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REVIEW ON IMMUNOMODULATION AND IMMUNOMODULATORY ACTIVITY OF SOME MEDICINAL PLANT

Singune Shantilal*, Vaghela J. S. and Sisodia S. S.

B N College of Pharmacy, B N University, Udaipur, Rajsthan, India.

***Corresponding Author: Singune Shantilal**
B N College of Pharmacy, B N University, Udaipur, Rajsthan, India.

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ABSTRACT
Alteration in the immune system can be achieved by immunomodulatory agents from plant source, The use of phytochemicals has been a supportive practice for our immune system against infections since centuries as these drug substances enhance the immune response against infections. There are abundant plants which possess immunomodulatory and immunostimulatory activities. The present review summarizes some of Indian medicinal plants with immunomodulation action and also to provide insights into the future research in this area.

Keywords: Immune system , Immunomodulation,medicinal plants.

INTRODUCTION
Immune system is a remarkably sophisticated defence system within vertebrates, to protect them from invading agents. It is able to generate varieties of cells and molecules capable of recognizing and eliminating limitless varieties of foreign and undesirable agents. Modulation of the immune system denotes to any change in the immune response that can involve induction, expression, amplification or inhibition of any part or phase of the immune response. Thus, immunomodulatory is a substance used for its effect on the immune system. There are generally of two types immunomodulators based on their effects: immunosuppressants and immunostimulators. Immunopharmacology is a comparatively new and developing branch of pharmacology aims at searching for immunomodulators. The potential uses of immunodulators in clinical medicine include the reconstitution of immune deficiency (e.g. the treatment of AIDS) and the suppression of normal or excessive immune function (e.g. the treatment of graft rejection or autoimmune disease). Specific immunomodulators administered together with antigens known as immunological adjuvants to boost the immune response to the vaccine constituents.[1] The basic function of immune system is to protect against foreign pathogens and infectious agents. This is achieved either through innate or natural immunological mechanisms which essentially serve as a short term first line defence or through elaborate adaptive mechanisms which are highly specific, complex, and marked by diversity and memory. In both types of immunity, cells and molecules play important roles.[2] Immunology is thus probably one of the most rapidly developing areas of biomedical research and has great promises with regard to the prevention and treatment of a wide range of disorders.[3]

According to the World Health Organization (WHO), about three-quarters of the world population relies upon traditional remedies (mainly herbs) for the health care of its people. In fact, herbs and/or plants are the oldest friends of mankind. They not only provided food and shelter but also served to cure different ailments. Herbal medicine, sometimes called traditional or natural medicine, has always existed in one way or another in different cultures and civilizations, such as Ayurvedic (India), Egyptian, Western, Chinese, Kampo (Japan) and Greco-Arab or Unani- Tibb (south Asia). Traditional medicine all over the world is currently being revalued through extensive research activity on various plant species and their therapeutic properties. Various plants identified in the Indian Ayurvedic system of medicine display a wealth of pharmacological properties. The ayurvedic system of medicine is one of the oldest systems of medicine and includes various ethnopharmacological activities such as immunostimulation, tonic, neurostimulation, anti-ageing, antibacterial, antiviral, antirheumatic, anticancer, adaptogenic, etc.[4]

IMMUNE SYSTEM
The immune system is composed of many interdependent cell types that collectively protect the body from bacterial, parasitic, fungal, viral infections and from the growth of tumor cells. Many of these cell types have specialized functions. The cells of the

immune system can engulf bacteria, kill parasites or tumour cells, or kill viral infected cells. Often, these cells depend on the T helper subset for activation signals in the form of secretions formally known as cytokines, lymphokines, or more specifically interleukins.

The Innate Immune System

Innate immunity comprises a series of host defenses including barrier function, cytokines, complement, phagocytes, natural killer (NK) cells, and gamma-delta(gd) T cells to provide the initial (nonspecific) response to a pathogen or injury. These responses are phylogenetically ancient and have been developed to cope with pathogens that are encountered regularly but that rarely cause disease. Unlike the adaptive (specific) immune system, responses are generic and leave no memory; nonetheless the innate immune system functions effectively to keep organisms healthy. Indeed a failing in innate immunity is hypothesized to contribute to secondary infections in critical illness and death in sepsis.Stimulation of the active components of the innate immune system occurs by way of pathogen-associated molecular pattern (PAMP) receptors or damageassociated molecular pattern (DAMP) receptors. PAMPs are recognized by membrane bound or vesicular pathogen recognition receptors (PRRs) including the Tolllike receptors (TLRs), nucleotide binding oligomerization domain (NOD)-like receptors, and RIG-I like receptors. Bacteria stimulate these PRRs to activate various intracellular signalling cascades, leading to a proinflammatory response. For example, the gramnegative bacteria endotoxin, lipopolysaccharide, binds to TLR 4, whereas the gram-positive peptidoglycan binds to TLR 2 In the setting of tissue damage from an infection or trauma, DAMPs activate the innate immune system through these PRRs. Indeed there is significant overlap in mechanisms stimulated by PAMPs and DAMPs. As sedatives are frequently administered during infection and surgery, investigation of their immune effects on these mechanisms of immune stimulation would seem prudent.

The Adaptive Immune System

Adaptive or acquired immunity differs from the innate response as it is specific, has an element of memory, and is unique to vertebrates. The humoral component involves the proliferation of antigen-stimulated B lymphocytes into antibody-secreting plasma cells. The cellular component is mediated by T lymphocytes, the predominant cell types being helper T cells (Th) and cytotoxic T cells. Recently, regulatory T cells that likely dampen the immune response have been identified. T cells recognize antigens bound to major histocompatibility complex (MHC) proteins by way of T cell receptors that are antigen specific. Th lymphocytes act through secretion of cytokines to elaborate and prime the immune response. This action includes inducing immunoglobin classs witching of B cells, activation of Tc,and optimization of bactericidal capacity of phagocytes. Th lymphocytes are characterized by expression of CD4 proteins and are activated when MHC type II molecules, expressed on professional antigen-presenting cells (dendritic cells, macrophages, and B cells), activate the specific T cellreceptor.Th1 cells are regarded as ”proinflammatory’’ secreting cytokines such as interferon-g and interleukin (IL)-12, and stimulate macrophage function and cytotoxic T cell function. Th2 cells have an “anti-inflammatory” phenotype and secrete cytokine such as IL-4 and IL-10, acting cooperatively to activate B cells. Further, Th cells include the regulatory T cells that act to dampen the immune response and the Th17 class that modulates neutrophil function. A shift from Th1 to Th2 cells has been observed in the latter stages of sepsis, possibly induced by the apoptotic cell death of lymphocytes, and the subsequent anti-inflammatory phenotype has been associated with secondary infections in this patients.[5]

The Organs of the Immune System

Bone Marrow: All the cells of the immune system are initially derived from the bone marrow. They form through a process called hematopoiesis. During hematopoiesis, bone marrow-derived stem cells differentiate into either mature cells of the immunesystem or into precursors of cells that migrate out of the bone marrow to continue their maturation elsewhere. The bone marrow produces B cells, natural killer cells, granulocytes and immature thymocytes, in addition to red blood cells and platelets.

