JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2025/35535

REVIEW ARTICLE

A Comprehensive Review of Indian Herbs as Immunomodulators

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Abstract

The immune system is a highly effective network of cellular components and substances created to protect the body's integrity from external shocks. Evidence from the literature indicates that immunological illnesses are currently on the rise, and much emphasis has been given to the discovery of molecules that can control the immune response. Herbal remedies are being explored as a potential solution to the global need for innovative, efficient treatments, such as integrative, supplementary, and preventative treatments. Utilising novel bioactive components with a variety of immunomodulatory capabilities, such as probiotics, polyunsaturated fatty acids, and other phytoconstituents, innovative functional meals are being created. Phytochemicals are naturally occurring substances that play a crucial role in regulating positive immunological responses.

Major Findings: Th e phytochemicals such as flavonoids, tannins, anthocyanins, vitamins and terpenoids play a crucial role in improving our health through immunity-modulating properties. Glycosides, alkaloids, phenolic acids, flavonoids, saponins, tannins and sterols are the phytochemicals that have been shown to have immunomodulatory action.

Keywords: Immune System, Immunostimulants, Immunosuppressant, Medicinal Herbs, Phytochemicals

1. Introduction

Immunity refers to the body's defense mechanisms against antigens, which may include microbial toxins, allergens and poisons[1]. The immune system produces antibodies against these antigens using various cells and processes. The initial line of defense against an invading infection is innate immunity. It is a defense mechanism that the host employs shortly after coming into contact with an antigen or within hours of doing so. It is antigen-independent (non-specific). Since the innate immune system lacks immunologic memory, it is unable to identify or "memorise" the same pathogen if the body comes into contact with it again in the future. The duration between exposure to the antigen and the maximum response occurs more slowly in adaptive immunity because it is antigen-dependent and antigen-specific. The potential for memory, which permits the host to produce a more prompt and effective immune response upon recurrent exposure to the antigen, is the distinguishing feature of adaptive immunity. Adaptive and innate immunity are complementary rather than antagonistic modes of host protection, and flaws in either system make the host more vulnerable or cause inappropriate reactions[2,3].

The immune system's basic structure is multilayered, with protections at several levels. The skin serves as the first and most evident defense against infection. Another is physiological, where the body's pH and temperature provide unfavorable living conditions for outside microbes. Once infections have successfully entered the body, the immune system fights them off. Both systems use a large number of cells and chemicals that interact in intricate ways to recognize and get rid of infections. Immune system cells have a variety of receptors on their surfaces, which are chemically

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Article Received on: 03.11.2023 Revised on: 12.12.2024 Accepted on: 17.02.2025

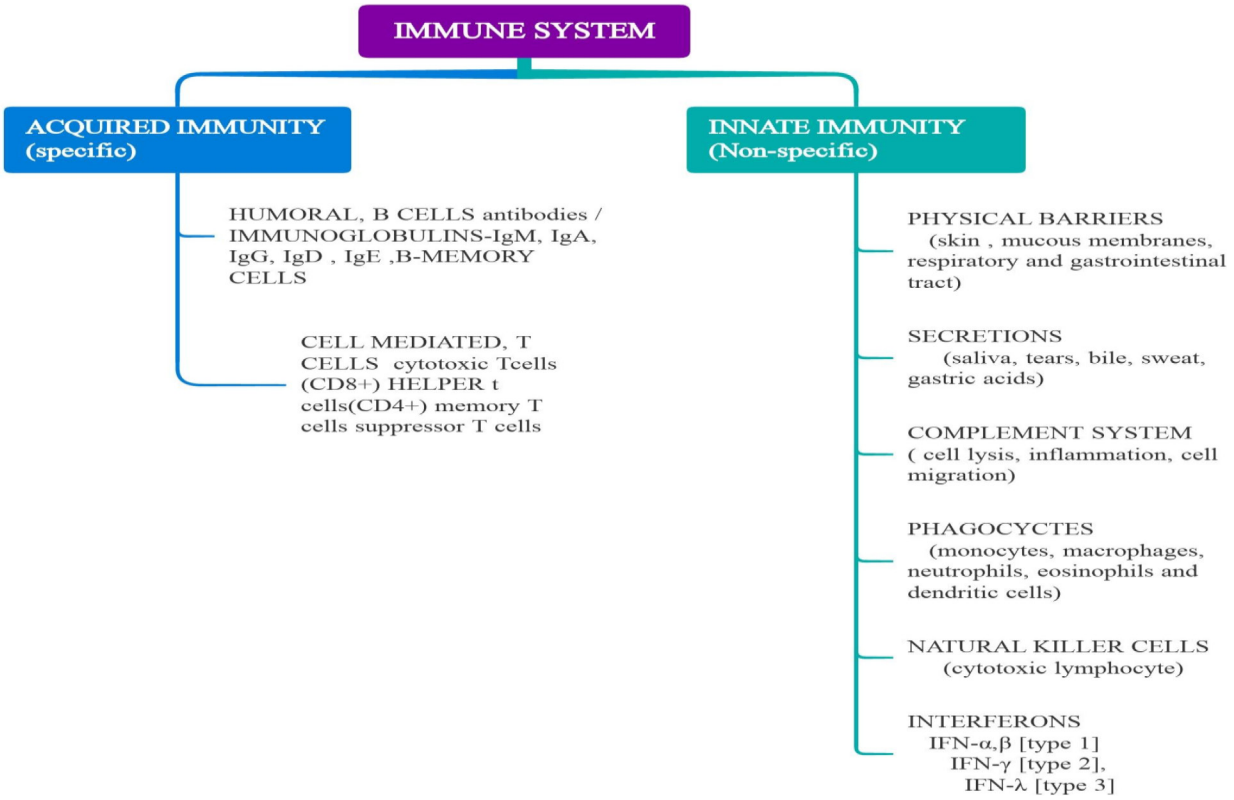


Figure 1. Types of immunity systems with their cellular components.

bonded to pathogens and other toxins to produce antibodies or substances to enable the complicated immune response[4]. Immunomodulators are biological or artificial chemicals that can activate, inhibit, or modify any immune system function, including the innate and adaptive immune systems. In healthy organisms, the immune system maintains homeostasis within the body. The function and efficiency of the immune system are influenced by various exogenous and endogenous factors resulting in either immunosuppression or immunostimulant. Several agents possessing an activity to normalize or modulate pathophysiological processes are called immunomodulators[5].

Immunoadjuvants are used to improve vaccine efficacy. It can modify the immune response and act as a modulator. They can be used between cellular components and immune helper cells to stimulate immune responses. So they may be immunoprotect ants, immune destructive and immunoglobulin E (IgE) and IgG type immune responses, and thus possess a significant challenge to vaccine designers[6]. Immunostimulants are essentially non-specific because they are designed to increase a body's ability to fight off infection. They can influence both innate and adaptive immune reactions. By boosting the fundamental level of immune response in healthy persons, immunostimulants are anticipated to work as preventative and promotional agents or as immunopotentiators. They are anticipated to function as immunotherapeutic agents in the person whose immune response is compromised[7]. Immunosuppressants are a physically and functionally varied class of medications that are frequently used to inhibit or prevent the activity of the immune system. These drugs suppress the body's response towards the organ transplant regimen, thereby improving our auto immune response[8]. The different types of immunity are exhibited in Figures 1 and 2. *Ayurveda*, a traditional Indian system of medicine, utilizes plant-based remedies with diverse therapeutic properties. It is one of the oldest medical systems, *Ayurveda* contains a variety of ethnopharmacological treatments such as adaptogenic, immunostimulant, tonic, neurostimulation, anti-aging, antibacterial, antiviral, anti-rheumatic, and anticancer[9]. The Materia Medica of *Ayurveda* contains an entire section devoted to "*Rasayana*," or medicines thought to increase body resistance[10]. It contains a list of plants

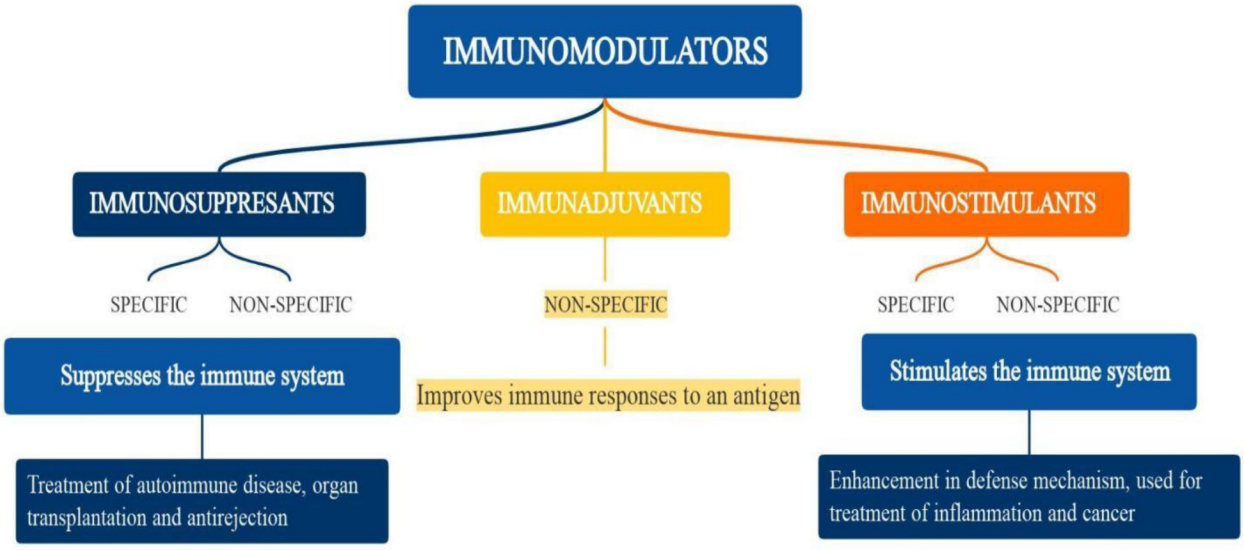


Figure 2. Types of immunomodulators.

that are said to improve our body's defense mechanisms and lifespan. These characteristics are comparable to the present idea of adaptogenic substances, which are recognized for protecting the human physiological system against various stresses[11]. Numerous medicinal herbs used as Rasayanas, such as *Withania somnifera*, *Tinospora cordifolia*, and *Mangifera indica*, have been said to have immunomodulatory properties[12,13]. They can react particularly to a foreign substance or suppress or enhance the host's natural ability to fight against infection and malignancies.

