethanollic extract	Decreased inflammation and pain response
In vivo	Collagen-induced arthritis (rats)	Standardized extract	Reduced joint swelling and cytokines
In vivo	Adjuvant-induced arthritis (rats)	Root powder	Improved mobility and reduced inflammation
In vivo	Oxidative stress model (rats)	Methanollic extract	↓ ROS and lipid peroxidation
Clinical	Rheumatoid arthritis patients	Standardized root extract	Reduction in pain and inflammation markers
Clinical	Stress-related inflammation	Ashwagandha capsules	Improved immune response and ↓ inflammation

## 8. Therapeutic Applications in Inflammation-Related Disorders

*Withania somnifera* has acquired significant interest in the context of its therapeutic roles in an enormous number of inflammation-related diseases. Its multi-targeted pharmacological effects such as anti-inflammatory, antioxidant and immunomodulatory effects make it a potential natural agent in the treatment of acute and chronic inflammatory diseases.<sup>[51]</sup>

### Arthritis

Arthritis especially rheumatoid arthritis and osteoarthritis is a disease that is marked by persistent joint inflammation, which results in pain, swelling, and limitations in movement. *Withania somnifera* has been used traditionally to treat disorders related to the joints. Its bioactive compounds particularly withanolides assist

in the suppression of the inflammatory mediators like TNF- $\alpha$  and IL-6 hence lowering the inflammation and stiffness of the joints. It also enhances the functionality of joints and decreases the degeneration of cartilages. It has been proven both clinically and experimentally to be effective in pain reduction and increasing mobility, and is, therefore, an effective complement to managing arthritis.<sup>[52]</sup>

### Neuroinflammation (Alzheimer's, Parkinson's)

Neuroinflammation is an essential aspect of neurodegenerative diseases like Alzheimer disease and Parkinson disease. Neuronal damage is caused by chronic activation of microglial cells and augmented oxidative stress. *Withania somnifera* has been shown to have neuroprotective effects through inhibition of inflammatory pathways, decreased oxidative stress and

increased neuronal survival. It aids with the inhibition of neuroinflammatory mediators and has a supporting effect on the cognitive functioning, thus demonstrating potential in the delay of the progression of neurodegenerative diseases.<sup>[53]</sup>

### Cardiovascular Inflammation

Cardiovascular diseases such as atherosclerosis and hypertension are important in the process of inflammation. Chronic inflammation causes endothelial malfunction, the development of plaque, and vascular damage. *Withania somnifera* has shown benefit in lowering systemic inflammation and oxidative stress, and safeguarding the vascular integrity. It is an antioxidant that inhibits lipid peroxidation and enhances endothelial performance. Additionally, it may help in regulating lipid profiles and reducing inflammatory markers associated with cardiovascular risk.<sup>[54]</sup>

### Metabolic Disorders

Diabetes mellitus and obesity are examples of chronic low-grade inflammation. Inflammatory cytokines and oxidative stresses are some of the factors that cause insulin resistance and metabolic disequilibrium. *Withania somnifera* has been demonstrated to alter the metabolic parameters to be beneficial in terms of reducing inflammation and increasing antioxidant defenses. It aids in reducing the level of blood glucose, enhancing insulin sensitivity and lipid metabolism. Its adaptogenic action also contributes to general metabolism, decreasing hormonal imbalance caused by stress.<sup>[55]</sup>

## 9. Formulation Approaches and Safety Aspects

To increase its therapeutic efficacy, stability and patient compliance, *Withania somnifera* has been extensively used in several pharmaceutical and herbal preparations. Evaluation of safety and toxicity should also be done in tandem with formulation development to facilitate its clinical use in the inflammation-related disorders.<sup>[56]</sup>

### Capsules, Tablets, and Extracts

The classical and recent preparations of *Withania somnifera* comprise mainly powders (*churna*), capsules, tablets, and standardized extracts. Tablets and capsules containing root extracts are the most widely used dosage forms because of their convenience, precise dosing and enhanced patient compliance. In clinical practice, standardized extracts, especially those fortified with withanolides are desirable because they offer good supply of therapeutic results.

