



Review Article

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A REVIEW ON IMMUNOMODULATORY PLANTS IN INDIA AND THEIR SIGNIFICANCE

V. Sruthi ^{1*}, G. Baba Shankar Rao ²

¹ Department of Pharmacognosy, MNR College of Pharmacy, Sangareddy, Telangana, India

² Department of Pharmacognosy and Phytochemistry, School of Pharmacy, Anurag Group of Institutions, Ghatkesar, Telangana, India

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*Corresponding author

E-mail: reachsruthireddy@gmail.com

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ABSTRACT

An immunomodulator is a substance that either suppresses or stimulates immunity components. Currently, immune system modulation using different herbal constituents is an investigational scientific subject. Several herbal plants belonging to India were found to have an immunomodulatory effect. Various therapeutic effects of plant extracts were found because of their wide range of immunomodulatory effects. Plants' immunomodulatory activities are due to phytochemicals like lactones, flavonoids, alkaloids, and glycosides. A remarkable rise in understanding the phytoconstituents' knowledge and their effects and side effect began recently. Plants like *Morus alba*, *Acacia catechu*, *Tinospora cordifolia*, *Allium sativum*, *Mangifera indica* etc., have gained attention. This article mainly focuses on several herbal plants in India that enhance and suppress impaired immune systems under unfavourable conditions.

Keywords: Immunomodulators, Herbal plants, Phytochemicals, Immune system

INTRODUCTION

Plants are the oldest friends of humanity. Herbal medicine is also known as natural or traditional medicine. Immunity alteration using medicinal plants and their products has developed an accepted therapeutic approach¹. Since the early days, the use of plants and minerals for treating several diseases and ailments².

Immunity

The ability of the body to detect and fight many harmful and infectious microbes causing various diseases and protect the body is known as immunity. It is classified as humoral immunity (antibody mediated defence system) and cellular immunity (cell-mediated defence system)³. Immunomodulators work on the complex system of mechanisms of the immune system in a manner not described thoroughly. (Figure 1)

Immunomodulation

From the various developments that are taking place in experimental and clinical immunology, it has been found that traumatic environmental conditions related to the suppression of the immune system are the reason for the occurrence of several infectious diseases and disorders. Evolved because of the interest to provide more excellent protection against contagious agents through how nonspecific and specific immune mechanisms developed. Naturally occurring or synthetic compounds capable of altering those mechanisms offered further possibilities for modulating immune responses⁴.

Immunomodulators

These synthetic or biological substances modulate, stimulate and suppress the immune system (both adaptive and innate). They are classified as Immunosuppressants and Immunostimulants.⁵

Immunosuppressant

Immunosuppression reduces resistance to infections, stress, and environmental or chemotherapeutic factors. They have specific clinical applications as below:

- To suppress graft-versus-host disease in transplantation of bone marrow and also to stop its rejection along with other organs and tissues
- To treat a variety of autoimmune conditions. E.g., myasthenia gravis, rheumatoid arthritis, psoriasis etc.
- To prevent Rh haemolytic disease of the newborn.

Immunostimulant

Immunostimulant is a therapeutic concept having the objective of nonspecific immune system stimulation. This mainly means the non-antigen-dependent stimulation of various cells.

Mechanism of Immuno-stimulation

Immunological defence is a complex relationship between specific and nonspecific, humoral and cellular responses, suppression and stimulation of immunocompetent cells, and the effect of endocrine and other mechanisms on the immune system. Immunostimulants mainly target T or B lymphocytes, and phagocytosis increases, which plays a vital role in immunostimulation. To remain in contact with the reactive cell, macrophage activation is possibly critical for the stimulating agents, along with T lymphocytes stimulation, which can be achieved through macrophages either directly or indirectly⁵.

Side Effects of Immunomodulator Drugs

Alopecia, Pulmonary toxicity, Myelosuppression, Lymphoma, Nephrotoxicity, neurotoxicity, hyperuricemia, elevated LDL cholesterol etc. are the side effects associated with the use of Immunomodulator drugs⁶.