2. Phytochemicals - The Effective Immunomodulators

The term "phytochemical" refers to a group of chemicals or agents that are derived from plants and have unique structures and functions[14]. These are the chemical substances, whether natural or synthetic, that can activate or modulate immune responses. In plants, growth and metabolism are regulated by primary metabolites, while secondary metabolites often contribute to plant defense mechanisms, including colour and odour of the plants to induce pollination and protection against stressors like wounds or environmental changes[15]. These substances are frequently referred to as secondary metabolites[16]. Based on their chemical properties, Phytochemicals are divided into six major classes shown in Figure 3, which include lipids, alkaloids, terpenoids, phenolics and steroids. Secondary metabolites are biosynthesized in plants from primary metabolism, they are used as protectants to the plants whenever it gets shock from environmental changes. So far, more than 5000 phytochemicals have been reported and studied scientifically[17,18]. When consumed by people, phytochemicals also display strong biological effects like antioxidants, anti-inflammatory properties, and immunomodulatory properties. The management of some chronic conditions, such as cancer and cardiovascular diseases, may be aided by the potential effects of these medications[19,20]. Recently, it has been extensively studied by *in vivo* and *in vitro* models, which has revealed its potential health effects in treating a variety of diseases and improving quality of life.

2.1 Glycosides

Glycosides are hemiacetal and are formed as a result of the binding of the sugar and no sugar moiety. It contains glycone moiety as well as the aglycone moiety of alcoholic or phenolic hydroxyl group. In plants, glycosides occur in an inactive form with glycosidic linkage that can be activated by bodily enzymes. These substances have a variety of beneficial effects on both humans and animals[21]. According to aglycone moiety, glycosides can be divided into flavonoid, steroidal, terpenoid and anthocyanin glycosides with specific pharmacological activity. Plant glycosides primarily

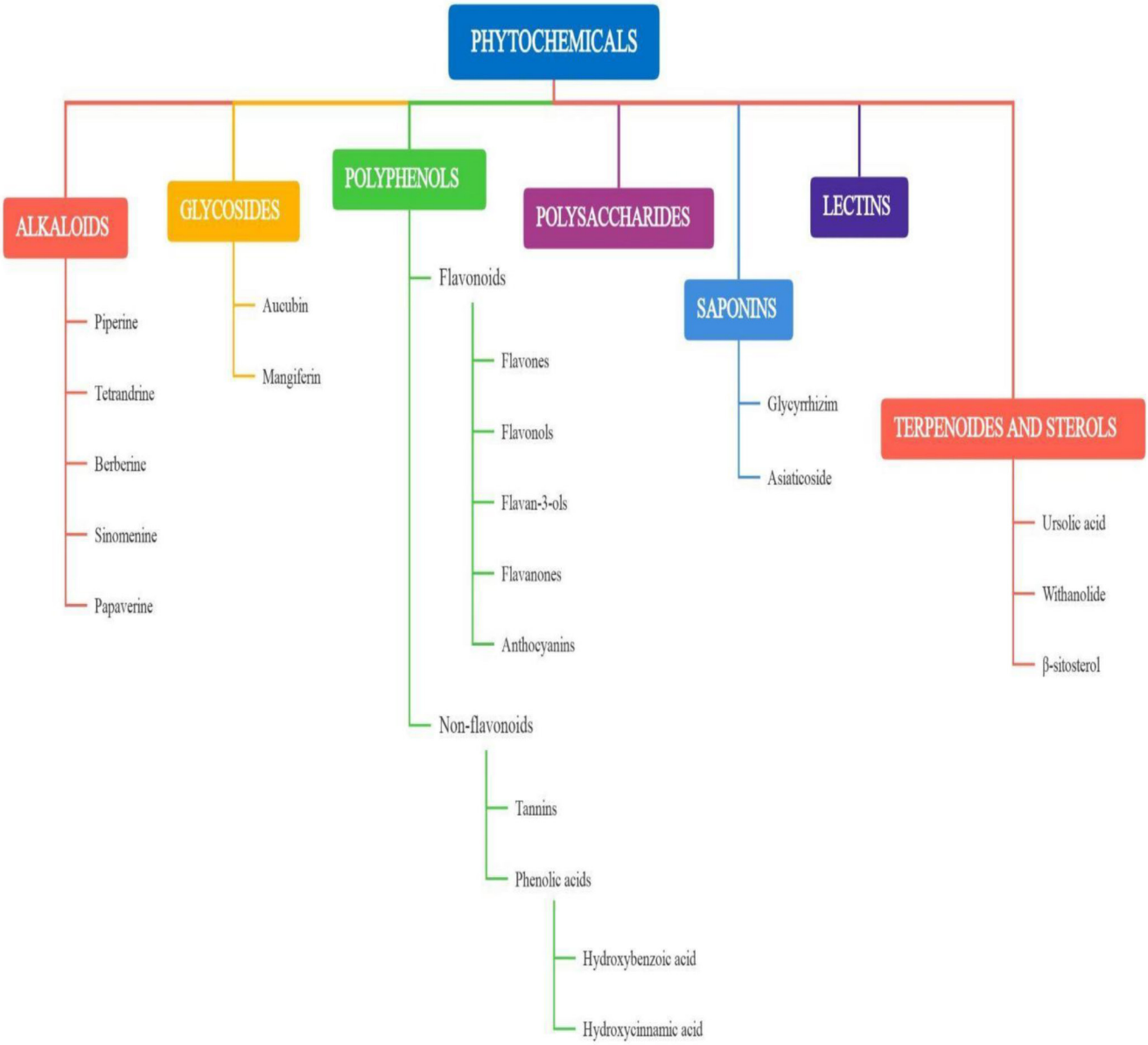


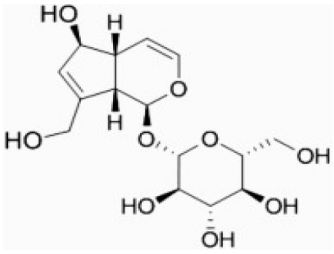
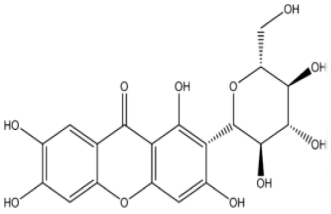
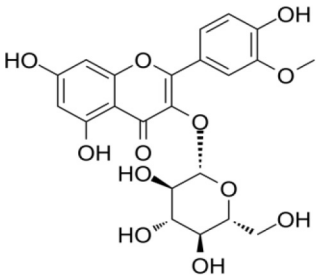
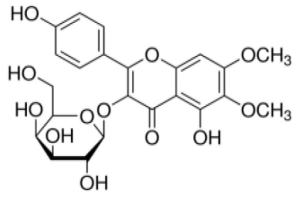
Figure 3. List of phytochemicals as immunomodulators.

affect the cardiac and neurological systems, while some flavonoids exhibit immunological properties[22] (Table 1).

2.2 Alkaloids

These are nitrogen-containing, heterocyclic basic phytocompounds widely distributed in flora. They are typically bitter and can be toxic, providing defense against herbivores. Because of their toxicity, they protect the plants from numerous infections and insects. More than 10,000 alkaloid molecules have been identified. Noscapine was the first alkaloid isolated from opium, They form a major group of secondary plant compounds with heterocyclic structure with one or more nitrogen in the ring structure[27,28]. Alkaloids are a major source of boosting the immune system and performance. Common alkaloids include tropane, phenanthrene, indole, and quinidine, which exhibit antibacterial, anti-tumor, and analgesic properties, such as catharanthine, vincristine, and vinblastine (e.g. morphine). Due to their anti-inflammatory and immunomodulatory properties, many different alkaloids have recently been studied[29,30] (Table 2).

Table 1. List of potent herbal glycosides as immunomodulators

Plant source	Active compound	Mode of action	Chemical structure	References
Plantago major	Aucubin	Increased lymphocyte proliferation and IL-γ production Immunostimulatory effects		23,24
Mangifera indica	Mangiferin	Decrease in the imbalance of the cytokines Th1/Th2		25
Urtica	Isorhamnetin-3-*O*-glucoside	Immunomodulatory effects and an increase in intracellular killing activity		26
Boerhaavia species	Eupalitin-3-*O*-β-d-galactopyranoside	Substantial suppression of human PBMC proliferation, TNF-, and IL-2		27

2.3 Polysaccharides

The bioactive substances known as polysaccharides are collections of monosaccharides (10 or more) bound together by glycosidic linkage[37]. Polysaccharides are complex organic molecules composed of simple monosaccharides. These primary metabolites can elevate proinflammatory cytokine levels while reducing inflammatory markers in disease conditions[38]. The engagement of polysaccharides in the control of innate immunity, particularly macrophage function, is the mechanism behind their immunomodulatory effect. These substances have the power to increase the levels of the cytokines and interleukins while suppressing TNF- and IL-6 levels. Additionally, these molecules control the growth of macrophages. A correlation between the administration of polysaccharides and the immune system. In light of this, it can be concluded that plant-derived polysaccharides can serve as the basis for evaluating potential medicinal compounds that frequently display immunomodulatory action[37,39].

