CHAPTER

2

Recommended and Scientifically Validated Medicinal Plants as an Immunostimulant

2.1 INTRODUCTION

Traditional herbal drugs are an essential and integral part of health care system. Almost every civilization and country has its own methods and descriptions about the use of plant-based medicines. The World Health Organization reported that around three-quarter of the world population relies on the herbal medicines. The Indian Ayurvedic system of medicines also stresses on the use of rich Indian medicinal plants. The ethnopharmacological activities and scientific exploration of valuable plants drag the attention of world and these herbal remedies are gaining popularity across the globe.

One of the major health issue challenged by almost all the population is drug resistance. It has been observed that antibiotic resistance and antiviral drug resistance are few important medical threats that the entire world is facing. The improvement in the defense system of our body could be a way out to face the condition and thus making an individual adaptogenic against various dreadful pathogens.

Traditionally, many plants have been reported to have an immunomodulatory properties that can either stimulate or depresses the immune system depending upon the physiological and medical conditions. But we are more focused on immunostimulation properties of plants. Herbal immunomodulators work on immune system and its complicated network in order to achieve the stimulation and thus preparing the body to effectively fight with the invading pathogen and thus forming a protective shield against antigens.

The immunostimulants are thus act as a prophylactic agent or in other words they act as immunopotentiators. The action of herbal plants on immune system includes both innate and adaptive responses (Dinesh Kumar *et al*, 2012). These herbs enhance the basic immune responses and in a person with low immunity or impaired immunity, these plant-based medicines act as a immunotherapeutic agents.

2.2 TRADITIONALLY RECOMMENDED MEDICINAL PLANTS AS AN IMMUNOSTIMULANT

Many herbal drugs are used in Indian traditional system of medicines. The traditional literatures indicate the use of immunoherbs in order to achieve specific or nonspecific manner and act on both innate as well as adaptive immunity of our body (Agarwal SS, 1999). Indian Ayurvedic system of medicine is considered as one of the most

primitive system. People are practicing it in modern era as well and its existence is proved philosophically and scientifically (Chulet R, 2010). In Ayurveda, drugs are categorized as 'Rasayana' meaning enhancement of resistance of the body. The word Rasayana is made-up of two words 'Rasa' meaning elixier and 'Ayana' meaning transportation. If we explain the concept of Rasayana in terms of Charaka, it is the preparation that improves longevity, strength like horse, freedom from any disease. Similarly in terms of Sushruta, Rasayana is an anti-aging and quality of life improving concept (Shastri AK, 1993).

If we try to understand the concept of immunomodulation with the help of Rasayana, then around 34 herbs are identified traditionally under this category (Gulati K, 2002). A very famous Rasayana formulation Chyawanprash is used from around 4000 years. This preparation contains *Emblica officinalis* (Amla) as major ingredient along with other powder and herbal extracts (Mishra LC, 2004).

Table 2.1: List of Rasayana herbs as described in traditional system of medicine

S. No.	Plant name	S. No.	Plant name
1.	*Acorus calamus* (Bach)	18.	*Glycyrrhiza glabra* (Yashtimadhu)
2.	*Cissampelos pareira* (Akanadi)	19.	*Gmelina arborea* (Gaman)
3.	Aloe vera (Ghrit-kuman)	20.	*Hemidesmus indicus* (Ananta mul)
4.	*Ipomoea digitata* (Ajvayan)	21.	*Argyreia speciosa* (Samander ka Pat)
5.	*Semecarpus anacardium* (Bhilawa)	22.	*Leptademia reticulate* (Don)
6.	*Azadirachta indica* (Nimba, Neem)	23.	*Piper longum* (Piplamul)
7.	Plumbago zeylenica (Chita)	24.	*Bacopa monerri* (Brahmi)
8.	*Pterocarpus marsupium* (Bijasar)	25.	*Psoralea corylifolia* (Babchi)
9.	*Allium sativum* (Lahsun)	26.	*Boerhavia diffusa* (Sant)
10.	*Commiphora mukul* (Guggul)	27.	*Asparagus racemosus* (Satawar)
11.	*Solanum nigram* (Makoi)	28.	*Sida spinosa* (Gulsakan)
12.	*Curculigo orchiodes* (Krishna Musli)	29.	*Convolvulus phuricaulis* (Shankhapusp)
13.	*Terminalia belirica* (Bahera)	30.	*Spheranthus indicus* (Mandi)
14.	*Desmodium gangeticum* (Shalaparni)	31.	*Curcuma longa* (Haldi)
15.	*Tinospora cordifolia* (Gaduchi)	32.	*Terminalia chebulica* (Haritaki/Panhara)
16.	*Emblica officinalis* (Amla)	33.	*Dioscora bulbifera* (Ratalu)
17.	*Withania somnifera* (Ashwagandha)	34.	*Emblica ribes* (Vidang)

Apart from Rasayana, many non-Rasayana herbs also traditionally recommended to improve the immune system. They work on the concept of 'Ama'. The Ama is the immunologically active complexes generated in the intestine. Around 60 non-Rasayana herbs are mentioned in ancient literatures.