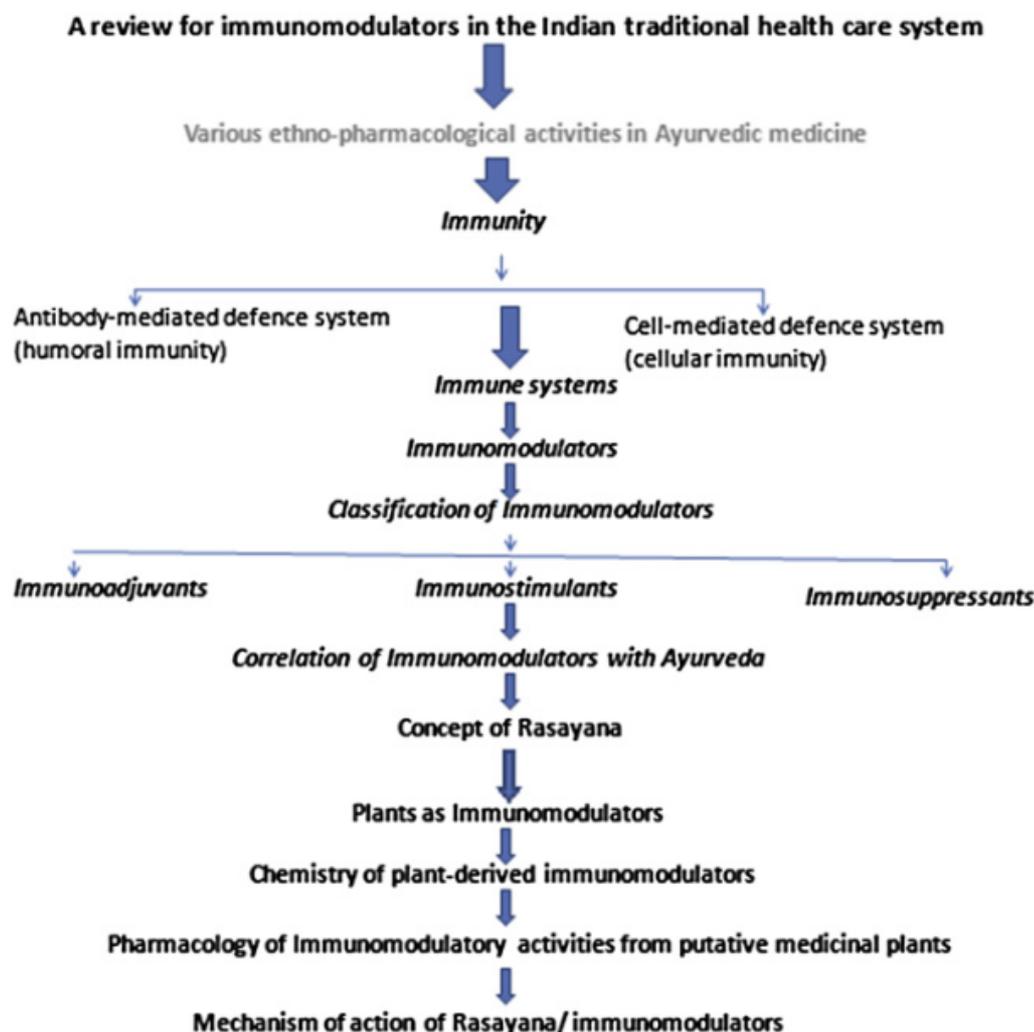


Figure 1: Immunomodulators mechanism⁴

Methods for Testing Immunological Factors

Several *in vitro* and *in vivo* methods for immunological factors testing are listed below ⁷.

In vitro methods

- Inhibition of dihydro-orotate dehydrogenase, T cell proliferation and histamine release inhibition from mast cells
- Mitogen-induced lymphocyte proliferation
- *In vitro* Plaque Forming Colony (PFC) test

In vivo methods

- Spontaneous autoimmune diseases in animals
- Acute systemic anaphylaxis in rats
- Anti-anaphylactic activity (Schultz-Dale reaction)
- Adjuvant arthritis in rats
- Collagen type II-induced arthritis in rats etc.

Types of Immunomodulators

1. Based on Microbial Products source

Bacteria-related immunomodulators were found to either improve or prevent immune cell functions. Antimicrobials have specific nature, while immunomodulators provide broad spectrum competence against microbial diseases ^{8,9}.

2. Synthetic chemical compounds

They are specified drugs and have fewer drug interactions than previous immunomodulators. However, specific side effects like activating latent infections etc., are seen. Immunomodulators affect the cells by producing soluble mediators such as cytokines. They have many side effects associated with them ¹⁰.

3. Therapy using Cow urine

Cow urine stimulates the production of interleukin 1 and 2. It has excellent immunomodulatory properties. It protects against oxidative damage of the DNA responsible for ageing and cancer. It was also found to improve the cell-mediated and humoral immune response in mice and increase B, and T lymphocyte blastogenesis in mice studies ¹¹.

4. Medicinal Plants as Immunomodulators

Immunomodulators have a direct anti-proliferative effect on tumour cells, and the host's ability is enhanced to tolerate damage by toxic chemicals. Various Indian medicinal plants, like *Withania somnifera*, *Tinospora cordifolia*, *Mangifera indica* etc., have been cited for having immunomodulatory activity. Multiple targets of plants' active components are given in Figure 2.