Thymus: The function of the thymus is to produce mature T cells. Immature thymocytes, also known as prothymocytes, leave the bone marrow and migrate into the thymus. Through a remarkable maturation process sometimes referred to as thymic education, T cells that are beneficial to the immune system are spared, while those T cells that might evoke a detrimental autoimmune response are eliminated. The mature T cells are then released into the bloodstream.

Spleen: The spleen is an immunologic filter of the blood. It is made up of B cells, T cells, macrophages, dendritic cells, natural killer cells and red blood cells. In addition to capturing foreign materials (antigens) from the blood that passes through the spleen, migratory macrophages and dendritic cells bring antigens to the spleen via the bloodstream. An immune response is initiated when the macrophage or dendritic cells present the antigen to the appropriate B or T cells. This organ can be thought of as an immunological conference center. In the spleen, B cells become activated and produce large amounts of antibody. Also, old red blood cells are destroyed in the spleen.

Lymph nodes: The lymph nodes function as an immunologic filter for the bodily fluid known as lymph. Lymph nodes are found throughout the body. Composed mostly of T cells, B cells, dendritic cells and macrophages, the nodes drain fluid from most of our tissues. Antigens are filtered out of the lymph in the

lymph node before returning the lymph to the circulation. In a similar fashion as the spleen, the macrophages and dendritic cells that capture antigens present these foreign materials to T and B cells, consequently initiating an immune response.[6,7,8]

The Cells of the Immune System

T-Cells: T lymphocytes are usually divided into two major subsets that are functionally and phenotypically (identifiably) different. The T helper subset, also called the CD4+ T cell, is a pertinent coordinator of immune regulation. The main function of the T helper cell is to augment or potentiate immune responses by the secretion of specialized factors that activate other whiteblood cells to fight off infection. Another important type of T cell is called the T killer/suppressor subset or CD8+ T cell. These cells are important in directly killing certain tumor cells, viral-infected cells and sometimes parasites. The CD8+ T cells are also important in down-regulation of immune responses. Both types of T cells can be found throughout the body. They often depend on the secondary lymphoid organs (the lymph nodes and spleen) as sites where activation occurs, but they are also found in other tissues of the body, most conspicuously the liver, lung, blood, and intestinal and reproductive tracts.

Natural Killer Cells: Natural killer cells, often referred to as NK cells, are similar to the killer T cell subset (CD8+ T cells). They function as effector cells that directly kill certain tumors such as melanomas, lymphomas and viralinfected cells, most notably herpes and cytomegalovirusinfected cells. NK cells, unlike the CD8+ (killer) T cells, kill their targets without a prior "conference" in the lymphoid organs. However, NK cells that have been activated by secretions from CD4+ T cells will kill their tumor or viralinfected targets more effectively. B Cells: The major function of B lymphocytes is the production of antibodies in response to foreign proteins of bacteria, viruses, and tumor cells. Antibodies are specialized proteins that specifically recognize and bind to one particular protein that specifically recognize and bind to one particular protein. Antibody production and binding to a foreign substance or antigen, often is critical as a means of signalling other cells to engulf, kill or remove that substance from the body. Granulocytes or Polymorphonuclear (PMN) Leukocytes: Another group of white blood cells is collectively referred to as granulocytes or polymorphonuclear leukocytes (PMNs). Granulocytes are composed of three cell types identified as neutrophil, eosinophils and basophils, based on their staining characteristics with certain dyes. These cells are predominantly important in the removal of bacteria and parasites from the body. They engulf these foreign bodies and degrade them using their powerful enzymes.

Macrophages: Macrophages are important in the regulation of immune responses. They are often referred to as scavengers or antigen-presenting cells (APC) because they pick up and ingest foreign materials and present these antigens to other cells of the immune system such as T cells and B cells. This is one of the important first steps in the initiation of an immune response. Stimulated macrophages exhibit increased levels of phagocytosis and are also secretory.

Dendritic Cells: Another cell type, addressed only recently, is the dendritic cell. Dendritic cells, which also originate in the bone marrow, function as antigen presenting cells (APC). In fact, the dendritic cells are more efficient apcs than macrophages. These cells are usually found in the structural compartment of the lymphoid organs such as the thymus, lymph nodes and spleen. However, they are also found in the bloodstream and other tissues of the body. It is believed that they capture antigen or bring it to the lymphoid organs where an immune response is initiated. Unfortunately, one reason we know so little about dendritic cells is that they are extremely hard to isolate, which is often a prerequisite for the study of the functional qualities of specific cell types. Of particular issue here is the recent finding that dendritic cells bind high amount of HIV, and may be a reservoir of virus that is transmitted to CD4+ T cells during an activation event.[9-12]

Immunomodulators

These are biological or synthetic substances that can stimulate, suppress or modulate any aspect of the immune system including both adaptive and innate arms of the immune system.

Immunoadjuvant: These agents are used for enhancing vaccines efficacy and therefore, could be considered specific immune stimulants 31 example in this regard is of Freud's adjuvant. The immunoadjuvant hold the promise of being the true modulators of immune response. It has proposed to exploit them for selecting between cellular and humoral, Th1 (helper T1 cells) and Th2, (helper T2 cells) immunoprotective and immunodestructive, and reagenic (IgE) versus immunoglobin G (IgG) type of immune responses, which poses to be a real challenge to vaccine designers.[13]

Immunostimulant: These agents are inherently nonspecific in nature as they envisaged enhancing body's resistance against infection. They can act through innate immune response and through adaptive immune response. In healthy individuals the Immunostimulant are expected to serve as prophylactic and promoter agents i.e. as immunopotentiators by enhancing basic level of immune response, and in the individual with impairment of immune response as immunotherapeutic agents.[14-19]

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.[20]

Methods for Testing Immunological Factors[21]

The routine process for screening is to extract single ingredient or single distilled fraction from herbal drugs, determine its bioactivity by the classic pharmacological means. The whole animal model is the most classic pharmacological screening model, which is very important at the aspect of medicine evaluation because it can apparently respond to the efficacy, side effect and toxicity of medicines in whole. Although this method is high cost and low efficient, at present it is still a primary way to drug discovery and evaluation. Several *in vitro*, *in vivo* methods of pharmacological screening of medicinal plants having immunomodulatory activity have been listed.

