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A Review on Immunity and Immunomodulatory Remedies of Plant Origin

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Abstract
For nearly 4 decades, studies on iron preparations have been benchmarked against Ferrous Ascorbate. Properties of Ferrous Ascorbate are thus considered the Gold Standard in Iron therapy. Ferrous Ascorbate is the world's most widely recognized reference Iron. since Iron absorbed from the diet is inadequate to meet requirement of many individuals, so iron supplementation is essential to control iron deficiency anaemia. Actiferon slow release iron tablets are easy to swallow and easy on stomach. Actiferon rich in iron combines complete folic acid and physiologically active. Vitamin B12 and zinc in Actiferon in delayed release form avoiding the inhibition of iron absorption. Present article emphasized the role of Actiferon, slow relese iron therapy for better Absorption &Bioavailability.
Keywords: Actiferon, Anaemia, Iron absorption.

Contents

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1. Introduction
Immune system is composed of many interdependent cell types that collectively protect the body from bacterial, parasitic, fungal, viral infections and from the growth of tumor cells. Many of these cell types have specialized functions. The cells of the immune system can engulf bacteria, kill parasites or tumour cells, or kill viral infected cells. Often, these cells depend on the T helper subset for activation signals in the form of secretions formally known as cytokines, lymphokines, or more specifically interleukins.[1]

2. The Cells of the Immune System[2]
Phagocytes:
This is a group of immune cells specialized in finding and "eating" bacteria, viruses, and dead or injured body cells. There are three main types, the granulocyte, the macrophage, and the dendritic cell. The granulocytes often take the first stand during an infection. They attack any invaders in large numbers, and "eat" until they die. The pus in an infected wound consists chiefly of dead granulocytes. A small part of the granulocyte community is specialized in attacking larger parasites such as worms.
The macrophages: ("big eaters") are slower to respond to invaders than the granulocytes, but they are larger, live longer, and have far greater capacities. Macrophages also play a key part in alerting the rest of the immune system

of invaders. Macrophages start out as white blood cellscalled monocytes. Monocytes that leave the blood stream turn into macrophages.

The dendritic cells are "eater" cells and devour intruders, like the granulocytes and the macrophages. And like the macrophages, the dendritic cells help with the activation of the rest of the immune system. They are also capable of filtering body fluids to clear them of foreign organisms and particles.

Table 1. Organs of Immune System[2]

Bone Marrow	Thymus	Spleen	Lymph nodes
All the cells of the immune system are initially derived from the bone marrow. They form through a process called hematopoiesis. During hematopoiesis, bone marrow-derived stem cells differentiate into either mature cells of the immune system or into precursors of cells that migrate out of the bone marrow to continue their maturation elsewhere. The bone marrow produces B cells, natural killer cells, granulocytes and immature thymocytes, in addition to red blood cells and platelets**.**	The function of the thymus is to produce mature T cells. Immature thymocytes, also known as prothymocytes, leave the bone marrow and migrate into the thymus. Through a remarkable maturation process sometimes referred to as thymic education, T cells that are beneficial to the immune system are spared, while those T cells that might evoke a detrimental autoimmune response are eliminated. The mature T cells are then released into the bloodstream.	The spleen is an immunologic filter of the blood. It is made up of B cells, T cells, macrophages, dendritic cells, natural killer cells and red blood cells. In addition to capturing foreign materials (antigens) from the blood that passes through the spleen, migratory macrophages and dendritic cells bring antigens to the spleen via the bloodstream. An immune response is initiated when the macrophage or dendritic cells present the antigen to the appropriate B or T cells. This organ can be thought of as an immunological conference centre. In the spleen, B cells become activated and produce large amounts of antibody. Also, old red blood cells are destroyed in the spleen.	The lymph nodes function as an immunologic filter for the bodily fluid known as lymph. Lymph nodes are found throughout the body. Composed mostly of T cells, B cells, dendritic cells and macrophages, the nodes drain fluid from most of our tissues. Antigens are filtered out of the lymph in the lymph node before returning the lymph to the circulation. In a similar fashion as the spleen, the macrophages and dendritic cells that capture antigens present these foreign materials to T and B cells, consequently initiating an immune response

