



# Plant Archives

Journal homepage: <http://www.plantarchives.org>  
DOI Url : <https://doi.org/10.51470/PLANTARCHIVES.2021.v21.no2.122>

## SCREENING OF IMMUNOMODULATORY ACTIVITY OF DIFFERENT PLANT PARTS: A REVIEW

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(Date of Receiving : 09-05-2021; Date of Acceptance : 11-09-2021)

### ABSTRACT

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 allotransplantation. 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 phagocytes’ cells such as macrophages, monocytes, or related cells. In Indian medicinal literature a large number of plants promote the physical mental and defense mechanism into the body. In other hand a large number of medicinal plants included in Rasayanas have been claimed to possess immunomodulatory activities. Medicinal plants which are used as immunomodulatory effect to provide alternative potential to conventional chemotherapy for a variety of diseases, especially in relation to host defense mechanism. The present study thrust a review on the different plants being used as an alternative for immune development and to overcome the overburden expensis and threats of allopathay.

**Keywords:** Immunomodulatory, Immunosuppressant, Hypersensitivity, Haemagglutination

### INTRODUCTION

The Immune system is involved in the etiology as well as pathophysiology mechanisms of many diseases. Modulation of the immune responses to alleviate the diseases has been of interest for many years. Immunomodulation is a procedure which can alter the immune system of an organism by interfering with its function; if it results in an enhancement of immune reactions it is named as immunostimulative drug which primarily implies stimulation of non-specific system, that is, granulocytes, macrophages, complement, certain T-lymphocytes and different effector substances. Immunosuppression implies mainly to reduce resistance against infections, stress and may occur an account of environmental or chemotherapeutic factors. Immunostimulation and immunosuppression both need to be tackled in order to regulate the normal immunological functioning.

The medicinal properties of certain plants have been known centuries. More than a quarter of the medicines in use today come from plants i.e; from traditional medicine. Immunology is probably one of the most rapidly developing areas of biomedical research and has great promises with regard to prevention and treatment of wide range of disorders, inflammatory diseases of skin, gut, respiratory tract, joints and central organs. In addition infectious diseases are now primarily considered immunological disorders while neoplastic diseases and organ transplantation and several

autoimmune diseases may involve in an immunosuppressive state. The function of efficacy of immune system may be influenced by many exogenous factors like food and pharmaceuticals, physical and psychological stress and hormones etc. the healthy state is believed to be based on a sophisticated fine tuning of immunoregulatory mechanism.

Suppressive and cytotoxic activity affecting the function of immune system has been reported for many of the synthetic substances; azathioprin and cyclophosphamide are used, but these drugs have a number of side effects in long term treatment. Cyclophosphamide is an alkylating agent resulting in the cross linking of DNA and causes inhibition of DNA synthesis. The major drawback of these drugs is myelosuppression, which is undesirable.

In recent times, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional system. Today, we are witnessing a great deal of public interest in the use of herbal remedies. Now-a-days a large number of drugs in use are derived from plants. Plants play an essential role in the health care needs for the treatment of diseases and to improve the immunological response against much pathology (Bocher *et al.*, 2000). Plant extracts are potentially curative. Some of these extracts boost the humoral (Rehman *et al.*, 1999) and cell mediated immunity (Upadhyey *et al.*, 1992), against viruses (Calixto *et al.*, 1998), bacteria (Boyanova and Neshev, 1999), Fungi (Ali

*et al.*, 1999), protozoa (Sharma *et al.*, 1998) and cancer (Wong *et al.*, 1994).