Table 2.2: Some examples of non-Rasayana herb

S. No.	Plant name	S. No.	Plant name
1.	*Amoora rohituka* (Harin-hara)	6.	*Picrorrhiza kurao* (Kutki)
2.	*Bahuhania veriegata* (Kachnar)	7.	*Saraca indica* (Ashoka)
3.	*Ciser arientinum* (Chana)	8.	*Vitex negundo* (Nirgandi)
4.	*Mentha spicata* (Pudina)	9.	*Zingiber officinalis* (Adarak)
5.	*Ocimum sanctum* (Tulsi)	10.	*Hibiscus esculentum* (Bhindi)

India is a country of diverse cultures and rituals. If we take an example, after the birth of a child, it is our custom to give dry fruits like *Prunus amygdalus* and *Phoenix dactylifera* in a preparation with milk or jaggary. Another similar preparation called Hareera that contains seeds of *Buchanania lanzan*, *Euryale ferox*, *Prunus amygdalus* and *Phoenix dactylifera* and dried rhizome of *Zingiber officinalem*. The concept behind this alternate therapy is to make the mother overcome from the depressed immune system experienced after the childbirth. These plants were studied for immunostimulant property and promising results were obtained.

2.3 SCIENTIFICALLY VALIDATED MEDICINAL PLANTS AS AN IMMUNOSTIMULANT

Natural adjuvants, antibody reagents, synthetic agents, etc. are used as immune-stimulative agents but there are major limitation to the general use of those agents such as increased risk of infections, side effects and generalized effects throughout the immune system. To deal with these problems, a number of drugs obtained from the natural sources have been used to alter and improve the human immune system (Mukherjee *et al*, 2014). In different systems of medicine, several medicinal plants are employed to improve the immune system and deal with the immunological disorders. Medicinal plants are used as remedies since long time and is believed that Ayurveda, i.e. ancient science of life is prevalent for more than 5000 years in India (Mishra *et al*, 2001). In recent times, it is known that to cure various diseases, it is necessary to modulate the immune response, this concept of modulating immune Response to cure any disease is same as the concept of Rasayana in Ayurveda. According to Ayurvedic system of medicine plants with rejuvenating properties promote health by strengthening host defenses against various diseases (Singh *et al*, 2012). Plants with rejuvenating properties may also possess other effects such as improving mental functions by strengthening the psychoneuro immune axis or delaying the onset of senescence. Hence, a number of plants with their extracts, active fractions of extract and the active phytoconstituents are investigated for modifying immune responses. Biologically active compounds of medicinal plants are also been in focus of research to effectively treat infectious diseases by improving the immune functions (Taylor *et al*, 2001). Some medicinal plants possessing immunostimulant activities are listed in Table 2.3.

Table 2.3: Medicinal plants with active phytoconstituents responsible for immunostimulant properties

S. No.	Medicinal plants, botanical name and family	Part of plant used	Active phytoconstituent	Immunostimulant mechanism	References
1.	**Aloe vera** *Aloe barbadensis* (Liliaceae)	Leaves	Dihydro-coumarin derivatives	Stimulates the superoxide production and increases phagocytosis of macrophages	**Zhang *et al*, 2006**
2.	**Amla** *Phyllanthus emblica* (Phyllanthaceae)	Fruits	Ascorbic acid, emblicanins A and B and flavonoids	Restores the production of IL-2 and IFN-γ, produces immuno-suppressive effect on lymphocyte proliferation	**Madhuri *et al*, 2011; Sairam *et al*, 2002**

Contd.

Table 2.3: Medicinal plants with active phytoconstituents responsible for immunostimulant properties (Contd.)

