



## Review Article

**A Review on Immunomodulatory Activity Plants**

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**ABSTRACT**

Certain 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, lectins, 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*, *Azadirachta indica*, *Tinospora cordifolia*, *Polygala senega*, *Ocimum santum*, *Withania somnifera* 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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**INTRODUCTION**

Immunomodulation means that one can modulate immunity using various substances either of natural or synthetic origin. Immunomodulation using medicinal plants can provide an alternative to conventional chemotherapy for a variety of diseases, especially when the host defence mechanism has to be activated under conditions of impaired immune response, or when a selective immunosuppression is desired in situations such as autoimmune disorders. It appears that the normal way by which the immune system works is through its own modulation by factors usually synthesised by the immune cells.

Networking and interactions within the immune system are so complex that modulations of the immune response at will to achieve designed therapeutic success is still in the realm of philosophical editorials rather than of definitive efficacy studies.

The immune response requires timely interplay of multiple cell types within specific microenvironments to maintain immune homeostasis. The selectivity and flexibility that is necessary to regulate cell traffic under homeostatic and diseased conditions are provided by the differential distribution and regulated expression of cytokines and their receptors. As a consequence, cytokines are responsible for the development of phenotypes and are, therefore, logical targets for therapeutic immune modulation.

One of the most promising recent alternatives to classical antibiotic treatment is the use of immunomodulators for enhancing host defence responses. Several types of immunomodulators have been identified, including substances isolated and purified from natural sources such as plants including microorganisms. An immunomodulator may be defined as a substance, biological or synthetic, which can stimulate, suppress or modulate any of the components of the immune system including both innate and adaptive arms of the immune responses.

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### ***Abutilon indicum***

*Abutilon indicum* (AI) commonly known as "Atibala" in Sanskrit gives excessive tonic strength. Atibala is a stronger diuretic and heart tonic. AI reported in the Siddha system as a remedy for jaundice, piles, ulcer, leprosy, raktapitta dosha and blood purifier. Chemically it contains flavonoids (quercetin), saponins, alkaloids and phenolic compounds. The ethanolic and aqueous extract of leaves of *Abutilon indicum* was administered orally at the dosage levels of 200 mg/kg/day and 400 mg/kg/day body weight in mice. The assessment of immunomodulatory activity on specific and non-specific immunity were studied by hemagglutination antibody (HA) titer, delayed type hypersensitivity (DTH), neutrophil adhesion test and carbon clearance test. In order to induced immunosuppression in mice by using cyclophosphamide (100 mg/kg/day, *p.o.*) and levamisole (50 mg/kg/day, *p.o.*) used as immunostimulating agents. The study demonstrates that *A. indicum* triggers both specific and non-specific responses to a greater extent. The study comprised the acute toxicity and preliminary phytochemical screening of *A. indicum*. From the results obtained and phytochemical studies the immunostimulant effect of AI could be attributed to the flavonoid content [1].

### ***Actinidia macrosperma***

*Actinidia macrosperma* (AM) is a medicinal plant in China and has been well known for its activities against cancers, especially of lung, liver and digestive system. The immunomodulatory effects of AM aqueous extract were examined using S180-bearing mice. Young adult (20 ± 2 g) ICR mice inoculated with S180 cells were divided randomly into six groups: S180-bearing control group, normal control group, positive control group (Ginseng Radix Rubra 2000 mg/kg) and 50, 100, 250 mg/kg AM treatment groups. The results showed that the aqueous extract of AM was lack of significant inhibit on transplantable sarcoma S180, with a inhibit rate of 1.5%–14.8% (dose at 250 mg/kg was the best), but significantly increased the overall immune functions (especially at 100 and 250 mg/kg). The immunomodulatory effect was dose-dependent in a nonlinear fashion with the optimal dose of 100 mg/kg. The AM-induced antitumor effects were at least partially indirect and were associated with the modulation of immune functions [2].