2.4 Lectins

Lectins are common polysaccharides found in plants, animals, and microbes, including grains and cereals. It is chemically proteins and glycoproteins that are present in virtually all species of plants and animals[40]. Plant-derived lectin, found in foods including cereals, vegetables and fruits, is important for enhancing immune system performance. Numerous lectins have immunomodulatory and anticancer properties, which are scientifically evaluated by cellular, preclinical and clinical models as therapeutic agents. Preclinical and clinical trials

Table 2. Role of potent plant alkaloids with its mode of action for immune system

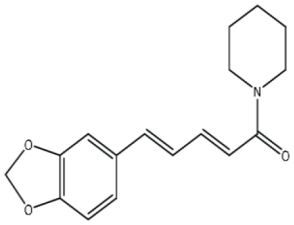
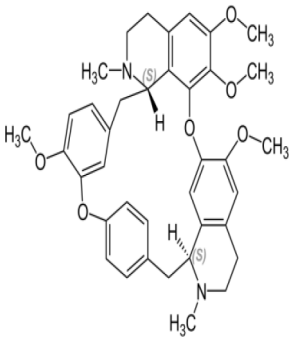
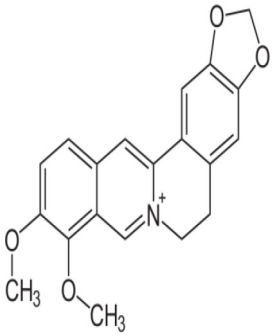
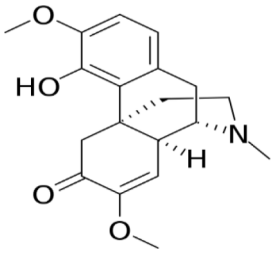
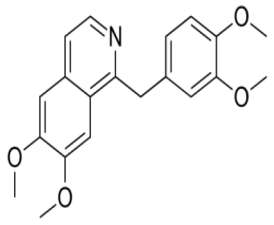
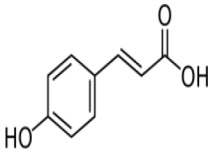
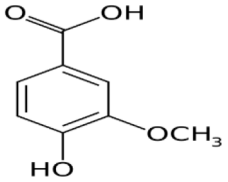
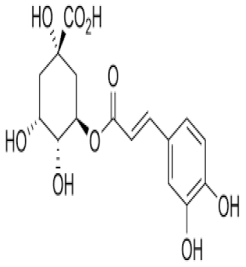
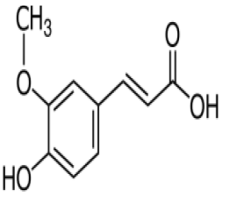
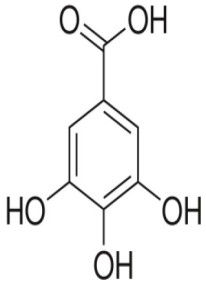
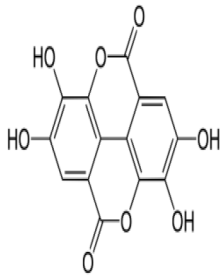
Plant source	Active compound	Mode of action	Chemical structure	References
Piper longum	Piperine	It improves the immunity by increasing leucocytes count at cellular level and thereby improve the antibody		31
Stephania tetrandra	Tetrandrine	Suppression levels of nitric oxide, interferon, and tumor necrosis factor		32
Hydrasti Canadensis	Berberine	Alkaloids reduce oxidative and inflammatory stress, mitigating damage to the respiratory and gastrointestinal systems		33
Sinomenium acutum	Sinomenine	Rejection prevention for cardiac grafts		34
Opium alkaloid	Papaverine	Anti-inflammatory and immunomodulatory effects		35
Fumaria capreolata	Alkaloid extract	reduction of intestinal inflammatory indicators at the microscopic and macroscale Inflammatory bowel disease treatment		36

Table 3. List of Polyphenols with their immunity property

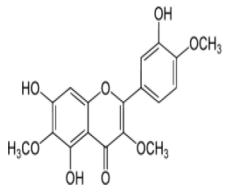
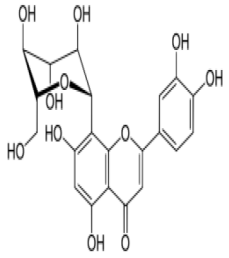
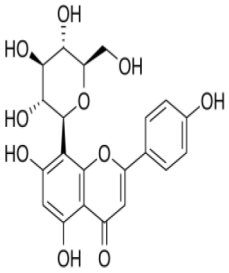
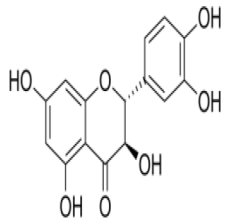
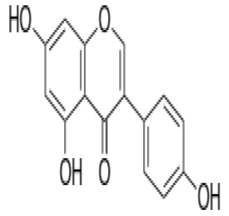
Plant source	Active compound	Mode of action	Chemical structure	References
Plantago ovata	Para hydroxy cinnamic acid	Increased lymph gland activity and its cell proliferation and inteferons - γ production		52
Plantago ovata	Vanillic acid	Interferons - γ production		52
Plantago ovata	Chlorogenic acids	Increased lymph gland activity and cell proliferation		52
Plantago ovata	Ferulic acid	IFN- γ production		52
Anacardium occidentale	Gallic acid	Increase immunological responses, nitrite release, and phagocytosis reduction of infection and macrophage infectiousness		53
Anacardium occidentale, Myracrodruon urundeuva, Anogeissus leiocarpus	Tannins	Increase immunological responses, nitrite release, and phagocytosis reduction of infection and macrophage infectiousness		53

have shown that lectins can modify cellular potential and increase oxygenation within cells[41,42]. Additionally, Garlic, derived from the *Allium* species, has demonstrated immunity-boosting effects in animal models[43]..

2.5 Phenolic compounds

Phenolic compounds, including polyphenols, are abundant in colored fruits, particularly those that are blue or red. These are complex polyhydroxy aromatic

Table 4. List of Bioflavonoids with their mode of action as immunity booster

Plant source	Active compound	Mode of action	Chemical structure	References
Bidens pilosa	Centaurein	Impact on immune modulation via controlling IFN-γ-expression		56
Jatropha curcas	Orientin	Immune responses that are cell- and humoral-mediated are stimulated the prevention of Newcastle disease		57
Jatropha curcas	Vitexin	Immune responses that are cell- and humoral-mediated are stimulated the prevention of Newcastle disease		57
Cedrus deodara	Dihydroquercetin	Improvement in immunological function and IgM levels Immunostimulant action to cure or prevent disease issues		58
Flavonoid	Genistein	Immune system development for the mucosa and humoral anti-Newcastle affliction antibodies against avian influenza		59

compounds that include flavonoids, tannins, phenolic acids, and aromatic acids[44]. Due to their diverse chemical structures, polyphenols exhibit a wide range of therapeutic actions, such as reducing inflammation by modulating nitric oxide levels and pro-inflammatory cytokine expression[45,46]. Shikimate, phenylpropanoid, and pentose phosphate are the major biogenetic pathway sources of these compounds in plants[47]. Tannins and flavonoids are the two basic classifications of polyphenols. Flavonoids are further subcategorized into flavones, flavanones, flavanols, isoflavones, flavanols, and anthocyanins, consisting of two aromatic rings that are attached to an oxygen heterocycle[48,49]. Due to their biological activity and use in the food business, polyphenols have recently attracted a great deal of attention. Polyphenols have exhibited extraordinary benefits in a wide range of chronic illnesses, including neurodegenerative disorders, diabetes, and cardiovascular diseases[50]. Numerous of these compounds are now exhibiting immunomodulatory action by modifying the nitric oxide inhibition activity and

cytokines modulator property as well as by limiting the expression of pro-inflammatory cytokines and genes[51].

2.6 Flavonoids

Flavonoids are widely dispersed polyphenols that are present in plant-based meals and drinks. There are about 8000 known flavonoid chemicals, most of which are found in fruits, including grapes, berries, cranberries, cherries, and plums. These substances frequently have a C6-C3-C6 carbon skeleton, 15 carbon atoms, and low molecular weight. Both the free-state and the glycoside form of them can be discovered[54]. Anthocyanins, which give plants and fruits their color, and canthaxanthins are the two major subcategories of flavonoids (colourless molecules). The classification of canthaxanthins includes flavanones, flavanols, flavones, isoflavones, and flavan-3-ols. According to their biological activity, the primary flavonoid molecules that have a special influence on human health include kaempferol, quercetin, myricetin, hesperidin, naringenin, epicatechin gallate, and anthocyanin. Flavonoids have anti-cancer effects as well as possible preventative action against oxidative cell death. They can also stop all of the mechanisms that lead to the development, stimulation, and spread of tumors. Flavonoids have recently been utilized to regulate a variety of chronic illnesses like atherosclerosis, diabetes, and Alzheimer's disease based on their anti-inflammatory and antioxidant properties[55]. Research is now being done to determine how they affect immune system function and whether they can operate as powerful immunomodulators. The list of plant flavonoids with their mode of action is exhibited in Table 4.