Several plants and their bioactive compound extracts have been reported for immunomodulatory activity and many formulations of these plants activity and many formulations

of these plant products are available to enhance the immune system. Some of the most commonly and important plants possessing a potential to alleviate the immunological disorders are as under in the Table 1 given below:

**Table 1:** List of plants having immunomodulatory activity;

S.No.	Name of the Plant (Common Name)	Family	Part Used
01.	<i>Adhatoda vasica</i> (Malabar Nut)	Acanthaceae	Leaf
02.	<i>Amorphophallus campanulatus</i> (Elephant yam)	Araceae	Tuber
03.	<i>Balanites roxburghii</i> (Desert date/ Hingot)	Simarubaceae	Stem bark
04.	<i>Cassia fistula</i> (Amaltus/Imli)	Leguminosae/ Caesalpinioideae	Fruit
05.	<i>Hibiscus sabdariffa</i> (Rosella/ Lal ambary)	Malvaceae	Dried Calyx
06.	<i>Moringa oleifera</i> (Munga/Horseradish tree)	Moringaceae	Leaf
07.	<i>Nyctanthus arbor tritis</i> Linn. (Night jasmine)	Oleaceae	Whole Plant
08.	<i>Ocimum sanctum</i> (Holi basil/ Tulsi)	Lamiaceae	Leaf
09.	<i>Tinospora cardifolia</i> (Common wheat/ Guduchi)	Menispermaceae	Whole plant
10.	<i>Terminalia chebulla</i> (Myrobalan)	Combretaceae	Fruit, Root
11.	<i>Trapa bispinosa</i> (Water chestnut)	Trapaceae	Fruit

***Adhatoda vasica* (Malabar Nut):** Immunomodulatory activity of various extracts of *Adhatoda vasica* Linn. in experimental rats. The Methanolic, chloroform and diethyl ether extracts of leaves of Indian medicinal plant *Adhatoda vasica* Linn. were pharmacologically validated for its immunomodulatory properties in experimental animals.

Oral administration of extracts at a dose of 400 mg/kg in adult male Wistar rats significantly increased the percentage neutrophil adhesion to nylon fibers ( $P < 0.001$ ).

Its extracts were also found to induce Delayed Type Hypersensitivity reaction by sheep erythrocytes ( $P < 0.001$ ). The observed results at different doses were significant when compared to control groups. These findings suggested that the extracts of this plant, *A. vasica* Linn positively modulates the immunity of the host.

***Amorphophallus campanulatus* (Elephant yam):** Immunomodulatory Activity of the Methanol Extract of *Amorphophallus campanulatus* (Araceae) Tuber. The present study was evaluated to design and to screen the immunomodulatory activity of the plant material of *Amorphophallus campanulatus*. The effect of the methanol extract (ME) of *Amorphophallus campanulatus* tuber on immunological function in mice was studied using charcoal clearance, spleen index and delayed-type hypersensitivity (DTH) response models. The extract was administered orally at doses of 250 and 500 mg/kg. The extract exhibited immunomodulatory activity by causing a significant decrease in charcoal clearance, spleen index and delayed-type hypersensitivity (DTH) response. *Amorphophallus campanulatus* caused decreases in the charcoal clearance rate

and cellular immunity by facilitating the footpad thickness response to sheep red blood cell (RBC) in sensitized mice.

***Balanites roxburghii* (Desert date/ Hingot):** Immunomodulatory potential of Ethanolic extract of Stem Bark of *Balanites roxburghii* plant. This work has done to investigate the immunomodulatory property of ethanolic extract of stem bark of *Balanites roxburghii* Planch (Family, Simarubaceae). The extract was given at the doses of 50, 100 and 200 mg/kg p.o. and sepielin (Himalaya, India) was used as a standard drug at a dose of 500mg/kg, p.o. for 14 days to wistar albino rats. The assessment of immunomodulatory activity were carried out by carbon clearance test for phagocytic index, haemagglutination antibody titre for humoral immune response and delayed type of hypersensitivity for cell mediated immune responses. The results of present study clearly indicates that the rate of elimination of carbon particles is more in ethanolic extract of stem bark of *Balanites roxburghii* treated group in dose dependent manner when compared with control group and standard drug. The augmentation of the humoral immune response to Sheep Red Blood Cells (SRBCs) by ethanolic extract is evidenced by significant ( $p < 0.05$ ) enhancement of antibody titres in the blood in dose dependent manner when compared with control group. In the cell mediated immunity; the extract showed increase in DTH reaction in rats. This study clearly indicates the immunomodulatory activity of *Balanites roxburghii*. Thus, the immunostimulatory effect produced by ethanolic extract of *Balanites roxburghii* may be due to cell mediated immune response by T- lymphocytes and humoral antibody mediated response by B-lymphocytes. It can therefore be

concluded that the ethanolic extract of *Balantes roxburghii* is potent immunostimulant and can be used as a complimentary therapeutic agent.

