

## Immunomodulatory Study of Some Herbal Medicinal Plants: A Review

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**ABSTRACT:** The immune system is one of the body's most complex biological systems. A substantial number of viruses, bacteria, and fungi attack the immune system during an infection. A chemical known as a herbal immunomodulator enhances or inhibits the immune system's innate and adaptive immunological responses. Phytochemicals including alkaloids, polyphenols, terpenoids, glucosinolates, and glycosides, which have a variety of pharmacological uses, are mostly found in plants. Clinical research demonstrates that these active ingredients can serve as immunomodulators. A number of Indian medicinal plants and various "Rasayana" have been claimed to possess immunomodulatory activity. Some of these plants are *Withania somnifera*, *Tinospora cordifolia*, *Echinacea purpurea*, *Nelumbo nucifera*, *Caesalpinia bonducella*, *Boerhaviadiffusa* etc.

**Keywords:** Immunomodulators, herbal plants, immunesystem, chemicalconstituents.

### I. INTRODUCTION:

Since the beginning of time, plants and minerals have been utilised to heal a wide variety of maladies. It is now understood that immune response immunomodulation may offer an alternative to traditional chemotherapy for a variety of disease conditions, particularly when the host's defense mechanism needs to be activated in the presence of impaired immune responsiveness or when a selective immunosuppressant needs to be induced in conditions like autoimmune disorders and organ transplantation[1].

Immunity is the body's built-in safeguard against several contagious diseases. An illness history, vaccinations, and a number of environmental stressors all serve as triggers for immunity. An immune system is a mechanism that helps an organism maintain homeostasis while fighting against these intruders. The immune system of the body distinguishes between self- and

non-self-cells in an organism. Hippocrates (460–377 BCE), the Father of Medicine, and Maharshi Charak (200 BCE), the Father of Indian Medicine, both make reference to the immune system's science in their respective works[2].

### Types Of Immune System

Immune systems have been divided into two major groups based on their functions: innate immune systems (also known as non-specific immune systems) and adaptive immune systems (also known as specific or acquired immune systems)[3].

- **Innate Immunity:** Since the innate immune response acts quickly and non-specifically in response to an antigen in the early stages, it is known as the first line of defence.
- **Adaptive Immunity:** All vertebrates have an adaptive immune response, which is a surveillance system and highly specific but weak to react to the antigen. Through a process of gene rearrangement, pathogen (antigen)-specific B and T cells are produced, resulting in the development of adaptive immunity. Active immunity is the process of exposing the body to an antigen with the goal of producing an adaptive immune response that may take weeks or months to mature but may endure for the rest of one's life. Either acquired or innate immunity may be active [4].
- **Immunomodulators:** Numerous exogenous and endogenous variables that affect the immune system's function and effectiveness can either inhibit or stimulate it. Immunomodulators are a class of substances with the ability to normalise or modify pathogenic processes[5]. Immunomodulators are substances, either natural or artificial, that inhibit, stimulate, or otherwise modify the immune response. They are also referred to as DMDs, or disease-modifying drug.

### Classification Of Immunomodulators on Basis of Their Mode of Action

- A. **Immunostimulants:** Are molecules that aid in triggering the body's defences against an antigen and boosting the intensity of the immunological response[6].
- B. **Immunosuppressant:** Molecules that suppress the immune response and are frequently given after organ transplantation and autoimmune diseases.
- C. **Immunoadjuvants:** Are specialised molecules that, when combined with a particular vaccination, increase the amount of immunity compared to the vaccines alone[2].

### Ayurveda and Immunomodulation

The Vedas and Samhita, which date from about 3500 BCE and 800 BCE, include numerous allusions to medicinal plants and their applications, making India well recognised for its ethnobotanical research. The first documentation of herbal medicine was described in "Vrikshayurveda," which is mostly covered in the Rigveda and Atharvaveda of the Vedic texts. Traditional herbal medicine is used in Ayurveda. Its history dates back to 3300 to 1300 BCE emerged in the Indus Valley. Ayur which means life, and Veda are the roots of the word ayurveda means expertise.

The four basic methods used by Ayurveda to avoid disease in humans and animals are Parakratishapanum (Health Maintenance), NaisthikaChikitsa (Spiritual Therapy), RoganasmaniChikitsa (Disease Cure), and RasayanaChikitsa (Herbal Product Therapy)[7]. Rasayana is a combination of the terms juice or extract (Rasa) and "way of life" (Ayana). Rasayana is known to as a rejuvenation therapy since it strengthens the body's internal system in a way that enhances vitality, lifespan, intellect, and skin health [8]. It has been established that the medicinal plant's immunostimulant characteristics work for both selective and non-specific regulation. Rasayana describes plants with immunomodulatory qualities as *Tinospora cordifolia*, *Withania somnifera*, *Phyllanthus emblica*, and *Mangifera indica*[9].