2.7 Anthocyanins

Anthocyanidins are water-soluble polyphenol pigments found in red and reddish-brown fruits. Common anthocyanidins include cyanidin glycosides, malvidin, and betanin. It is a subclass of hydrophilic pigments and phenolic hydroxy groups that may change the color of many fruits and vegetables from red to yellow. Anthocyanidin glycosides are the name for these anthocyanin pigments. By modifying several signaling

Table 5. List of herbal Anthocyanins and their immunomodulator mechanism

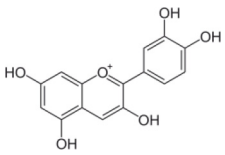
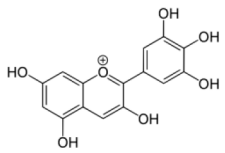
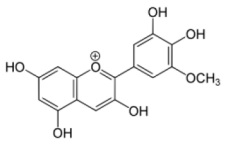
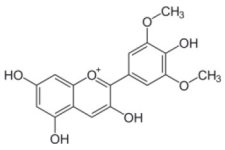
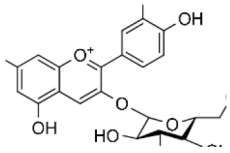
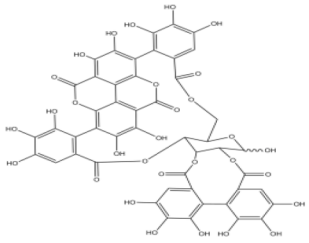
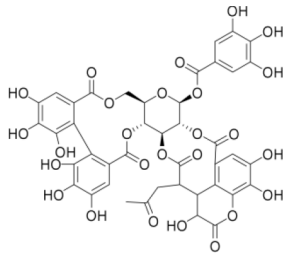
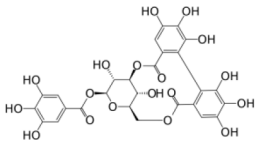
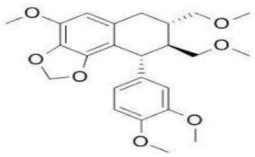
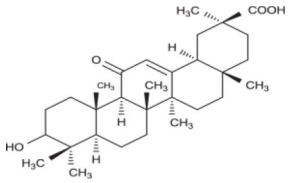
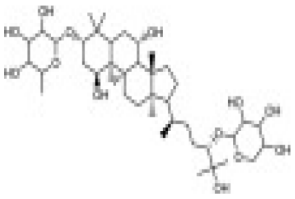
Plant source	Active compound	Mode of action	Chemical structure	References
Prunus cerasus	Cyanidin	Cytokine expression and paw swelling suppression		61-64
Prunus cerasus	Delphinidin	Cytokine expression and paw swelling suppression		61-64
Prunus cerasus	Petunidin	Cytokine expression and paw swelling suppression		61
Prunus cerasus	Malvidin	Cytokine expression and paw swelling suppression		61
Blackberr	cyanidin-3-glycoside	inflammatory-reduction capacity amplifies platelet activity		65

Table 6. List of Tannins and saponin as Immunity boosters

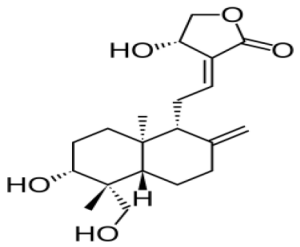
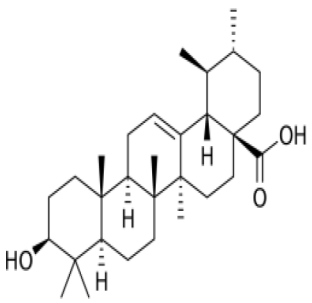
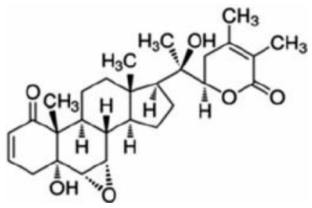
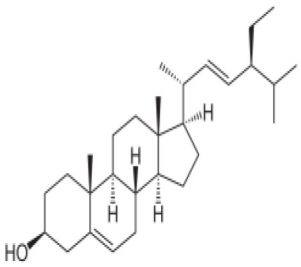
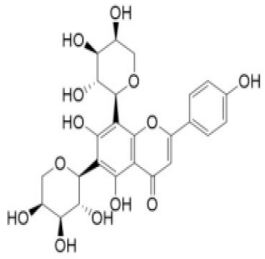
Plant source	Active compound	Mode of action	Chemical structure	References
Punica granatum	Punicalagin	Immunosuppressive action		70
Terminalia chebula	Chebulagic acid	IL-2, TNF-α, and ROS production are reduced		71
Terminalia chebula	Corilagin	Neuroprotection		72
Phyllanthus amarus	Hypophyllanthin	Immunomodulatory activity		73
Glycyrrhiza glabra	Glycyrrhizin	Classical complement pathway inhibition		74
Astragalus oleifolius	Macrophyllosaponin B	Attenuation of Th1/Th2 Cytokine Imbalance		75

pathways, these substances have demonstrated promising antioxidant and anti-inflammatory effects. These positive benefits lead people to look into anthocyanin's immunomodulatory action[60]. The list of herbs containing anthocyanins is mentioned in Table 5.

2.8 Tannins

Large-molecular-weight, water-soluble tannins are a common component of complexes with proteins, polysaccharides, and alkaloids in plants. Tannins are categorized into three groups: proanthocyanidins, phlorotannins, and hydrolysable tannins, depending on their solubility or hydrolysis result. Esters of phenolic acids are used to produce hydrolysable tannins, polyhydroxy flavan-3-ol monomers are combined to create condensed tannins, and brown algal extract phloroglucinol is used to create phlorotannins. The main sources of tannins include apples, grapes,

Table 7. List of Phto sterols and terpenoids as immunomodulators

Plant source	Active compound	Mode of action	Chemical structure	References
Andrographis paniculata	Andrographolide	Suppression of the generation of NO and iNOS		78
Terpenoids	Pentacyclic terpenoids	Stimulates macrophages' intracellular killing activity when Mycobacterium tuberculosis is present		79
Withania somnifera	Withanolide	Inhibition of the traditional complement pathway and sensitivity		80
Clinacanthus nutans	Stigmasterol	Immune cell proliferation is suppressed, and T Helper cells produce interferons responsible for defense system at intercellular level.		81
Clinacanthus nutans	Shaftoside	T helper cell produced interleukins responsible for allergic		81

berries, peaches, and walnuts[66,67]. Numerous preclinical investigations have demonstrated the immunomodulatory properties of these substances.

2.9 Saponins

These are plant-derived complex organic compounds. Most of them are found in plants as glycosides. They are distributed in almost all parts of the plants, including leaves, flowers, shoots, roots, tubers, and seeds. Based on their chemical property, two major classes of saponins occur in nature: triterpenoid saponins in dicotyledon plants and Steroidal saponins in Monocotyledon plants. Mostly, the glycone portion is mono or oligo saccharides, which are connected to

Table 8. An overview of plant-derived immunomodulators

Scientific Name	Family	Parts used	Active compound	Biological uses	References
Panax ginseng Wall.	*Araliaceae*	Fruits, root	Saponins such as ginsenosides, panaxdiol, panaxtriole and oleanolic acid	Adaptogenic properties, antiarrhythmic	84,85
Ocimum sanctum Linn.	*Labiateae*	Whole plant	Volatile oils containing mono and sesqui trepenes	Carminative, stomachic, antispasmodic, antiasthmatic, hepatoprotective	84,86-88
Aloe vera Linn.	*Liliaceae*	Dried juices of the leaves	Anthraquinone glycosides	Purgative, emmenagogue, emollient, antinflammatory	84,89-91
Murraya koenigii (L) Spreng.	*Rutaceae*	Leaves	Flavonoids, alkaloids, glucoside	Anthelmintic and antimicrobial	84,92
Artemisia annua Linn.	*Compositea*	Herb	Artemisinin	Immunosuppressive	93
Boerhaavia diffusa	*Nyctaginaceae*	Herb	Alkaloid	Immunostimulatory	94
Citrus natsudaidai Hayata	*Rutaceae*	Fruits	Auraptene, flavonoids	Antioxidant	95
Calendula Officinalis L.	*Asteraceae*	Flowers	Polysaccharides, , flavonoids, triterpenoids , proteins	Anticancer, Used against HIV virus	96
Cannabis sativa	*Cannabaceae*	Leaves	Cannabinoids	Immunomodulatory	97
Cistanche deserticola	*Orobanchaceae*	Herb	Polysaccharide	Immunomodulator, mitogenic and comitogenic activities	98
Centella asiatica Linn.	*Umbelliferae*	Herb	Terpenoids	Immunomodulator	99
Carpobrotus edulis L.	*Aizoaceae*	Flowers, fruit	Alkaloids	Immunomodulator	100
Cliona celata	*Clionaidae*	Sponge	Amino alkaloids	Bactericidal activity	101
Cordyceps militaris L.	*Clavicipitaceae*	Fungus	Phenolic acids	In inflammatory conditions	102
Crinum latifolium Andr.	*Amaryllidaceae*	Herb	Alkaloids	Immunomodulator	103
Dracocephalum Kotschyi	*Lamiaceae*	Herb	Essential oil	Immunomodulator	104
Echinacea angustifolia	*Asteraceae*	Flowers	Polysaccharide	Immunomodulator	105
Evolvulus alsinoides Linn.	*Convolvulaceae*	Herb	Alkaloids	Brain tonic	106
Haussknechtia elymatica	*Apioideae*	Herb	Phenolics	Immunomodulator	107
Lycium barbarum Linn.	*Solanaceae*	Fruits	Polysaccharide-protein complexes	Free radical scavenging property	108
Matricaria chamomilla	*Rhabdoviridae*	Flowers	Protein	Immunomodulator	109
Mollugo verticillata L.	*Molluginaceae*	Herb	Quercetin, triterpenoid glycosides	Immunomodulator	110

Table 8. Continued...