S. No.	Medicinal plants, botanical name and family	Part of plant used	Active phytoconstituent	Immunostimulant mechanism	References
3.	**Garlic** *Allium sativum* (Amaryllidaceae)	Fruits	Allicin, organosulphur compounds	Suppresses the production of leukocyte inflammatory cytokine	**Kyo *et al*, 2001; Hodge *et al*, 2002**
4.	**Ashwagandha** *Withania somnifera* (Solanaceae)	Root	Glycowithanolides (sitoindosides IX and X)	Increases WBC count, circulating antibodies, bone marrow cellularity, plaque forming cells in spleen and phagocytic activity of macrophages	**Ghosal *et al*, 1989; Tiwari *et al*, 2014**
5.	**Giloy** *Tinospora cordifolia* (Menispermaceae)	Stem and root	Magnoflorine, tinocordiside and syringin	Increases total WBC count, bone marrow cellularity and α-esterase positive cells. Increases macrophage activation	**Bishayi *et al*, 2002; Sharma *et al*, 2012**
6.	**Mulethi** *Glycyrrhiza glabra* (Fabaceae)	Bark and root	Glycyrrhizin, β-glycyrrhetinic acid	• Enhances activities of immune and antioxidant enzymes • Stimulates immune cells by CD69 expression on CD4 T cells, CD8 T cell and macrophages function	**Pandit *et al*, 2011**
7.	**Turmeric** *Curcuma longa* (Zingiberaceae)	Rhizome	Curcumin	Inhibits PMA and anti-CD28 antibody-induced proliferation, also inhibits PHA-induced T lymphocytes	**Ranjan *et al*, 1998; Yadav *et al*, 2005; Varalakshmi *et al*, 2008**
8.	**Papaya** *Carica papaya* (Caricaceae)	Leaves and seeds	α-tocopherol, ascorbic acid, phenolic acid, myricetin, kaempferol	Increases phytohemagglutinin responsiveness of lymphocytes and inhibits complement-mediated hemolytic pathway	**Otsuki *et al*, 2010**
9.	**Gotu Kola** *Centella asiatica* (Apiaceae)	Leaves	Asiaticoside	Increases WBC count and phagocytic index, inhibit production of IL-2 and TNFα and also inhibits human peripheral blood mononuclear cell (PBMC)	**Punturee *et al*, 2005**

Contd.

Table 2.3: Medicinal plants with active phytoconstituents responsible for immunostimulant properties (Contd.)

S. No.	Medicinal plants, botanical name and family	Part of plant used	Active phytoconstituent	Immunostimulant mechanism	References
10.	**Salai Guggul** *Boswellia serrata* (Burseraceae)	Bark	Boswellic acids (pentacyclic triterpene acid)	Inhibits mast cell protection	**Sharma *et al*, 1996**
11.	**Fenugreek** *Trigonella foenum graecum* (Fabaceae)	Seeds	Quercitin, rutin	• Increases the phagocytic capacity and phagocytic index of macrophages • Enhances thymus and bone marrow cellularities	**Bin-Hafeez *et al*, 2003**
12.	**Bhringraj** *Eclipta prostrata* (Asteraceae)	Whole plant	Wedelolactone and demethyl wedelolactone	• Increases non-immune response and lysosomal activity of humoral responses and induces phagocytic index	**Karthikumar *et al*, 2011**
13.	**Mango** *Mangifera indica* (Anacardiaceae)	Fruits	Magniferin	• Enhances production of IgG1 and IgG2b • Increases humoral antibody (HA) titre and DTH	**Garcia *et al*, 2003**
14.	**Punarnava** *Boerhaviadif fusa* (Nyctaginaceae)	Root	C-methyl flavones	• Inhibits production of NO, IL-2 and TNFα. • Inhibits human NK cell cytotoxicity	**Mehrotra *et al*, 2002**
15.	**Shatavari** *Asparagus racemosus* (Liliaceae)	Root	Steroidal saponins and sapogenins	Increases production of leucocytosis and phagocytic activity of macrophages	**Muruganandan *et al*, 2001**
16.	**Karela** *Momordica charantia* (Cucurbitaceae)	Fruit and seeds	α and β momorcharin	Inhibits the release of NO, TNF-α and proliferation of PHA induced spleen cells	**Pongnikorn *et al*, 2003**
17.	**Tulsi** *Ocimum sanctum* (Labiateae)	Aerial part	Eugenol	Inhibits antigen-induced histamine release from peritoneal mast cells and leucocyte migration	**Mediratta *et al*, 2002**
18.	**Black caraway** *Nigella sativa* (Ranunculaceae)	Seeds	Thymoquinone	Decreases synthesis of monocyte chemoattractant protein-1 (MCP-1), TNF-α, IL-1β and cyclooxygenase (COX)-2	**Salem, 2005**

Contd.

Table 2.3: Medicinal plants with active phytoconstituents responsible for immunostimulant properties (Contd.)

