



(REVIEW ARTICLE)



## Ethnopharmacological review of traditional medicinal plants as immunomodulator

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### Abstract

Medicinal plants play significant roles in the prevention of human beings from various pathogenic microorganisms and diseases. The immunomodulators are agents used to modulate the immune system and can be obtained from both natural as well as synthetic origin from plants and chemicals. Alteration within the system is often achieved by immunomodulatory agents from a plant source, low molecular weight compounds like alkaloids and other nitrogen-containing compounds, terpenes, phenols, and high molecular weight compounds like lectins, polysaccharides. The Immune system is a part of the body to detect the pathogen by using a specific receptor to produce an immediate response by the activation of immune components cells, cytokines, and chemokines and also release of an inflammatory mediator. This review also discusses various ethnopharmacological information of traditional medicinal plants being used as immunomodulators.

**Keywords:** Medicinal plants; Immunomodulators; Immunostimulants; Immunoadjuvants.

### 1. Introduction

Today, worldwide a novel coronavirus disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has emerged as havoc to humanity. The disease has unfolded globally and caused more than three lakh casualties. Worldwide many efforts and measures have been taken by the countries to control this pandemic but it is ceaselessly spreading. Now the dimension of pandemic forces us to explore the available options present in all knowledge systems practicing globally [1, 2]. A ray of hope has come from China wherever they used Traditional Chinese Medicine (TCM) to treat COVID-19 cases and to seek out better recovery results. This can also draw the attention of the scientific community to Ayurveda classics and their experimental knowledge to get explored for finding a cure for this pandemic [3].

Nowadays, the use of plants or parts thereof is being used worldwide, and in the COVID-19 situation, WHO recommending to use of herbal medicines for treatment or prophylactic use in the prevention of diseases or disorders. There are thousands of plants that are being used throughout the world as medicinal plants [4-10]. According to the World Health Organization, around 80% of the world population uses herbal medicines for primary health care, particularly across South Asia and Europe. Research studies indicate that along with building up the body's immunity, they also have anti-inflammatory properties and relatively have fewer side effects [11-12].

The System is one of the foremost complex biological systems within the body. At the time of infection, the immune system goes under the attack of a large number of viruses, bacteria, and fungi. Modulation of immune functions by utilizing medicinal plants and their products as a possible therapeutic measure has become an accepted therapeutic

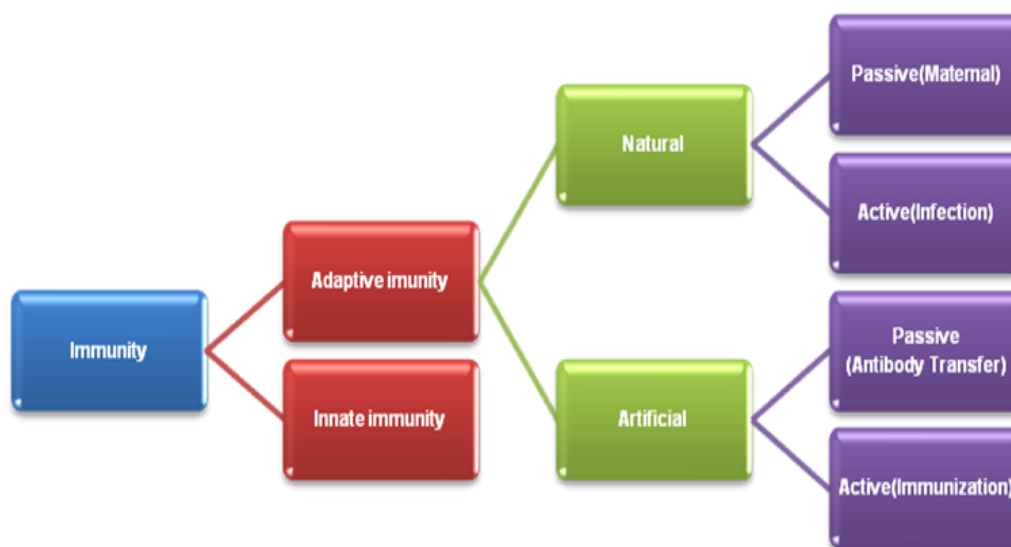
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approach. Plants and minerals have been used since ancient times for the treatment of many infirmities and diseases. It is now being that immunomodulation of immune response could provide an alternative to conventional chemotherapy for a variety of disease conditions, especially when the host's defense mechanism has to be activated under conditions of impaired immune responsiveness or when a Particular immunosuppressant has to be induced in a situation such as autoimmune disorders or organ transplantation. Immunity is a homeostatic process a series of finely balanced complex, multicellular and physiologic mechanisms that allow an individual to distinguish foreign material from "self" and neutralize and/or eliminate the foreign matter [13-14].