### ***Aegle marmelos***

*Aegle marmelos*, belongs to family Rutaceae is generally known as bael fruit. They were evaluated for potential immunomodulatory activity using the in vitro Polymorphonuclear leukocyte function test. Both Methanolic and Ethanolic extract of *Aegle marmelos* leaves were evaluated for their immunomodulatory activity. In *in vivo* studies, using rats as the animal model. The extract was tested for hypersensitivity and hemagglutination reactions, using sheep red blood cells (SRBC) antigen. The methanol extract exhibited a significant increase in the percentage phagocytosis versus the control. It was noted to exhibit a dose related increase in the hypersensitivity reaction, to the SRBC antigen, at concentration of 100 & 200 mg/kg. It also resulted in a significant increase in the antibody titer value, to SRBC, at doses of 100 and 200 ml/kg in animal studies. The Methanolic extract was found to stimulate cell mediated and antibody mediated immune responses in rats [3].

### ***Allium sativum***

Garlic (*Allium sativum*), an important medicinal spice of liliaceae family, displays a plethora of biological effects including immunomodulation. Although some immunomodulatory proteins from garlic have been described, their identities are still unknown. The present study was envisaged to isolate immunomodulatory proteins from raw garlic, and examine their effects on certain cells of the immune system (lymphocytes, mast cells, and basophils) in relation to mitogenicity and hypersensitivity. Three protein components of approximately 13 kD (QR-1, QR-2, and QR-3 in the ratio 7:28:1) were separated by Q-Sepharose chromatography of 30 kD ultrafiltrate of raw garlic extract. All the 3 proteins exhibited mitogenic activity towards human peripheral blood lymphocytes, murine splenocytes and thymocytes. The mitogenicity of QR-2 was the highest among the three immunomodulatory proteins. All these results indicate that the two major proteins QR-2 and QR-1 present in a ratio of 4:1 in raw garlic contribute to garlic's immunomodulatory activity, and their characteristics are markedly similar to the abundant *Allium sativum* agglutinins (ASA) I and II, respectively [4].

### ***Aloe vera***

To study the immunomodulatory activity of saline extracts of leaves of *Aloe vera* Linn. (Family: Liliaceae) on the albino mice. The saline extract of leaves of *Aloe vera* was administered

orally according to their body weight in mice. The assessment of immunomodulatory activity on specific and nonspecific immunity was studied by administration of test extract. The method of pyrogallol induced immunosuppression was employed with slight modification to study the immunomodulatory potential of the extract. Humoral antibody response to SRBC measurement of antibody titer by haemagglutination reaction was done and cellular immune response (Foot pad reaction test) the edema was induced in the right paw of mice by injecting SRBC ( $0.025 \times 10^9$  cells) in the sub planar region. Pyrogallol-induced suppression of humoral as well as cell mediated immune response was significantly attenuated by daily oral treatment with saline extract of *Aloe vera*. Vitamin E treated group exhibited similar attenuation of the suppression in immune responses. *Aloe vera* extract at the dose of 100 mg/kg was found to suppress delayed type hypersensitivity reaction induced by SRBCs in mice. As evidenced by marked increase in haemagglutination titers in mice was also observed. The study demonstrates that *A. vera* triggers both specific and non-specific responses to a greater extent. The study comprised the acute toxicity and preliminary phytochemical screening of *A.vera*. From the results obtained and phytochemical studies the immunostimulant effect of *Aloe vera* could be attributed to the alkaloids content [5].

#### ***Alstonia scholaris***

The immunostimulating effect of "Pule" (*Alstonia scholaris* (L.) R.Br, Family: Apocynaceae) bark extracts was studied in mice. The extracts were administered orally, once a day for 7 consecutive days. The results showed that at the same doses (50, 100 and 200 mg/kg b.w.) the aqueous extract had higher phagocytic index (1.39-1.79) than the ethanolic extracts (0.81-0.93) in normal mice. The results showed that *Alstonia scholaris* has a significant immunomodulatory activity [6].

#### ***Bauhinia variegata***

The traditional claim endowed upon the *Bauhinia variegata* (EBV) has an herbal drug as a *rasayana* in Ayurveda. The effect of the ethanolic extract of the stem bark of *Bauhinia variegata* (EBV) on the primary and secondary antibody responses was evaluated by the humoral antibody response for a specific immune response. The effect of EBV on the phagocytic activity was evaluated by the carbon clearance test and neutrophil activation was evaluated by

the neutrophil adhesion test for a nonspecific immune response. On oral administration, EBV showed a significant increase in the primary and secondary humoral antibody responses, by increasing the hemagglutinating antibody titre at doses of 250 and 500mg/kg/p.o. There was a significant increase in the phagocytic index and percentage neutrophil adhesion at doses of 250 and 500mg/kg/p.o. This study reveals that the ethanolic extract of the stem bark of *Bauhinia variegata* Linn holds a promise as an immunomodulatory agent, which acts probably by stimulating both the specific and nonspecific arms of immunity [7].