S. No.	Medicinal plants, botanical name and family	Part of plant used	Active phytoconstituent	Immunostimulant mechanism	References
19.	**Carpenter's herb** *Prunella vulgaris* (Lamiacease)	Fruits	Rhein	• Stimulates proliferation of T lymphocytes and supresses the production of NO in lipopolysaccharide-stimulated macrophages • Modulates various other immune factors like TNF-α, IgG, IgG1, IgG2b, LTB4, IFN- γ, IL2 and Src family protein kinase	**Harput *et al*, 2006**
20.	**Babchi** *Psoralea corylifolia* (Fabaceae)	Leaves	Furanocoumarin psoralen	• Increases cell-mediated humoral immune response • Up-regulates OVA-specific T_H1 cytokinie (IFN-γ) production and • down regulates OVA-specific T_H2 cytokine	**Latha *et al*, 2000; Lee *et al*, 2008**
21.	**Sage** *Salvia officinalis* (Lamiaceae)	Aerial part	Arabinogalactans	Induces thymocyte proliferation	**Capek *et al*, 2003**
22.	**Pomegranate** *Punica granatum* (Punicaceae)	Fruits	Punicic acid, anthocyanins	Stimulates cell-mediated immune response and inhibits leucocyte migration	**Ross *et al*, 2001**
23.	**Tamarind** *Tamarindus indica* (Leguminosae)	Fruits	B-setosterol, campesterol	• Stimulates functions of neutrophil, neutrophil NADPH oxidase activity and elastase activity. • Inhibits phorbol myristate acetate (PMA)	**Landi Librandi *et al*, 2007**
24.	**Jasmine** *Rhinacan thusnasutus* (Acanthaceae)	Fruits	Hyperforin	• Stimulates IL-8 expression in primary hepatocytes and human intestinal epithelial cells • Decreases adhesion function of epithelial cells and alters the function of NF-kB	**Zhou *et al*, 2004**
25.	**Sea-buckthorn** *Hippophaes* (Elaeagnaceae)	Leaves and fruits	B-carotene, ascorbic acid	Induces cellular and humoral immune response, inhibits production of chromium-induced free radicals	**Geetha *et al*, 2005**

Contd.

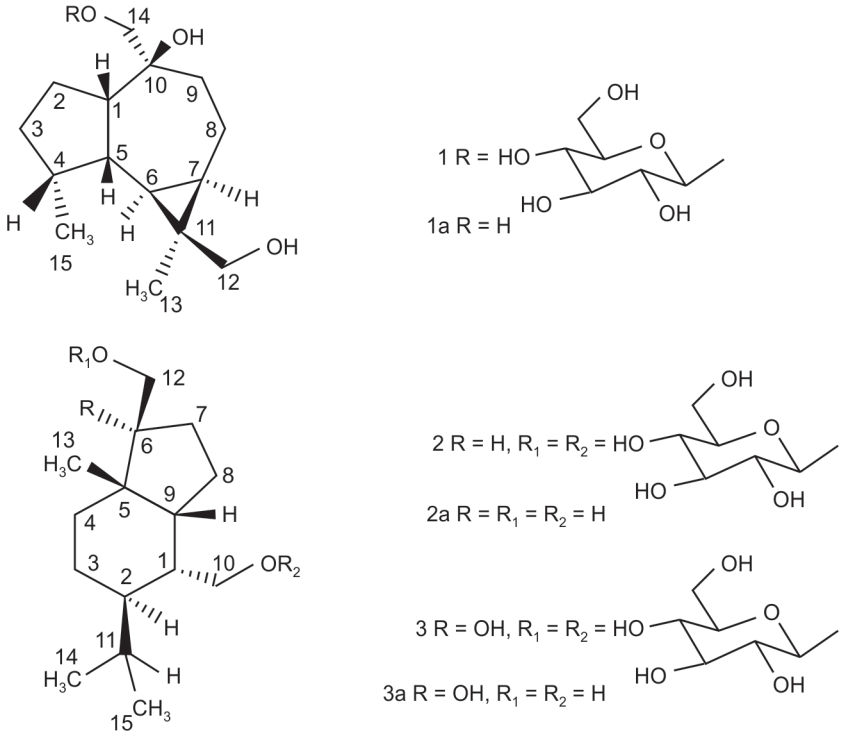
Table 2.3: Medicinal plants with active phytoconstituents responsible for immunostimulant properties (Contd.)

S. No.	Medicinal plants, botanical name and family	Part of plant used	Active phytoconstituent	Immunostimulant mechanism	References
26.	**Guldaudi** *Chrysanthemum indicum* (Compositae)	Aerial parts	α-Pinene, 1,8-cineol, and chrysanthenone	Increases antibody generation, DTH reactions and potentiates mononuclear phagocytosis function	**Choi *et al*, 2009**

2.4 PHYTOCONSTITUENTS AS AN IMMUNOSTIMULANT

GLYCOSIDES

Glycosides are the naturally occurring phytoconstituents consisting of a carbohydrate portion combined with a hydroxyl compound. The hydroxyl compound is usually a noncarbohydrate molecule (aglycon) like derivatives of phenol, alcohol, etc. They are widely distributed in plant and animal sources. Many glycosides exhibit immunomodulation property. Few examples include iridoid glycosides (HS Garg *et al*, 1994), anthraquinone glycosides, sesquiterpene glycosides, etc.