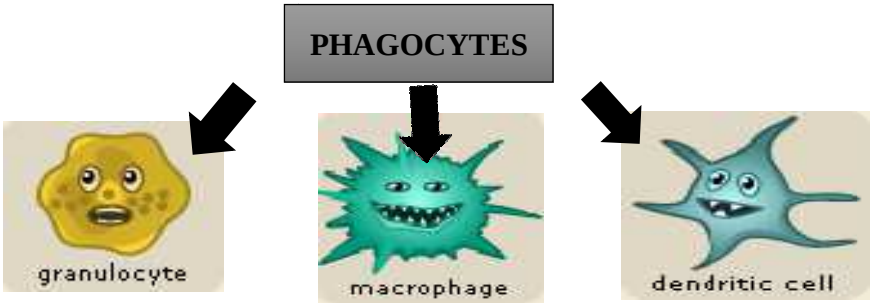

Figure 1

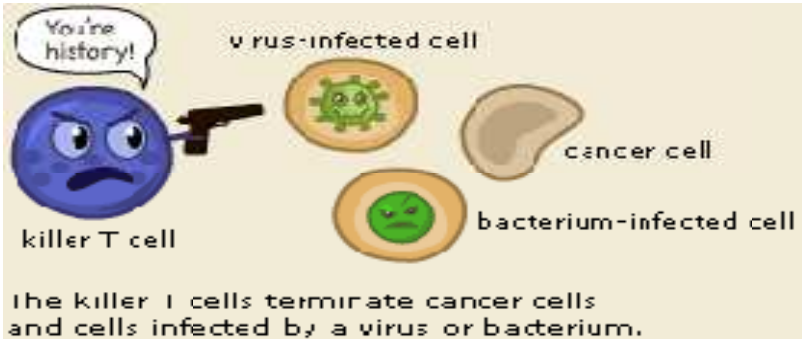

Figure 2

Lymphocytes:

White blood cells called lymphocytes originate in the bone marrow but migrate to parts of the lymphatic system such as the lymph nodes, spleen, and thymus. There are two main types of lymphatic cells, T cells and B cells. The lymphatic system also involves a transportation system - lymph vessels - for transportation and storage of lymphocyte cells within the body. The lymphatic system feeds cells into the body and filters out dead cells and invading organisms such as bacteria. On the surface of each lymphatic cell are receptors that enable them to recognize foreign substances. These receptors are very specialized - each can match only one specific antigen.In this included T cell and B cells.**T cells:**T cells come in two different types, helper cells and killer cells. They are named T cells after the thymus, an organ situated under the breastbone. T cells are produced in the bone marrow and later move to the thymus where they mature. Helper T cells are the major driving force and the main regulators of the immune defense. Their primary task is to activate B cells and killer T cells. However, the helper T cells themselves must be activated. This happens when a macrophage or dendritic cell, which has eaten an invader, travels to the nearest lymph node to present information about the captured pathogen. The phagocyte displays an antigen fragment from the invader on its own surface, a process called antigen presentation. When the receptor of a helper T cell recognizes the antigen, the T cell is activated. Once activated, helper T cells start to divide and to produce proteins that activate B and T cells as well as other immune cells**.**

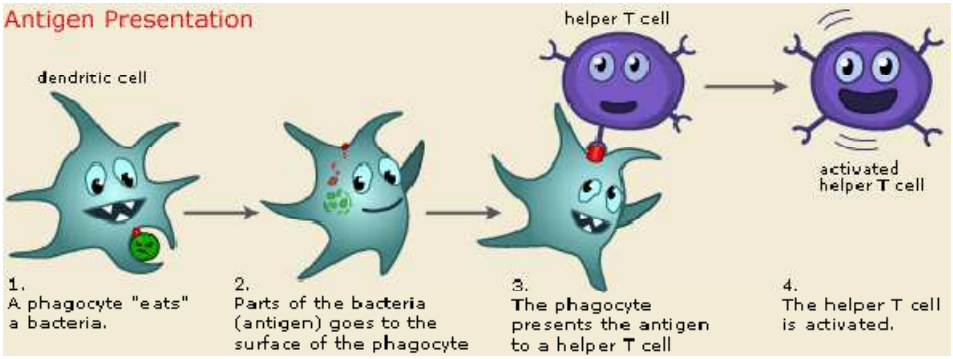

Figure 3

The killer T cell:

The killer T cell is specialized in attacking cells of the body infected by viruses and sometimes also by bacteria. It can also attack cancer cells. The killer T cell has receptors that are used to search each cell that it meets. If a cell is infected, it is swiftly killed. Infected cells are recognized because tiny traces of the intruder, antigen, can be found on their surface.