## 2. Immune system

The immune system is multi-layered, with defenses on numerous levels. The most primary is the skin, which is the first barrier to infection. Another one is a physiological condition such as pH and temperature provide living conditions for foreign organisms. Once pathogens enter the body, they deal with the innate immune and acquired or adaptive immune system. Both systems are composed of a mess of cells and molecules that interact in a complex manner to detect and eliminate pathogens. Both detection and elimination of pathogen depend upon chemical bonding: surfaces of immune system cells are engulfed with various receptors, some of them chemically bound with pathogens and some of which bind to other immune system cells or molecules to delegate the complex system of signaling that mediates the immune response [15-17] (See Fig. 1).



**Figure 1** Types of immunity

### 2.1. Innate immune system

The term "innate" refers to that part of the system, with which we are born; that means, it doesn't change or adapt to specific pathogens like an adaptive system. The innate system gives a rapid first line of defense, to keep the early infection in check, giving the adaptive immune system time to build up a more specific response [18]. Innate immunity comprises primarily of a chemical response system called complement, and the endocytic and phagocytic systems, which involve roaming "scavenger" cells, such as macrophages, that detect and immerse extracellular molecules and materials, clearing the system of both debris and pathogens [19].

### 2.2. Adaptive immune system

The adaptive immune system adapts or "learns" to concede specific kinds of pathogens, and retains a "memory" of them for speeding up future responses. The learning occurs during a primary response to a kind of pathogen not encountered before by the system. The primary response is slow, often first only becoming apparent several days after the initial infection, and taking over three weeks to clear an infection. After the primary response clears an infection, the immune system keeps a memory of the kind of pathogen that caused the infection. Should the body be infected again by the equivalent kind of pathogen, the system doesn't need to re-learn to acknowledge the pathogens, because it remembers their specific appearance, and will mount a way more rapid and efficient secondary response [20].

The secondary response is often quick enough so that there are no clinical indications of a re-infection. Immune memory can confer protection up to the lifetime of the organism (measles is a good example in this regard). The adaptive immune system primarily consists of certain types of white blood cells, called lymphocytes, which circulate the body via the blood and lymph systems [21].

### 3. Classification of immunomodulators

The immune system may be a complex system that involves an interwoven network of biochemical mechanisms. The modulation of immune response by various agents to diminish the disease has been of interest for many years, to modulate and potentiate the weapons of your immune system keeping them in a highly prepared state for any threat it may confront with this balancing effect, all subsequent immune responses improve [22].

When your immune system is in this highly prepared state, the invading organisms do not have the time to build up force and strength before the immune system attack demolishes and/or weakens the invader. Immunomodulation is the process of improving immune response in a positive or negative approach by the administration of a drug or compound. Many proteins, amino acids, and natural compounds have shown a huge potential to manage immune responses including interferon- $\gamma$  (IFN- $\gamma$ ) and steroids. These substances, which can stimulate, suppress, or modify any of the immune systems, including both adaptive and innate arms of the immune response. Clinically, immunomodulators can be classified into the following three categories (See Fig. 2) [23-24].



**Figure 2** Classification of immunomodulators

#### 3.1. Immunoadjuvants

These agents are used to increase the efficacy of vaccines and, therefore, could be considered specific immunostimulants. Immunoadjuvants act as true modulators of the immune response [25].

#### 3.2. Immunostimulants

Immunostimulants are inherently non-specific as they are envisaged as enhancements to a body's resistance to infection. They can act through innate and adaptive immune responses. In healthy individuals, Immunostimulants are expected to serve as prophylactic and promoter agents by boosting the basic level of an immune response. In the individual with impairment of immune response, they are expected to act as immunotherapeutic agents [26].

#### 3.3. Immunosuppressants

These are a structurally and functionally heterogeneous group of drugs, which are often concomitantly administered in combination regimens to treat various types of organ transplant rejection and autoimmune diseases [27].

### 4. Methods for testing immunological factors

The routine method for screening is to extract one ingredient and single distilled fraction from flavoring medicine and verify its bioactivity by the classic medical specialty means that the total animal model is that the foremost classic medical specialty screening model, which is extraordinarily vital within the facet of drug analysis as a result of it will answer to the efficaciousness, facet impact, and toxicity of medicines as a full. Though this methodology is high value and low potency, it's still a primary due to drug discovery and analysis [28].