Sesquiterpene glycosides from *Dendrobium nobile* plant

1. Dendroside A; 2. Dendronobilosides A; 3. Dendronobilosides B

Fig. 2.1: Immunomodulatory glycosides

FLAVONOIDS

Flavonoids are important secondary metabolites and widely distributed in herbal medicinal plants, fruits, vegetables, etc. They have shown many health promoting advantages and are widely used by nutraceutical, cosmetic and pharmaceutical industry. Since flavonoids have broad spectrum advantages, so immunostimulatory activity is also one of its potential areas of its applications. Flavonoids are divided into different types on the basis of carbon of the C-ring carbon at which the B ring is attached, degree of unsaturation and also oxidation of the C ring. The basic nucleus is shown in figure 2.2 (AN Panche, 2016). Immunomodulatory flavonoids include isoflavonoids, anthocyanins and flavones (Dinesh Kumar *et al*, 2012).

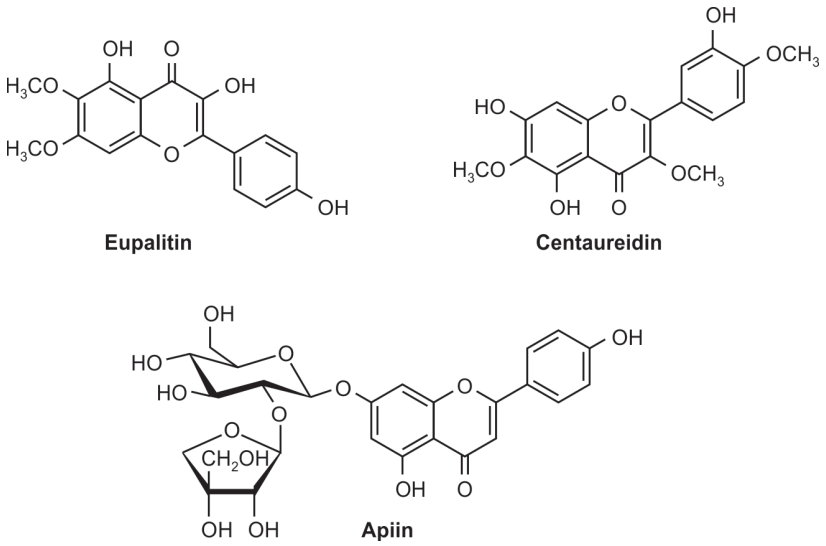


Fig. 2.2: Some common immunomodulatory flavonoids

COUMARINS

Chemically, coumarins are 1-benzopyran-2-one and belongs to benzopyrone class and distributed in many plant species of medicinal importance (Hervé Martial Poumale Poumale *et al*, 2013) (Fig. 2.3).

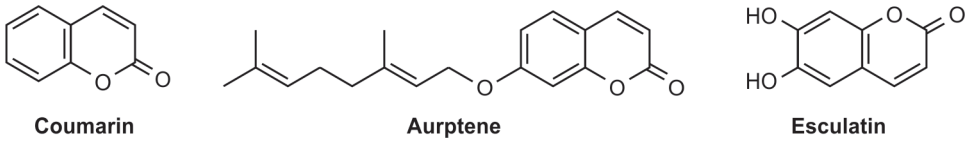


Fig. 2.3: Coumarin and its derivatives

Coumarins like aurptene, coumarin derivatives, esculatin also exert immunomodulatory activities (Leung K *et al*, 2005).

SAPOGENINS

Sapogenins are nonsaccharide parts of natural products known as saponins (Fig. 2.4). Chemically, they contain steroid or triterpene structure as their vital organic feature. Many medicinal plants contain sapogenins and exhibit immunomodulatory activity like *Gymnema sylvestre*, *Randia dumetorum*, etc.

