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HERBAL IMMUNOMODULORS: A REVIEW

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ABSTRACT: The traditional Indian system of medicine (Ayurveda) describes different modalities involved in the prevention and treatment of disease and stresses upon the role of diet, life style and drugs as cornerstones of therapy. Medicinal plant products are known to modify different aspects of human physiology and exert an alleviating influence on several pathophysiological states, and concepts of immunity and immune-modulation can be traced back several hundred years to the history of medicine. However, it is only in recent years that the scientific concept of immune modulation has been forwarded, and it now appears that some of the beneficial effects of Indian medicinal plants, proposed in Ayurveda by Charaka and Sushruta Samhita, may be due to these "immunomodulatory" effects. Several research groups have worked on the scientific basis of such immunomodulatory effects of plant products, and as a result, considerable data has accrued. The present review summarizes some of these experimental data in an attempt to justify some of their beneficial effects in health and disease, and also to provide insights in to the future research in this area.

INTRODUCTION: The prime objective of Ayurveda, the ancient Indian system of medicine is the prevention of the disease process. To achieve this, it advocates a vast range of health care practices. These measures include systematized daily routine to govern the life style of the individuals, and a seasonal routine to harmonize the physiology with the circadian rhythm that governs the nature. Thus complete harmonization both at systemic and cellular levels is involved [1]. The system also explores various natural resources, both pharmacological and non-pharmacological, to optimize the inherent physiological abilities of living systems, to modify the overall quality of life.

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The different health care measures to be adopted by an individual are grouped together under the heading of "Rasayana." The word Rasayana in Sanskrit literally implies to the circulation of Rasa, the nutrient. Rasayana aims at optimizing the circulation of nutrients to all components of the physiology, whether in a system, in any tissue or even within a cell. In the words of Charaka with a Rasayana "One obtains longevity, regains youth, gets a sharp memory and intellect and freedom from disease, gets a lustrous complexion and the strength of a horse". Sushruta was more specific, describing a Rasayana as one, which is anti-aging, increases the life-span, promotes intelligence and memory, and increases resistance to diseases (indicating immunostimulant effect) [2]. Rasayana plants are particularly recommended for the treatment of epidemic diseases. Apart from immunostimulant activity, they have also been evaluated for their anabolic, anti-stress adaptogenic, no tropic, antioxidant and anti-aging effects.

The modern system of medicine had always been enthusiastic to evoke nonspecific defense mechanisms of human physiology, which led to the discovery of active immunization using microbial preparation to enhance the host defense against infection. Recently, the same enthusiasm has taken an important leap towards exploring a novel group of substances from natural resources that modulate the immune response of living systems and influence the disease process. An immunomodulator can be defined as a substance, which can influence any constituent or function of the immune system in a specific or nonspecific manner including both innate and adaptive arms of the immune response [3]. It can cause immuno-stimulation by stimulating effector cells or production of their metabolic inducers or by inhibiting the immunity limiting factors. Immunosuppression can be achieved by stimulating the inhibitor cells and humoral factors, or inhibition of effector cells. In clinical practice, both aspects of immunomodulation, *viz.* immune-stimulation and immunosuppression are equally important.

Immuno-stimulation may be required during conventional chemotherapy when the host defence mechanisms are to be activated under conditions of impaired immune responsiveness. In addition, it may help in prophylaxis of opportunistic infections in risk-prone, sensitive patients. on the other hand, immunosuppression may be of choice in treatment of autoimmune disorders such as rheumatoid arthritis, multiple sclerosis etc [4].

Immune System: The immune system is designed to protect the host from invading pathogens and to eliminate disease. The primary object in the past has been to suppress immune system to permit all transplantation. Activation of immune system by "non-self" antigen (alloantigen) or "self" antigen (auto antigen) is generally believed to require processing of the antigen by the phagocytic cells such as macrophages, monocytes, or related cells. Human immune system is quite able to maintain immunity against various infections certain bacteria and virus can affect adversely. The immune system is one of our most complex biological systems in the body that protect against Disease [5]. The cellular component of acquired immunity consists of T-Lymphocyte while the humoral component of this immunity involves the role of β-Lymphocyte.

Immunology is one of the most rapidly developing areas of medicinal biotechnology research and has great promises with regard to the prevention and treatment of a wide range of disorder such as inflammatory disease of skin, gut, respiratory tract and central organ. Infectious diseases are now primarily considered immunological disorders while neoplastic disease and organ transplantation and several autoimmune diseases. Smaller fragment which then activate adaptive immune system to neutralize or kill the pathogens [6]. Disorders of the immune system can result in autoimmune disease and inflammatory disease cancer.

Immunodeficiency occurs when the immune system is less active than normal, resulting in recurring and life-threatening infections. In humans, immunodeficiency can either be the result of a genetic disease such as severe combined immunodeficiency, acquired conditions such as HIV/AIDS, or the use of immunosuppressive medication. In contrast, autoimmunity results from a hyperactive immune system attacking normal tissues as if they were foreign organisms. Common autoimmune diseases include Hashimoto's thyroiditis, rheumatoid arthritis, diabetes mellitus type 1, and systemic lumps erythematosus. Immunology covers the study of all aspects of the immune system [7].