Many *in-vitro* and *in-vivo* strategies of medical specialty screening of healthful plants having immunomodulatory activity are listed below:

#### 4.1. *In-Vitro* Methods

(i) Inhibition of histamine release from mast cells, (ii) Mitogen induced lymphocyte proliferation, (iii) Inhibition of T cell proliferation, (iv) Chemiluminescence in macrophages PFC (plaque-forming colony) test *in vitro*, (v) Inhibition of dihydro-orotate dehydrogenase.

#### 4.2. *In-Vivo* Methods

(i) Spontaneous autoimmune diseases in animals, (ii) Acute systemic anaphylaxis in rats, (iii) Anti-anaphylactic activity (Schultz-Dale reaction), (iv) Passive cutaneous anaphylaxis, (v) Arthus type immediate hypersensitivity, (vi) Delayed type hypersensitivity, (vii) Reversed passive Arthus reaction, (viii) Adjuvant arthritis in rats, (ix) Collagen type II-induced arthritis in rats, (x) Proteoglycan-induced progressive polyarthritis in mice, (xi) Experimental autoimmune thyroiditis, (xii) Coxsackievirus B3-induced myocarditis, (xiii) Porcine cardiac myosin-induced autoimmune myocarditis in rats, (xiv) Experimental allergic encephalomyelitis, (xv) Acute graft versus host disease (GVHD) in rats, (xvi) Influence on SLE-like disorder in MRL/LPR mice, (xvii) Prevention of experimentally induced myasthenia gravis in rats, (xviii) Glomerulonephritis induced by anti-basement membrane antibody in rats, (xix) Auto-immune uveitis in rats, (xx) Inhibition of allogeneic transplant rejection.

### 5. Pharmacology of immunomodulatory plants

There is associate excessive would like for understanding plant-based drug medical specialty profile, administration, and dosage, since high doses tend to be immunological disorder and low doses of constant, tend to become immunostimulatory. Finally, it ought to be noted that the bulk of *in vitro* or *in vivo* models are not adequate or not straightforward enough to form certain that the same is commonly used as a drug. Several phytoconstituents from plants like polysaccharides are taken into consideration to be biological response modifiers and are reportable to bolster varied immune responses, like complement activation, a proliferation of lymphocytes, and stimulation of macrophages [29].

The immunopharmacological activities of phenolic are complicated and are still not fully understood. *In-Vitro* study does not forever settle for as true with observations *in vivo* study. Moreover, the consequences of various flavonoids could also be antagonistic; in some cases, they're an immunological disorder, and in others, an immunostimulatory. Varied flavonoids a square measure seen to influence the performance of protein systems that a square measure critically concerned at intervals the immunologic response, and at intervals the generation of inflammatory processes, particularly within the transduction of cellular activation signals [30]. The Asteraceae family is the largest flowering plant having immunomodulatory activity. This family consists of about 900 genera and some 13,000 species [31]. Different plants having immunomodulatory activity are listed in Table 1.

**Table 1** List of plants having immunomodulatory activity

SN	Plant name	Family	Part use
1	<i>Boerhaavia diffusa</i>	Nyctaginaceae	Root
2	<i>Curcuma longa</i>	Zingiberaceae	Rhizome
3	<i>Rhododendron spiciferum</i>	Ericaceae	Leaf
4	<i>Caesalpinia bonducella</i>	Caesalpinaceae	Whole plant
5	<i>Tinospora cordifolia</i>	Menispermaceae	Whole plant
6	<i>Capparis zeylanica</i>	Capparidaceae	Whole plant
7	<i>Luffa cylindrical</i>	Cucurbitaceae	seed and fruit (bulb)
8	<i>Withania somnifera</i>	Solanaceae	Whole plant
9	<i>Asparagus racemosus</i>	Asparagaceae	Root
10	<i>Panax ginsengs</i>	Araliaceae	Root
11	<i>Nelumbo nucifera</i>	Nymphaeaceae	rhizome and seed
12	<i>Azadiracta indica</i>	Meliaceae	Leaf
13	<i>Arnica montena</i>	Compositae	Dried flowers head
14	<i>Calendula officinalis</i>	Asteraceae	Flower
15	<i>Echinacea purpurea</i>	Asteraceae	Flowering top
16	<i>Euphorbia tirucalli</i>	Euphorbiaceae	Latex
17	<i>Ocimum sanctum</i>	Lamiaceae	Leaf