#### ***Caesalpinia bonducella***

*Caesalpinia bonducella* Fleming (Family: Caesalpiaceae) is a plant well known for its medicinal value in Indian Ayurveda. However, to prove its efficiency for the clinical utilization, more experimental data will be beneficial. The evaluation of immunomodulatory potential by oral administration of ethanolic seed extract of *Caesalpinia bonducella* (200-500 mg/kg) evoked a significant increase in percent neutrophil adhesion to nylon fibers as well as a dose-dependent increase in antibody titre values, and potentiated the delayed-type hypersensitivity reaction induced by sheep red blood cells. Also it prevented myelosuppression in cyclophosphamide drug treated rats and good response towards phagocytosis in carbon clearance assay. The results obtained in this study indicate that *Caesalpinia bonducella* possesses potential immunomodulatory activity and has therapeutic potential for the prevention of autoimmune diseases [8].

#### ***Carica papaya***

Various parts of *Carica papaya* Linn. (CP) have been traditionally used as ethnomedicine for a number of disorders, including cancer. There have been anecdotes of patients with advanced cancers achieving remission following consumption of tea extract made from CP leaves. However, the precise cellular mechanism of action of CP tea extracts remains unclear. The aim of this study is to examine the effect of aqueous-extracted CP leaf fraction on the growth of various tumor cell lines and on the anti-tumor effect of human lymphocytes. The observations showed significant growth inhibitory activity of the CP extract on tumor cell lines. In peripheral blood mononuclear cells, the production of IL-2 and IL-4 was reduced following the addition of CP extract, whereas that of IL-12p40, IL-12p70,

IFN-gamma and TNF-alpha was enhanced without growth inhibition. In addition, cytotoxicity of activated PBMC against K562 was enhanced by the addition of CP extract. Moreover, microarray analyses showed that the expression of 23 immunomodulatory genes, classified by gene ontology analysis, was enhanced by the addition of CP extract. Since *Carica papaya* leaf extract can mediate a Th1 type shift in human immune system, our results suggest that the CP leaf extract may potentially provide the means for the treatment and prevention of selected human diseases such as cancer, various allergic disorders, and may also serve as immunoadjuvant for vaccine therapy [9].

### ***Cinnamomum tamala***

The leaves of *Cinnamomum tamala* Linn. (CT) (Family: Lauraceae) clinically used in Ayurveda as antidiabetic and diuretic, but no reports are available towards immunomodulating property. Its hexane fraction (CTH) was orally given to rats for 10 days and delayed type of hypersensitivity (DTH), antibody production against sheep red blood cells (SRBCs), mitotic index in bone marrow cells and concanavalin A (Con A) mediated proliferation of lymphocytes were assessed. Further on 30 days treatment, change in body weight (BW), spleen weight, thymus weight, bone marrow cellularity and hematological changes were observed. It inhibited significantly the DTH response (IC (50) 1475 +/- 57.19 mg kg (-1) BW), antibody production, suppressed mitotic index in bone marrow cells along with the suppression of lymphocyte proliferation against Con A (IC(50) 63.33 +/- 1.95 microg mL(-1)). In all experiments, cyclophosphamide and dexamethasone had been used as reference drug for in vivo and in vitro studies, respectively. On 30 days treatment, the CTH (800 mg kg (-1) BW and above) significantly suppressed growth rate, increase of spleen and thymus weight and low bone marrow cellularity. In hematological examination, it inhibited total white blood cell and lymphocytes count and increased per cent of polymorphs. Thus, it could be suggested that the fraction possesses immunosuppressive property at doses, higher than 800 mg kg (-1) BW in rats [10].