Organs of Immune System: Although functioning as a system, the organs of immune system are distributed at different places in the body. These are as under:

a) Primary lymphoid organs:

i. Thymus

ii. Bone marrow

b) Secondary lymphoid organs

i. Lymph nodes

ii. Spleen

iii. Malt (mucosa associated lymphoid tissue located in the respiratory tract and GIT)

There are the types of immune response are occurs in the human body: (Figure 1)

1. Innate immune response
2. Adaptive immune response
3. Humoral immunity
4. Cellular immunity [13]

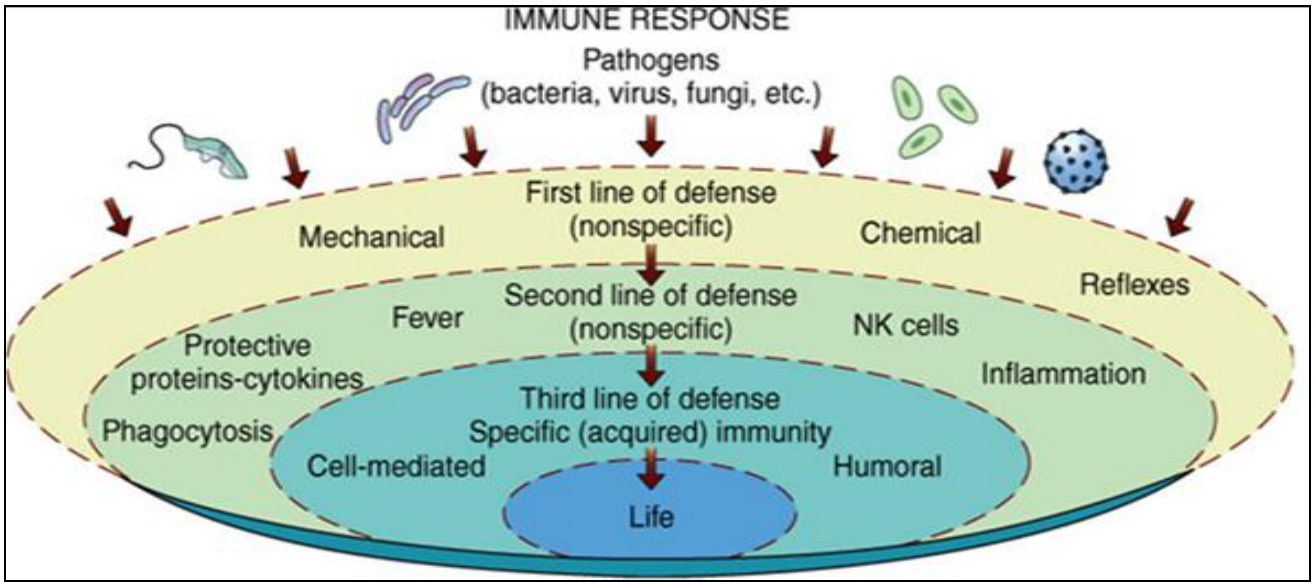
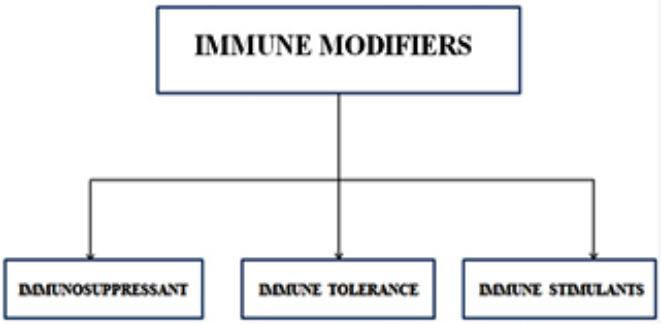


FIGURE 1: HOW THE IMMUNE SYSTEM WORK

Immunomodulation: Immunomodulation is a therapeutic approach in which we try to intervene in auto regulating processes of the defense system. Immunomodulator are the extrinsic or intrinsic substances which regulate or alter the scope type duration or competency of the immune response. Immunomodulator correct immune system that is out of balance. Immunomodulators modulate the activity of the immune system. That, in turn decreases the inflammatory response. Hence, immunomodulator is to maintain a disease Free State & modulation of immune response by stimulation & suppression. Immunomodulator can provide supportive therapy to the chemotherapy. Immunomodulator are natural or synthetic substances that help regulate or normalize the immune system. Natural immunomodulator are less potent then prescription immunomodulator and also less likely to cause side effects. Synthetic immunomodulator medication works by suppressing the immune system and decreasing inflammation in the digestive tract, ulcerative colitis, and chrons disease [9].

Immunomodulator stem from their ability to stimulate natural and adaptive defence mechanism which enables the body to help itself. Natural immunomodulator found in some raw fruits and vegetables and in the alga, sprulina, *Aloe vera*, *Plumbago indica* and *Aegle marmalose* etc. There are two types of immunomodulators are as follows.