Ayurvedic practice is also popular in the use of liquid extracts and tinctures to achieve faster absorption, although powdered root formulations are also common. These are formulations that are aimed at maximizing bioavailability and providing long lasting pharmacological actions particularly in long term inflammatory diseases.<sup>[57]</sup>

### Nano-formulations (Recent Trends)

Recent innovations in drug delivery systems have resulted in the creation of nano-formulations of *Withania somnifera*, to increase its bioavailability, stability, and targeted delivery. They consist of nanoparticles, nanoemulsions, liposomes and polymer-based delivery systems.

Nano-formulations help in improving the solubility of poorly water-soluble compounds like withanolides and enable controlled and sustained release of active constituents. Moreover, they enable the targeted delivery to inflamed tissues, enhancing the therapeutic efficacy and reducing the side effects. These novel strategies have the potential of becoming the future in designing herbal medicines.<sup>[58]</sup>

### Toxicity Studies

*Withania somnifera* has shown a good safety profile in preclinical and clinical trials of toxicology. The research of acute and sub-chronic toxicity in the animal models has shown that the plant extracts are safe in most cases when used at the recommended doses, without any toxicity or organ damage reported.

Minimal side effects such as the occurrence of mild gastrointestinal discomfort in isolated instances are reported in most studies. Moreover, the mutagenic or genotoxic effects are not significant. Nonetheless, the differences in the extraction procedures and dosage form can affect the safety outcomes, and the standardisation is essential.<sup>[59]</sup>

### Safe Dosage

Safe and effective dose of *Withania somnifera* is contingent on the formulation and concentration of active constituents. Generally, standardized root extracts are usually given in the dosage of 300-600 mg/day, usually in two doses. Ayurvedic use Traditional Ayurvedic use might be of larger amounts of crude powder, typically 36 grams per day.

Though *Withania somnifera* is believed to be safe in most people, it is recommended that caution should be observed in certain groups like pregnant or lactating women, those with autoimmune conditions and those under immunosuppressive medication. To achieve safety and the best therapeutic effects, proper dosage standardization and medical supervision are crucial.<sup>[60]</sup>

## 10. Future Perspectives

The accumulating scientific literature points to the apparent huge therapeutic promise of *Withania somnifera* in treating inflammation-related conditions. Nonetheless, there are still a few gaps to be filled in to make it easier to translate traditional medicine into the modern clinical practice.

### Need for Clinical Trials

Despite the many *in vitro* and *in vivo* research studies that have proven the anti-inflammatory effect of *Withania somnifera*, there remains a deficit of well-designed and large-scale clinical research. Majority of the available clinical data are small and short term. Future studies need to concentrate on randomized controlled trials (RCTs) to determine its safety, effectiveness, optimum dosage, and long-term outcomes in various patient groups. These studies are needed to make it acceptable in evidence-based medicine.<sup>[61]</sup>

### Standardization of Extracts

The variability in the composition of phytochemicals because of the difference in the plant source, growing conditions, and extraction is one of the biggest issues of herbal medicine. To achieve consistency, reproducibility, and quality control, standardization of *Withania somnifera* extracts, especially in terms of major bioactive markers (withanolides), is essential. Reliability of extraction, processing and formulation protocols should be developed to facilitate reliability of the protocol as a therapeutic agent.<sup>[62]</sup>

### Molecular Mechanism Studies

Although some of the mechanisms of action have been suggested to include the inhibition of NF- $\kappa$ B complex measurements like genomics, proteomics and metabolomics can be utilized to determine particular molecular targets and signaling pathways. A better insight into these processes will empower scientific verification and help to create specific treatments.<sup>[63]</sup>