### 5.1. *Boerhaavia diffusa*

*Boerhaavia diffusa*, (Punarnava; Family Nyctaginaceae), could also be a crawl weed found profusely each ever India. In Indian ancient medication, roots of this weed are used for the treatment of indigestion, jaundice, enlargement of spleen, abdominal pain, and associate degree as an anti-stress agent. Extraction of *Boerhaavia diffusa* in methane series, chloroform & grain alcohol solvents, they isolated two different compounds, i.e. Bd-I (eupalitin-3-O-h-Dgalactopyranoside) and Bd-II (eupalitin) by Flash action. The methane series extract stifled considerably PHA-stimulated proliferation of human peripheral blood mononucleate cells at the concentration of ten µg/ml, whereas chloroform and grain alcohol extract offer this activity at the concentration of fifty µg/ml. The suppression by Bd-I and Bd-II is dose-dependent and ranged from 63 to 98 you have to attempt a five hundred µg / milliliter to 7–14 attempt five µg /ml. On the opposite hand, the impact of chloroform extract on NK cell is eighty-four, the ethanolic extract is forty-eighth however, the Bd-I & Bd-II is incredibly low [32].

### 5.2. *Curcuma longa*

Curcumin could be a main active constituent of *Curcuma longa* Linn belonging to the family Zingiberaceae. Asian nations are the largest country that produces turmeric (about ninetieth of the whole output of the world). Liliopsid genus is also a genus of concerning seventy species of stalk herbs distributed in South East Asia particularly China, Thailand, and Asian nation. Curcumin is employed for the treatment of medicine, antiarthritic, common colds & coughs, jaundice [33]. The inhibition of IL-2 induced proliferation of cells was dose-dependent; since the increasing suppressive effect was observed at increasing concentration of curcumin from 6.25 to 25 mol/L. IL-2 induced proliferation of spleen cells was completely inhibited by curcumin at 25 mol/L (See Table 2).

**Table 2** Effect of curcumin on proliferation (p) of splenic lymphocytes

Compound	Dose	Effect
Curcumin	6.25 µmol/L, 12.5 µmol/L, 25 µmol/L	P<0:001, P < 0:0001, completely blocked

### 5.3. *Rhododendron spiciferum*

The plant *Rhododendron spiciferum* belonging to the Ericaceae. They will be widely used as a medicinal plant due to their active constituent's proanthocyanidin A-1 (PAA-1) is very used for health. Proanthocyanidin A-1 (PPA-1) is used attributable to the unconventional scavengers, anti-bacterial agents, and effective protein inhibitors. They conjointly exhibit the activity of vasodilators, anti-allergic, medicinal drug, cardio-protective, immune-stimulating, antiviral, and sex hormone activities [34-35].

### 5.4. *Caesalpinia bonducella*

*Caesalpinia bonducella* belonging to the Caesalpiniaceae. It's commonly referred to as Nata Karanja. It's an indigenous plant of India but also found to be Myanmar, Sri Lanka. The *Caesalpinia* prickly shrub, globular-shaped seeds with a smooth shining surface. The Seeds of those plants contain thick, brittle shells with a yellowish-white bitter fatty kernel. *Caesalpinia bonducella* has employed the shows following therapeutic activity like antipyretic, antidiuretic, anthelmintic and antibacterial, anti-anaphylactic and antidiarrheal, antiviral, antiasthmatic, antiamebic, and anti-estrogenic.

Within the treatment of liver disorder and tumor, bonduc has been traditionally used. Extraction of *Caesalpinia bonducella* by the recent extraction process using ethanol as a solvent. This extract is employed for the activity of immunomodulatory within the mouse. The oral administration of *Caesalpinia bonducella* (ethanolic extract) within the mouse the effect of this is often given below (see Table 3) [36].

**Table 3** Phagocytic response of extract in mouse

Compound	Dose	Phagocytic index
<i>Caesalpinia bonducella</i> extract(ethanolic)	200 mg/kg	4.72±0.66,
	300mg/kg	5.15±0.27
	400mg/kg	6.19±0.45
	500mg/kg	8.13±0.39

### 5.5. *Tinospora cordifolia*

*Tinospora cordifolia* belonging to the family of Menispermaceae. This is often a perennial climber distributed throughout the tropical Indian subcontinent. It's categorized as in Ayurveda and documented for its adaptogenic and immunomodulatory activity in fighting infection. The activity of this drug appears to flow from to alkaloid. The drug shows immunomodulatory activity. It's shown to be effective against various sorts of experimental induce infection [37].

In *Tinospora cordifolia* extract is referred to as a-d-glucan RR1. The recent extraction process employed for the extraction. In the extraction process the methanol, trichloroacetic acid is employed as a solvent .the compound RRA-1 is isolated from this extract by the tactic of chromatography & lyophilization process [38].