B Cells:

The B lymphocyte cell:

The B lymphocyte cell searches for antigen matching its receptors. If it finds such antigen it connects to it, and inside the B cell a triggering signal is set off. The B cell now needs proteins produced by helper T cells to become fully activated. When this happens, the B cell starts to divide to produce clones of itself. During this process, two new cell types are created, plasma cells and B memory cells.

The plasma cell:

The plasma cell is specialized in producing a specific protein, called an antibody, that will respond to the same antigen that matched the B cell receptor. Antibodies are released from the plasma cell so that they can seek out intruders and help destroy them. Plasma cells produce antibodies at an amazing rate and can release tens of thousands of antibodies per second. When the Y-shaped antibody finds a matching antigen, it attaches to it. The attached antibodies serve as an appetizing coating for eater cells such as the macrophage. Antibodies also neutralize toxins and incapacitate viruses, preventing them from infecting new cells. Each branch of the Y-shaped antibody can bind to a different antigen, so while one branch binds to an antigen on one cell, the other branch could bind to another cell - in this way pathogens are gathered into larger groups that are easier for phagocyte cells to devour. Bacteria and other pathogens covered with antibodies are also more likely to be attacked by the proteins from the complement system.

The Memory Cells:

The Memory Cells are the second cell type produced by the division of B cells. These cells have a prolonged life span and can thereby "remember" specific intruders. T cells can also produce memory cells with an even longer life span than B memory cells. The second time an intruder tries to invade the body, B and T memory cells help the immune system to activate much faster. The invaders are wiped out before the infected human feels any symptoms. The body has achieved immunity against the invader.