### Nano-Drug Delivery Systems

Emerging nanotechnology-based drug delivery systems offer promising opportunities to enhance the therapeutic efficacy of *Withania somnifera*. Nano-formulations such as nanoparticles, liposomes, and nanoemulsions can improve the bioavailability, stability, and targeted delivery of active compounds like withanolides. These systems may also enable controlled release and reduced toxicity, thereby improving patient outcomes. Future research should focus on optimizing nano-drug delivery platforms and evaluating their clinical applicability.<sup>[64]</sup>

## 11. CONCLUSION

*Withania somnifera* emerges as a highly promising medicinal plant with significant anti-inflammatory potential, supported by both traditional knowledge and modern scientific evidence. Its rich phytochemical composition, particularly withanolides, alkaloids, and saponins, contributes to its ability to modulate key inflammatory pathways, suppress pro-inflammatory cytokines, and reduce oxidative stress.

The importance of *Withania somnifera* in modern medicine is increasingly recognized due to its multi-targeted mechanism of action, favorable safety profile, and wide range of therapeutic applications in inflammation-related disorders such as arthritis,

neurodegenerative diseases, cardiovascular conditions, and metabolic disorders. Unlike conventional synthetic drugs, it offers a more holistic approach with comparatively fewer side effects, making it an attractive alternative or complementary therapy.

The strong pharmacological significance of *Withania somnifera* lies in its combined anti-inflammatory, antioxidant, and immunomodulatory activities, which work synergistically to control inflammation and improve overall physiological balance. These properties position it as a valuable candidate for the development of novel therapeutic agents.

However, despite encouraging findings, there remains a critical need for further research. Well-designed clinical trials, standardization of extracts, and advanced molecular studies are essential to validate its efficacy and safety on a larger scale. Addressing these gaps will help in establishing *Withania somnifera* as a scientifically validated and widely accepted therapeutic option in modern healthcare systems.

**ACKNOWLEDGEMENT:** Nil.

**Conflict of Interest:** Nil.

## REFERENCES

1. Harvanová G, Duranková S. Inflammatory process: Factors inducing inflammation, forms and manifestations of inflammation, immunological significance of the inflammatory reaction. *Alergologia Polska-Polish Journal of Allergology*, 2025; 12(1): 54-61.
2. Furman D, Campisi J, Verdin E, Carrera-Bastos P, Targ S, Franceschi C, Ferrucci L, Gilroy DW, Fasano A, Miller GW, Miller AH. Chronic inflammation in the etiology of disease across the life span. *Nature medicine*, Dec. 2019; 25(12): 1822-32.
3. Fołta J, Rzepka Z, Wrześniok D. The role of inflammation in neurodegenerative diseases: Parkinson's disease, Alzheimer's disease, and multiple sclerosis. *International journal of molecular sciences*, May 28, 2025; 26(11): 5177.
4. Ahmadi M, Bekeschus S, Weltmann KD, von Woedtke T, Wende K. Non-steroidal anti-inflammatory drugs: recent advances in the use of synthetic COX-2 inhibitors. *RSC medicinal chemistry*, 2022; 13(5): 471-96.
5. Khan MA, Siddique HR. The Multi-Targeting Efficacy and Therapeutic Effects of Ayurveda and Chinese Medicine: An Integrated Approach for Cancer Treatment and Management. In *Ethnic Knowledge and Perspectives of Medicinal Plants*, Oct. 20, 2023; 389-417. Apple Academic Press.
6. Bashir A, Nabi M, Tabassum N, Afzal S, Ayoub M. An updated review on phytochemistry and molecular targets of *Withania somnifera* (L.) Dunal