***Cassia fistula* (Amaltus/Imli):** Modulation of Humoral Immunity by *Cassia fistula* and *Amoxy-cassia*. Immunomodulatory effect of fruit of *C. fistula*, a traditional medicinal plant and its synergistic antimicrobial combination with amoxicillin named 'Amoxy-cassia (Patent # 1371240, Government of Pakistan) studied on humoral immune system of BALB/c mice. Animal immunized with sheep RBC and treated with *C. fistula* fruit, amoxycassia, amoxicillin and saline. Number of activated anti - SRBC producing cell in spleen calculated by haemolytic plaque assay. Antibody titer in blood was measured by haemagglutination test. Number of plaques formed by the animal treated with Amoxy-cassia, amoxicillin, *C. fistula*, and normal saline were 191, 86, 53, 34 per 105 spleen cells respectively. Haemagglutinating Antibody (HA) titer was evaluated on post-immunized day 4, 6, 8, 10. Rising antibody titer was observed in all animals but Amoxy-cassia treated mice serum had the highest HA titer throughout the experiment suggesting its therapeutic usefulness. *C. fistula* and amoxy-cassia treatment improved the haemagglutination antibody titer in blood collected before and after treating the immunized animal and the rising titer in number of specific antibody reflected an overall elevation of humoral immune response.

***Hibiscus sabdariffa* (Rosella/ Lal ambary):** Immunomodulatory Effect of Extracts of *Hibiscus sabdariffa* L. (Family Malvaceae) in a Mouse Model. The immunomodulatory activity of water and alcohol extracts (including its fractions) of the dried calyx of the plant was evaluated in mice. The ability of the extracts to inhibit or enhance the production of two cytokines, namely tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-10 (IL-10), respectively, implicated as proinflammatory and anti-inflammatory interleukins were also evaluated. The extracts at doses of 50 mg/kg were found to possess higher immunostimulatory activities in comparison with levamisole (positive control), with significant effects when compared with the vehicle-treated group ( $p < 0.01$ ). Increased activity was observed with increase in doses of the 50% ethanol and absolute ethanol extracts. The insoluble fraction exhibited a significant dose-dependent immunostimulatory activity ( $p < 0.05$ ), while the residual water-soluble fraction exhibited activity at 100 mg/kg body weight. The production of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), was low in all the extract groups tested, while the production of interleukin 10 (IL-10) was high compared with the control. The production of IL-10 was high in 300 mg/kg aqueous extract. The insoluble fraction exhibited a profound dose-dependent immunostimulatory activity higher than the positive control at 100 mg/kg. This study established the immunoenhancing properties of the extracts of this plant confirming that the immunomodulatory activity is cell mediated and humoral. The insoluble fraction could find use as an immunostimulatory agent in humans. The study revealed that, to some extent the extracts, and to a large extent, two fractions of the plant possess the ability to stimulate the immune system *in vivo*. The activity may be as a result of interplay between the production of interleukin 10, inhibition of tumor necrosis factor- $\alpha$  and the effect of B-cells responsible for antibody

***Moringa oleifera* (Munga/Horse radish tree):** Immunomodulatory activity of Methanolic Leaf Extract of *Moringa Oleifera* in animals. The aim of 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 above 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 production. However, the extract, as it is taken in humans as a beverage may be of benefit in enhancing immunity.