1. Immunosuppressants
2. Immunostimulants



Immunosuppressant: Immunosuppressant have already employed in transplantation surgery. An immunosuppressant is any substance that performs immunosuppression of the immune system. They may be either exogenous, as immunosuppressive drugs, or endogenous, as, e.g., testosterone. Immunosuppressants are the agent which suppress the immune system and are used for the control of pathological response in autoimmune disease. The term immunotoxin is also sometimes used (incorrectly) to label undesirable immuno-suppressants, such as various pollutants and the herbicide DDT are immunosuppressants [10].

Immune tolerance: Immune tolerance or immunological tolerance is the process by which the immune system does not attack an antigen .It can be either 'natural' or 'self-tolerance', in which the body does not mount an immune response to self-antigens, or 'induced tolerance', in which tolerance to external antigens can be created by manipulating the immune system.

Immunostimulants: Immunostimulants, also known as immunostimulators, are substances (drugs and nutrients) that stimulate the immune system by inducing activation or increasing activity of any of its components. One notable example is the granulocyte macrophage colony-stimulating factor. An immune disorder such as immunodeficiency state autoimmune disease cancer and viral infection can be treated with immunostimulant drug. **Fig. 1** shows that the how many types immune system present in human body and how it works to stable our body against foreign particle [11].

Immunomodulation by drug-biological response modifires:

- Immunoaugmenting agent
- Immunosuppressive agent
- Interferons and interform inducers
- Lymphokines and monokines
- Growth factor
- Tnymic factor
- Tumor antigens
- Maturation factors
- T cell immunoregulator

Immunomodulation Therapy: The development of agents that modulate the immune responses rather than suppress it has become an important area of pharmacology. The rationale underlying this approach is that such drug may increase the immune responsiveness of patients who have either selective or generalized immunodeficiency. The major potential uses are in immune deficiency disorder, chronic infectious disease, and cancer. The AIDS epidemic has greatly increased interest in developing more effective immunomodulating drugs [12]. Many plants present in the world to show Immunomodulatory action and these are enlisted in **table 1.**

LIST OF PLANTS HAVING IMMUNOMODULATORY ACTIVITY:

S. no.	Name of drug	Family	Part used	Ethno medicinal Uses
1	*Boerhaavia diffussa*	Nyctaginaceae	Root	Anticancer, Antistrogenic Immunomodulatory, Hepatoprotective Antibacterial
2	*Curcuma longa*	Zingiberaceae	Rhizomes	Anticancer, Alzheimer, Diabeties, Cardioprotective Vasodilator, Immune stimulating
3	*Rhododendron spiciferum*	Ericaceae	Leaf	Immunomodulatory Anti-inflammatory Anti-asthmatic
4	*Caesalpinia bonducella*	Caesalpiniaceae	whole plant	Anti-anaphylactic Antiviral Anti asthmetic Immune stimulant
5	*Tinospora cordifolia*	Menispermaceae	Whole plant	Immunosupressant Tuberculosis Anti-cancer Hyperglycemic Anti-inflammatory Liver disorder
6	*Capparis zeylanica*	Capparidaceae	Whole plant	Immunostimulant Antipyretic Antimicrobial Asthma

7	*Luffa cylindrical*	Cucurbitaceae	Seed & fruit	Jaundice Anti-fungus Anti-microbial Anti-allergy Anti-stimulation
8	*Withania somnifera*	Solanaceae	Whole plant	Antioxidant activity Anti-carcinogenic Anti-aging Immune regulator
9	*Asparagus racemosus*	Asparagaceae	Root	Immunomodulator Amenorrhea Chemo preventive
10	*Panax ginsengs*	Araliaceae	Root	Immune modulator Anti-cancer Anti-diabetic
11	*Nelumbo nucifera*	Nymphaeaceae	Rhizome, seed	Anti-inflammatory Anti-ischemic Antioxidant Hepato protective Immunomodulator
12	*Azadiracta indica*	Meliaceae	Leaf	Anti-cancer Anti-oxidant wound healing
13	*Arnica montena*	Compositae	Dried flower head	Broken bone Anti-inflammatory Treatment of bruises
14	*Calendula officinalis*	Asteraceae	Flower	Reproductive health Astringent Anti-cancer
15	*Echinacea purpurea*	Asteraceae	Flowering top	Immune stimulant Heal wound and burn Skin infection
16	*Euphorbia tirucalli*	Euphorbiaceae	Latex	Lymphoma Asthma
17	*Ocimum sanctum*	Lamiaceae	Leaf	Immune stimulant Hypoglycemic Radiation poisoning Anti-oxidant Anti tussive
18	*Crocus sativus*	Iridaceae	Flower	Anti-inflammatory Anti-depression Anti-convulsant Ant mutagenic
19	*Picrorhiza kurroa*	Scrophulariaceae	Leaf	Anti-allergy Liver cirrhosis Dyspepsia
20	*Allium sativum*	Amaryllidaceae	Bulb	Anti-septic Anti-spasmodic Anti tumors
21	*Hibiscusrosa sinensis*	Malvaceae	Flowers	Increase blood circulation Liver disorder
22	*Cleome gynandra*	Cleomaceae	Aerial parts	Anti-inflammatory Anti-cancer Anti-diabetic
23	*Trikatu mega*	Piperaceae	Aerial parts	Immune modulation Anti-oxidant Rheumatism Intestinal worms