- (Ashwagandha). *Frontiers in Pharmacology*, Mar. 29, 2023; 14: 1049334.
- Saha P, Ajgaonkar S, Maniar D, Sahare S, Mehta D, Nair S. Current insights into transcriptional role (s) for the nutraceutical *Withania somnifera* in inflammation and aging. *Frontiers in Nutrition*, May 3, 2024; 11: 1370951.
  - Wiciński M, Fajkiel-Madajczyk A, Kurant Z, Liss S, Szyperski P, Szambelan M, Gromadzki B, Rupniak I, Słupski M, Sadowska-Krawczenko I. Ashwagandha's multifaceted effects on human health: impact on vascular endothelium, inflammation, lipid metabolism, and cardiovascular outcomes—a review. *Nutrients*, Jul. 31, 2024; 16(15): 2481.
  - Syed AA, Reza MI, Singh P, Thombre GK, Gayen JR. *Withania somnifera* in neurological disorders: Ethnopharmacological evidence, mechanism of action and its progress in delivery systems. *Current drug metabolism*, Jun. 1, 2021; 22(7): 561-71.
  - Hermont AP, Cruz PV, Occhi-Alexandre IG, Bendo CB, Auad SM, Pordeus IA, Martins CC. The importance of full text screening when judging eligibility criteria in a systematic review: a systematic survey. *Arquivos em Odontologia*, Sep. 20, 2022; 58: 160-5.
  - Khabiya R, Choudhary GP, Jnanesha AC, Kumar A, Lal RK. An insight into the potential varieties of Ashwagandha (Indian ginseng) for better therapeutic efficacy. *Ecological Frontiers*, Jun. 1, 2024; 44(3): 444-50.
  - Mehmood F, Abdullah, Ubaid Z, Bao Y, Poczai P, Mirza B. Comparative plastomics of Ashwagandha (*Withania*, Solanaceae) and identification of mutational hotspots for barcoding medicinal plants. *Plants*, Jun. 15, 2020; 9(6): 752.
  - Alamgir AN. Pharmacognostical Botany: Classification of medicinal and aromatic plants (MAPs), botanical taxonomy, morphology, and anatomy of drug plants. In *Therapeutic use of medicinal plants and their extracts: Volume 1: Pharmacognosy*, Sep. 8, 2017; 177-293. Cham: Springer International Publishing.
  - SINGH RK. Evaluation of productivity and quality of *Withania somnifera* (L.) Dunal under different plant populations, irrigation levels and moisture conservation practices in sub-tropical plains of North India. *Journal of Medicinal and Aromatic Plant Sciences*, 2021; 43(1-2): 37-48.
  - Poojari P, Kiran KR, Swathy PS, Muthusamy A. *Withania somnifera* (L.) dunal: an overview of bioactive molecules, medicinal properties and enhancement of bioactive molecules through breeding strategies. In *vitro Plant Breeding towards Novel Agronomic Traits: Biotic and Abiotic Stress Tolerance*, Nov. 24, 2019; 1-25.
  - Banik B, Das S, Das MK. Medicinal Plants with Potent Anti-inflammatory and Anti-arthritic Properties found in Eastern Parts of the Himalaya: An Ethnomedicinal Review. *Pharmacognosy Reviews*, Jul. 1, 2020; 14(28).
  - Ahmad M, Dar NJ. *Withania somnifera*: Ethnobotany, pharmacology, and therapeutic functions. In *Sustained energy for enhanced human functions and activity*, Jan. 1, 2017; 137-154. Academic Press.
  - Kumar V, Dey A, Hadimani MB, Emeraldjavascrip M. Chemistry and pharmacology of *Withania somnifera*: An update. *CellMed.*, Feb. 28, 2015; 5(1): 1-.
  - Dhanani T, Shah S, Gajbhiye NA, Kumar S. Effect of extraction methods on yield, phytochemical constituents and antioxidant activity of *Withania somnifera*. *Arabian journal of chemistry*, Feb 1, 2017; 10: S1193-9.
  - Hardiningsih DT, Hidayat AT, Delfira A. Qualitative identification of alkaloid compounds in *Moringa oleifera* leaf extract. *Proceedings Academic Universitas Jambi*, Nov. 27, 2025; 1(2): 468-75.
  - Kumar P, Banik SP, Goel A, Chakraborty S, Bagchi M, Bagchi D. Revisiting the multifaceted therapeutic potential of Withaferin A (WA), a novel steroidal lactone, W-ferinAmax ashwagandha, from *Withania Somnifera* (L) Dunal. *Journal of the american nutrition association*, Feb. 17, 2024; 43(2): 115-30.
  - Uddin Q, Samiulla L, Singh VK, Jamil SS. Phytochemical and pharmacological profile of *Withania somnifera* Dunal: a review. *Journal of Applied Pharmaceutical Science*, Jan. 2012; 30: 170-5.
  - Ghosal S, Lal J, Srivastava R, Bhattacharya SK, Upadhyay SN, Jaiswal AK, Chattopadhyay U. Immunomodulatory and CNS effects of sitoindosides IX and X, two new glycowithanolides from *Withania somnifera*. *Phytotherapy Research*, 1989; 3(5): 201-6.
  - Antony B, Benny M, Kuruvilla BT, Sebastian A, Aravindakshan Pillai AA, Joseph B, Edappattu Chandran S. Development and validation of an RP-HPLC method for the simultaneous determination of total withanolide glycosides and Withaferin A in *Withania somnifera* (Ashwagandha). *Current Chromatography*, Sep. 1, 2020; 7(2): 106-20.
  - Ezeokonkwo MA, Kabir D. Applications of FTIR, GC-MS, and LC-MS in the identification of antimicrobial phytochemicals. *Arab J. Chem. Environ Res.*, 2026; 13(2): 194-216.
  - RANJAN S, Chaitali RO, SINHA SK. Gas chromatography–mass spectrometry (GC-MS): a comprehensive review of synergistic combinations and their applications in the past two decades. *Journal of Analytical Sciences and Applied Biotechnology*, Dec. 30, 2023; 5(2): 72-85.
  - Srivastava M, editor. *High-performance thin-layer chromatography (HPTLC)*. Springer Science & Business Media, 2010 Nov 15.
  - Gaurav N, Kumar A, Tyagi M, Kumar D, Chauhan UK, Singh AP. Morphology of *Withania somnifera* (distribution, morphology, phytosociology of