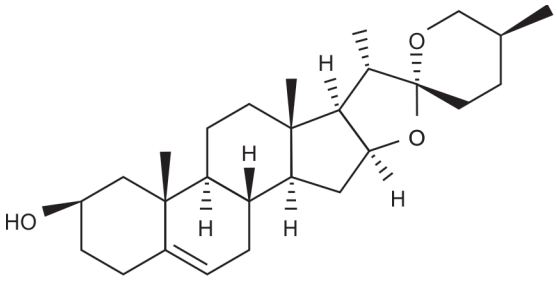


Fig. 2.4: Structure of sapogenin

ALKALOIDS

Alkaloids (Fig. 2.5) are a large group of compounds that contains nitrogen atom/s in their organic arrangement and found abundantly in nature (Kokate CK, 2004). Because of the presence of nitrogen, these compounds are alkaline in nature. The nitrogen is available in cyclic ring structure like indole alkaloid in which nitrogen is available in indole ring system, etc. Alkaloids are also further divided into many classes like steroids, terpenoids, quinolines, pyridines, etc. Scientific studies suggested that the alkaloids also have immunomodulatory activity. Alkaloids isolated from plants like *Achillea millefolium*, *Cissampelos pareira*, *Actinidia macrosperma*, etc. have significant immunomodulatory properties.

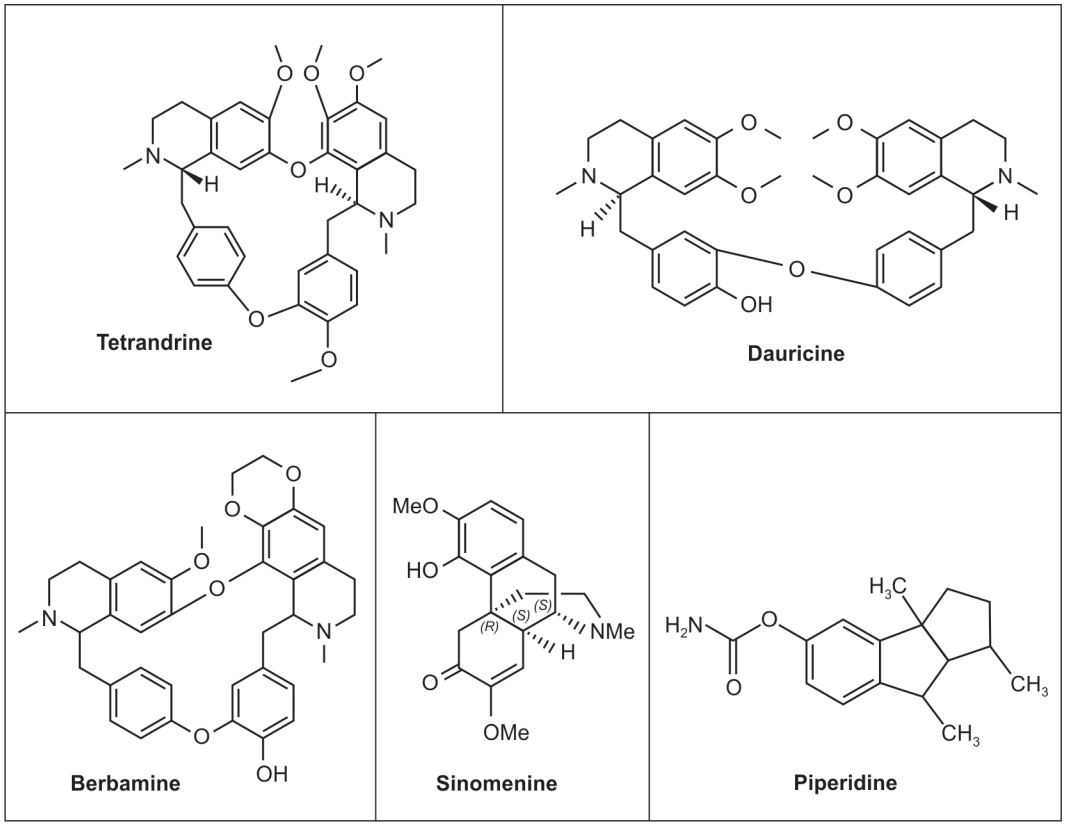
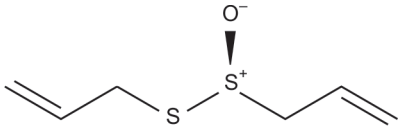


Fig. 2.5: Immunomodulatory alkaloids

THIOSULFINATES

Chemically, thiosulfinates contain functional group linkage R-S(O)-S-R, where R are organic substituents. Many acyclic and cyclic thiosulfinates occur in medicinal plants species, e.g. allicin obtained from garlic. Thiosulfinates have immunomodulatory and adaptogenic activities. Plant like *allium hirtifolium* is a well known example of immunomodulators that are rich in thiosulfinates (Jafarian A, 2003) (Fig. 2.6).