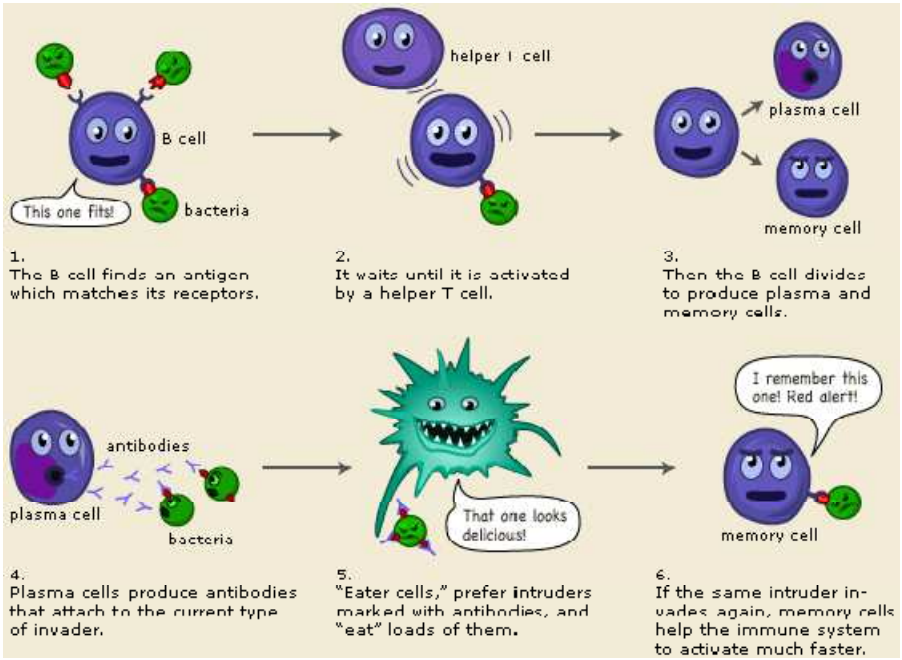

Figure 4

3. Methods for Testing Immunological Factors[6]

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

Table 2 Methods for Testing Immunological Factors

In vitro methods	In vivo methods
• Inhibition of histamine release from mast cells • Mitogens induced lymphocyte proliferation • Inhibition of T cell proliferationChemiluminescence in macrophages • PFC (plaque forming colony) test *in vitro* • Inhibition of dihydro-orotate dehydrogenase	• Spontaneous autoimmune diseases in animals • Acute systemic anaphylaxis in rats • Anti-anaphylactic activity (Schultz-Dale reaction) • Passive cutaneous anaphylaxis • Arthus type immediate hypersensitivity • Delayed type hypersensitivity • Reversed passive arthus reaction • Adjuvant arthritis in rats • Collagen type II induced arthritis in rats • Proteoglycan-induced progressive polyarthritis in mice • Experimental autoimmune thyroiditis • Coxsackievirus B3-induced myocarditis • Porcine cardiac myosin-induced autoimmunemyocarditis in rats • Experimental allergic encephalomyelitis • Acute graft versus host disease (GVHD) in rats. • Influence on SLE-like disorder in MRL/lpr mice • Prevention of experimentally induced myastheniagravis in rats • Glomerulonephritis induced by anti-basementmembrane antibody in rats • Auto-immune uveitis in rats • Inhibition of allogenic transplant rejection.

Table 3 Immunomodulatory Remedies of Plant Origin[9-31]

S.no	Plant name	Family	Plant part used	Solvent used	Model performed
1	*Aloe vera*	Liliaceae	Leaves	Saline extract	Haematological, Serological studies.
2	*Abutilon indicum*	Malaceae	Leaves	Aqueous and ethanolic extract	heamagglutination antibody (HA) titer, delayed type hypersensitivity (DTH),
3	*Aeglemarmelos*	Rutaceae	Leaves	Methanolic and ethanolic extract.	In vivo study, hemagglutination reactions
4	*Alstoniaschloris*	Apocynaceae	Bark	Aqueous and ethanolic extract	heamagglutination antibody (HA) titer,
5	*Aloe vera*	Liliaceae	Leaves	Powder dissolved in Phosphate	Humoral antibody response to SRBC,Cellular immune response (Foot pad reaction test)
6	*Actinidiamacrosperma*	Actinidiaceae	Whole plant	Aqueous extract	AM induced antitumor
7	*Allium sativum*	Liliaceae	Whole plant	Hydro-alcoholic Extract	Hemagglutination
8	*Andographispaniculata*	Acanthaceae	Whole plant	Andrographolides Extract	Delayed type hypersensitivity (DTH) mouse model
9	*Asparagus racemosus*	Liliaceae	Root	Aqueous extract	SRBC sensitized animals
10	*Aesculusindica*	Sapindaceae	Leaf	Petroleum ether and ethanol	Haemagglutination antibody Neutrophil index, Neutrophil Adhesion,
11	*Actinidiamacrosperma*	Actinidiaceae	Whole plant	Aqueous extract	immunomodulator, Sarcoma-180 (S180),
12	*Azadirachtaindica*	Meliaceae	Leaf	Hydro acetone Extract	WST-1-based cytotoxicity assay
13	*Bauhinia Vareigata*	Fabaceae	Stem bark	Acetone: water (70:30)	Human Neutrophils
14	*BalaniteRoxburghi*	Zygophylaceae	Leaf	Ethanolic extract	Carbon clearance test, serum immunoglobulin
15	*Bauhinia variegate*	Fabaceae	Stem bark	Ethanolic extract	Neutrophil adhesion , Phagocytic activity
16	*BaliospermumMontanum*	Euphorbiaceae	Root	Aqueous extract	Nitro blue tetrazolium test
17	*Boerhaaviadiffusa*	Nyctaginaceae	Whole plant	Hydro-alcoholic Extract	Circulating antibody titer
18	*Boswelliacarteri*	Burseraceae	Bark	Methylene chloride extract	Reagents for lymphocyte transformation assay
19	*Cleome gynandra*	Cleomceae	Aerial parts	Ethanolic extract	Carbon clearance method, Cellular mediated immunity,Immunostimulatory
20	*Cissampelosparreira*	Minispermaceae	Roots	Alkaloidal fraction	Humoral antibody titre
21	*Cinnamomumtamala*	Lauraceae	Leaves	Hexane fraction	delayed type of hypersensitivity
22	*Curculigoorchioides*	Amaryllidaceae	Root	Methanolic extract	Haemagglutination antibody titre, phyto- Haemagglutination induced blast transformation of lymphocytes.
23	*CapparisZeylanica*	Capparidaceae	Leaf	Alcoholic extract	Phagocytosis; Delayed hypersensitivity
24	*ChlorophytumBorivilianum*	Liliaceae	Roots	Ethanolic extract	In Vivo Phagocytosis Using Carbon Clearance Method
25	*Citrus aurantifolia*	Rutaceae	Fruits	Concentrated juice	Cell proliferation assay, Immunoblotting.
26	*Cissampelosparreira Linn*	Menispermaceae	Roots	methanol extract	Humoral antibody titre, Superoxide, Lipid peroxidation.
27	*Cappariszeylani*	Capparidace	Leaf	Aerial parts	Immunomodulatory activity;