### Herbal Plant as Immunomodulators

About three-fourths of the world's population, according to the WHO, employs conventional home remedies to treat health-related Issues. Many different ailments and illnesses have been successfully treated using plant extracts. New drugs may be discovered by combining

conventional knowledge with modern technology in multidisciplinary practise. The use of plant-based immunomodulators as an alternative to traditional treatments is possible[9].

Numerous plants have been shown to contain phytochemicals including flavonoids, lactones, alkaloids, and glycosides that are thought to be the cause of the plants' immunomodulating effects. As a result, there is growing scientific interest in the search for plant-derived natural compounds that might serve as fresh leads for the creation of effective and secure immunosuppressive and immunostimulant drugs[10].

### Herbal Plants as Immunomodulator

#### 1. *Withania somnifera*:

Numerous indigenous preparations widely utilize *Withania somnifera* (L.) Dunal, sometimes referred to as Ashwagandh, which belongs to the Solanaceae family. According to reports, *W. somnifera* has anti-inflammatory, anti-arthritic, and antitumor properties[11]. Ashwagandha, also known as *Withania somnifera* or WS, is a herb that is listed in the Rasayana family of Indian Ayurvedic medicines and has been widely studied as an immunomodulatory agent. The major withanolide glycosides present in WS cause macrophages to mobilize and become activated, which has an immunomodulatory effect. This also causes mouse splenocytes to proliferate. The concept of its usage as a Rasayana in Ayurveda has been proposed as the cause of this effect[12].

**Mohammad Ali et al.** discovered that although cyclophosphamide is an effective anti-cancer medication and is used in a range of cancer cases, it is hazardous and can lead to myelosuppression, mucosal ulcers, baldness, and other side effects. Their objective of the study was to develop an adjuvant treatment using an aqueous extract of the immunomodulator herb Ashwagandha to reduce the toxicity of cyclophosphamide. Five days before cyclophosphamide was administered, ashwagandha (300 mg/kg b.w.) was given, and it was continued for ten days. After treatment, a significant increase in the total count of WBC, ALC, and platelets was seen, but there was no statistically significant difference in the RBC count between any of the groups over the course of the study. The results of the study therefore demonstrated that Ashwagandha's therapeutic effectiveness can reduce the bone marrow depression caused by cancer chemotherapy, thereby reducing the toxicity[13].

## 2. *Tinosporacordifolia*:

The Ayurvedic plant *Tinospora cordifolia* (Menispermaceae) is found in China and the Indian subcontinent. The whole plant is utilised both alone and in conjunction with other plants in folk and Ayurvedic medicine. Due to its commercial significance, *T. cordifolia* has attracted intense research interest for the past 40 years. Alkaloids, sesquiterpenoids, diterpenoids, phenolics, steroids, aliphatic compounds, and polysaccharides have been isolated, and a wide range of pharmacological properties including immunomodulation, anticancer, hepatoprotective, and hypoglycemic properties have been discovered[14].

Common names for *Tinospora cordifolia* are Amrita, Guduchi (Sanskrit), and Giloe (Hindi). Syringin of guduchi and cordifolioside A are two isolated chemical compounds that have been described as immunomodulating agents in clinical studies. The stem of *T. cordifolia* affects the number of immune-supporting enzymes like catalase and activates lymphocyte cells, demonstrating the immuno-protective function of this shrub. *T. cordifolia* is a powerful medication for the prevention of immunological sensitive disorders since it may also boost immune cell and neutrophil activity. White blood cell (WBC) count, bone marrow cells, and foot pad thickness all rise after oral administration of *T. cordifolia* alcoholic extract (100 mg/kg), showing a stimulatory impact on the haemopoietic system that has a strong immunomodulatory effect. When evaluated on an edoema rat model, a traditional preparation of an aqueous extract of *T. cordifolia* known as "Ghana" in Ayurveda decreased the edematogenic agents and as a result had a strong immunostimulatory effect[15].

## 3. *Echinacea purpurea*:

*Echinacea purpurea* (L.) Moench is belonging to Asteraceae (Compositae) family is one most important well-known medicinal plants in the world[17]. *Echinacea* is herbal medicine which is also known as the purple coneflower. It has been used for the treatment of infections of upper respiratory system, cough and cold, bronchitis and certain inflammatory diseases[16].