### ***Cissampelos pareira***

The alkaloidal fraction (AFCP) of roots of *Cissampelos pareira* Linn. (Family: Menispermaceae) was screened for immunomodulatory activity in mice. The HPTLC finger print profile

was also established for the identification of AFCP which was found to contain 0.176 % of berberine. AFCP was found to have significant immunosuppressive activity at lower doses (25 and 50 mg/kg) while no activity was observed at higher doses (75 and 100 mg/kg). Humoral antibody titre was significantly ( $p < 0.01$ ) lowered by AFCP at the doses of 25 and 50 mg/kg. Delayed type hypersensitivity response was also significantly ( $p < 0.01$ ) suppressed by the AFCP at the dose of 75 mg/kg. Thus the present study revealed the immunosuppressive and antioxidant activities of the alkaloidal fraction of *C. pareira* roots [11].

### ***Cleome gynandra***

The assessment of immunomodulatory activity of ethanolic extracts of aerial parts of *Cleome gynandra* Linn. (Family: Capparidaceae) at the doses of 50, 100 and 200 mg/kg, *p.o.* was done by carbon clearance method for non-specific immunity, haemagglutination antibody titre method for humoral immunity and footpad swelling method for cell mediated immunity on wistar albino rats. Results of present studies suggest that the ethanolic extract of *Cleome gynandra* Linn. exhibited significant immune suppression effect in dose dependent manner when compare with control group [12].

### ***Curcuma langa***

Curcumin is a polyphenol derived from the dietary spice turmeric. It has been shown to regulate numerous transcription factors, cytokines, adhesion molecules, and enzymes that have been linked to inflammation. In addition to inhibiting the growth of a variety of pathogens, curcumin has been shown to have nematocidal activity. The present study was designed to evaluate the schistosomicidal activity of curcumin in vivo as well as immunomodulation of granulomatous inflammation and liver pathology in acute schistosomiasis mansoni. Mice were infected each with 80 *Schistosoma* (S.) mansoni cercariae and injected intraperitoneally with curcumin at a total dose of 400mg/kg body weight. Curcumin was effective in reducing worm and tissue-egg burdens, hepatic granuloma volume and liver collagen content by 44.4%, 30.9%, 79%, and 38.6%, respectively. Curcumin treatment restored hepatic enzymes activities to the normal levels and enhanced catalase activity in the liver tissue of infected mice [13].

### ***Dodonaea viscosa***

The immunomodulatory activity of an Indian medicinal plant i.e. ethanolic extract from *Dodonaea viscosa* L.F. namely DV was studied for their phagocytic activity, cell mediated and humoral immune system on rat/mouse. Immunomodulatory effect was assessed in carbon clearance test, delayed type of hypersensitivity (DTH), T-cell population test, and sheep erythrocyte agglutination test (SEAT) in animal treated with DV at doses of 200 and 400 mg/kg. In carbon clearance test, *D.viscosa* exhibited significantly high phagocytic index against control group, indicating stimulation of the reticuloendothelial system. Significant decrease in mean difference, in the foot paw thickness in DTH indicates its anti-inflammatory activity. In SEAT *D. viscosa* treated groups at 200, 400 mg/kg doses showed significant increase in antibody titer against control in normal immune status animals while In T-cell population test, showed significant increase in T-cell rosette formation against control. These results confirm the immunomodulatory activity of *D. viscosa* extract, which is a known immunomodulator in indigenous medicine [14].

### ***Echinacea purpurea***

*Echinacea purpurea* extracts are used in the production of standardized herbal medicines for the prevention and treatment of upper respiratory infections. Unsaturated N-alkylamide lipids, the main constituent of *E. purpurea* and *E. angustifolia* preparations capable of activating the cannabinoid receptor type-2 (CB<sub>2</sub>) have been suggested to play a role as potential anti-inflammatory and immunomodulatory principles. Here that the ethanolic *E. purpurea* radix and herbal extracts produce synergistic pharmacological effects on the endocannabinoid system *in vitro*. Superadditive action of N-alkylamide combinations was seen at the level of intracellular calcium release as a function of CB<sub>2</sub> receptor activation. Likewise, synergism of the radix and herba tinctures was observed in experiments measuring LPS-stimulated cytokine expression from human PBMCs. Here they showed that N-alkylamides act in concert and exert pleiotropic effects modulating the endocannabinoid system by simultaneously targeting the CB<sub>2</sub> receptor, endocannabinoid transport and degradation [15].