	ca	ae	extracts		Phagocytosis; Delayed hypersensitivity;
28	*Couroupitaguinensis*	Lecythidaceae	Flowers	Pet. ether, Benzene, Choloroform, Ethyl acetate, 70% ethanol and water	Allergic reaction, Haemagglutination
29	*Cappariszeylanica*	Capparidaceae	Aerial part	Methanolic and aqueous extracts	Haemagglutination antibody titre
30	*Carica papaya*	Caricaceae	Leaves	consumption of tea extract	Immunoadjuvant for vaccine therapy, microarray analyses
31	*Caesalpiniabonducella*	Caesalpiniaceae	Seed	Ethanolic extract	Neutrophil adhesion test, Haemagglutinating antibody (HA)
32	*Curcuma longa*	Zingiberaceae	Balb	Hydro-alcoholic Extract	Humoral antibody response to SRBC
33	*Clerodendrumphlomidis*	Verbanaceae	Root	Methanolic extract	Haemagglutinating antibody (HA) test
34	*Dodonaceae viscose*	Dodonaceae	Leaf	Ethanolic extract	Carbon clearance test, DTH test, T-cell population test.
35	*Eclipta alba*	Asteraceae	Whole plant	Methanolic extracts	phagocytic index and antibody titer
36	*Euphorbia hirta*	Euphorbiaceae	Herb	Aqueous extract.	macrophage activity testing, carbon clearance 35test and mast cell de-granulation assay
37	*Echinapurpurea*	Asteraceae		Ethanolic extract	Haemagglutinating antibody (HA)
38	*Epilobiumangustifolium*	Onagraceae	Whole plant	Hydro-alcoholic Extract	Chemotaxis, NF-kappa B activation
39	*Ficuscarica*	Moraceae	Leaf	Ethanolic extract	Cellular immune response, Humoral antibody response
40	*Ficusbenghalensis*	Moraceae	Roots	Methanolic extract	Hypersensitivity and hemagglutination reactions.
41	*GymnemaSylvestre*	Asclepiadaceae	Leaves	Water extract	Neutrophil locomotion and chemotaxis test
42	*Hibiscus rosasinensis*	Malvaceae	Flowers	Hydro-alcoholic Extract	Carbon clearance method, Cellular mediated immunity, Immunostimulatory
43	*HeracleumPersicum*	Apiaceae	Fruits	Aqueous Extract	Haemagglutination titre, Delayed, type hypersensitivity
44	*Janakiaarayayalpathra*	Periplocaceae	Root	Ethanolic extract	Humoral antibody titre, antibody secreting spleen cells in the PFC assay.
45	*Morus alba linn.*	Moraceae	Leaf	Methanolic Extract	Humoral immunity, serum immunoglobulin
46	*Mangiferaindica*	Anacardiaceae	Stem bark	Alcoholic extract	Humoral antibody response to SRBC
47	*Morindacitrifolia*	Rubiaceae	Fruit	Hydro-alcoholic extract	In vivo (cell mediated immune response) techniques
48	*Momordicacharantia*	Cucurbitaceae	Enzyme	-	RIP displayed strong apoptosis inducing activity.
49	*Moringaoleifera*	Moringaceae	Leaves	Methanolic extract	Neutrophil adhesion test, cyclophosphamide induced neutropenia and carbon clearance assay, mice lethality test
50	*Nyctanthesarbortristis*	Scrophulariaceae	Leaf	Ethanolic extract	Humoral immunity, delayed-type hypersensitivity
51	*Ocimum sanctum*	Lamiaceae	Whole plant	Aqueous extract	Enhance the production of RBC, WBC and haemoglobin