They have according to that the result of *Tinospora cordifolia* extracts on leucocyte activation. The dose of the extract is one hundred µg/ml can offer the result of leucocyte activation i.e. the activation of β-cells is thirty-ninth, T-cells one hundred and fifth, and NK cells is 331% severally. Throughout this result the result of the extract on the NK cells is high; this might be vital|a crucial|a vital|a very important feature as a result of the NK cells square measure important effectors of innate immune system [39].

### 5.6. *Capparis zeylanica*

*Capparis zeylanica*, family Cappridaceae is typically mentioned as Indian caper, perhaps an ascent bush found throughout Republic of India and has been used as a 'Rasayana' drug at intervals the standard in Northern India; the leaves square measure wide used as counter-irritant, medicine and as a plaster, in swellings, boils, and piles. The varied Fig.6 *Capparis zeylanica* species of *Capparis* square measure helpful at intervals the treatment of cough, asthma, inflammation, fevers, and infectious disease and additionally helpful as poultice in urarthritis [40].

The result of immunomodulatory activity of ethanolic and water extracts of *Capparis zeylanica* leaves. This extract was used to the determination of cellular and body substance reaction victimization white blood corpuscle adhesion take a look at, somatic cell activity in sheep RBCs. The solvent used for the extraction fossil fuel ether, ethanol, and so the processes square measure hot extraction (Soxhlet). A big ( $P < \text{zero}.05$ ) increase within the *in vitro* white blood corpuscle adhesion to nylon fibers by water extract (at a dose of three hundred mg/kg, oral). However, ethanolic extract (150–300 mg/kg) doesn't show any important increase in white blood corpuscle adhesion [41].

### 5.7. *Nelumbo nucifera*

*Nelumbo nucifera* is a plant belonging to the family of Nymphaeaceae. This plant could also be a well-known aquatic healthful plant that has been used as a typical medication in The Republic of India. The stalk extract of the sacred lotus, be employed for the activity of symptom, antidiarrheal, antimicrobial, diuretic, antipyretic, pharmacological medicine, medication. The seed of this plant is in addition, used for resultant activity as well as an anti-ischemic, inhibitor, hepatoprotective, antiproliferative, medication. The plant contains betulinic acid and hormone pentacyclic triterpenoid. Every extract of this plant is utilized for immunomodulatory activity [42].