Pestalotiopsis leucothes	*Amphisp haeriaceae*	Fungus	Terpenes	Immunomodulator	111
Piper longum L.	*Piperaceae*	Fruits	Alkaloids	Free radical scavenging property	112
Rhodiola imbricate Gray.	*Crassulaceae*	Rhizomes	Phenolics	Immunostimulant	113
Silybum marianum L.	*Asteraceae*	Flowers	Flavonoid	Free radical scavenging property	114
Salicornia herbacea	*Chenopodiaceae*	Herb	Polysaccharides	Immunomodulator	115
Viscum album L.	*Loranthaceae*	Leaves and young twigs, berries	polyphenols, polysaccharides	Anticancer	116
Thuja occidentalis L.	*Arborvitae*	Leaves	Polysaccharides	Immunomodulator	117
Bidens pilosa L.	*Asteraceae*	Flowers, leaves	Polyacetylenes	Inflammatory conditions, Immunomodulators, antibacterial and antimalarial	118

the hydroxyl group of genin by an acetal linkage. One of the most well-known functions of saponins is acting as immunoadjuvants, which modulate the immune system produced by cells and aid in the production of antibodies[68,69]. The list of saponin-containing herbs with their phytocompounds is shown in Table 6.

2.10 Terpenoids

These are building blocks of isoprene units obtained mostly from plants naturally via the isoprenoid pathway. It is classified based on the number of isoprene units and includes monoterpenes, sesquiterpenes, diterpenes, and triterpenes[76,77]. Carvone, limonene, and B-carotene are very common mono terpenoids. Triterpenoids are the most active terpenoids as immunomodulators. Terpenoids act by modifying the T-Cell and production of antibodies expressed in Table 7. Terpenoids also have potent anti-inflammatory properties by acting on cytokine expression. These compounds are biosynthesized by mevalonate pathways', di and triterpenoids are synthesized from acetate pathway whereas phosphate pathway leads to the formation of tri and sesquiterpenoids[76,77]. In plants, triterpenoids act as defensive and healing properties. The effects of terpenoids on the immune system mainly occurred either in the production of antibodies or in improving immune cell response and its suppression. Terpenoids have beneficial effects on the immune system, which mostly occur when antibodies are produced or when T helper -cell response suppression is improved[77,78].

2.11 Sterol ins and sterols

Plant steroids have properties of modifying immune system also reducing expression of inflammatory marker cytokines. The entry of glucocorticosteroids have the pathway for number steroidal derivatives in medical field. Numerous scientific data proved that the plant steroids act by modify the T-cell proliferation and immune cell mediated cytokines. Sterols and sterolins are found in food because they are mostly found in plants and not animals. Scientific reports and investigations have documented for their effect by modifying T-cell cellular proliferation and boosting NK-cell activity. Additionally, it has been suggested that sterols and sterolins have the capacity to control the amounts of Th1 and Th2 mediated cytokines, aiding in the enhancement of immune responses. T-cell proliferative responses can be enhanced by phytosterols, -Sitosterol, and its glycoside at even extremely low concentrations[82,83]. It was exhibited in Table 7.

3. Discussion

Immunity plays a vital role in many pathogenic diseases. Our immunity is enhanced by nature's gift, *e.g.*, mother's milk. So, natural source plays a crucial role in developing the immunity in humans from birth to old age. Immunity responds to a variety of antigens from outside of our body in a coordinated manner, so it is crucial for good health. Medicinal plants cure many metabolic disorders

with immunomodulator properties. The identification of existing molecules and discovery of new prodrugs from the plants and their purification for lead molecules as immunity was now more focused instead of taking medicine for disease treatment. Recently, people have had a keen interest in increasing their immunity power through food supplement nutraceuticals. So, this review emphasizes the use of Indian medicinal plants and its phytochemical used in animal and human health system as an immunity enhancer. In the present review work, we have collected the list of plants based on their phytocompounds and mode of action as immunomodulators, shown in Table 8. Out of reviewed scientific data, phytocompounds such as flavonoids, tannin, anthocyanin, vitamins, and terpenoids play a role in immunity modulation in human health. Over time, a number of substances of plant origin have been recognized for their immunomodulatory properties. Instead of employing chemotherapy, medicinal plants with immunomodulation can cure a variety of ailments. The identification and purification of more focused immunomodulatory molecules derived from plants have the potential to mitigate the negative effects and high expense of synthetic substances. It is necessary to study and work on the immunomodulators derived from plants. However, the transition from conventional treatments to modern pharmaceutical techniques is not always straightforward. If the standards for phytochemical enriched fractions and its extract standardization are systematically followed, this can be reduced.

4. Conclusion

Medicinal plants with immunomodulators can cure a variety of diseases. The identification of existing molecules and discovery of new prodrugs from the plants and their purification for lead molecules as immunity was now more focused instead of taking medicine for a longer duration. Nowadays, people have a keen interest in increasing their immunity with food supplements and nutraceuticals. In the present review, we have collected the list of plants based on their phytocompounds with their mode of action as immunomodulators. The review concludes that the phytochemicals such as flavonoids, tannins, anthocyanins, vitamins and terpenoids play a crucial role in improving our health through immunity-modulating properties.

5. Acknowledgement

The authors would like to acknowledge the library facilities provided by Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai, Tamil Nadu, for the collection of literature.

6. Author Contribution

Jayakumari: Writing, manuscript correction, editing and complete correspondence. Sakthi Priya: Data collection and literature review: Sharmila: Collection of literature data and compiling. Mahesh: Editing and writing. All authors have read and agreed to the published version of the manuscript.

7. References

1. Turvey SE, Broide DH. Innate immunity. J Allergy Clin Immunol. 2010; 125(2):S24-S32. https://doi.org/10.1016/j.jaci.2009.07.016 PMid:19932920 PMCid:PMC2832725
2. Bonilla A, Oettgen HC. Adaptive immunity. J Allergy Clin Immunol. 2010; 125(2):S33-S40. https://doi.org/10.1016/j.jaci.2009.09.017 PMid:20061006
3. Murphy KM, Travers P, Walport M. Janeway's immunobiology. New York: Garland Science; 2007.
4. Hofmeyr, SA. An interpretative introduction to the immune system, I Cohen, L Segel (Eds.). Design principles for the immune system and other distributed autonomous systems, USA: Oxford University Press; 2001.
5. Puri A, Saxena R, Saxena RP, Saxena KC, Srivastava V, Tandon JS. Immunostimulant activity of *Nyctanthes arbor-tristis* L. J Ethnopharmacol. 1994; 42(1):31-37. https://doi.org/10.1016/0378-8741(94)90020-5 PMid:8046941
6. Alfons B, Patrick M. Modes of action of Freund's adjuvants in experimental models of autoimmune diseases. J Leukoc Biol. 2001; 70(6):849-860. https://doi.org/10.1189/jlb.70.6.849 PMid:11739546
7. Juyal PD, Singla LD. Herbal immunomodulatory and therapeutic approaches to control parasitic infection in livestock; 2006.
8. El-Sheikh ALK. Renal transport and drug interactions of immunosuppressants [thesis]. Nijmegen, Netherlands: Radbound University; 2008.
9. 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; 65:179-204.
10. Thatte UM, Dahanukar SA. *Rasayana*. Concept: Clues from immunomodulatory therapy. SN Upadhyay (Ed.). Immunomodulation, New Delhi: Narosa Publishing House; 1997.