- Withania somnifera L. Dunal). *Int J Current Sci Res.*, 2015; 1(7): 164-73.
29. A. Dar P, R. Singh L, A. Kamal M, A. Dar T. Unique medicinal properties of *Withania somnifera*: Phytochemical constituents and protein component. *Current pharmaceutical design*, Feb. 1, 2016; 22(5): 535-40.
  30. Chandran U, Patwardhan B. Network ethnopharmacological evaluation of the immunomodulatory activity of *Withania somnifera*. *Journal of ethnopharmacology*, Feb. 2, 2017; 197: 250-6.
  31. Srivastav AK, Das P. Phytochemical extraction and characterization of roots of *Withania Somnifera* for its Anti-Bacterial, Anti-Oxidant, Anti-Inflammation and Analgesic activity. *Int J Innov Res Dev.*, Jul. 19, 2014; 3(7): 22-33.
  32. Mulabagal V, Subbaraju GV, Rao CV, Sivaramakrishna C, DeWitt DL, Holmes D, Sung B, Aggarwal BB, Tsay HS, Nair MG. Withanolide sulfoxide from *Aswagandha* roots inhibits nuclear transcription factor-kappa-B, cyclooxygenase and tumor cell proliferation. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*, Jul. 2009; 23(7): 987-92.
  33. Chatterjee S. Oxidative stress, inflammation, and disease. In *Oxidative stress and biomaterials*, Jan. 1, 2016; 35-58. Academic Press.
  34. Chovatiya R, Medzhitov R. Stress, inflammation, and defense of homeostasis. *Molecular cell*. 2014 Apr 24; 54(2): 281-8.
  35. Alanazi HH, Elfaki E. The immunomodulatory role of *withania somnifera* (L.) dunal in inflammatory diseases. *Frontiers in pharmacology*, Feb. 22, 2023; 14: 1084757.
  36. Moudgil KD, Venkatesha SH. The anti-inflammatory and immunomodulatory activities of natural products to control autoimmune inflammation. *International journal of molecular sciences*, Dec. 21, 2022; 24(1): 95.
  37. Verma S, Panchpuri M, Dwibedi V, Rath SK, Devi A. Exploring herbal synergies in the management of rheumatoid arthritis: a multifaceted approach to inflammation and joint health. *Inflammopharmacology*, Nov. 2025; 33(11): 6457-84.
  38. Singh S, Singh TG. Role of nuclear factor kappa B (NF- $\kappa$ B) signalling in neurodegenerative diseases: an mechanistic approach. *Current Neuropharmacology*, Sep. 1, 2020; 18(10): 918-35.
  39. Balkrishna A, Solleti SK, Singh H, Sharma N, Varshney A. Withanolides from *Withania somnifera* ameliorate neutrophil infiltration in endotoxin-induced peritonitis by regulating oxidative stress and inflammatory cytokines. *Planta Medica*, May 2022; 88(06): 466-78.
  40. Bennett JM, Reeves G, Billman GE, Sturmberg JP. Inflammation–nature’s way to efficiently respond to all types of challenges: implications for understanding and managing “the epidemic” of chronic diseases. *Frontiers in medicine*, Nov. 27, 2018; 5: 316.