***In vitro* methods**

1. Inhibition of histamine release from mast cells
2. Mitogens induced lymphocyte proliferation
3. Inhibition of T cell proliferation
4. Chemiluminescence in macrophages
5. PFC (plaque forming colony) test *in vitro*
6. Inhibition of dihydro-orotate dehydrogenase

***In vivo* methods**

1. Spontaneous autoimmune diseases in animals
2. Acute systemic anaphylaxis in rats
3. Anti-anaphylactic activity (Schultz-Dale reaction)
4. Passive cutaneous anaphylaxis
5. Arthus type immediate hypersensitivity
6. Delayed type hypersensitivity
7. Reversed passive arthus reaction
8. Adjuvant arthritis in rats
9. Collagen type II induced arthritis in rats
10. Proteoglycan-induced progressive polyarthritis in mice
11. Experimental autoimmune thyroiditis
12. Coxsackievirus B3-induced myocarditis
13. Porcine cardiac myosin-induced autoimmune myocarditis in rats
14. Experimental allergic encephalomyelitis
15. Acute graft versus host disease (GVHD) in rats
16. Influence on SLE-like disorder in MRL/lpr mice
17. Prevention of experimentally induced myasthenia gravis in rats
18. Glomerulonephritis induced by antibasement membrane antibody in rats
19. Auto-immune uveitis in rat

Table 1 A brief description of immunomodulator plants

a.	**Botanical (Family) Ayurvedic/**	**Common name**	**Part used**	**Chemical constituents**	**Other biological activities**	**References**
1.	Achillea millefolium C. Koch (Compositae)	Yarrow	Leaves	Flavonoids, alkaloids, polyacetylenes, coumarins, triterpenes	Anti-inflammatory, antispasmodic, antipyretic, diuretic.	[22]
2.	Aloe vera Tourn.ex Linn. (Liliaceae	Kumaari	Gel from leaves	Anthraquinone glycosides	Purgative, emmenagogue, emollient, antinflammatory.	[23,24,25]
3.	Andrographis paniculata Nees (Acanthaceae)	kallmegha	Leaves	Diterpenes	Hepatoprotective, antispasmodic, blood purifier, febrifuge.	[26,27]
4.	Asparagus racemosus Wild. (Liliaceae)	Shatavaari	Roots	Saponins, sitosterols	Ulcer healing agent, nervine tonic, antigout.	[28,29]
5.	Abutilon indicum linn. (Malvaceae)	Atibalaa	Whole plant	Flavonoids triterpenoids	Diuretic antibacterial.	[30]
6.	Alternanthera tenella Colla (Amaranthaceae	Snow Ball Herb	Herb	Flavonoids, triterpenes	Antitumor, anti-inflammatory.	[31]
7.	Actinidia macrosperma C. F. Liang (Actinidiaceae)	Actinidia	Fruits	Alkaloids, saponins	Antileprotic.	[32]
8.	Acacia catechu Willd. (Leguminosae)	Khadira	Leaf	Flavonoids, quercetin	Hypoglycaemic, astringent.	[33,34,35]
9.	Allium hirtifolium Boiss. (Alliaceae)	Persian shallot	Herb	Thiosulfinates, flavonoids	Antirheumatic, anti-inflammatory.	[36]
10.	Acanthopanax sessiliflorus (Rupr.	Prickly spine	Shoots and roots	Biopolymers	Lympho-proliferative activity.	[37]

	& Maxim.) (Araliaceae)					
11.	Agelas mauritianus (Porifera)	Agelas	Sponge	Glycolipid (a-galactosylceramide)	Phagocytotic activity.	[38]
12.	Aphanothece halophytica (Chroococcales)		Cyanobacterium	Exopolysaccharide	Inhibits influenza virus.	[39]
13.	Apium graveolens Linn. (Apiaceae)	Celery Seeds	Leaves, seeds	Flavonoids, coumarins	Anti-inflammatory.	[40]
14.	Artemisia annua Linn. (Compositea)	Wormwood	Herb	Artemisinin	Immunosuppressive	[41]
15.	Bauhinia variegata Linn. (Caesalpiniaceae)	Kaanchana	Roots, bark, buds	Flavonoids, beta-sitosterol, lupeol	Antifungal, astringent.	[42]
16.	Botryllus schlosseri (Botryllidae)	Botryllus	Tunicates	Cytokines	Antioxidant, antiviral, antimicrobial and antitumoral.	[43]
17.	Bidens pilosa L. (Asteraceae)	Beggar-ticks	Flowers, leaves	Polyacetylenes	Anti-inflammatory, immunosuppressive, antibacterial and antimalarial.	[44]
18.	Boerhaavia diffusa (Nyctaginaceae)	Punarnava	Herb	Alkaloid	Immunostimulatory	[45]
19.	Bugula neritina L. (Bugulidae	Brown bryozoans	Marine invertebrates	Macrocyclic lactones	Immunomodulator.	[46]
20.	Byrsonima crassa Nied. (Malpighiaceae)	Byrsonima	Leaves	Flavonoids, tannins, terpenes	Antimicrobial, antioxidant.	[47]
21.	Couroupita guianensis Aubl. (Lecythidaceae)	Nagalinga	Fruits, flowers	Steroids, flavonoids, phenolics	Antifungal.	[48]
22.	Cleome gynandra Linn. (Capperdiceae)	Tilaparni	Leaf, seeds, rots	Hexacosanol, kaempferol	Anti-inflammatory.	[49]
23.	Citrus natsudaidai Hayata (Rutaceae	Japanese summer grape fruit	Fruits	Auraptene, flavonoids	Antioxidant.	[50]
24.	Calendula Officinalis L. (Asteraceae)	Garden Marigold	Flowers	Polysaccharides, proteins, fatty acids, carotenoids, flavonoids, triterpenoids	Antitumor antiviral activity, anti-HIV properties.	[51]
25.	Cistanche deserticola (Orobanchaceae)	Cistanche	Herb	Polysaccharide	Immunomodulator, mitogenic and comitogenic activities.	[52]
26.	Cliona celata (Clionaidae)	Borimg sponge	Sponge	Clionamide, dehydrodopamine	Antibacterial activity.	[53]
27.	Cordyceps militaris L. (Clavicipitaceae)	Militaris	Fungus	Cordycepin, cordyceps acid	Anti-inflammatory.	[54]
28.	Crinum latifolium Andr. (Amaryllidaceae)	Milk and Wine Lily	Herb	Alkaloids	Immunomodulator.	[55]
29.	Cordia superba Cham. and C. rufescens A. DC. (Boraginaceae	Shleshmaataka	Leaf, fruit, bark	Alpha-amyrin	Anti-inflammatory, antimicrobial.	[56]
30.	Cissampelos pareira	Paatha	Roots	Hayatine alkaloids	Analgesic,antilithic.	[57]