11. Bhattacharya SK, Bhattacharya A, Chakrabarti A. Adaptogenic activity of Siotone, a polyherbal formulation of Ayurvedic *rasayanas*. Indian J Exp Biol. 2000; 38:119-128.
12. Davis L, Kuttan G. Immunomodulatory activity of *Withania somnifera*. J Ethnopharmacol. 2000; 71(1-2):193-200. https://doi.org/10.1016/S0378-8741(99)00206-8 PMid:10904163
13. Makare N, Bodhankar S, Rangari V. Immunomodulatory activity of alcoholic extract of *Mangifera indica* L. in mice. J Ethnopharmacol. 2001; 78(2-3):133-137. https://doi.org/10.1016/S0378-8741(01)00326-9 PMid:11694357
14. Tyagi S, Singh G, Sharma A, Aggarwal G. Phytochemicals as candidate therapeutics: An overview. Int J Pharm Sci Rev Res. 2010; 3:53-55.
15. Kurmukov AG. Phytochemistry of medicinal plants. Uzbekistan and Kyrgyzstan: Medicinal Plants of Central Asia; 2013; p. 13-14. https://doi.org/10.1007/978-1-4614-3912-7_4
16. Liu R. Health-promoting components of fruits and vegetables in the diet. Adv Nutr. 2013; 4:384S-392S. https://doi.org/10.3945/an.112.003517 PMid:23674808 PMCid:PMC3650511
17. Martinez K, Mackert J, McIntosh M. Polyphenols and intestinal health. Nutr Funct Foods Healthy Aging. 2017; p. 191-210.
18. Wiseman H. Phytochemicals: Health effects. Encyclopedia Hum Nutr. 2013; p. 47-51. https://doi.org/10.1016/B978-0-12-375083-9.00227-0 PMid:27481023
19. Koche D, Shirsat R, Kawale M. An overview of major classes of phytochemicals: Their types and role in disease prevention. Hislopia J. 2018; 9:1-11.
20. Xiao J, Bai W. Bioactive phytochemicals. Crit Rev Food Sci Nutr. 2019; 59(6):827-829. https://doi.org/10.1080/10408398.2019.1601848 PMid:31070480
21. Brito-Arias M. Synthesis and characterisation of glycosides. Springer; 2007.
22. Nenaah G. Antimicrobial activity of *Calotropis procera* Ait. (Asclepiadaceae) and isolation of four flavonoid glycosides as the active constituents. World J Microbiol Biotechnol. 2013; 29:1255-1262. https://doi.org/10.1007/s11274-013-1288-2 PMid:23417281
23. Pandey R, Maurya R, Singh G, Sathiamoorthy B, Naik S. Immunosuppressive properties of flavonoids isolated from *Boerhaavia diffusa* Linn. Int Immunopharmacol. 2005; 5(3):541-553. https://doi.org/10.1016/j.intimp.2004.11.001 PMid:15683850
24. Chiang LC, Ng LT, Chiang W, Mchang MY, Lin CC. Immunomodulatory activities of flavonoids, monoterpenoids, triterpenoids, iridoid glycosides and phenolic compounds of *Plantago* species. Planta Med. 2003; 69(7):600-704. https://doi.org/10.1055/s-2003-41113 PMid:12898413
25. Akbay P, Basaran A, Undeger U, Basaran N. *In vitro* immunomodulatory activity of flavonoid glycosides from *Urtica dioica* L. Phytother Res. 2003; 17(1):34-37. https://doi.org/10.1002/ptr.1068 PMid:12557244
26. Guo H, Yun C, Hou G, Du J, Huang X, Lu Y. Mangiferin attenuates Th1/Th2 cytokine imbalance in an ovalbumin-induced asthmatic mouse model. PLoS One. 2014; 9:300-315. https://doi.org/10.1371/journal.pone.0100394 PMid:24955743 PMCid:PMC4067356
27. Cushnie TPT, Cushni B, Lamb AJ. Alkaloids: An overview of their antibacterial, antibiotic-enhancing and antivirulence activities. Int J Antimicrobial Agent. 2014; 44:377-386. https://doi.org/10.1016/j.ijantimicag.2014.06.001 PMid:25130096
28. Rida PCG, LiVecche D, Ogden A, Zhou J, Aneja R. The noscapine chronicle: A pharmaco-historic biography of the opiate alkaloid family and its clinical applications. Med Res Rev. 2015; 35:1072-1096. https://doi.org/10.1002/med.21357 PMid:26179481 PMCid:PMC4778555
29. Souto AL, Tavares JF, da Silva MS, Diniz MdFM, de Athayde-Filho PF, Filho JMB. Anti-inflammatory activity of alkaloids: An update from 2000 to 2010. Molecules. 2011; 16:8515-8534. https://doi.org/10.3390/molecules16108515 PMid:21989312 PMCid:PMC6264344
30. Zhao Z, Xiao J, Wang J, Dong W, Peng D, An D. Anti-inflammatory effects of novel sinomenine derivatives. Int Immunopharmacol. 2015; 29(2):354-360. https://doi.org/10.1016/j.intimp.2015.10.030 PMid:26525983
31. Sunila ES, Kuttan G. Immunomodulatory and antitumor activity of *Piper longum* Linn. and piperine. J Ethnopharmacol. 2024; 90(2-3):339-346.
32. Xue Y, Wang Y, Feng D-c, Xiao B-g, Xu L-y. Tetrandrine suppresses lipopolysaccharide-induced microglial activation by inhibiting NF-κB pathway. Acta Pharmacol Sin. 2008; 29:245-251. https://doi.org/10.1111/j.1745-7254.2008.00734.x PMid:18215355
33. Li F, Wang H, Lu D, Wang Y, Qi R, Fu Y. Neutral sulfate berberine modulates cytokine secretion and increases survival in endotoxemic mice. Acta Pharmacol Sin. 2006; 27:1199-1205. https://doi.org/10.1111/j.1745-7254.2006.00368.x PMid:16923341
34. Mark W, Schneeberger S, Seiler R, Stroka DM, Amberger A, Offner F, *et al*. Sinomenine blocks tissue remodeling in a rat model of chronic cardiac allograft rejection. Transplantation. 2003; 75:940-945. https://doi.org/10.1097/01.TP.0000056610.22062.03 PMid:12698077
35. Guan S, Liu Q, Gu H, Zhang Y-y, Wei P-l, Qi Y-f, *et al*. Pluripotent anti-inflammatory immunomodulatory effects of papaverine against cerebral ischemic-reperfusion injury. J Pharmacol Sci. 2020; 144:69-75. https://doi.org/10.1016/j.jphs.2020.07.008 PMid:32713799
36. Bribi N, Rodríguez-Nogales A, Vezza T, Algieri F, Rodriguez-Cabezas M, Garrido-Mesa J, *et al*. Intestinal anti-inflammatory activity of the total alkaloid fraction from *Fumaria capreolata* in the DSS model of colitis in mice. Bioorg Med Chem Lett. 2020; 30(18):1-13. https://doi.org/10.1016/j.bmcl.2020.127414 PMid:32717615

37. Zhong K, Wang Q, He Y, He X. Evaluation of radicals scavenging, immunity-modulatory and antitumor activities of longan polysaccharides with ultrasonic extraction on in S180 tumour mice models. Int J Biol Macromol. 2010; 47(3):356-360. https://doi.org/10.1016/j.ijbiomac.2010.05.022 PMid:20685359
38. Gan L, Zhang SH, Yang XL, Xu HB. Immunomodulation and antitumor activity by a polysaccharide-protein complex from *Lycium barbarum*. Int J Immunopharmacol. 2004; 4(4):563-569. https://doi.org/10.1016/j.intimp.2004.01.023 PMid:15099534
39. Schepetkin IA, Quinn MT. Botanical polysaccharides: Macrophage immunomodulation and therapeutic potential. Int Immunopharmacol. 2006; 6(3):317-333. https://doi.org/10.1016/j.intimp.2005.10.005 PMid:16428067
40. De EMejía V. Prisecaru, lectins as bioactive plant proteins: A potential in cancer treatment. Crit Rev Food Sci Nutr. 2005; 45(6):425-445. https://doi.org/10.1080/10408390591034445 PMid:16183566
41. Gupta G. Animal lectins: Form, function and clinical applications. Springer Science and Business Media; 2012. https://doi.org/10.1007/978-3-7091-1065-2
42. Lavastre V, Pelletier M, Saller R, Hostanska K, Girard D. Mechanisms involved in spontaneous and *Viscum album* agglutinin-I-induced human neutrophil apoptosis: *Viscum album* agglutinin-I accelerates the loss of antiapoptotic Mcl-1 expression and the degradation of cytoskeletal paxillin and vimentin proteins via caspases. J Immunol. 2002; 168(3):1419-1427. https://doi.org/10.4049/jimmunol.168.3.1419 PMid:11801684
43. Clement F, Venkatesh YP. Dietary garlic (*Allium sativum*) lectins, ASA I and ASA II, are highly stable and immunogenic. Int Immunopharmacol. 2010; 10(10):1161-1169. https://doi.org/10.1016/j.intimp.2010.06.022 PMid:20615490
44. Ilja CWA, Peter CHH. Polyphenols and disease risk in epidemiologic studies. Am J Clin Nutr. 2005; 81(1):317S-325S. https://doi.org/10.1093/ajcn/81.1.317S PMid:15640497
45. Graf B, Milbury P, Blumberg J. Flavonols, flavones, flavanones, and human health: Epidemiological evidence. J Med Food. 2005; 8(3):281-290. https://doi.org/10.1089/jmf.2005.8.281 PMid:16176136
46. Habauzit V, Morand C. Evidence for a protective effect of polyphenols-containing foods on cardiovascular health: An update for clinicians. Ther Adv Chronic Dis. 2011; 38:7-106. https://doi.org/10.1177/2040622311430006 PMid:23251771 PMCid:PMC3513903
47. Tangney CC, Rasmussen HE. Polyphenols, inflammation, and cardiovascular disease. Curr Atheroscler Rep. 2013; 15:324. https://doi.org/10.1007/s11883-013-0324-x PMid:23512608 PMCid:PMC3651847
48. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: Food sources and bioavailability. Am J Clin Nutr. 2004; 79(5):727-747. https://doi.org/10.1093/ajcn/79.5.727 PMid:15113710
49. Tsao R. Chemistry and biochemistry of dietary polyphenols. Nutrients. 2010; 2(12):1231-1246. https://doi.org/10.3390/nu2121231 PMid:22254006 PMCid:PMC3257627
50. Mohamed S. Functional foods against metabolic syndrome (obesity, diabetes, hypertension and dyslipidemia) and cardiovascular disease. Trends Food Sci Technol. 2014; 35(2):114-128. https://doi.org/10.1016/j.tifs.2013.11.001
51. Chuang C, McIntosh M. Potential mechanisms by which polyphenol-rich grapes prevent obesity-mediated inflammation and metabolic diseases. Annu Rev Nutr. 2011; 31(4):155-176. https://doi.org/10.1146/annurev-nutr-072610-145149 PMid:21548775
52. Rezaeipoor R, Saeidnia S, Kamalinejad M. The effect of *Plantago ovata* on humoral immune responses in experimental animals. J Ethnopharmacol. 2000; 72(1): 283-286 https://doi.org/10.1016/S0378-8741(00)00224-5
53. Alves MMd, Brito LM, Souza AC, Queiroz BCSH, Carvalho TP de, Batista JF, *et al*. Gallic and ellagic acids: Two natural immunomodulator compounds solve infection of macrophages by Leishmania major. Naunyn Schmiedebergs Arch Pharmacol. 2017; 390(2):893-903.
54. Marzocchella L, Fantini M, Benvenuto M, Masuelli L, Tresoldi I, Modesti A, *et al*. Dietary flavonoids: Molecular mechanisms of action as anti-inflammatory agents. Recent Pat Inflamm Allergy Drug Discov. 2011; 5:200-220. https://doi.org/10.2174/187221311797264937 PMid:21827399
55. Panche AN, Diwan AD, Chandra SR. Flavonoids: An overview. J Nutr Sci. 2016; 5. https://doi.org/10.1017/jns.2016.41 PMid:28620474 PMCid: PMC5465813
56. Chang S-L, Chiang Y-M, Chang CL-T, Yeh H-H, Shyur L-F, KuoY-H, *et al*. Flavonoids, centaurein and centaureidin, from *Bidens pilosa*, stimulate IFN-γ expression. J Ethnopharmacol. 2007; 112:232-236. https://doi.org/10.1016/j.jep.2007.03.001 PMid:17408892
57. Abd-Alla HI, Moharram FA, Gaara AH, El-Safty MM. Phytoconstituents of *Jatropha curcas* L. leaves and their immunomodulatory activity on humoral and cell-mediated immune response in chicks. Z Naturforsch C. 2009; 64(7-B):495-501. https://doi.org/10.1515/znc-2009-7-805 PMid:19791499
58. Awad E, Awaad AS, Esteban MA. Effects of dihydroquercetin obtained from deodar (*Cedrus deodara*) on immune status of gilthead seabream (*Sparus aurata* L.). Fish Shellfish Immunol. 2015; 43(1):43-50. https://doi.org/10.1016/j.fsi.2014.12.009 PMid:25530582
60. Khoo HE, Azlan A, Tang ST, Lim SM. Anthocyanidins and anthocyanins: Colored pigments as food, pharmaceutical ingredients, and the potential health benefits. Food Nutr Res. 2017; 61(4):234-245. https://doi.org/10.1080/16546628.2017.1361779PMid:28970777 PMCid:PMC5613902