24	*Nyctanthes arbortristis*	Oleaceae	Leaf	Anti-inflammatory Immune stimulant Anti-diabetic Hepato protective
25	*Cissampelos pareira*	Menispermaceae	Roots	Uterine relaxant Diuretic Hypotensive Anti hemorrhagic
26	*Bauhinia Vareigata*	Fabaceae	Stem bark,	Blood purifier Asthma Skin disease
28	*Balanite roxburghi*	Zygophyllaceae	Leaf	Immunomodulator Anti-inflammatory Analgesic effect
29	*Ficus carica*	Moraceae	Leaf	Anti-fungal Anti agiogenic Erythropoitic Humoral antibody response Hepato protective Anticancer Hypocholestrolemic
30	*Chenopodium album*	Amaranthaceae	Leaf & stem	Anti-nociceptive effect Cytogenetic activity Mucosal immune Response
31	*Trapa bispinosa*	Trapaceae	Fruits	Analgesic activity Anti-diabetic activity Morphological activity Immunomodulatory activity
33	*Chlorophytum borivilianum*	Asparagaceae	Roots	Analgesic activity Boost the immune system Health promoting
34	*Morus alba linn*	Moraceae	Fruits	Immunonutrition activity Hepatoprotective activity Neuroprotective activity Anti-depressant activity
35	*Aesculus indica*	Aesculus	Leaf	Anti-inflammatory activity Anti tumor activity Anti-viral activity Anti angeiogenic activity
36	*Ficus benghalensis*	Moraceae	Roots	Immunomodultory Wound healing Hypolipidemic Anti-diarrhoeal Anti-stress Anti-allergy
37	*Citrus aurantifolia*	Rutaceae	Fruits	Cardiovascular disease Anti-Cancer Anti-Obesity Sedative and hypnotics
38	*Cissampelos pareira*	Menispermaceae	Roots	Antihistaminic Hypotensive Anticonvulsant Smooth muscle relaxant
39	*Actinidia macrosperma*	Actinidiaceae	Whole plant	Anti-cancer Immunomodulatory
41	*Prunella vulgaris*	Labiatae	Fruit spikes	Anti-viral (HIV) Immunomodulator
42	*Rhaphido phorakorthalsii*	Araceae	Leaf extracts	Anti-cancer Immunomodulatory effect Treatment of snake bite

43	*Selaginella species*	Selaginellaceae	Whole plant	Herat disease Tonic for malaria patient Treated to snake bite Jaundice Acute hepatitis
44	*Couroupita guinensis*	Lecythidaceae	Flowers	Analgesic Antiseptic Skin disease
47	*Aloe vera*	Xanthorrhoeaceae	Leaves	Adaptogens Skin burn (1°) Constipation Immunomodulator
48	*Angelica dahurica*	Apiaceae	Root	Diuretic Reduce gallbladder pain Relive anemia Dyspepsia Blood builder
49	*Baliospermum montanum*	Euphorbiaceae	Root	Diaphoretic Leprosy Jaundice Skin disorder Leucoderma
50	*Caesalpinia bonducella*	Caesalpiniaceae	Seed	Adaptogenic Anti-diabetic Anti-filarial activity Immunomodulatory Anxiolytic activity Anti-malarial activity
51	*Eclipta alba*	Asteraceae	Whole plant	Rheumatism Relives burning urine Spleen and skin disorder
52	*Epilobium angustifolium*	Onagraceae	Whole plant	Sedative Hypnotic Anti-androgen
53	*Mangifera indica*	Anacardiaceae	Stem bark	Anti-oxidant Radioprotective Immunomodulatory Lipolytic Anti boneresorption
54	*Salicornia herbacea*	Chenopodiaceae	Whole plant	Anti-oxidant Anti-inflammatory Immunomodulatory Anti hyperlipidemic
56	*Boswellia carterii*	Burseraceae	Bark	Arthritis Asthma Ulcerative colitis Aromatherapy
57	*Gymnema sylvestre*	Asclepiadaceae	Leaves	Anti-diabetic Diuretic Metabolic syndrome
58	*Tridax procumbens*	Asteraceae	Aerial part	Immunomodulator Hepatoprotective Anticancerous
59	*Clerodendrone Multiflorum*	Lamiaceae	Stem	Anit malarial Anti-diabetic Anti-hypertensive Antitumor
60	*Emblica officinalis*	Phyllanthaceae	Fruit	Immunomodulation Anti-Diabetes Antipyretic Cytoprotective

				Snake venom neutralizer
61	*Heracleum persicum*	Apiaceae	Whole plants	Anti-inflammatory Anticonvulsant Modulate immune system
62	*Morinda citrifolia*	Rubiaceae	Fruit	Tuberculosis Hypertension Rheumatism Fibromyalgia
64	*Centella asiatica*	Mackinlayaceae	Whole plant	Improving memory Treating mental fatigue Skin disease Treatment of burn
66	*Curculigo orchioides*	Hypoxidaceae	Root stocks	Stimulate immune response Skin disease Asthma Dyspepsia Opthalmia
67	*Randia dumetorum*	Rubiaceae	Leaf	Analgesic Anti-allergic Immunomodulatory activity
68	*Piper longum*	Piperaceae	Fruit	Hepatitis Anti-allergic Intestinal disorder Antitumor
69	*Terminalia arjuna*	Combretaceae	Stem bark	Heart disease Anti-inflammatory Anti-bacterial
70	*Ficus religiosa*	Moraceae	Leaf	Anti actylcholinesterase Protolytic activity Anti-amnesic activity Anticonvulsant activity
71	*Moringa olifera*	Moringaceae	Pods	Antiviral disease Nervous disorder Immune stimulant Reproductive health
72	*Bryophyllum pinnatum*	Crassulaceae	Leaf	Rheumatism Anti-ulcer Anti-cancer
73	*Camellia sinensis*	Theaceae	Leaf and leaf buds	Anti-aging activity Anti-Alzheimer activity Cardiovascular disease