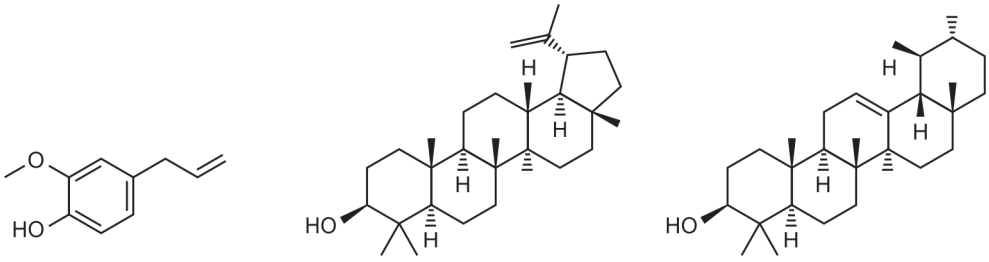


Allicin

Fig. 2.6: Thiosulfinates (allicin) as immunomodulator

VOLATILE OILS AND TERPENOIDS

Chemically, terpenes are the hydrocarbons (C_5H_8) and terpenoids include the hydrocarbon along with their oxygenated derivatives. Terpenes and the terpenoids are volatile oils of plant and animal source (Kokate CK, 2004). These phytochemicals also exhibit effects on immune system and immunomodulation properties have been reported. Common examples are eugenol isolated from *Ocimum sanctum*, triterpenes isolated from *Ganoderma lucidum*, lupeol and amyrine present in *Bauhinia variegate* also demonstrated immunomodulation (Fig. 2.7).



Eugenol **Lupeol** **Amyrine**

Fig. 2.7: Some common immunomodulatory volatile oils and terpenoids

POLYSACCHARIDES

Recent studies on polysaccharides as an significant bioactive compound available in medicinal plants have initiated its wide spectrum applications. Scientists have validated the polysaccharides to have anticancer, antioxidant, radioprotective, hypolipidemic and immunomodulatory activities. Many other biological activities are also conducted and promising results were obtained that made the bioactive compound suitable or its medicinal application. As far as immunomodulatory activity is concerned, studies suggest that the polysaccharides modulate innate immunity and macrophage functioning. Murine-thymus-lymphocyte proliferation enhancement due to polysaccharides obtained from plant *Cistanche deserticola* was studied (Alamgir M, 2010). High molecular weighted polysaccharides of plant *Salicornia herbacea* also activates monocytes and initiates its differentiation into macrophages. Wide range of naturally occurring pectic polysaccharides obtained from medicinal plants

act on human immune system. Many acidic polysaccharides like RG-I, RG-II and homogalacturonans purified from medicinal plants have their activity on complement system (Sophie, Aboughe Angone, 2011).

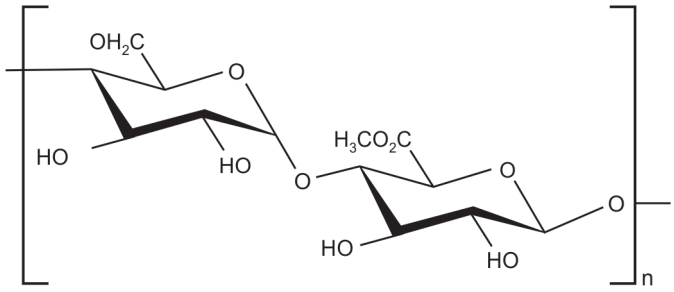


Fig. 2.8: Polysaccharide immunomodulator

2.5 POSSIBLE MECHANISMS OF ACTION OF MEDICINAL PLANTS AS AN IMMUNOSTIMULANT

Plants have been used from ancient times to treat various ailments and diseases. Medicinal plants and their products are now an accepted therapeutic approach to modulate immune responses and functions. It is also known that modulation of immune response may provide an alternative to a number of conventional therapies for several disease conditions, especially when there is a need of activating the host's defense mechanism under impaired immune response conditions or the conditions when there is a need of inducing selective immunosuppressant to tackle the autoimmune disorders or organ transplantation (Singh *et al*, 2016).

Naturally occurring compounds have the ability to modify the cellular and humoral immune responses in animals and humans that are evolved to confer the protection against infectious agents via various mechanisms such as specific and nonspecific immune mechanisms. Bioactive compounds from medicinal plants are capable to alter those mechanisms in order to modulate the immune responses (Quinn, 1990).

Bioactive compounds from medicinal plants may modulate the immune response either by suppressing or stimulating the antigen recognition and phagocytosis, synthesis of antibodies, ag–ab interaction, proliferation of lymphocytes, release of several mediators such as TNF-α, IgG, IgG1, IgG2b, LTB4, IFN-γ, IL2, Src family protein kinase, etc. and modification of target tissue response. Natural products may also enhance the ability to stimulate host's natural and adaptive defense mechanisms including cytokines which enable body to help itself.