52	*Prunella vulgaris*	Lamiaceae	Fruit-spikes	Aqueous extract	Inhibition of HIV-1 reverse transcriptase activity
53	*Picrorhizakurroa*	Scrophulariaceae	Leaf	Ethanolic extract	Cell-mediated and humoral components
54	*Punicagranatum*	Lithraceae	Fruit	Aqueous suspension	Delayed hypersensitivity test with Purified Protein Derivative (PPD)
55	*Plumbagozelanica*	Plumbaginaceae	-	-	phytohemagglutinin (PHA)-stimulated cell proliferation
56	*Rhaphidophora korthalsii*	Araceae	Leaf extracts	Methanolic Extract	In vitro splenocyte cytokine (IL-2, IL-12 and IFN-γ) Determinations, In vitro Splenocytes, thymocytes and bone marrow cell viability assay.
57	*Randiadumetorum*	Rubiaceae	Fruit	Chloroform, methanol, pet ether.	Delayed hypersensitivity test, hemagglutination reactions
58	*Sellaginella species*	Sellaginecea e	Whole plant	Powdered in gum Acacia	Immunomodulatory, short term toxicity
59	*Saracaindica*	Fabaceae	Seeds	Saracin, obtained from seed integument lectin	FACS analysis
60	*Solanumtorum*	Solanaceae	Leaves	Aqueous extract.	levamisole and dexamethasone. Phenylhydrazine (PHZ)-induced anemia in rats
61	*Syzygiumaromaticum*	Myrtaceae	Buds	Essential of clove	Humor- and cellmediated immune responses
62	*Salicorniaherbacea*	Chenopodiaceae	Whole plant	Hydro-alcoholic Extract	Phagocytic activity on opsonised
63	*Trikatu mega*	-	Aerial parts	Pe.Ether, Benzene, Choloroform	Carbon clearance assay, delayed hypersensitivity test
64	*TriAmrit (Terminalia, Allium, Tinospora*)	Minispermaceae	Aerial parts	Pe.Ether, Benzene, Choloroform	Carbon clearance assay, delayed hypersensitivity test
65	*TinosporaCordifolia*	Minispermaceae	Stems	Ethanolic extract	DTH, Bone marrow cellularity and α-Esterase cells, Zinc sulphate turbidity test.
66	*TrapaBispinosa*	Tropaceae	Fruits	Aqueous extract	Neutrophils, Haemagglutination titre.
67	*Triticumvulgare*	Poaceae	Wheat	Bran extract	delayed-type hypersensitivity (DTH) model
68	*Tinosporacordifolia*	Minispermaceae	Whole plant	Alcoholic extract	macrophage activation; lysozyme;
69	*Tridax procumbens*	Compositae	Aerial part	Alcoholic extract	delayed-type hypersensitivity (DTH) model
70	*Withaniasomnifera*	Solanaceae	Root	Alcoholic extract	Bone marrow cellularity
71	*Withaniacoagulans*	Solanaceae	Root	Crude extract	Spectroscopic techniques including 1D- and 2D-NMR (1H, 13C, HMQC, and HMBC) and MS experiments

4. Conclusion

According to literature survey some medicinal plants are believed to promote positive health and maintain organic resistance against infection by re-establishing body equilibrium and conditioning the body tissues. It is tempting to speculate that the restorative and rejuvenating power of these herbal remedies might be due to their action on the immune system and some of the medicinal plants are believed to enhance the natural resistance of the body to infections. Plant derived materials (proteins, lections, polysaccharides, etc.) have been shown to stimulate the immune system. Ayurveda and other Indian literature mention the use of plants in treatment of various human ailments. Some of the plants with established immunomodulatory activity are Viscum album, Panax ginseng, Asparagus racemosus, Azadirachtaindica, Tinosporacordifolia, Polygala senega, Ocimumsantum, Withaniasomnifera among others. There are a number of plants that have been reported to have immunomodulatory activity. The present paper review plants which have shown experimental and clinical immunomodulatory activity.

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