***Panax ginseng*:**

Geographical source: Ginseng is dried root of the various species of *Panax ginseng* belonging to family areliaceae [1].

Description: It is a perennial geophites with a short rhyzomes attached to freshly root and has single stem that immersed every year with compound leaves a single cluster of small white flowers that develop into bright red fruits.

Geographical source: American ginseng grows in the mountain of eastern United States & Canada. Asian ginseng grows on mountain slope of China and Korea [13].

Chemical constituents: Ginseng contains mixture of several saponins, glycosides belonging to terpenoid glycoside. They are grouped as follows.

Ginsenosides (structure is given in **fig. 2**), Panaxocides, Chikusetsusaponin

Ginsenoside contain dammarolpanaxosides have oleanoic acid as aglycone panaxdiol and panaxtriol on decomposition.

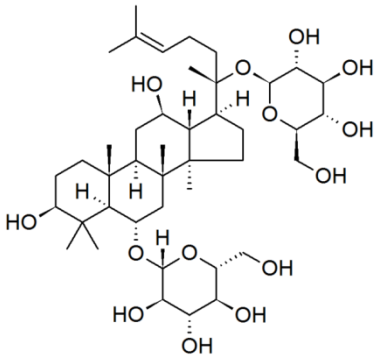


FIG. 2: GINSENOSIDE

Therapeutic uses: It is an important immunomodulatory drug. Ginseng is used for lack of apatite, insomnia, cholesterol; ginseng extract and ginsenoside to effective in stimulate learning[14].

***Curcuma longa*:**

Biological source: Turmeric consists of dried as well as fresh rhizomes of the plant known as *Curcuma longa belonging* to family zingeiberaceae. It contains not less than 1.5 % of curcumin.

Geographical source: curcuma is a genous of about 70 species of rhizomatous herbs distributed in South East Asia and especially India, China, Italy, Malaysia, Australia. In India, it accounts for as much as 90 % of total output of the world. Tamil Nadu and Andhra Pradesh together contribute about 70 % of the Indian production [15].

Chemical constituents: Turmeric contains about 5 % volatile oil, resin and yellow coloring substances known as curcuminoids. The chief component of curcuminoids is known as curcumin (50-60 %) structure is mentioned in **Fig. 3** and some sesquiterpenes such as α and β pinene, zingiberene.

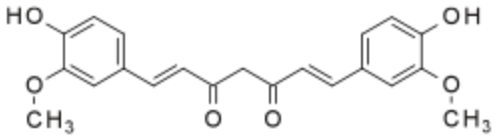


FIG. 3: CURCUMIN

Chemical test: The aqueous solution of turmeric with boric acid gives reddish brown color on addition of alkali changes to greenish blue.

With acetic anhydride and conc. Sulphuric acid gives violet color.

Therapeutic uses: Turmeric is used as anti-inflammatory anti arthritic immunomodulator and has been used in cervical cancer [16].

***Tinospora cardifolia*:**

Biological source: These are the dried leaves and stem pieces of woody climber *Tinospora cordifolia* (guduchi) belonging to family menispermaceae. It contains not less than 0.02 % of cordifolioside.

Geographical source: It is found in deciduous and dry forests of India. It is spread throughout India from Kumaun to Assam, Bihar, Konkan and also in Sri Lanka and Indonesia.

Chemical constituents: It consists of tinosporine, tinosporic acid, syringin the main constituents is codifolioside (mentioned in **fig. 4**) and pinosoridine. The stems are rich in proteins, starch, calcium and phosphorus.

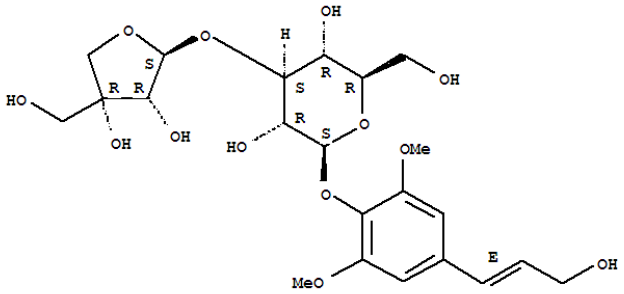


FIG. 4: CORDIFOLIOSIDE A

Therapeutic uses: It is used in general debility, pyrexia and skin disease. It also used in rheumatoid arthritis, jaundice and diabetes. The drug is gaining popularity due to its potent immunostimulant activity [17, 7, 8].