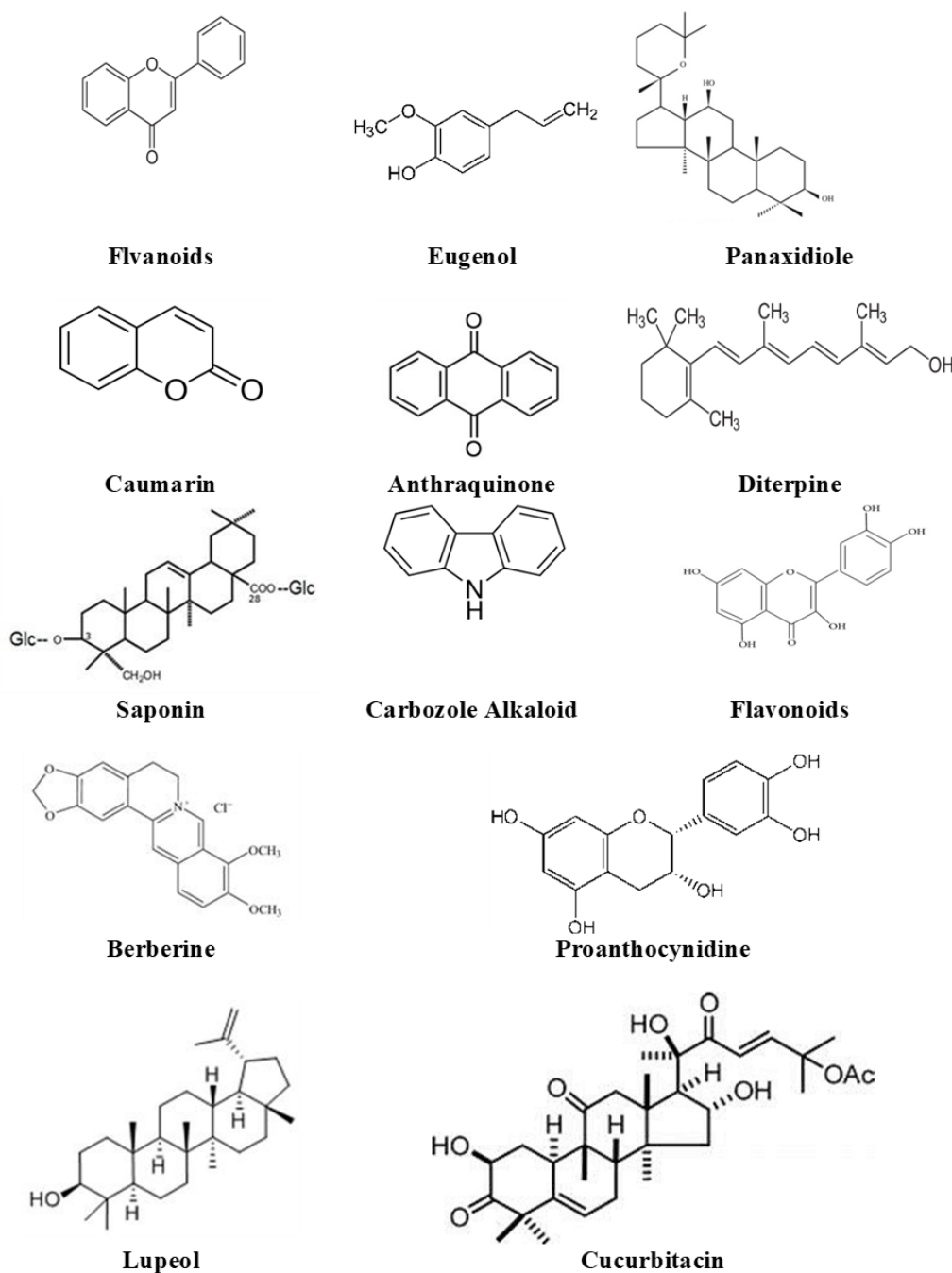
The immunomodulatory effect of the plant extracts *Nelumbonucifera*, in Swiss albino mice. The extract (NNSE and NNRE) of rhizome and seeds was extracted with 70% ethanol by cold maceration process. It has been reported the activity is dose-dependent, i.e. the improvement of NBT (Nitro blue tetrazolium reduction test) a reduction was determined additional considerably at higher doses of each the extracts, three hundred mg/kg NNSE,  $P < 0.001$ ; NNREP  $< 0.01$ ) and then that of their lower dose 100 mg/kg when compared to control 100 mg/kg ( $P < 0.01$ ), 300 mg/kg ( $P < 0.001$ ) [43].

During their study, they were determined that adherence of neutrophils to the nylon fiber was augmented in each NNRE and NNSE treated teams as compared to the management and ended that hydroalcoholic extracts of a rootstock and seeds of a lotus showed stimulation of weapons system by modulating the medicine parameters and shows potential therapeutic edges of the plant components on immunomodulation [44].

### 5.8. *Allium sativum*

*Allium sativum* a crucial medicinal plant having immunomodulatory effects. Three proteins showing immunomodulatory were discrete from garlic by Q-Sepharose chromatography of 30 kD ultrafiltrate of raw garlic extract of these proteins shows the mitogenic activity towards human peripheral blood lymphocytes, murine splenocytes, and thymocytes [45-46].

The extraction of garlic was prepared by blending the bulbs in phosphate buffer saline (pH, 7.4). Followed by ammonium sulfate precipitation and were isolated by ultra-filtration, and anion exchange chromatography using Q-Sepharose (High Performance) column taking unbuffered 20 mm 1, 3-diamino propane taken in 1:10 ratio (w/v), Tris-HCl buffer, pH 8, and NaCl. The eluted fractions were monitored by absorbance at 280 nm [47]. The richly present garlic ImPs, QR-1 and QR-2, identified in the present study agglutinins ASA II and ASA I, was found to be potent mutagenic activity having potential utility in therapeutic immunomodulation [48]. Many other plants show immunomodulation activities (See Table 4)