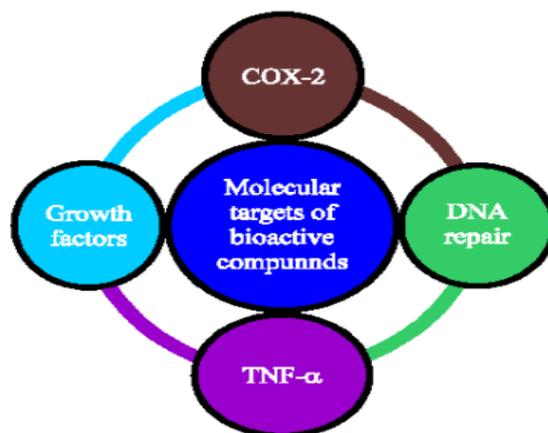


Figure 2: Various targets of plants' active components¹²

Table 1: Some Medicinal essential plants and their uses¹³

Plant	Chemical compound	Medicinal uses
<i>Allium sativum</i>	Organosulfur compounds, extracts	Inhibit the growth of the tumour, modulate the activity of diverse chemical carcinogens, augment macrophages and T lymphocytes and enhance the production of IL-2
<i>Aloe vera</i>	Carboxypeptidase, salicylate, polysaccharides, acemannan, oligosaccharides etc	The anti-inflammatory, immunostimulatory effect, and immunosuppressive help in antibody production and induction of delayed-type hypersensitivity
<i>Andrographis paniculata</i>	Ethanol extract, Purified andrographolides	Stimulation of antibody DTH macrophages migration, phagocytosis of 14C labelled E.coli, inhibits NO production and proliferation of splenic lymphocytes
<i>Asparagus racemosus</i>	Extracts	Induces lag in tumour development, inhibits ochratoxin-induced suppression of IL-1, TNF- α and macrophage chemotaxis, causes the production of TNF
<i>Azadirachta indica</i>	Oils	Stimulates cytokines, activates the immune system
<i>Curcuma longa</i>	Diferuloylmethane, sodium curcumin, volatile oil	Increased mitogenic response of lymphocytes shows anti-inflammatory activity, anti-tumour
<i>Nyctanthes arbor-tristis</i>	Lipids	Stimulates macrophages migration, stimulates response I <i>in vivo</i> studies
<i>Ocimum sanctum</i>	Steroids	Inhibits tumour development in mice, enhances survival of viral encephalitis patients
<i>Panax ginseng</i>	Saponins and steroids	Stimulates T cells proliferation, augments NK cells, chemotaxis, production of cytokines
<i>Phyllanthus embilica</i>	Vitamin C	Enhances NK Cells and ADCC activity against Dalton lymphoma ascites tumour
<i>Tinospora cordifolia</i>	Syringin, cordial	Immunomodulatory property

Immunomodulatory Herbal Plants

In Table 1, some essential herbal plants are listed along with their uses

Withania somnifera

Withania somnifera (Ashwagandha) of the family Solanaceae. It is found to have anti-inflammatory, antiarthritic and antitumor activities. Administration of *Withania* could also enhance the total WBC count, bone marrow cellularity, and esterase-positive cells in mice treated with cyclophosphamide.^{14, 15}

Morus alba Linn. (Mulberry)

Its methanolic extract was administered orally, and as a standard drug, *Ocimum sanctum* (100 mg/kg, PO) was used. *Morus alba* increases both humoral immunity and cell-mediated immunity.¹⁶

Acacia catechu

Acacia catechu (Katha or Karangali) belongs to the family Leguminosae. Its extract exhibited a rise in adhesion of neutrophils to the nylon fibres, which has shown a substantial upsurge in the phagocytic index and considerable protection against cyclophosphamide-induced neutropenia. It also produced a significant rise in serum immunoglobulin levels, indicating its effect on the humoral arm of the immune system. It is widely used in India for its various pharmacological effects.^{17, 18}

Curcuma longa

It is a polyphenol obtained from turmeric. It regulates several transcription factors, cytokines, enzymes etc., related to inflammation and nematocidal activity. Treating with curcumin modifies cellular and humoral immune responses¹⁹.

Allium sativum (Garlic)

Allium Sativum L. (garlic) is the most commonly used plant in traditional medicine and belongs to the family Alliaceae. Garlic is an essential medicinal spice and also exhibits immunomodulation activity. Various studies have confirmed the exciting, helpful properties of garlic on immunity.²⁰

Tinospora cordifolia (Guduchi)

It contains a protein in the stem with lymphoproliferative and macrophage activating properties. This protein was obtained from dry stem powder extract by anion-exchange chromatography on Q-Sepharose and further purified.^{21,22}

CONCLUSION

Alternative medicines are used today as an adjunct therapy for various diseases, including autoimmune diseases. Immunity alteration with the help of herbal plants can provide a substitute for regular chemotherapy for several illnesses. Drugs that modify

the immunity of an organism by increasing the immune response (immunostimulants) or decreasing (immunosuppressants) are called immunomodulatory drugs. They are widely used in autoimmune diseases, allergic reactions, AIDS, cancer and some viral infections. From the present study, it can be confirmed that various available herbal plants have immunomodulatory activity, but insufficient information hinders their practices in clinical practice. Hence these agents will gain more advantages in future research.

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