Immunological defense mechanism is a complex interaction between (i) specific and nonspecific and humoral and cellular immune responses, (ii) suppression and stimulation of immunocompetent cells, (iii) endocrine influence and several other mechanisms on the immune system. T and B lymphocytes are the primary targets of the immunostimulants and the central role in immunostimulation is played by increase in phagocytosis by macrophages and granulocytes (Smyth *et al*, 2004). For the stimulating agent to be in contact with reactive cells, activation of macrophage is of paramount importance and the stimulation of T lymphocytes is another important step that can be achieved directly or indirectly via macrophages (Wagner *et al*, 1985).

2.6 CLINICALLY INVESTIGATED MEDICINAL PLANTS AS AN IMMUNOSTIMULANT

Medicinal plants are well known for treating a number of diseases with no or minimum side effects. Immunostimulant characteristics of the plant and plant-based therapeutic agents have gathered the focus of researchers. A large number of medicinal plants are known in traditional system of medicines and many of them are also clinically proven. Capsaicin is isolated from chili-peppers, i.e. *Capsicum* species; vinblastine, vincristine from Madagascar periwinkle, i.e. *Catharanthus roseus*; galantamine from Caucasian snowdrop, i.e. *Galanthus caucasicusare*; are some of the examples of plant-based compounds that are clinically investigated as immunostimulants (Jantan *et al*, 2015).

Kalikar *et al*, assessed immunomodulatory effect in HIV-positive patients by treating them with *Tinospora cordifolia* extract in a randomized double-blind placebo controlled trial. They treated the patients with *Tinospora cordifolia* extract or placebo. As a result, they found 60 % patents treated with *Tinospora cordifolia* and 20% of placebo-treated patients reported decrease in various symptoms based on weak immunity. The researchers concluded that *Tinospora cordifolia* extract may be considered as plant-derived immunostimulant which was validated by clinical evaluation (Kalikar *et al*, 2008).

Ishikawa *et al* studied effect of aged garlic extract (AGE) on human subjects, i.e. patients with inoperable liver, colorectal or pancreatic cancers. In randomized double blind trial they administered AGE to one group and to the other group administered placebo for 6 months. Primarily (endpoint) they looked quality of life questionnaire based on the functional assessment of cancer therapy (FACT) and the subendpoints were changes in the activity of NK cells and change in the salivary cortisol level from before and after AGE administration. Total subjects consented for the trial were 50 out of which 42 patients with liver cancer, 7 patients with pancreatic cancer and 1 patient was suffering from colon cancer. As a result, they found good drug compliance in both the groups and no adverse effects in either group. Increase in number of NK cells and NK cell activity were observed in AGE group. The study concluded improved activity of NK cells in the patients with advanced cancer of digestive system when administered with AGE (Ishikawa *et al*, 2006).

2.7 CONCLUSION AND FUTURE PROSPECTIVE

Traditional herbal medicines are the popular source of medicine and as per WHO a major proportion of population relies on herbal drugs. The ancient literatures and Ayurveda are helping in the scientific development of drug and its formulation and around every year 20% rise in this sector is observed. Indian herbal medicines have a distinct position if we talk about research on ethnopharmacological evidences in scientific validation process. Many of our herbs are now included in International pharmacopoeia.

Rejuvenation and leading a quality life is everyone's dream. Disease-free life is now difficult to achieve due to many external factors like microbial load, stress, etc. Immunoherbs are giving their contribution in order to boost immune system so that a shield can be made around our body that prohibits the entry of any disease causing element in our body system.

Traditional literatures have mentioned many Rasayana and non-Rasayana herbs that are being used from ages to impart stimulated immune system and to build ability inside an individual to either be protected from the disease or can readily cured with

the help of immune system components. These drugs act on both innate as well as adaptive immune responses and give a long-lasting effect.

Immunostimulatory plants have found to possess many important categories of phytochemicals including glycosides, polysaccharides, volatile oil and terpenoids, coumarins, thiosulfinates, alkaloids, etc. The scientific validation of indicated plants have successfully demonstrated the activity of these rich medicinal herbs as immunomodulators and preclinical investigation provides promising scientific evidence related to its pharmacological activities. The scientists are getting success in identifying the responses of immune cells and mediators like phagocytes, T and B cells, NK cells, etc. due to immunoherbs.

The clinical trials of many immunomodulatory phytochemicals are under process incluing curcumin, resveratrol, epigallocatechin-3-gallate, quercetin, colchicine, etc. (Jantan I, 2015). We can conclude that the immunoherbs have potentiated discovery engine to formulate effective, safe and cheap herbal solution to fight against human invasive pathogen and hence improve the quality of life.

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