***Boerhaavia diffusa*:**

Biological source: It consists of fresh as well as dried herb *Boerhaavia diffussa* (Punarnava) belonging to family nyctaginaceae. It should contain not less than 0.005 % of boervinone on dried basis.

Geographical source: It is found wild throughout India and Sri lanka. Punarnava is found in Himalayan valleys upto 2000-2500 m. the weed also grows in Malaysia, China and Africa [18].

Chemical constituents: Punarnava contain about 0.04 – 0.1 % of alkaloid known as punarnavine and punernavoside (mentioned in **fig. 5**), an antifibrinolytic agent. It also contain about 6% of potassium nitrate an oily substances and ursolic acid.

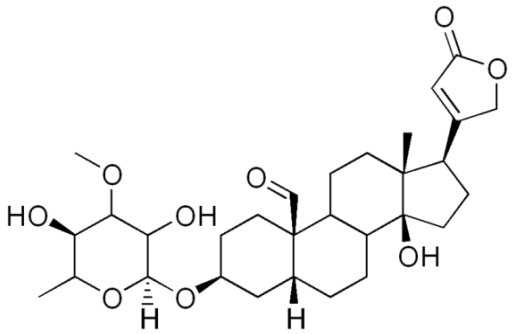


FIG. 5: PUNERNAVOSIDE

Therapeutic uses: The herb used as diuretic and as an expectorant and used in the treatment of jaundice. It gives the effect of anti-cancer immunomodulatory and hepatoprotective [19].

***Withania somnifera*:**

Biological source: It consists of dried root and stem bases of *Withania somnifera* belonging to family Solanaceae. It should contain not less than 0.02 % of total withanolide A and withaferin A on dried basis [1, 23].

Geographical source: This plant grows in Congo, Africa, Egypt, Jordan, Pakistan, Afghanistan and India. In India, it grows widely in all dry parts and subtropical regions [20].

Chemical constituents: The main constituents of ashwagandha are alkaloidal and steroidal lactones. Among the various alkaloids withanine (mentioned in **fig. 6**) is the main constituents. The other alkaloids are somniferine, somnine, somniferinine, tropine [6].

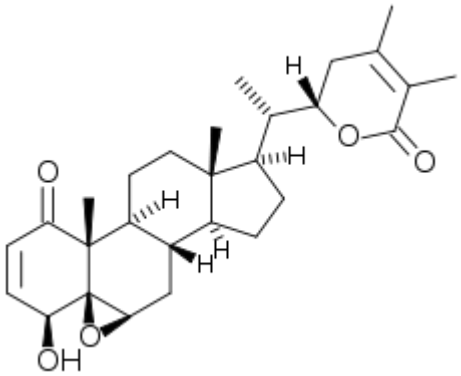


FIG. 6: WITHAFERIN A

Therapeutic uses: Ashwagandha has sedative and hypnotic effect.it has hypotensive, respiratory stimulant. It is an immunomodulatory agent. It has used in treatment of rheumatism hypertension, nerve and skin disease.it has widely used as sex stimulant [21].

***Asparagus racemosus*:**

Biological source: Shatavari consist of dried root and leaves of the plant known *Asparagus racemosus* belonging to family liliaceae. It contains not less than 0.1 % of shatavarin.

Geographical source: It is found distributed throughout tropical Asia, Africa, and Australia. In India it is found in Himalaya's upto an altitude of 1300 – 1400 m and all tropical parts of India [22].

Chemical constituents: Shatavari root contain 4 steroid saponins : shatavarin I-IV(0.2 %) and structure is given in **fig. 7**. Shatavarin-I is the major glucose and rhaminose moieties attached to sarsapogenin.the flower and fruit contain quercetin, rutin and hyperoside.

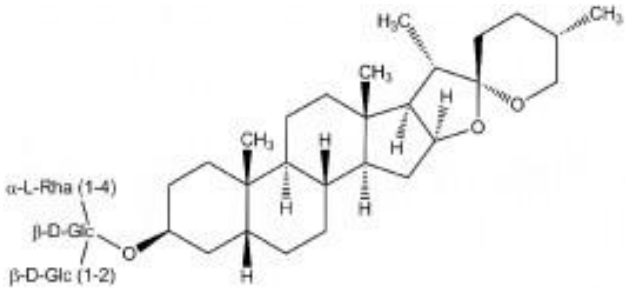


FIG. 7: SHATAVARIN-IV

Therapeutic uses: Shatavari roots are used as tonic and diuretic. Root is largely used for treatment of rheumatism and nervine disorder and it give immunomodulatory property [23].

***Echinacea purpurea*:**

Biological source: Echinaceae consist of dried underground parts of *Echinacea purpurea* belonging to family Asteraceae (Compositae).

Geographical source: It is perennial herb of south western and central parts of United States of America especially Kansas, Arkansas, Missouri and Oklahoma. It also found in Canada [24].

Chemical constituents: Echinacea species contain various type of phytochemicals among which the polysaccharides namely arabinogalactan the other constituents are echinacoside (structure is mentioned in **fig. 8**) called echinacin [6].