**Figure 3** Bioactive molecules showing immunomodulatory activity

**Table 4** A brief descriptions of common plant-derived immunomodulators

<b>Botanical (Family) name</b>	<b>Ayurvedic/ Common name</b>	<b>Part used</b>	<b>Chemical constituents</b>	<b>Other biological activities</b>
<i>Ocimum sanctum</i> Linn. (Labiatae)	Tulasi	Entire Plant	Essential oils such as eugenol, carvacrol	Carminative, stomachic, antispasmodic, antiasthmatic, hepatoprotective.
<i>Morus alba</i> Linn. (Moraceae)	Brahmdaru	Fruits, leaves, bark, Fruits,	Flavonoids, anthocyanin's	Expectorant, hypocholesterolaemic, diuretics.
<i>Panax ginseng</i> Wall. (Araliaceae)	Ninjin	Fruits, root	Saponins such as ginsenosides, panaxdiol, panaxtriol and oleanolic acid	Adaptogenic properties, antiarrhythmics.
<i>Achillea millefolium</i> C. Koch (Compositae)	Yarrow	Leaves	Flavonoids, alkaloids, polyacetylenes, coumarins, triterpenes	Anti-inflammatory, antispasmodic, antipyretic, diuretics.
<i>Aloe vera</i> Tourn. Ex Linn. (Liliaceae)	Kumaari	Gel from leaves	Anthraquinone glycosides	Purgative, emmenagogue, emollient, anti-inflammatory.
<i>Andrographis paniculata</i> Nees (Acanthaceae)	Kaalmegha	Leaves	Diterpenes	Hepatoprotective, antispasmodic, blood purifier, febrifuge
<i>Asparagus racemosus</i> Wild. (Liliaceae)	Shatavari	Roots	Saponins, sitosterols	Ulcer healing agent, nervine tonic, antigout
<i>Murraya koenigii</i> (L) Spreng. (Rutaceae)	Surabhini-nimba	Leaves	Coumarin, carbazole alkaloids, glucoside	Antifungal, insecticidal, insecticidal.
<i>Couroupita guianensis</i> Aubl. (Lecythidaceae)	Nagalinga	Fruits, flowers	Steroids, flavonoids, phenolics	Antifungal.
<i>Tinospora cordifolia</i> Miers. (Menispermaceae)	Amrita, guduuchii	Entire herb	Alkaloidal constituents such as berberine, tinosporic acid	Hypoglycaemic agent, antipyretic.
<i>Lagenaria siceraria</i> Mol. (Cucurbitaceae)	Katu-tumbi	Leaves, fruit	Cucurbitacin, beta-glycosidase	Purgative, emetic.
<i>Terminalia arjuna</i> Roxb. (Combretaceae)	Arjuna	Leaves, bark	Flavonoids, oligomeric	Cardiotonic, diuretic
<i>Bauhinia variegata</i> Linn. (Caesalpiniaceae)	Kaanchana	Roots, bark, buds	Flavonoids, beta-sitosterol, lupeol	Antifungal, astringent.
<i>Urena lobata</i> Linn. (Malvaceae)	Naagabala	Roots, flowers	Flavanoids	Diuretic, emollient, antispasmodic.
<i>Gymnema sylvestre</i> R.Br. (Asclepiadaceae)	Gurmaar	Leaves	Sapogenins	Antidiabetic, diuretic, antibilious.
<i>Cordia superba</i> Cham. And <i>C. rufescens</i> A. DC. (Boraginaceae)	Shleshmaataka	Leaf, fruit, bark	Alpha-amyrin	Anti-inflammatory, antimicrobial.
<i>Picrorhiza scrophulariiflora</i> Benth. (Scrophulariaceae)	Kutki	Roots	Iridoid glycosides, amphicoside	Antioxidant.
<i>Heracleum persicum</i> Desf. (Apiaceae)	Golpar	Shurb	Flavonoids, furanocoumarins	Antimicrobial.
<i>Cissampelos pareira</i> Linn. (Menispermaceae)	Paatha	Roots	Hayatine alkaloids	Antipyretic, analgesic, antilithic.