61. He Y, Ciao C, Wang Y, Zhao L, Hao H, Tong Y. Antioxidant and anti-inflammatory effects of cyanidin from cherries on rat adjuvant-induced arthritis. Zhongguo Zhongyao Zazhi. 2005; 30(20):1602-1605.
62. DeFuria J, Bennett G, Strissel KJ, James II WP, Milbury PE, Greenberg AS, *et al.* Dietary blueberry attenuates whole-body insulin resistance in high fat-fed mice by reducing adipocyte death and its inflammatory sequelae. J Nutrition. 2009; 139(8):1510-1516. https://doi.org/10.3945/jn.109.105155 PMid:19515743 PMCid:PMC2709302
63. Dragano NRV, Marques AyC, Cintra DEC, Solon C, Morari J, Leite-Legatti AV, *et al.* Freeze-dried jaboticaba peel powder improves insulin sensitivity in high-fat-fed mice. Braz J Nutrition. 2013; 110(3):447-455. https://doi.org/10.1017/S0007114512005090 PMid:23415177
64. Karunarathne WAHM, Lee KT, Choi YH, Jin C-Y, Kim G-Y. Anthocyanins isolated from *Hibiscus syriacus* L. attenuate lipopolysaccharide-induced inflammation and endotoxic shock by inhibiting the TLR4/MD2-mediated NF-κB signaling pathway. Phytomed. 2020; 76(4):340-356. https://doi.org/10.1016/j.phymed.2020.153237 PMid:32540784
65. Rechner AR, Kroner C. Anthocyanins and colonic metabolites of dietary polyphenols inhibit platelet function. Thromb Res. 2005; 116(4):327-334. https://doi.org/10.1016/j.thromres.2005.01.002 PMid:16038718
66. Onaolapo AY, Onaolapo OJ. Herbal beverages and brain function in health and disease. Funct Med Bev. 2019; 2(6):313-349. https://doi.org/10.1016/B978-0-12-816397-9.00009-1
67. Serrano J, Puupponen-Pimiä R, Dauer A, Aura A, Saura-Calixto F. Tannins: Current knowledge of food sources, intake, bioavailability and biological effects. Mol Nutr Food Res. 2009; 53(1):310-329. https://doi.org/10.1002/mnfr.200900039 PMid:19437486
68. Oleszek M, Oleszek W. Saponins in food. Handbook of Dietary Phytochemical. Springer Nature Link; 2020. https://doi.org/10.1007/978-981-13-1745-3_34-1
69. Sparg S, Light M, Van Staden J. Biological activities and distribution of plant saponins. J Ethnopharmacol. 2004; 94(2-3):219-243. https://doi.org/10.1016/j.jep.2004.05.016 PMid:15325725
70. Lee S, Kim B, Kim K, Lee S, Shin K, Lim J. , Immune-suppressive activity of punicalagin via inhibition of NFAT activation. Biochem Biophy Res Commun. 2008; 371(4):799-803. https://doi.org/10.1016/j.bbrc.2008.04.150 PMid:18466764
71. Reddy D, Reddanna P. Chebulagic Acid (CA) attenuates LPS-induced inflammation by suppressing NF-κB and MAPK activation in RAW 264.7 macrophages, Biochem Biophy Res Commun. 2009; 381(1):112-117. https://doi.org/10.1016/j.bbrc.2009.02.022 PMid:19351605
72. Chang CL. Phytochemical composition, antioxidant activity, and neuroprotective effect of *Terminalia chebula* plant extracts. Evid Based Complement Alternat Med. 2012; 6(3):1-7. https://doi.org/10.1155/2012/125247 PMid:21754945 PMCid:PMC3132459
73. Ilangkovan M, Jantan I, Mesaik M, Bukhari S. Inhibitory effects of the standardized extract of *Phyllanthus amarus* on cellular and humoral immune responses in Blab/C mice. Phytother Res. 2016; 30(8):1330-1338. https://doi.org/10.1002/ptr.5633 PMid:27137750
74. Ablise M, Leininger-Muller B, Wong C, Siest G, Loppinet V, Visvikis S . Synthesis and *in vitro* antioxidant activity of glycyrrhetinic acid derivatives tested with the cytochrome P450/NADPH system, Chem Pharm Bull. 2004; 52(12):1436-1439. https://doi.org/10.1248/cpb.52.1436 PMid:15577240
75. Nalbantsoy A, Nesil T, Yılmaz-Dilsiz O, Aksu G, Khan S, Bedir E. Evaluation of the immunomodulatory properties in mice and *in vitro* anti-inflammatory activity of cyclooctane type saponins from *Astragalus species*. J Ethnopharmacol. 2012; 139(2):574-581. https://doi.org/10.1016/j.jep.2011.11.053 PMid:22155389
76. Singh B, Sharma R. Plant terpenes: Defense responses, phylogenetic analysis, regulation and clinical applications. Biotechnol. 2014; 5(2):129-151. https://doi.org/10.1007/s13205-014-0220-2:28324581 PMCid:PMC4362742
77. Ludwiczuk A, Skalicka K, Georgiev M. Terpenoids, Pharmacog; 2017. p. 233-266. https://doi.org/10.1016/B978-0-12-802104-0.00011-1
78. Chiou W, Chen C, Lin J. Mechanisms of suppression of inducible nitric oxide synthase (iNOS) expression in RAW 264.7 cells by andrographolide Brazilian. J Pharmacol. 2000; 129(2):1553-1560. https://doi.org/10.1038/sj.bjp.0703191PMid:10780958 PMCid:PMC1571992
79. Podder B, Jang WK, Lee B, Song H. Ursolic acid activates intracellular killing effect of macrophages during Mycobacterium tuberculosis infection. J Microbiol Biotechnol. 2015; 25(5):738-744. https://doi.org/10.4014/jmb.1407.07020PMid:25406534
80. Rasool M, Varalakshmi. Immunomodulatory role of *Withania somnifera* root powder on experimental induced inflammation: an *in vivo* and *in vitro* study, Vascular. Pharmacol. 2006; 44(6):406-410. https://doi.org/10.1016/j.vph.2006.01.015 PMid:16713367
81. Le C, Kailaivasan TS, Chow S, Abdulla Z, Sling S, Fang C. Phytosterols isolated from *Clinacanthus nutans* induce immunosuppressive activity in murine cells. Int J Immunopharmacol. 2017; 44(5):203-210. https://doi.org/10.1016/j.intimp.2017.01.013 PMid:28119186
82. Bouic P. Sterols and Sterolins: New drugs for the immune system. Drug Discov. Today. 2002; 7(14):775-778. https://doi.org/10.1016/S1359-6446(02)02343-7 PMid:12547034
83. Patel S, Plant sterols and stanols: their role in health and disease, J Clin Lipidol. 2008; 2(2):S11-S19. https://doi.org/10.1016/j.jacl.2008.01.007PMid:19343077 PMCid:PMC2390824