### ***Eclepta alba***

An attempt has been made to assess the immunomodulatory activity of methanol extracts of whole plant of *Eclepta alba* (1.6% wedelolactone) at five dose levels (dose-response relationship) ranging from 100 to 500 mg/kg body wt. using carbon clearance, antibody titer and cyclophosphamide immunosuppression parameters. In the case of *E. alba*, the phagocytic index and antibody titer increased significantly and the F ratios of the phagocytic index and WBC count were also significant. Regression analysis showed linearity in patterns of the dose-response relationship, greatest in the case of the phagocytic index, moderate in the WBC count and lowest in the antibody titer [16].

### ***Euphorbia hirta***

*Euphorbia hirta*, a pantropic herb has been reported to be pharmacologically active (Family: Euphorbiaceae. This study reports one another not widely reported property of the plant, immunomodulatory activity, which has been proved using simple techniques like the macrophage activity testing, carbon clearance test and mast cell de-granulation assay [17].

### ***Ficus benghalensis***

Various extracts of the aerial roots of *Ficus benghalensis* (Family Moraceae) were evaluated for potential immunomodulatory activity, using the *in vitro* polymorphonuclear leucocyte (human neutrophils) function test. The methanol extract was evaluated for immunomodulatory activity in *in vivo* studies, using rats as the animal model. The extracts were tested for hypersensitivity and hemagglutination reactions, using sheep red blood cells (SRBC) as the antigen. Distilled water served as a control in all the tests. The successive methanol and water extracts exhibited a significant increase in the percentage phagocytosis versus the control. In the *in vivo* studies, the successive methanol extract was found to exhibit a dose related increase in the hypersensitivity reaction, to the SRBC antigen, at concentrations of 100 and 200 mg/kg. It also resulted in a significant increase in the antibody titer value, to SRBC, at doses of 100 and 200 mg/kg in animal studies. The successive methanol extract was found to stimulate cell mediated and antibody mediated immune responses in rats. It also enhanced the phagocytic function of the human neutrophils, *in vitro* [18].

### ***Ficus carica***

The Immunomodulatory effect of ethanolic extract of the leaves of *Ficus carica* (Family: Moraceae) was investigated in mice. The study was carried out by various hematological and serological tests. Administration of extract remarkably ameliorated both cellular and humoral antibody response. The present study show that *Ficus carica* leaves ethanolic extract (100mg/kg/*i.p.*, daily) produces stimulatory effect on the humoral and cells mediated immune response in the experimental animals and suggest its therapeutic usefulness in disorders of immunological origin. Further studies using *in vivo* and *in vitro* models of immunomodulation are needed to confirm the Immunomodulatory activity of *Ficus carica* leaves and its mechanism of action [19].

### ***Heracleum persicum***

*Heracleum persicum* Desf. (Family: Apiaceae), a medicinal plant native to Iran, was studied for its immunomodulatory activity. Immunomodulatory activity of different doses of an aqueous extract of *H. persicum*, was evaluated in female Swiss albino mice. Mice were treated with three doses (50, 100 and 200 mg/kg body weight) for 5 days. Body weight, relative organ weight, delayed type hypersensitivity (DTH) response and haemagglutination titre (HT) were studied in various groups of animals. No significant body weight gain differences were recorded in various groups of animals. The results obtained showed a significant stimulatory effect on both humoral and cellular immune functions in mice [20].

### ***Hibiscus rosa sinensis***

The assesement of immunomodulatory activity of hydro-alcoholic extract of flowers of *Hibiscus rosa sinensis* Linn. (75, 150 and 300 mg/kg, *p.o.*) was done by carbon clearance method for non-specific immunity, haemagglutination antibody titre method for humoral immunity and footpad swelling method for cell mediated immunity on wistar albino rats. Results of present studies suggest that the hydro-alcoholic extract of *Hibiscus rosa sinensis* Linn. was found to possess significant immunostimulatory action on immune system [21].