	Linn. (Menispermiaceae)		Antipyretic,			
31.	Chlorophytum borivilianum Sant. F (Liliaceae)	Safed musli	Roots	Sapogenins	Antifungal.37	[58]
32.	Camellia sinensis L. (Theaceae)	Tea	Leaves	(_)Epigallocatechin gallate, quercetin, gallicacid	Anticancer activity, lipid lowering activity, anticataract activity, hepatoprotective and antioxidant.	[59]
33.	Cannabis sativa (Cannabaceae)	Common hemp	Leaves	Cannabinoids	Immunomodulatory	[60]
34.	Carpobrotus edulis L. (Aizoaceae)	Fig Marigold	Flowers, fruit	Alkaloids	Immunomodulator.	[61]
35.	Centella asiatica Linn. (Umbelliferae),	Brahmi	Herb	Triterpenoid saponins	Immunomodulator.	[62]
36.	Dracocephalum Kotschyi (Lamiaceae)	Dragon Head	. Herb	Essential oil	Immunomodulator.	[63]
37.	Echinacea angustifolia (Asteraceae)	Cone flower	Flowers	Polysaccharide	Treatment for common cold,immunomodulator.	[64]
38.	Eclipta alba L. (Compositae)	Bringraja	Leaves	Triterpenoid glucoside	Anticancer, antileprotic, analgesic, antioxidant, antimyotoxic.	[65]
39.	Euphorbia hirta linn. (Euphorbiaceae)	Asthma weed	Herb	Quercitol, myricitrin, gallic acid	Anti-inflammatory activity, sedative and anxiolytic activity.	[66]
40.	Evolvulus alsinoides Linn. (Convolvulaceae)	Shankhpushpi	Herb	Alkaloids	Brain tonic.	[67]
41.	Ganoderma lucidum (Fr.) P. Karst. (Polyporaceae)	Reishi mushroom	Whole plant	Flavonoids, triterpenes	Antioxidant.	[68]
42.	Genus Ardisia (Myrsinaceae)	Marlberry	Shrub, Branches and leaves	Peptides, saponins, Isocoumarins, quinones and alkyl phenols	Antimetastatic drug, anti-HIV property.	[69]
43.	Genus Aristolochia (Aristolochiaceae)	Pipevine	Leaves	Aristolochic acid	Antiangiogenic, employed in prostate cancer.	[70]
44.	Genus Aspergillus (Trichocomaceae)	Aspergillus	Fungus	Polyene triazole	Antifungals.	[71]
45.	Hibiscus rosa sinensis Linn. (Malvaceae)	Japaa	Flowers	Cyclopropanoids	Antidiarrheal, anti inflammatory.	[72]
46.	Hyptis suaveolens (L.) Poit. (Lamaceae)	Tumbaaka	Leaf, flowers	Lupeol, beta sitosterol.	Carminative, antispasmodic.	[73]
47.	Heracleum persicum Desf. (Apiaceae)	Golpar	Shurb	Flavonoids furanocoumarins	Antimicrobial.	[74]
48.	Inonotus obliquus Pers. (Hymenochaetaceae)	Chaga Mushroom	Mushroom	Polysaccharide	Antitumor.	[75]
49.	Larrea divaricata DC.	Creosote Bush	Herb	Lignans	Anti inflammatory.	[76]

	(Zygophyllaceae)					
50.	Lycium barbarum Linn. (Solanaceae) Fruits Polysaccharide	protein complexes Antioxidant.79	Lycium barbarum Linn. (Solanaceae) Fruits Polysaccharide	protein complexes Antioxidant.79	Lycium barbarum Linn. (Solanaceae) Fruits Polysaccharide	[77]
51.	Matricaria chamomilla (Rhabdoviridae)	Chamomile	Flowers	Protein	Immunomodulator.	[78]
52.	Mollugo verticillata L. (Molluginaceae)	Carpetweed	Herb	Quercetin, triterpenoid glycosides	Immunomodulator.	[79]
53.	Moringa oleifera L. (Moringaceae)	Sahijan	Leaves	Vitamin A carotenoids saponins	Antioxidant.	[80]
54.	Nyctanthes arbor tristis L. (Oleaceae)	Paarijaata Anti	Leaf, seeds	Iridoid glucosides	inflammatory, antispasmodic.	[81]
55.	Ocimum sanctum Linn. (Labiateae)	Tulasi	Entire plant	Essential oils such as eugenol, cavacrol, derivatives of ursolic acid, apigenin	Carminative, stomachic, antispasmodic, antiasthmatic, hepatoprotective.	[82,83]
56.	Piper longum L. (Piperaceae)	Pipali	Fruits	Alkaloids	Antioxidant.	[84]
57.	Panax ginseng Wall. (Araliaceae)	Ninjin	Fruits,, root	Saponins such as ginsenosides, panaxdiol, panaxtriole and oleanolic	Adaptogenic properties antiarrhythmic.	[85,86]
58.	Picrorhiza scrophulariiflora Benth. (Scrophulariaceae)	Kutki	Roots	Iridoid glycosides, amphicoside	Antioxidant.	[87]
59.	Rhodiola imbricate Gray. (Crassulaceae)	Roseroot	Rhizomes	Phenolics	Immunostimulating properties.	[88]
60.	Randia dumetorum Lamk. (Rubiaceae)	Madana	Fruits	Saponins triterpenes Chlorosis	antiarthritic.	[89]
61.	Silybum marianum L. (Asteraceae)	Milk Thistle	Flowers	Flavonoid	Antioxidant.	[90]
62.	Salicornia herbacea (Chenopodiaceae)	Glasswort	Herb	Polysaccharides	Immunomodulator.	[91]
63.	Tinospora cordifolia Miers. (Menispermiaceae)	Amrita, guduuchii	Entire herb	Alkaloidal constituents such as berberine, tinosporic acid	Hypoglycaemic agent, antipyretic.	[92,93]
64.	Terminalia arjuna Roxb. (Combretaceae)	Arjuna	bark Leaves,	Flavonoids, oligomeric proanthocyanidins,	Cardiotonic, diuretic, prescribed for hypertension.	[94]
65.	Thuja occidentalis L. (Arborvitae)	White cedar	Leaves	Polysaccharides	Immunomodulator.	[95]