<i>Abutilon indicum</i> linn. (Malvaceae)	Atibalaa	Whole plant	Flavonoids, triterpenoids	Diuretic, antibacterial.
<i>Chlorophytum borivillianum</i> Sant. F (Liliaceae)	Safed musli	Roots	Sapogenins	Antifungal.
<i>Alternanthera tenella Colla</i> (Amaranthaceae)	Snow Ball	Herb	Flavonoids, triterpenes	Antitumor, anti-inflammatory.
<i>Ganoderma lucidum</i> (Fr.) P. Karst. (Polyporaceae)	Reishi mushroom	Whole plant	Flavonoids, triterpenes	Antioxidant.
<i>Nyctanthes arbor-tristis</i> L. (Oleaceae)	Paarijaata	Leaf, seeds	Iridoid glucosides	Anti-inflammatory, antispasmodic
<i>Actinidia macrosperma</i> C. F. Liang (Actinidiaceae)	Actinidia	Fruits	Alkaloids, saponins	Antileprotic.
<i>Acacia catechu</i> Willd. (Leguminosae)	Khadira	Leaf	Flavonoids, quercetin	Hypoglycaemic, astringent.
<i>Boswellia</i> spp. (Burseraceae)	Shallaki	Gum resin	Triterpenes, ursanes	Hypoglycaemic.
<i>Hibiscus rosa sinensis</i> Linn. (Malvaceae)	Japaa	Flowers	Cyclopropanoids	Antidiarrheal, anti-inflammatory.
<i>Cleome gynandra</i> Linn. (Capperdiceae)	Tilaparni	Leaf, seeds, rots	Hexacosanol, kaempferol	Anti-inflammatory.
<i>Hyptis suaveolens</i> (L.) Poit. (Lamaceae)	Tumbaaka	Leaf, flowers	Lupeol, beta-sitosterol	Carminative, antispasmodic.
<i>Randia dumetorum</i> Lamk. (Rubiaceae)	Madana	Fruits	Saponins, triterpenes	Chlorosis, antiarthritic.
<i>Allium hirtifolium</i> Boiss. (Alliaceae)	Persian shallot	Herb	Thiosulfinates, flavonoids	Antirheumatic, anti-inflammatory.
<i>Acanthopanax sessiliflorus</i> (Rupr. & Maxim.) (Araliaceae)	Prickly spine	Shoots and roots	Biopolymers	Lymphoproliferative activity.
<i>Agelas mauritanus</i> (Porifera)	Agelas	Sponge	Glycolipid (a-galactosylceramide)	Phagocytotic activity.
<i>Aphanothece halophytica</i> (Chroococcales)		Cyanobacterium	Exopolysaccharide	Inhibits influenza virus.
<i>Apium graveolens</i> Linn. (Apiaceae)	Celery Seeds	Leaves, seeds	Flavonoids, coumarins	Anti-inflammatory.
Genus Ardisia (Myrsinaceae)	Marlberry	Shrub, Branches, and leaves	Peptides, saponins, Isocoumarins, quinones, and alkylphenols	The antimetastatic drug, anti-HIV property.
Genus Aristolochia (Aristolochiaceae)	Pipevine	Leaves	Aristolochic acid	Antiangiogenic, employed in prostate cancer.
<i>Artemisia annua</i> Linn. (Compositae)	Wormwood	Herb	Artemisinin	Immunosuppressive.
Genus Aspergillus (Trichocomaceae)	Aspergillus	Fungus	Polyene, triazole	Antifungals.

<i>Botryllus schlosseri</i> (Botryllidae)	Botryllus	Tunicates	Cytokines	Antioxidant, antiviral, antimicrobial and antitumoral.
<i>Bidens pilosa L.</i> (Asteraceae)	Beggar-ticks	Flowers, leaves	Polyacetylenes	Anti-inflammatory, immunosuppressive.
<i>Boerhaavia diffusa</i> (Nyctaginaceae)	Punarnava	Herb	Alkaloid	Immunostimulatory.
<i>Bugula neritina L.</i> (Bugulidae)	Brown bryozoans	Marine invertebrates	Macrocyclic lactones	Immunomodulator.
<i>Byrsonima crassa Nied.</i> (Malpighiaceae)	Byrsonima	Leaves	Flavonoids, tannins, terpenes	Antimicrobial, antioxidant.
<i>Calendula Officinalis L.</i> (Asteraceae)	Garden Marigold	Flowers	Polysaccharides, proteins, fatty acids, carotenoids, flavonoids, triterpenoids	Antitumor antiviral activity, anti-HIV properties.
<i>Camellia sinensis L.</i> (Theaceae)	Tea	Leaves	Epigallocatechingallate, quercetin, gallicacid	Anticancer activity, lipid- lowering activity, anticataract activity, hepatoprotective and antioxidant.
<i>Cannabis sativa</i> (Cannabaceae)	Common hemp	Leaves	Cannabinoids	Immunomodulatory.
<i>Carpobrotus edulis L.</i> (Aizoaceae)	Fig Marigold	Flowers, fruit	Alkaloids	Immunomodulator.
<i>Centella asiatica Linn.</i> (Umbelliferae)	Brahmi	Herb	Triterpenoid saponins	Immunomodulator.

## 6. Conclusion

From this discussion, it's evident that many medicinal plants exert an immunomodulatory effect in experimental models at a specific dose. Different types of *in vivo* and *in vitro* screening methods are employed in determining their pharmacological activity. Some medicinal plants may stimulate the system like *Ocimum sanctum*, *Tinospora cordifolia* and a few of them may suppress the immune responses (Eg. *Alternanthera tenella*). The review also reveals an update of the present immunomodulator plants and their pharmacological aspects. Thus successful results are achieved by following an appropriate screening approach.

## Compliance with ethical standards

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### Disclosure of conflict of interest

The author declares no conflict of interest.

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