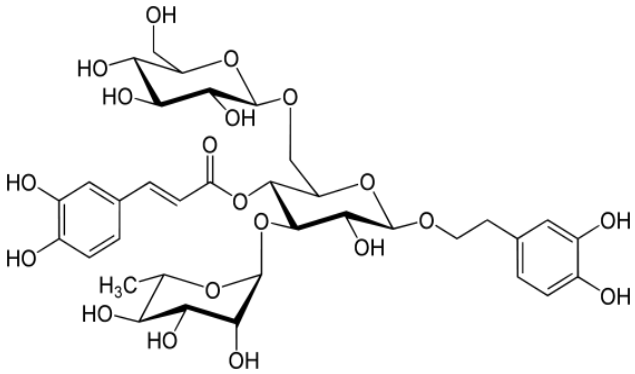


FIG. 8: ECHINACOSIDE

Therapeutic uses: Echinacea is used as immunostimulant mainly for prevention or treatment of viral disease. It also acts as antiseptic and peripheral vasodilator causing migration of neutrophils from bone marrow to blood stream [25].

***Ocimum sanctum*:**

Biological source: Tulsi consist of fresh and dried leaves of *Ocimum sanctum* belonging to family lamiaceae. It contains not less than 0.40 % eugenol.

Geographical source: It is an herbaceous, much branched annual plant found throughout India. It is considered as sacred by Hindu's. The plant is commonly cultivated in garden and also grown near temples. It is propagated by seed [26].

Chemical constituents: Tulsi leaves contains pleasant volatile oil (0.1 – 0.9%). It contains approximately 70 % eugenol, carvacrol (3%) (**fig. 9**) and caryophyllin also present.

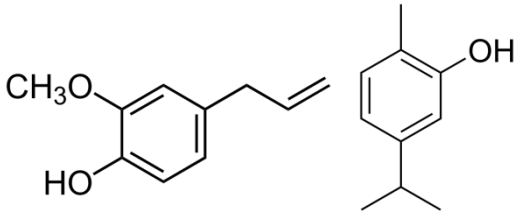


FIG. 9: EUGENOL CARVACROL

Therapeutic uses: The fresh leaves are used as stimulant, aromatic, anticatarrhal, spasmolytic, skin disease. The drug is a good immunomodulatory agent [27].

***Aloe vera*:**

Biological source: Aloes is the dried juice of the leaves of *Aloe barbadensis, Aloe perryi, Aloe ferox, aloe Africana and Aloe spicata* belonging to family liliaceae.

Geographical source: Aloe is endogenous to eastern and southern Africa and grown in cape colony, Zanzibar and island of Socotra. It is also cultivated in Caribbean island, Europe and many parts of India [5, 4].

Chemical constituents: All the varieties of aloe are the major source of anthraquinone glycosides. The principal active composition of aloe is aloin, which is a mixture of glycoside among barbaloin is the chief constituent (structure is mentioned in **Fig. 10**). The drug also contains aloetic acid, homonataloin, aloesone, chrysamminic acid etc [28, 1].

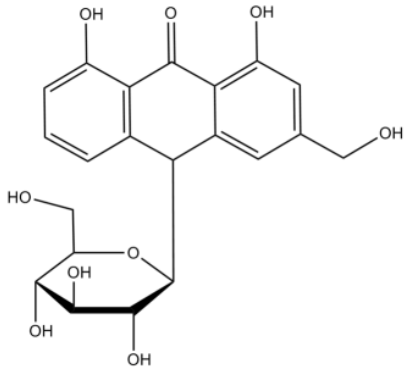


FIG. 10: BARBALOIN

Chemical test: The chemical tests for aloes are performed either for general detection or detection of specific variety of aloes.

General test: For these tests, 1 g of aloe powder is boiled with 10 ml water and filtered with help of kieselguhr. The filtrate is used for bromine test and Schoenteten's reaction.

Bromine test: Freshly prepared bromine solution is added to a small quantity of above filtrate. The test gives a pale yellow precipitate to tetrabromalin.

Borax test: Little quantity of above filtrate is treated with borax and shaken well till the borax dissolves. When few drops of this solution added to a test tube nearly filled with water a green fluorescence appears.

Special test: These tests are meant for distinguishing varieties of aloe vera.

Nitrous acid test: Crystal of sodium nitrate along with small quantity of acetic acid is added to aqueous solution of aloes.

Curacao aloe – sharp pink to carmine color

Cape aloe – faint pink color

Zanzibar aloe – very less change in color

Nitric acid test: This test carried out either by directly applying nitric acid to drug or to its aqueous solution.

Curacao aloes – deep brownish red color

Cape aloes – brownish color changing to green

Socotrine aloe – pale brownish to yellow color

Zanzibar aloes – yellowish brown color

Modified anthraquinone test: The aqueous solution of aloes is treated with ferric chloride solution and dilute hydrochloric acid to bring out the oxidative hydrolysis of aloe emodine. The hydrolysis sets free anthraquinones which are collected in organic solvent like carbon tetrachloride .The organic layer is separated and shaken with dilute ammonia. The ammonical layer rose – pink to cherry red color.

Therapeutic uses: Aloe is used as a purgative its effect is mainly on colon. It is used in the treatment of burns and wound, pain and itching. It also used in painful inflammation and it give immunomodulatory effect [29].