DISCUSSION

Allopathic drugs are available for counteracting the oxidative stress and hence improve immunity, but the side effects and prohibitive cost of these allopathic drugs makes it necessary to search for an alternative. The Ayurvedic system of medicines not only provides that alternative, but also scores over the side effects and cost factor of allopathic medicine.[96,97] Immunomodulators

are becoming very popularin the worldwide natural health industry as people start to realize the importance of a healthy immune system in the maintenance of health and the prevention of diseases. Although extensive work has been carried out in the field of chemotherapy during this century, it is only in the last two decades that a number of compounds with immunomodulatory activity have been identified from the plant materials. From ancient times, medical treatment in India has relived to a large extent on the use of plants.

Indian medicinal plants are a rich source of substances that are claimed to induce paraimmunity, the non-specific immunomodulation of granulocytes, macrophages, natural killer cells and complement function in mammalian models.[98] In the recent past, scientific studies on plants used in ethno medicine have led to the discovery of many valuable drugs. Several structural analogues are also in clinical use and most notable of these are vinorelbine and vindesine. The current practice of prescribing photochemicals to support the immune system or to fight infections is based on centuries old traditions.[99]

Immunomodulation using medicinal plants can provide an alternative to conventional chemotherapy for a variety of diseases especially when host defense mechanism has to be acquired under the conditions of impaired immune responsiveness.[100] Indian medicinal plants are a rich source of substances which are claimed to induce paraimmunity, the non-specific immunomodulation of especially granulocytes, macro-pages, natural killer cells and competent functions. Immunostimulation and immunosuppression both need to be tackled in order to regulate the normal immunological functioning. Therefore, stimulatory or suppressive agents have been shown to possess activity to normalize or modulate pathophysiological processes and are hence called' 'immunomodulatory agents'. Among the suppressive synthetic substances, cyclophosphamide has been extensively studied. However; the major drawback of this drug is myelosuppression, which is undesirable. Moreover, natural adjuvants, synthetic agents, antibody reagents are used as immunomodulatory agents. Nevertheless, there are major limitations to the general use of these agents such as increased risk of infection and generalized effect throughout the immune system. As an upshot, there is high pre-valence of usage of herbal plants to treat diseases of immune system for hundreds of years. Besides, compared to synthetic drugs, herbal drugs are frequently considered to be less toxic with fewer side effects. Therefore; the search for more effective and safer agents exerting immunomodulatory activity is becoming a field of major interest all over the world. Number of plants used in Indian traditional system of medicines for upgrading therapy and chronic diseases has been shown to stimulate immune responses and several active substances have also been isolated.[101] In recent years, immunomodulatory activity has been reported in a number of plants listed in table no.1.

CONCLUSION

Immunomodulatory drugs are agents that could alter immune system of an organism, if it increases the immune response are called as immunostimulants or if it decreases immune response are called as immunosuppressants. These drugs are most commonly used in autoimmune diseases, allergic reactions, AIDS, cancer and some viral infections. Modern medical healthcare in developing countries such as India is still a far reaching goal due to economic constraints. Only a few plants have been screened for immunomodulatory activities. From the above review, it is evident that there are several medicinal plants and marine products which have immunomodulatory activity but inadequate evidence does not allow their uses in clinical practice. Therefore immunomodulatory agents will gain more importance in the future research of herbal medicine.

REFERENCES

1. Manu KA, Kuttan G, Immunomodulatory activities of Punarnavine, an alkaloid from *Boerhaavia diffusa*. Immunopharmacology and Immunotoxicology, 2009; 2: 377–87.
2. Roshan N, Savitri P, review on Chemical Constituents and Parts of Plants as Immunomodulators. Res. Jour. of Pharm., Bio. and Chem. Sci, 2013; 4: 76-89.
3. Hashemi SR, Davoodi H, (2012), Herbal Plants as New Immunostimulator in Poultry Industry: A Review. Asian Journal of Animal and Veterinary Advances, 2012; 7: 105-116.
4. Agarwal SS, Singh VK. Immunomodulators: a review of studies on Indian medicinal plants and synthetic peptides. Part I: medicinal plants. Proc Indian Natl Sci Acad, 1999; 65: 179e204.
5. Bafna Anand, Mishra Shrihari, Antioxidant and Immunomodulatory Activity of the Alkaloidal Fraction of Cissampelos pareira Linn. Sci Pharm, 2010; 78: 21–31.
6. More P, Pai K, Immunomodulatory effects of Tinospora cordifolia (Guduchi) on macrophage activation, Biology and Medicine, 2011; 3: 134-140.
7. Lu Yin, Fan Jie, Zhao Yunpeng, Chen Shaoyuan, Zheng Xiaodong, Yin Yuanming and FuChengxin, Immunomodulatory activity of aqueous extract of Actinidia macrosperma, Asia Pac J Clin Nutr, 2007; 16: 261- 265.
8. Agrawal S. Surendra, Khadase C. Saurabh and S.Gokul, Studies on Immunomodulatory Activity of Capparis zeylanica Leaf Extracts, International Journal of pharmaceutical Sciences and Nanotechnology, 2010; 3: 887-892.
9. Cheng Chuen-lung, Xu Hongxi, Antiviral and Immunomodulatory Properties of Prunella vulgaris, Asian Journal of Traditional Medicines, 2006; 1: 1-5.
10. Shrivastav Preeti, Tinospora cordifolia (Amrita)-A miracle herb and lifeline to many diseases, International Journal of Medicinal and Aromatic Plants, 2011; 1: 57-61.