### ***Momordica charantia***

*Momordica charantia*, called bitter melon or bitter gourd is a tropical and subtropical vine of the family Cucurbitaceae. This is one of the most important local medicinal plants both for ritual and ethnomedical practices.

There was a high degree of consensus (>50%) for use in the treatment of gastrointestinal and viral disease among 47 groups of village informants in the general population, while 19 traditional healers reported a larger and broader set of uses. Ribosome-inactivating proteins (RIPs) are a family of enzymes that depurinate rRNA and inhibit protein biosynthesis. Here they report the purification, apoptosis-inducing activity, and polyethylene glycol (PEG) modification of RIP from the bitter melon seeds. The protein has a homogenous N-terminal sequence of N-Asp-Val-Ser-Phe-Arg. Moreover, the RIP displayed strong apoptosis-inducing activity and suppressed cancer cell growth. This might be attributed to the activation of caspases-3. To make it available for *in vivo* application, the immunogenicity of RIP was reduced by chemical modification with 20 kDa (mPEG)<sub>2</sub>-Lys-NHS. The inhibition activity of both PEGylated and non-PEGylated RIP against cancer cells were much stronger than against normal cells, and the antigenicity of PEGylated RIP was reduced significantly. Their results suggested that the PEGylated RIP might be potentially developed as anti-cancer drug [22].

### ***Morinda citrifolia***

*Morinda citrifolia* Linn (Family: Rubiaceae) is a traditional medicinal herb that has been purported to be beneficial in the treatment of infections due to its immune enhancing properties. However, detailed studies highlighting the effect of different compounds isolated from the plant on the immune system are lacking. In this study, the stimulatory effects of the extracts and fractions of *M. citrifolia* fruits on important components of the adaptive immune system such as T lymphocytes and B lymphocytes were studied. The effects of the plant extracts on lymphocytes were assessed by *in vitro* (MTT assay) and *in vivo* (cell mediated immune response) techniques. Results of the MTT study indicated that the hydroalcoholic (0.5 and 1.0 mg/ml) and aqueous extracts (0.5 and 1.0 mg/mL) significantly ( $p < 0.05$ ) increased *in vitro* splenocyte proliferation to the extent of 43.6, 54.5, 32.7, and 36.4%, respectively. Moreover, the hydroalcoholic (200 mg/kg) and the aqueous (200 mg/kg) extracts significantly ( $p < 0.05$ ) increased the cell-mediated immune response to the extent of 33.52 and 18.56%, respectively. The study revealed that the hydroalcoholic extract (200 mg/kg) and fraction F I (40 mg/kg) significantly increased the humoral response to the extent of 33.33 and

35.12%, respectively. The results of this study confirm the cellular and humoral immunostimulant properties of *M. citrifolia* fruits and justify its usage in traditional medicine [23].

### ***Moringa oleifera***

The present study was to investigate the immunomodulatory action of methanolic extract of *Moringa oleifera* (MEMO) in an experimental model of immunity. The cellular immunity was evaluated using neutrophil adhesion test, cyclophosphamide induced neutropenia and carbon clearance assay, whereas, humoral immunity was tested by mice lethality test, serum immunoglobulin estimation and indirect haemagglutination assay in animals. Administration of MEMO (250 and 750 mg/kg, po) and *Ocimum sanctum* (100 mg/kg, po) significantly increased the levels of serum immunoglobulins and also prevented the mortality induced by bovine *Pasteurella multocida* in mice. They also increased significantly the circulating antibody titre in indirect haemagglutination test. Moreover, MEMO produced significant increase in adhesion of neutrophils, attenuation of cyclophosphamide induced neutropenia and an increase in phagocytic index in carbon clearance assay. From the results, it can be concluded that MEMO stimulate both cellular and humoral immune response. However, low dose of MEMO was found to be more effective than the high dose [24].