***Emblica officinalis*:**

Biological source: This consist of dried as well as fresh fruit of the plant *Emblica officinalis* belonging to family Euphorbiaceae. It contains not less than 1.0 % w/w of gallic acid [5].

Geographical source: It is a small or medium size tree found in all deciduous forest of India. It is also found in Sri lanka and Myanmar. The leaves are feathery with small oblong pinnately arranged leaflets.

Chemical constituents: Amal fruit is a rich source of vitamin C (structure of ascorbic acid is mentioned in **fig. 11**). A fruit also contain 0.5% fat phyllemblin and 5% tannin. The fresh fruit contain about 75% moisture. It may be due to the presence of tannins which retards oxidation of vitamin C.

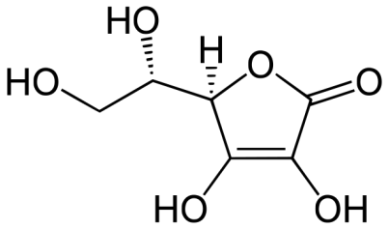


FIG. 11: ASCORBIC ACID

Chemical test:

- Alcoholic or aqueous extract of the drug gives blue color with ferric chloride solution.
- To aqueous extract add gelatin and sodium chloride milky white color is produced [1].

Therapeutic uses: Amla fruit are largely used in Indian medicine. It is used as a diuretic, laxative, jaundice, dyspepsia, immunomodulator, and anaemia. Seed of the fruit are given in treatment of asthma and bronchitis. Alcoholic extract of the fruit is anti – viral [30, 2, 15].

***Piper longum*:**

Biological source: This consists of dried fruiting spikes of climbing vine called as *Piper longum b*elonging to family Piperaceae. It contains not less than 1.0 % of piperine.

Geographical source: It found in India, Singapore, Sri Lanka, Indonesia, Malaysia and in part of East Nepal. In India it is found in Bengal, Bihar, Cherapunji in Assam [5].

Chemical constituents: It consist of alkaloid piperine and piplasterol (about 6%) 1% essential oil and pungent resin. Large variety contains not less than 1.0% while small variety contains not less than 0.4% of piperine (structure is mentioned in **fig. 12**).

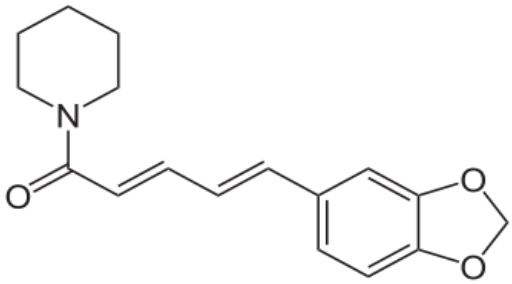


FIG. 12: PIPERINE

Therapeutic uses: It is widely used in Ayurvedic and Unani medicine, especially in diseases of respiratory tract. The roots are used for bronchitis, stomach – ache, disease of spleen and tumors. It improves appetite, used in pickles [31, 15].

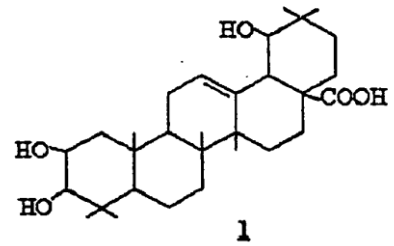
***Terminalia arjuna*:**

Biological source: Arjuna consists of dried stem bark of the plant known as *Terminalia arjuna* belonging to family Combretaceae. It contains not less than 0.02 % of arjungenin on dried basis [8].

Geographical source: The tree is common in Indian peninsula. It is grown by the side of streams and very common in chotta – Nagpur region.

Chemical constituents: Arjuna contains about 15 % of tannins (hydrolysable). It also contains triterpenoid saponin, arjunolic acid, arjunic acid, arjunogenin.

It contains β – sitosterol, ellagic acid and arjunic acid. Crystallisable compound reported are arjunine and arjunetine. Arjunolone and arjunone (structures are mentioned in **fig. 13**) are the flavonoids reported in Arjuna bark [32].



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ARJUNIC ACID

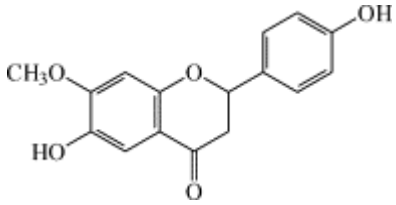

FIG. 13: ARJUNOLONE

Chemical test: Etherial extract of Arjuna shows pinkish fluorescence under UV light [1].

Therapeutic uses: Arjuna bark used as cardiotonic. It is also used in antidysentric and diurectic. The drug exhibit hypotensive action with vasodilation and decreased heart rate [33].

Conclusion: After this study, it is clear that the medicinal plants play a prominent role against various diseases. A variety of medicinal plants and plants extracts have been reported for its significant Many studies have been performed to identify Immunomodulator compounds with desired pharmacological activity and a limited toxicity. This review makes an attempt to give scientific account of use of different valuable Immunomodulatory sources. Some natural sources (plants) may stimulate the Immune system like *Boerhaavia diffussa, Rhododendron spiciferum, Caesalpinia bonducella, Capparis zeylanica, Luffa cylindrical, Withania somnifera* and *Asparagus racemosus* etc.

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