11. V.Gayahtri, Asha V.V. Subramoniam A.Prerliminary study on the Immunomodulatory antioxidant properties of Sellaginella species.Indian Journal of Pharmacol, 2005; 16: 261-265.
12. Pradhan D. Panda K.P.Thripathi G. Evaluation of Immunomodulatory activity of the methanolic extract of Couroupita guinensis Flowers in Rats.Natural Products Radiance, 2009; 8: 37-42.
13. Agrawal Surendra S, Khadase Saurabh C., Gokul S., Studies on Immunomodulatory Activity of Capparis zeylanica Leaf Extracts, International Journal of Pharmaceutical Sciences and Nanotechnology, 2010; 3: 887-892.
14. Chandua S, Kailash H, Studies on immunomodulatory activity of Aloe vera (Linn), International Journal of Applied Biology and Pharmaceutical Technology, 2011; 2: 19-22.
15. Lu Y, Fan J, Zhao Y, Chen S, Zheng X, Yin Y, Fu C., Immunomodulatory activity of aqueous extract of Actinidia macrosperma, Asia Pac J Clin Nutr, 2007; 16: 261-5.
16. Clement F, Pramod SN., Venkatesh YP., Identity of the immunomodulatory proteins from garlic (Allium sativum) with the major garlic lectins or agglutinins, Int Immunopharmacol, 2010; 10: 316-24.
17. Naik Suresh R, Hule Amolkumar, Evaluation of Immunomodulatory Activity of an Extract of Andrographolides from Andographis paniculata, Planta Med, 2009; 75: 785-791.
18. Gautam M, Praveen G, Immunomodulatory activity of Asparagus racemosus on systemic Th1/Th2 immunity: implications for immunoadjuvant potential, J Ethnopharmacol, 2009; 121: 241-7.
19. Patil Alpena S., Jalalpure S. S., Wadekar R. R., Effect of Baliospermum montanum Root extract on Phagocytosis by Human Neutrophils, Indian J Pharm Sci, 2009; 71: 68–71.
20. Manu KA., Kuttan G., Immunomodulatory activities of Punarnavine, an alkaloid from boerhaavia diffusa, Immunopharmacol Immunotoxicol, 2009; 31: 377-87.
21. Pathirage Kamal Perera, Yunman Li, Cheng Peng, Weirong Fang, Caifeng Han. Immunomodulatory activity of a Chinese herbal.
22. Sharififar F, Pournournohammadi S, Arabnejad M. Immunomodulatory activity of aqueous extract of Achiella wilhelmsii C. Koch in mice. Indian J Exp Biol, 2009; 47: 668-71.
23. Khare CP. Indian Medicinal Plants. An illustrated dictionary. New York: Springer Publications, 2007.
24. Sikarwar Mukesh S, Patil MB, Shalini Sharma, Vishnu Bhat. Aloe vera: plant of immortality. IJPSR, 2010; 1: 7-10.
25. Cooper JC, Turcasso N. Immunostimulatory effects of b-1,3 glucan and acemannan. JANA, 1999; 2: 5-11.
26. Khare CP. Indian Medicinal Plants. An illustrated dictionary. New York: Springer Publications, 2007.
27. Varma A, Padh H, Shrivastava N. Andrographolide: A new plant-derived antineoplastic entity on horizon. Evid Based Complement Alternat Med, 2011; 2011: 815390.
28. Nadkarni KM, Nadkarni AK. Indian Materia medica. 3rd ed. Mumbai: Popular Prakashan, 2005.
29. Bopana N, Saxena S. Asparagus racemosusdethnopharmacological evaluation and conservation needs. J Ethnopharmacol, 2007; 110: 1-15.
30. Dashputre NL, Naikwade NS. Immunomodulatory activity of Abutilon indicum Linn. On albino mice. IJPSR, 2010; 1(3): 178-84.
31. Guerra RNM, Pereira HAW, Silveria LMS, Olea RSG. Evaluation of immunomodulatory and anti-inflammatory effects and phytochemical screening of Alternanthera tenella Colla (Amaranthaceae) aqueous extract. Braz J Med Biol Res, 2003; 36: 1215-9.
32. Lu Y, Fan J, Zhao Y, Chen S, Zheng X, Yin Y, Fu C. Immunomodulatory activity of aqueous extract of Actinidia macrosperma. Asia Pac J Clin Nutr, 2007; 16(1): 261-5.
33. Khare CP. Indian Medicinal Plants. An illustrated dictionary. New York: Springer Publications, 2007.
34. Nadkarni KM, Nadkarni AK. Indian Materia medica. 3rd ed. Mumbai: Popular Prakashan, 2005.
35. Syed I, Mohammed A. Immunomodulatory activity of Acacia catechu. Indian J Physicol Pharmacol, 2009; 53(1): 25e33.
36. Jafarian A, Ghannadi A, Elyasi A. The effects of Allium hirtifolium Boiss. on cell-mediated immune response in mice. IJPR, 2003; 2: 51-5.
37. Jeong SC, Jeong YT, Yang BK, Song CH. Chemical characteristics and immuno-stimulating properties of biopolymers extracted from Acanthopanax sessiliflorus. J Biochem Mol Biol, 2005; 39(1): 84-90.
38. Hung LC, Lin CC, Hung SK, Wu BC, Jan MD, Liou SH. A synthetic analog of a galactosylceramide induces macrophage activation via the TLR4-signaling pathways. Biochem pharmacol, 2007; 73(12): 1957-70.
39. Zheng W, Chen C, Cheng Q, Wang Y, Chu C. Oral administration of exopolysaccharide from Aphanothece halophytica Chroococcales significantly inhibits influenza virus H1N1- induced pneumonia in mice. Int Immunopharmacol, 2006; 6(7): 1093-9.
40. Cherng JM, Chiang W, Chiang LC. Immunomodulatory activities of common vegetables and spices of Umbelliferae and its related coumarins and flavonoids. Food Chem, 2007; 106(3): 944-50.
41. Noori S, Naderi GA, Hassan ZM, Habibi Z, Bathaie SZ, Mahmoud S. Immunosuppressive activity of a molecule isolated from Artemisia annua on DTH responses compared with cyclosporin A. Int Immunopharmacol, 2004; 4(10-11): 1301-6.
42. Ghaisas MM, Saikh SA, Deshpande AD. Evaluation of immunomodulatory activity of ethanolic extract of stem bark of Bauhinia variegata Linn. IJGP, 2009; 3(1): 70-4.