  41. Devkar ST, Kandhare AD, Zanwar AA, Jagtap SD, Katyare SS, Bodhankar SL, Hegde MV. Hepatoprotective effect of withanolide-rich fraction in acetaminophen-intoxicated rat: decisive role of TNF- $\alpha$ , IL-1 $\beta$ , COX-II and iNOS. *Pharmaceutical Biology*, Nov. 1, 2016; 54(11): 2394-403.
  42. Akhtar N, Baig MW, Haq IU, Rajeeve V, Cutillas PR. Withanolide metabolites inhibit PI3K/AKT and MAPK pro-survival pathways and induce apoptosis in acute myeloid leukemia cells. *Biomedicines*, Sep. 6, 2020; 8(9): 333.
  43. Wang L, Lu S, Wang L, Xin M, Xu Y, Wang G, Chen D, Chen L, Liu S, Zhao F. Anti-inflammatory effects of three withanolides isolated from *Physalis angulata* L. in LPS-activated RAW 264.7 cells through blocking NF- $\kappa$ B signaling pathway. *Journal of ethnopharmacology*, Aug. 10, 2021; 276: 114186.
  44. Rasool M, Varalakshmi P. Immunomodulatory role of *Withania somnifera* root powder on experimental induced inflammation: An in vivo and in vitro study. *Vascular pharmacology*, Jun. 1, 2006; 44(6): 406-10.
  45. Sharma PK, Kumar L, Goswami Y, Pujani M, Dikshit M, Tandon R. The aqueous root extract of *Withania somnifera* ameliorates LPS-induced inflammatory changes in the in vitro cell-based and mice models of inflammation. *Frontiers in Pharmacology*, Jun. 12, 2023; 14: 1139654.
  46. Nile SH, Liang Y, Wang Z, Zheng J, Sun C, Nile A, Patel G, Kai G. Chemical composition, cytotoxic and pro-inflammatory enzyme inhibitory properties of *Withania somnifera* (L.) Dunal root extracts. *South African Journal of Botany*, Dec. 1, 2022; 151: 46-53.
  47. Abd-Allah AA, El-Deen NA, Mohamed WA, Naguib FM. Mast cells and pro-inflammatory cytokines roles in assessment of grape seeds extract anti-inflammatory activity in rat model of carrageenan-induced paw edema. *Iranian journal of basic medical sciences*, Jan. 2018; 21(1): 97.
  48. Du H, Zhang X, Zeng Y, Huang X, Chen H, Wang S, Wu J, Li Q, Zhu W, Li H, Liu T. A novel phytochemical, DIM, inhibits proliferation, migration, invasion and TNF- $\alpha$  induced inflammatory cytokine production of synovial fibroblasts from rheumatoid arthritis patients by targeting MAPK and AKT/mTOR signal pathway. *Frontiers in immunology*, Jul. 23, 2019; 10: 1620.
  49. Orrù A, Marchese G, Ruiu S. Alkaloids in *Withania somnifera* (L.) Dunal root extract contribute to its anti-inflammatory activity. *Pharmacology*, May 30, 2023; 108(3): 301-7.
  50. Dar NJ, Hamid A, Ahmad M. Pharmacologic overview of *Withania somnifera*, the Indian Ginseng. *Cellular and molecular life sciences*, Dec. 2015; 72(23): 4445-60.
  51. Nisar A, Jagtap S, Vyavahare S, Deshpande M, Harsulkar A, Ranjekar P, Prakash O.