Alkamides, ketoalkenes, caffeic acid derivatives, polysaccharides, and glycoproteins are the complex chemical composition of roots and herbs of *Echinacea*, which are thought to be the cause of the observed immunostimulatory and anti-inflammatory effects. The effective mechanism of immunomodulation is due to the effectiveness of alkamides on cannabinoid type 2 receptors

(CB2)[17]. Alkylamides is a main active ingredient which suppress the release of inflammatory cytokine such as TNF –  $\alpha$  and also stimulate the macrophages phagocytosis. It also has antiviral activity, promote circulating leukocytes and elevates NK cells[18].

## 4. *Nelumbo nucifera*:

*Nelumbo nucifera* is also called as lotus and sacred lotus. It is an aquatic perennial herb belonging to the family Nelumbonaceae. In India it is commonly known as Kamal or Padam in different regional languages. Lotus grow on the surface of the water with thick and yellow rhizomes, it has a fruit of a green colour[19].

The *Nelumbo nucifera* extract of rhizomes and seeds is found to be having the antipyretic, antidiarrhoeal, diuretic, antioxidants, psychopharmacological, anticancer, hypoglycaemic anti-inflammatory activities[20,21,22]. All of these activities are due to the presence of chemical constituents such as betulinic acid, steroidal pentacyclic triterpenoids, alkaloids, flavonoids and phenolic acids. Different types of extracts such as alcoholic, hydroalcoholic have the immunomodulatory effect[20].

**Debajyoti et.al** in 2010 shows that the rhizome and seed extract of *nelumbo nucifera* have the significant immunomodulatory effect. He found in his study that the count of lymphocytes increases in the treatment group when compared to the control group, but also decreases the neutrophil count[23].

## 5. *Caesalpinia bonducella*:

*Bonducella Caesalpinia Fleming* (Caesalpinaceae), often referred to as "nata karanja," "molucca bean," "bonduc nut," and "fevernut," is a prickly shrub that may be found all throughout the drier regions of India and Sri Lanka. The seeds have a smooth, shiny surface, are globular in shape, and are grey, hard, and brittle. The kernel is a yellowish-white colour and is bitter and greasy[24].

The most prevalent alkaloid in *Caesalpinia bonducella* L. natin, is known to be present in the shell, seed, and twigs. According to reports, the seed contains a potent glycoside called bonducin, which is the active chemical. Seed is also known to contain terpenoids and saponins. Fatty oils, starches, sucrose, phytosterols, stearic, palmitic, oleic, linoceric, and a combination of unsaturated acids with low molecular weights are known to be present in the shell. The plant is also known to have anti-oxidant, antifilarial, anticonvulsive, and

anti-microbial properties, as well as anti-tumor, anti-ulcer, anti-tumor, anti-immunomodulatory, and anticataract action[25].

The percentage of neutrophils adhering to nylon fibres increased noticeably as ethanolic extract of *C. bonducella* seed was evaluated for its immunomodulatory activity. Additionally, there was a dose-dependent rise in antibody titer values. The extract stopped myelosuppression in cyclophosphamide-treated rats and its Immunomodulatory properties make it useful in preventing autoimmune diseases[26].

#### 6. *Boerhaviadiffusa*:

In traditional Indian medicine as well as other parts of the world, such as Southern America and the African continent, *Boerhaviadiffusa* (BD) Linn. (Nyctaginaceae) is a well-known medicinal plant. Raktapunarnava, Shothaghni, Kathillaka, Kshudra, Varshabhu, Raktapushpa, Varshaketu, and Shilatika are some of the names that *Boerhaviadiffusa* is also known by. The plant is also known as "Punarnava" because, once its aerial portions fully dry out in the summer, it may regenerate during the rainy season with the aid of perennial roots[27]. According to Ayurveda, BD is a "rasayana" herb with qualities like "antiaging," "restoring youth," "strengthening life and intellectual capacity," and "preventing disease." These qualities all suggest that they raise the body's tolerance to any attack, or provide hepatoprotection and immunomodulation[28]. A novel class of isoflavonoids called rotenoids, flavonoids, flavonoid glycosides, xanthenes, purine nucleoside, lignans, ecdysteroids, and steroids are derived from the roots.