43. Ballarin L. Immunobiology of compound ascidians, with particular reference to Botryllus schlosseri: state of art. ISJ, 2008; 5: 54-74.
44. Chang SL, Chiang YM, Chang CLT, Yeh HH, Shyur LF, Kuo YH, Wu TK, Yang WC. Flavonoids, centaurein and centaureidin, from Bidens pilosa, stimulate IFN expression. J Ethnopharmacol, 2007; 112: 232-6.
45. Mungantiwar AA, Nair AM, Shinde UA, Dikshit VJ, Saraf MN, Thakur VS, Sainis KB. Studies on the immunomodulatory effects of Boerhaavia diffusa alkaloidal fraction. J Ethnopharmacol, 1999; 65(2): 125-31.
46. Sredni B, Kalechman Y, Albeck M, Gross O, Aurbach D, Sharon P, Sehgal SN. Cytokine Secretioneffected by synergism of the immunomodulator AS101 and the protein kinase C inducer bryostatin. Immunology, 1990; 70: 473-7.
47. Bonacorsi C, Raddi MSG, Carlos IZ, Sannomiya M, Vilegas W. Anti-Helicobacter pylori activity and immunostimulatory effect of extracts from Byrsonima crassa Nied. (Malpighiaceae). BMC Complement Altern Med, 2009; 9(2): 1-7.
48. Pradhan D, Panda PK, Tripathy G. Evaluation of immunomodulatory activity of methanolic extract of Couroupita guianensis Aubl flowers in rat. NPR, 2009; 8(1): 37-42.
49. Gaur K, Kori ML, Nema RK. Comparative screening of immunomodulatory activity of hydro-alcoholic extract of Hibiscus rosa sinensis Linn. and ethanolic extract of Cleome gynandra Linn. GJP, 2009; 3(2): 85-9.
50. Tanaka T, Sugiura H, Inaba R, Nishikawa A, Murakami A, Koshimizu K, Ohigashi H. Immunomodulatory action of Citrus auraptene on macrophage functions and cytokine production of lumphocytes in female BALB/c mice. Carcinogenesis, 1999; 20(8): 1471-6.
51. Medina EJ, Lora AG, Paco L, Algarra I, Collado A, Garrido F. A new extract of the plant Calendula officinalis produces a dual in vitro effect: cytotoxic anti-tumor activity and lymphocyte activation BMC Complement Altern Med, 2006; 6(119): 1e14.
52. Ebringerova A, Hromadkova Z, Hribalova V, Hirsch J. An immunomodulating pectic arabinogalactan from roots Cistanche deserticola. Chem Pap, 2002; 56(5): 320e5.
53. Sugumaran M, Robinson WE. Bioactive dehydrotyrosyl and dehydrodopyl compounds of marine origin. Mar Drugs, 2010; 8: 2906-35.
54. Hsu CH, Sun HL, Sheu JN, Ku MS, Hu CM, Chan Y, Lue KH. Effects of the immunomodulatory agent Cordyceps militaris on airway inflammation in a mouse asthma model. Pediatr Neonatol, 2008; 495(5): 171-8.
55. Zvetkova E, Wirleitner B, Tram NT, Schennach H, Fuchs D. Aqueous extracts of Crinum latifolium L and Camellia sinensis show immunomodulatory properties in human peripheral blood mononuclear cells. Int Immunopharmacol, 2001; 1(12): 2143-50.
56. Costa JFO, David JPL, David JM, Giulietti AM, Queiroz LP, Santos RR, Soares MBP. Immunomodulatory activity of extracts from Cordia superba Cham. and Cordia rufescens A. DC. (Boraginaceae), plant species native from Brazilian semiarid. Rev Bras Farmaacogn, 2008; 18(1): 11-5.
57. Bafna A, Mishra S. Antioxidant and immunomodulatory activity of the alkaloidal fraction of Cissampelos pareira Linn. O¨PhG, 2009; 78: 21-31.
58. Thakur M, Bhargava S, Dixit VK. Immunomodulatory activity of Chlorophytum borivilianum Sant. F. Evid Based Complement Alternat Med, 2006; 4(4): 419-23.
59. Bhatt RP, Pandya BK, Sheth RN. Camellia sinensis L: the medicinal beverage: a review. IJPSRR, 2010; 3(2): 6-9.
60. Killestein J, Hoogervorst ELJ, Reif M, Blauw B, Smits M, Uitdehaag BMJ, Nagelkerken L, Polman CH. Immunomodulatory effects of orally administered cannabinoids in multiple sclerosis. J Neuroimmunol, 2003; 137(1-2): 140-3.
61. Ordway D, Hohmann J, Viveiros M, Viveiros A, Molnar J, Leandro C, Arroz MJ, Gracio MA, Amaral L. Carpobrotus edulis methanol extract inhibits the MDR efflux pumps, enhance killing of phagocytosed S aureus and promotes immune modulation. Phytother Res, 2003; 17(5): 512-9.
62. Mali RJ, Hatapakki BC. An in vitro study of effect of Centella asiatica on phagocytosis by human neutrophils. IJPSN, 2008; 1(3): 297e302.
63. Amirghofran Z, Azadbakht M, Karimi MH. Evaluation of the immunomodulatory effects of five herbal plants. J Ethnopharmacol, 2000; 72(1-2): 167-72.
64. Senchina DS, McCann DA, Asp JM, Johnson JA, Cunnick JE, Kaiser MS, Kohut ML. Changes in immunomodulatory properties of Echinacea spp root infusions and tinctures stored at 4 degrees C for four days. Clinica Chimica Acta, 2005; 355(1(2): 67-82.
65. Jayathirtha MG, Mishra SH. Preliminary immunomodulatory activities of methanol extracts of Eclipta alba and Centella asiatica. Phytomedicine, 2004; 11: 361-5.
66. Patil SB, Naikwade NS, Magdum CS. Review on phytochemistry and pharmacological aspects of Euphorbia hirta Linn. JPRHC, 2009; 1(1): 113-33.
67. Ganju L, Karan D, Chanda S, Srivastava KK, Sawhney RC, Selvamurthy W. Immunomodulatory effects of agents of plant origin. Biomed Pharmacother, 2003; 57(7): 296-300.
68. Habijanic J, Berovic M, Wraber B, Hodzar D, Boh B. Immunostimulatory effects of fungal polysaccharides from Ganoderma lucidum submerged biomass cultivation. Food Technol Biotechnol, 2001; 39(9): 327-31.
69. Kobayashi H, Mejia ED. The genus Ardisia: a novel source of health-promoting compounds and phytopharmaceuticals. J Ethnopharmacol, 2005; 96: 347-54.