84. Khare CP. Indian medicinal plants. An illustrated dictionary, Springer Publications, New York; 2007. p. 653-655. https://doi.org/10.1007/978-0-387-70638-2 PMCid:PMC2705749
85. Anonymous. *Panax ginseng.* Monograph. Altern Med Rev. 2009; 14(2):172-176. PMID: 19594226
86. Vaghasiya J, Datani M, Nandkumar K, Smalaviya S, Jivani N. Comparative evaluation of alcoholic and aqueous extracts of *Ocimum sanctum* for immunomodulatory activity, Int J Pharm Biol Res. 2010; 1(1):25-29. http://www.kejapub.com/ijpbr/docs/IJPBR10-01-01-05
87. Singh S, Taneja M, Majumdar DK. Biological activities of Ocimum *sanctum* Linn. fixed oil - An overview. Indian Journal of Experimental Biology. 2007; 45(5):403-412. PMID: 175692
88. Nadkarni KM, Nadkarni AK. Indian Materia médica (3rd ed.), Popular Prakashan, Mumbai; 2005. p. 108-110
89. Mukesh SS, Patil MB, Shalini S, Vishnu B. Aloe vera: Plant of immortality. Int J Pharm Sci Res. 2010; 6(1):7-10.
90. Hammam JH. Composition and applications of Aloe vera leaf gel. Molecules. 2008; 13(8):1599-1616. https://doi.org/10.3390/molecules13081599. PMid:18794775 PMCid:PMC6245421
91. Cooper JC, Turcasso. Immunostimulatory effects of β-1,3 glucan and ace Mannan. J Amer Nutr Assoc.1999; 2(10):5-11.
92. Shah SA, Wakade AS, Juvekr AR. Immunomodulatory activity methanolic extract of *Murraya koenigii* (L) Spreng. Leaves. Ind J Exper Biol. 2007; 46:505-509.
93. Noori S, Naderi GA, Hassan ZMZ, Habibi Z, Mathaie 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);1301-1306. https://doi.org/10.1016/j.intimp.2004.05.003. PMid:15313428
94. Mungantiwar AA, Nair AM, Shinde UA, Dikshit VJ, Saraf MNV, Thakur VS, *et al*. Studies on the immunomodulatory effects of *Boerhaavia diffusa* alkaloidal fraction. J Ethnopharmacol. 1999; 65(2):125-131. https://doi.org/10.1016/S0378-8741(98)00153-6 PMid:10465652
95. Tanaka T, Sugiura H, Rinaba R, Aishikawa A, Murakami A Koshimizu K, *et al*. Immunomodulatory action of *Citrus auraptene* on macrophage functions and cytokine production of lymphocytes in female BALB/c mice. Carcinogen. 1999; 20(8):1471-1476. https://doi.org/10.1093/carcin/20.8.1471. PMid:10426794
96. Jiménez-Medina E, Garcia-Lora A, 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):1-14. https://doi.org/10.1186/1471-2407-6-119 PMid:16677386 PMCid:PMC1513589
97. Killestein J, Hoogervorst ELJ, Reif M, Blauw BM, Smits M, Uitdehaag BMJ, *et al*. Immunomodulatory effects of orally administered cannabinoids in multiple sclerosis. J Neuroimmunol. 2003; 137(1-2):140-143. https://doi.org/10.1016/S0165-5728(03)00045-6. PMid:12667658
98. Ebringerova A. Hromadkov Z, Vhribalova V, Hirsc J. An immunomodulating pectic arabinogalactan from roots *Cistanche deserticola.* Chem Pap. 2002; 56(3):320-325.
99. Mali RJ, Hatapakki BC. An *in vitro* study of effect of *Centella asiatica* on phagocytosis by human neutrophils. Int J Pharm Sci Nanotechnol. 2008; 1(3):297-302. https://doi.org/10.37285/ijpsn.2008.1.3.13
100. Ordway D, Hohmann J, Viveiros M, Viveiros A, Molnar J, Leandro C, *et al*. Amaral. *Carpobrotus edulis* methanol extract inhibits the MDR efflux pumps, enhances killing of phagocytosed S aureus and promotes immune modulation. Phytother Res. 2003; 17(5): 512-519. https://doi.org/10.1002/ptr.1314. PMid:12748989
101. Sugumaran M, Robinson WE. Bioactive dehydrotyrosyl and dehydrodopyl compounds of marine origin. Mar Drugs. 2008; 8(3):30-35. https://doi.org/10.3390/md8122906 PMid:21339956 PMCid:PMC3039461
102. Hsu CH, Sun HL, Sheu JN, Ku MS, Hu CM, Chan Y, *et al*. Effects of the immunomodulatory agent *Cordyceps militaris* on airway inflammation in a mouse asthma model. Pediat Neonatol. 2008; 495(5):171-178. https://doi.org/10.1016/S1875-9572(09)60004-8. PMid:19133568
103. 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):2143-2150. https://doi.org/10.1016/S1567-5769(01)00140-0 PMid:11710543
104. Amirghofran Z, Zadbakht M, Karimi MH. Evaluation of the immunomodulatory effects of five herbal plants. J Ethnopharm. 2000; 2(1-2):167-172. https://doi.org/10.1016/S0378-8741(00)00234-8 PMid:10967468
105. Senchina, DS, 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. Clin Chim Acta. 2005; 355(2):67-82. https://doi.org/10.1016/j.cccn.2004.12.013. PMid:15820480
106. Ganju L, Karan D, Chanda S, Srivastava KK, Sawhney RC, Selvamurthy W. Immunomodulatory effects of agents of plant origin, Biomed Pharmacother. 2023; 57(7):296-300. https://doi.org/10.1016/S0753-3322(03)00095-7. PMid:14499177
107. Amirghofran Z, Azadmeh A, Javidnia K. *Haussknechtia Elymatica*: A plant with immunomodulatory effects. Iran J Immunol. 2007; 4(1):26-31.
108. Gan L, Zhang SH, Liu Q, Xu HB. A polysaccharide-protein complex from *Lycium barbarum* upregulates cytokine expression in human peripheral blood

mononuclear cells. Eur J Pharmacol. 2003; 471(6):217-222. https://doi.org/10.1016/S0014-2999(03)01827-2 PMid:12826241

109. Reis LSLd, Frazatti-Gallina NM, Paoli Rd, Giuffrida R, Albas A, Oba E. Efficiency of *Matricaria chamomilla* CH12 and number of doses of rabies vaccine on the humoral immune response in cattle. J Vet Sciences. 2008; 9(4):433-435. https://doi.org/10.4142/jvs.2008.9.4.433 PMid:19043320 PMCid:PMC2811788
110. Ferreira AP, Soares GLG, Salgad CA, Goncalve LS, Teixeira FM, Teixeira HC, Kaplan MAC. Immunomodulatory activity of *Mollugo verticillata* L. Phytomed. 2003; 10(2-3):154-158. https://doi.org/10.1078/094471103321659861 PMid:12725569
111. Kumar DS, Lau CS, Wan JM, Yang D,Hyde,KD. Immunomodulatory compounds from Pestalotiopsis leucothes, an endophytic fungus from *Tripterygium wilfordii*. Life Sciences.2005; 78 (2): 147-56. https://doi.org/10.1016/j.lfs.2005.04.050. PMid:16107268
112. Sunila ES, Kuttan G. Immunomodulatory and antitumor activity of *Piper longum* Linn and piperine. J Ethnopharmacol. 2004; 90(2):339-346. https://doi.org/10.1016/j.jep.2003.10.016 PMid:15013199
113. Mishra KP, Padwad YS. Dutt A, Ganj L, Sairam M, Banerjee PK, *et al.* 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, Immunobiol. 2003; 213(2):125-131. https://doi.org/10.1016/j.imbio.2007.07.003. PMid:18241696
114. 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; 9(5):1161-1168. https://doi.org/10.1158/1535-7163.MCT-06-0095 PMid:16891451
115. Im SA, Kim K, Lee CK. Immunomodulatory activity of polysaccharides isolated from *Salicornia herbacea*. Int J Immunopharmacol. 2006; 6(9):1451-1458. https://doi.org/10.1016/j.intimp.2006.04.011. PMid:16846839
116. Elluru S, Huyen JPD, Wootla B, Delignat S, Prost F, Negi VS, *et al*. Tumor regressive effects of *Viscum album* preparations exploration of immunomodulatory mechanisms. Medicina. 2007; 67(2):85-89.
117. Gohla SH, Zeman RA, Bogel M, Jurkiewicz E, Schrum S, Haubeck HD, *et al.* Modification of the *in vitro* replication of the human immunodeficiency virus HIV-1 by TPSg, a polysaccharide fraction isolated from the Cupressaceae *Thuja occidentalis* L. Arborvitae. Haematol Blood Transfus. 1992; 35(2):140-149. https://doi.org/10.1007/978-3-642-76829-3_24
118. Chang SL, Chiang YM, Chang CLT, Yeh HH, Shyur HL, Kuo YH, *et al*. Flavonoids, centaurein and centaureidin, from *Bidens pilosa*, stimulate IFN expression. J Ethnopharmacol. 2007; 112(2):232-236. https://doi.org/10.1016/j.jep.2007.03.001 PMid:17408892