In vivo studies Mungantiwar and colleagues investigated the immunomodulation by BD (aqueous extract, 50–200 mg/Kg/day orally) and found significant leucocytosis and decreased morbidity (50%) in pretreated mice using an *E. coli*-induced abdominal sepsis stress condition. Additionally, the extract restored the rise in glucose, cholesterol, SGPT, and BUN levels as well as the decrease in triglycerides brought on by the cold and forcedswimming stress in rats. In another study, Sumanth and colleagues evaluated the effects of BD and ashwagandha and discovered that when mice were administered an alcoholic extract, both substances increased the amount of time spent swimming collectively. The total WBC count, blood glucose level, and plasma cortisol level all indicated that the extract had a more powerful impact. Similar to levamisole, the extract also induced macrophage phagocytic activity [29].

**7 *Capparis zeylanica*:** The climbing shrub *Capparis zeylanica*, Linn. (Family: Capparidaceae), often known as Indian caper, may be found all over India. It has been used as a "Rasayana" drug in the conventional Ayurvedic system of medicine. The leaves are frequently used in Northern India as a cataplasm in swellings, boils, and piles as well as a counterirritant and febrifuge. Modern phytochemical analysis of the plant has revealed that the leaves contain fatty acids and flavonoids[30]. Flavonoids are recognised to have antioxidant, anti-cancer, anti-inflammatory, anti-ulcer, and antibacterial properties. It is also traditionally used as a treatment for cholera, colic, hemiplegia, neuralgia, sores, pneumonic and pleurisy, small pox, boils, cholera, and testicular enlargement [31].

In their investigation, B.V. Ghule and colleagues found that the *Capparis zeylanica* ethanolic and water extract significantly improved the total WBCs count, RBCs count, haemoglobin and platelets count as well as reversed the myelosuppressive effects brought on by cyclophosphamide. Immune responses to *Capparis zeylanica* may be cellular and humoral. According to the study's results, *Capparis zeylanica* is an effective immunostimulant that activates both specific and non-specific immune systems[32].

**8. *Moringa Oleifera*:** The family Moringaceae only has one genus, *Moringa*, which is a native plant to both Africa and Asia and is the most frequently cultivated species in Northwestern India. The "horse-radish tree" is the common name for *Moringa oleifera*[33]. It consists of 13 species, from tiny herbs to enormous trees, that are native to tropical and subtropical regions. It has been established that MO contains a significant number of bioactive substances. The leaves of the plant, which are the most commonly utilised components, are abundant in saponins, vitamins, carotenoids, flavonoids, polyphenols, phenolic acids, glucosinolates, alkaloids, isothiocyanates, and tannins[34]. This plant's many parts, including the leaves, roots, seed, bark, fruit, flowers, and immature pods, operate as cardiac and circulatory stimulants, have anticancer, antipyretic, antiepileptic, antiinflammatory, antiulcer, antispasmodic, diuretic, antihypertensive, cholesterol-lowering, antioxidant, antidiabetic, hepatoprotective, antibacterial, and antifungal effects, and are used to treat various illnesses[35]. Joshua Nfambi and co-workers investigated in their study, that the *M. oleiferamethanolic* extract of leaf



increased both the cell-mediated and humoral immune reactions in rats. The many macronutrients, micronutrients, and phytochemicals that the plant contains may be too responsible for the immunomodulatory activity. Therefore, the methanolic leaf extract of *M. oleifera* has potential therapeutic efficacy in a number of clinical diseases that depress the immune system[36].

**9. Eupatorium cannabinum:** The genus *Eupatorium* belongs to the family Asteraceae and comprises about 60 species that have mostly been used in folk medicine or as ornamental plants. Among species, many possess a wide range of pharmacological activities, such as cytotoxic, antifungal, insecticidal, antibacterial, antiinflammatory, and antinociceptive activities. *E. cannabinum* L., commonly known as hemp-agrimony, is a perennial herbaceous species distributed in the northern hemisphere, especially in Europe and North America [37]. A study of the essential oil of *E. cannabinum* subsp. *Cannabinum* L. obtained from the aerial parts identified high percentage of terpenoids, such as germacrene, monocyclic sesquiterpene, found in large amount. *Eupatoriumcannabinum* is currently used as an ingredient of immunostimulatory drug preparation. Of the two homogeneous polysaccharides (PI and PII) isolated from *E. cannabinum* and *E. perfoliatum*, PI has been reported to differntiately to enhance the microphagocytosis chemiluminescence by a much larger margin than PII[38].

## II. CONCLUSION:

Several biomolecules (herbs) are employed to improve the body's response to infection. Many medications derived from plants are now being introduced to the market through appropriate clinical trials. A higher level of protective antibodies against various infections, as well as the production and development of a more potent cell-mediated immune response, may be obtained through the use of various plant extracts and herbal supplemented additives in specific doses during the prescribed vaccination regimen. As a result, using herbal formulations as effective immunomodulators may be advised.

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