70. Wang C, Tao W, Wang Y, Bikow J, Lu B, Keating A, Verma S, Parker TG, Han R, Wen XY. Rosuvastatin, identified from a zebrafish chemical genetic screen for antiangiogenic compounds, suppresses the growth of prostate cancer. Eur Urol, 2010; 58: 418-26.
71. Steinbach WJ, Stevens DA. Review of newer antifungal and immunomodulatory strategies for invasive Aspergillosis. ClinInfect Dis, 2003; 37(3): 157-87.
72. Gaur K, Kori ML, Nema RK. Comparative screening of immunomodulatory activity of hydro-alcoholic extract of Hibiscus rosa sinensis Linn. and ethanolic extract of Cleome gynandra Linn. GJP, 2009; 3(2): 85-9.
73. Jain V, Bhagwat D, Jat RC, Bhardwaj S. The immunomodulation potential of Hyptis suaveolens. IJPRD, 2005; 1(11): 1-6.
74. Sharififar F, Pournournohammadi S, Arabnejad M. Immunomodulatory activity of aqueous extract of Achiella wilhelmsii C. Koch in mice. Indian J Exp Biol, 2009; 47: 668-71.
75. Chen C, Zheng W, Gao X, Xiang X, Sun D, Wei J, Chu C. Aqueous extract of Inonotus obliquus (Fr.) Pilat (Hymenochaetaceae) significantly inhibits the growth of sarcoma 180 by inducing apoptosis. Am J Pharmacol Toxicol, 2007; 2(1): 10-7.
76. Davicino R, Mattar A, Casali Y, Porporatto C, Correa SG, Micalizzi B. In vivo immunomodulatory effects of aqueous extracts of Larrea divaricata Cav. Immunopharmacol Immunotoxicol, 2007; 29(3(4)): 351-66.
77. Gan L, Zhang SH, Liu Q, Xu HB. A polysaccharide-protein complex from Lycium barbarum upregulates cytokine expression in human peripheral blood mononuclear cells. Eu J Pharmacol, 2003; 471: 217-22.
78. Reis LSLS, Frazatti-Gallina NM, Paoli RL, Giuffrida AA, Oba E, Pardo PE. Efficiency of Matricaria chamomilla CH12 and number of doses of rabies vaccine on the humoral immune response in cattle. J Vet Sci, 2008; 9(4): 433-5.
79. Ferreira AP, Soares GLG, Salgado CA, Goncalves LS, Teixeira FM, Teixeira HC, Kaplan MAC. Immunomodulatory activity of Mollugo verticillata L. Phytomedicine, 2003; 10: 154-8.
80. Gupta A, Gautam MK, Singh RK, Kumar MV, Rao CV, Goel RK, Anupurba S.Immunomodulatory effect of Moringa oleifera extract on cyclophosphamide induced toxicity in mice. Ind J Exp Biol, 2010; 48: 1150-67.
81. Kannan M, AJA Ranjit Singh, Ajith Kumar TT, Jegatheswari P, Subburayalu S. Studies on immuno-bioactivities of Nyctanthes arbortristis (Oleaceae). Afr J Microbiol Res, 2007; 1(6): 88-91.
82. Vaghasiya J, Datani M, Nandkumar K, Malaviya S, Jivani N. Comparative evaluation of alcoholic and aqueous extracts of Ocimum sanctum for immunomodulatory activity. Int J Pharm Biol Res, 2010; 1(1): 25-9.
83. Nadkarni KM, Nadkarni AK. Indian Materia medica. 3rd ed. Mumbai: Popular Prakashan, 2005.
84. Sunila ES, Kuttan G. Immunomodulatory and antitumor activity of Piper longum Linn and piperine. J Ethnopharmacol, 2004; 90(2,3): 339-46.
85. Khare CP. Indian Medicinal Plants. An illustrated dictionary. New York: Springer Publications, 2007.
86. Panax ginseng. Monograph. Altern Med Rev, 2009; 14: 172-6.
87. Smit HF. Picrorhiza scrophularii flora from traditional use to immunomodulatory activity [doctoral thesis]. Utrecht, Netherlands: University of Utrecht, 2000.
88. Mishra KP, Padwad YS, Dutta A, Ganju L, Sairam M, Banerjee PK, Sawhney RC. Aqueous extract of Rhodiola imbricata rhizome inhibits proliferation of an erythroleukemic cell line K-562 by inducing apoptosis and cell cycle arrest at G2/M phase. Immunobiology, 2008; 213(2): 125-31.
89. Satpute KL, Jadhav MM, Karodi RS, Katare YS, Patil MJ, Rukhsana Rub, Bafna AR. Immunomodulatory activity of fruits of Randia dumetorum Lamk. JPP, 2009; 1(3): 36-40.
90. Meeran SM, Katiyar S, Elmets CA, Katiyar SK. Silymarin inhibits UV radiation-induced immunosuppression through augmentation of interleukin-12 in mice. Mol Cancer Ther, 2006; 5(7): 1161-8.
91. Im SA, Kim K, Lee CK. Immunomodulatory activity of polysaccharides isolated from Salicornia herbacea. Int Immunopharmacol, 2006; 6(9): 1451-8.
92. Nadkarni KM, Nadkarni AK. Indian Materia medica. 3rd ed. Mumbai: Popular Prakashan, 2005.
93. Sinha K, Mishra NP, Singh J, Kanjua SPS. Tinospora cordifolia,a reservoir plant for therapeutic applications: A review. IJTK, 2004; 3(3): 257-70.
94. Halder S, Bharal N, Mediratta PK, Kaur I, Sharma KK. Antiinflammatory, Immunomodulatory and anti-nociceptic activity of Terminalia arjuna Roxb. Bark powder in mice and rats. Indian J Exp Biol, 2009; 47: 577-83.
95. Gohla SH, Zeman RA, Bogel M, Jurkiewicz E, Schrum S, Haubeck HD, Schmitz H, Hunsmann G, Neth RD. Modification of the in vitro replication of the human immunodeficiency virus HIV-1 TPSg, a polysaccharide fraction isolated from the Cupressaceae Thuja occidentalis L Arborvitae. Haematol Blood Transfus, 1992; 35: 140-9.
96. Meera S, Gupta A, Kumar NS. Immunomodulatory and antioxidant activity of a polyherbal formulation. International Journal of Pharmacology, 2008; 4: 287-91.
97. Balakrishnan B, Indap M. Evaluation of Leucas aspera extracts for immunomodulatory activity. Int J Pharmacol Biol Sci, 2007; 3: 1-4.
98. Vrushali D, Madhavi I. Immunostimulatory activity of Amoora rohituka and Azadirachta indica. Adv Pharmacol Toxicol, 2006; 7: 5-12.

99. Vattem, DA, Shetty K, Biological Function of Ellagic Acid: A Review. *J. Food Biochem,* 2005; 29: 234-266.
100. Miller LE, Ludke HR. In: Manual of Immunology. II edition. London: Lea and Fibiger, 1991; 1-57.