### ***Plumbago zeylanica***

*Plumbago zeylanica*, commonly known as Ceylon Leadwort or Doctorbush, is a species of plumbago with a pantropical distribution (Family: Plumbaginaceae). Effects of seselin identified from *Plumbago zeylanica* on phytohemagglutinin (PHA)-stimulated cell proliferation were studied in human peripheral blood mononuclear cells (PBMC). The data demonstrated that seselin inhibited PBMC proliferation-activated with PHA with an IC<sub>50</sub> of 53.87±0.74 µM. Cell viability test indicated that inhibitory effects of seselin on PBMC proliferation were not through direct cytotoxicity. The action mechanisms of seselin may involve the regulation of cell cycle progression, interleukin-2 (IL-2) and interferon-gamma (IFN-gamma) production in PBMC. Since cell cycle analysis indicated that seselin arrested the cell cycle progression of activated PBMC from the G<sub>1</sub> transition to the S phase. Seselin suppressed IL-2 and IFN-gamma production in a concentration-dependent manner. Furthermore,

seselin significantly decreased the IL-2 and IFN-gamma gene expression in PHA-activated PBMC. Therefore, results elucidated for the first time that seselin is likely an immunomodulatory agent for PBMC [25].

### ***Punica granatum***

*Punica granatum* L. (Punicaceae) fruit rind powder (PGFRP) at the dose of 100 mg/kg orally as aqueous suspension was found to stimulate the cell-mediated and humoral components of the immune system in rabbits. PGFRP elicited an increase in antibody titer to typhoid-H antigen. It also enhanced the inhibition of leucocyte migration in Leucocyte Migration Inhibition test and induration of skin in delayed hypersensitivity test with Purified Protein Derivative (PPD) confirming its stimulatory effect on cell-mediated immune response [26].

### ***Randia dumetorum***

*Randia dumetorum* Lamk., (Family: Rubiaceae) a plant widely used in the traditional medicinal systems of India, has been reported to possess antiviral, antibacterial and anti-inflammatory activities. In present study, the attempt was made to screen immunomodulatory activity of methanol extract and its petroleum ether, chloroform, ethyl acetate and methanol fraction of fruits of *R. dumetorum*. The effects of *R. dumetorum* on cell mediated and humoral components of the immune system in mice were observed. Administration of chloroform fraction at dose 100 mg/kg produced statistically significant results as evidenced by increase in humoral antibody (HA) titre ( $p < 0.05$ ), delayed type hypersensitivity (DTH) response ( $p < 0.001$ ). This fraction also enhanced the total WBC level in cyclophosphamide induced myelosuppression model ( $p < 0.001$ ) at dose 100 mg/kg. Petroleum ether fraction and methanol fraction affected only cell mediated immunity. Present study, therefore reveals that drug holds promise as immunomodulatory agent [27].

### ***Saraca indica***

*Saraca indica* is a genus in the family Fabaceae (legume family). Saracin, a seed integument lectin from *Saraca indica* is highly specific for binding N-acetyl-neuraminyl-N-acetylglucosamine [Neu5Ac- $\alpha$ -(2-6)/(2-3)-D-Gal-beta-(1-4)-D-GlcNAc]. This lectin has been found to be mitogenic for human lymphocytes, and this mitogenic activity could be inhibited in presence of fetuin. Further, treatment with saracin could induce secretion of IL-2 in a culture

of resting human peripheral blood mononuclear cells (PBMC) after 48 h. Saracin has a higher affinity for the CD8(+) than CD4(+) T cells as revealed by FACS analysis. Agarose gel electrophoresis of DNA isolated from lymphocytes cultured under different conditions has shown that this lectin could induce apoptosis in activated T-lymphocytes, as also confirmed by flow cytometric studies. Phenotypic analysis of the apoptotic cells reveals that they belong to CD8 (+) T cells lineage. Four surface glycoproteins of PBMC have been found to interact with saracin in a trisaccharide [Neu5Ac-alpha-(2-6)/(2-3)-D-Gal-beta-(1-4)-D-GlcNAc]-sequence specific manner. Saracin seems to be an interesting immunomodulator for the mammalian immune system [28].