- Phytochemicals in the treatment of inflammation-associated diseases: the journey from preclinical trials to clinical practice. *Frontiers in pharmacology*, May 9, 2023; 14: 1177050.
52. Shrivastava AK, Pandey A. Inflammation and rheumatoid arthritis. *Journal of physiology and biochemistry*, Jun. 2013; 69(2): 335-47.
53. Chen WW, Zhang XI, Huang WJ. Role of neuroinflammation in neurodegenerative diseases. *Molecular medicine reports*, Apr. 1, 2016; 13(4): 3391-6.
54. Castellon X, Bogdanova V. Chronic inflammatory diseases and endothelial dysfunction. *Aging and disease*, Jan. 2, 2016; 7(1): 81.
55. Castro AM, Macedo-De la Concha LE, Pantoja-Meléndez CA. Low-grade inflammation and its relation to obesity and chronic degenerative diseases. *Revista Médica del Hospital General de México*, Apr. 1, 2017; 80(2): 101-5.
56. Tandon N, Yadav SS. Safety and clinical effectiveness of *Withania Somnifera* (Linn.) Dunal root in human ailments. *Journal of ethnopharmacology*, Jun. 12, 2020; 255: 112768.
57. Zaigham H, Tauheed A, Ali A. Recent trend in traditional medicine dosage form and present status of Unani and Ayurvedic medicine. *Int J Pharm Sci & Res.*, 2019; 10(4): 1640-49.
58. Kumari S, Goyal A, Sönmez Gürer E, Algin Yapar E, Garg M, Sood M, Sindhu RK. Bioactive loaded novel nano-formulations for targeted drug delivery and their therapeutic potential. *Pharmaceutics*, May 19, 2022; 14(5): 1091.
59. Nohmi T. Thresholds of genotoxic and non-genotoxic carcinogens. *Toxicological research*, Oct. 2018; 34(4): 281-90.
60. Bernstein N, Akram M, Yaniv-Bachrach Z, Daniyal M. Is it safe to consume traditional medicinal plants during pregnancy?. *Phytotherapy research*, Apr. 2021; 35(4): 1908-24.
61. Khan MA, Ahmed RS, Chandra N, Arora VK, Ali A. In vivo, extract from *Withania somnifera* root ameliorates arthritis via regulation of key immune mediators of inflammation in experimental model of arthritis. *Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Inflammatory and Anti-Allergy Agents)*. Fe. 4, 2019; 18(1): 55-70.
62. Liebelt DJ, Jordan JT, Doherty CJ. Only a matter of time: the impact of daily and seasonal rhythms on phytochemicals. *Phytochemistry Reviews*, Dec. 2019; 18(6): 1409-33.
63. Verhoeckx KC, Bijlsma S, Jespersen S, Ramaker R, Verheij ER, Witkamp RF, van der Greef J, Rodenburg RJ. Characterization of anti-inflammatory compounds using transcriptomics, proteomics, and metabolomics in combination with multivariate data analysis. *International Immunopharmacology*, Nov. 1, 2004; 4(12): 1499-514.
64. Anand A, Gautam P, Ojha S. Application of nanotechnology for herbal medicine development: A review. *Letters in Drug Design & Discovery*, Jun. 1, 2024; 21(8): 1325-33.