### ***Solanum torvum***

The effect of *Solanum torvum* (Family: Solanaceae) on delayed type hypersensitivity (DTH) response, hemagglutinating antibody (HA) titer, white blood cells (WBC), red blood cells (RBC) and hemoglobin concentration was investigated in Sprague-Dawley rats to establish immune modulatory and erythropoietic activity. Sheep red blood cells (SRBC)-immunized and challenged rats were treated with *Solanum torvum* extract, levamisole and dexamethasone. Phenylhydrazine (PHZ)-induced anemia in rats was treated with the extract. The aqueous *Solanum torvum* extract and levamisole significantly enhanced DTH response, increased HA titer and WBC count, while dexamethasone significantly decreased DTH response, did not increase HA titer, and did not enhance WBC profile. The extract and Feroglobin, the reference heamatinic, were able to reverse PHZ-induced anemia, and increase the RBCs and Hb concentration above baseline values within 24 days. *Solanum torvum* extract showed a concentration-dependent immunostimulant and erythropoietic activity [29].

### ***Syzygium aromaticum***

The immunomodulatory effect of clove, *Syzygium aromaticum* (Family: Myrtaceae) essential oils was evaluated by studying humor- and cell-mediated immune responses. Essential oils were administered to mice (once a day, orally, for a week) previously immunized with sheep red blood cells (SRBCs). Clove essential oil increased the total white blood cell (WBC) count and enhanced the delayed-type hypersensitivity (DTH) response in mice. Moreover, it restored cellular and humoral immune responses in

cyclophosphamide-immunosuppressed mice in a dose-dependent manner. The findings were established that the immunostimulatory activity found in mice treated with clove essential oil is due to improvement in humor- and cell-mediated immune response mechanisms [30].

### ***Triticum vulgare***

*Triticum Vulgare* (Wheat) Bran Extract is an extract of the bran of the wheat (Family: Poaceae). The investigation aimed to the antitumor activity of wheat bran arabinoxylans, including the role of its immunostimulatory effect. In S<sub>180</sub> tumor-bearing mice arabinoxylan administration significantly inhibited the growth of mouse transplantable tumors and remarkably promoted thymus and spleen indexes, splenocyte proliferation, natural killer cell and macrophage phagocytosis activity, interleukin<sub>2</sub> production, and delayed-type hypersensitivity reaction. In addition, it increased peripheral leukocyte count, and bone-marrow cellularity in tumor-bearing mice. As the antitumor activity of arabinoxylans may be mediated via the improvement in the immune response, they can be considered an antitumor agent with immunomodulatory activity [31].

### ***Withania coagulans***

*Withania coagulans* Dun. (Stocks.) Vegetable Rennet. (Fam. Solanaceae.) This shrub has the property of coagulating milk, and has been used for preparing vegetable rennet ferment for making cheese. Six new withanolides, withacoagulins A-F (1-6, resp.), together with ten known withanolides, 7-16, were isolated from the aerial parts of *Withania coagulans*. Their structures were determined by spectroscopic techniques including 1D- and 2D-NMR (1H, 13C, HMQC, and HMBC) and MS experiments. These compounds, including the crude extracts of this herb, exhibited strong inhibitory activities on the T- and B-cell proliferation. From, that the results showed *Withania coagulans* has a immunosuppressive activity [32].

## **CONCLUSION**

Allopathic drugs are available for counteracting the oxidative stress and hence improve immunity, but the side effects and prohibitive cost of these allopathic drugs makes it necessary to search for an alternative. The Ayurvedic system of medicines not only provides that alternative, but also scores over the side effects and cost factor of allopathic medicine [33,34]. Immunomodulators are becoming very popular



in the worldwide natural health industry as people start to realize the importance of a healthy immune system in the maintenance of health and the prevention of diseases. Although extensive work has been carried out in the field of chemotherapy during this century, it is only in the last two decades that a number of compounds with immunomodulatory activity have been identified from the plant materials. From ancient times, medical treatment in India has relied to a large extent on the use of plants. Indian medicinal plants are a rich source of substances that are claimed to induce paraimmunity, the non-specific immunomodulation of granulocytes, macrophages, natural killer cells and complement function in mammalian models [35]. In the recent past, scientific studies on plants used in ethno medicine have led to the discovery of many valuable drugs. Several structural analogues are also in clinical use and most notable of these are vinorelbine and vindesine. The current practice of prescribing photochemicals to support the immune system or to fight infections is based on centuries old traditions [36]. The last factor is very important, since high doses tend to be immunosuppressive and low doses of the same tend to become immunostimulatory. Finally it should be noted that most in-vitro or in-vivo models are not adequate or not simple enough to ensure that the same can be used as a drug [37].

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