***Nyctanthus arbor tritis* Linn. (Night jasmine):** An Immuno-Pharmacological Investigation of Indian Medicinal Plant *Nyctanthes arbor-tristis* Linn. The immunopharmacological properties of ethanolic extract of *Nyctanthes arbor-tristis* Linn. (NA) have been investigated. After administration of *Nyctanthes arbor-tristis* in doses of 0.25 and 0.5 g/kg body weight (BW) a significant increase in phagocytic index, leukocyte count and splenic antibody secreting cells were noticed. Stimulation of humoral immune response was further observed with haemagglutination antibody titer. This extract was further submitted to Thin Layer Chromatography (TLC) and High performance liquid chromatography (HPLC) and it confirmed the presence of methoxylated flavonoid quercetin-3,3'-dimethoxy-7-O-rhamnoglucopyranose. The results suggest that bio active compound flavonol glycoside of *Nyctanthes arbor-tristis* influences both humoral as well as cell mediated immune system.

***Ocimum sanctum* (Holi basil/ Tulsi):** Immunomodulatory activity of aqueous extract of *Ocimum sanctum* in rat. To evaluate the immunomodulatory effect of *Ocimum sanctum* in rat. Aqueous extract of *Ocimum sanctum* were administered orally at doses of 100, 200 mg/kg/day for 45 days in wistar albino rats. Immunomodulatory effect and biochemical and haematological changes were tested by standard methods. Aqueous extract of the *Ocimum sanctum* showed increasing antibody production in dose dependent manner. It enhance the production of RBC, WBC and haemoglobin. It does not affect the biochemical parameters. An oral administration of the aqueous extract of *O. sanctum* showed immunomodulatory effect in rat.

***Tinospora cardifolia* (Common wheat/ Guduchi):** Pharmacological Study of *Tinospora cordifolia* as an Immunomodulator. Immunomodulators are natural or synthetic agents, which by modifying the immune system affect a therapeutic benefit. They may have ability to augment (immune stimulant and /or immune enhancer), restore (immune restorative), inhibit (immune suppressant) or

help to produce (adjuvant) the desired immune response. The present work described that *Tinospora cordifolia* alcoholic extract shows immunomodulator activity. The various parameters determined were Delayed Type Hypersensitivity (DTH), effect on the bone marrow cellularity and  $\alpha$ -esterase cells and zinc sulphate turbidity test. Orally administration of *T. cordifolia* alcoholic extract (100 mg/kg, p. o) was found to increase in the there was distinct increase in foot pad thickness after treatment with *T. cordifolia* alcoholic extracts which indicates immunomodulatory effects of *T. cordifolia* as compared to vehicle and cyclophosphamide treated groups. Also significant increase in the WBC counts and bone marrow cells significantly indicating stimulatory effect on haemopoietic system. In zinc sulphate turbidity test *T. cordifolia* treated rats serum showed the more turbidity (cloudy) which indicate the increase in the immunoglobulin level as compared to vehicle, SRBC sensitized and cyclophosphamide treated group. Finally it can be concluded that *Tinospora cordifolia* (stem) mango plant climber shows potent immunomodulatory action.

***Terminalia Chebulla* (Myrobalan):** Immunomodulatory effect of alcoholic extract of *Terminalia chebula* ripe fruits. Most of the synthetic chemotherapeutic agents are immunosuppressants and exerts variety of side effects. The herbal based immunomodulators are employed as supportive or adjuvant therapy to overcome the undesired effects of chemotherapeutics agents. Herbal drugs will be significantly more effective and highly efficacious supplement to use as a general adaptogen and immune strengthener in healthy people and as a very useful, safe and effective nutrient support tonic for those challenged by disease. The present work described that *Terminalia chebula* alcoholic extract shows immunomodulator activity. The various parameters determined were differential leukocyte count (DLC), phagocytic activity and zinc sulphate turbidity test. Oral administration of *T. chebula* alcoholic extract (100 mg/kg, p.o.) was found to increase the neutrophils and lymphocytes as compared to vehicle and cyclophosphamide treated groups. *T. chebula* alcoholic extract showed linear time dependent significant phagocytic activity as compared to SRBC sensitized and cyclophosphamide treated group. In zinc sulphate turbidity test *T. chebula* treated rats serum showed more turbidity (cloudy) which indicate the increase in the immunoglobulin level as compared to vehicle, SRBC sensitized and cyclophosphamide treated group. Finally it can be concluded that *Terminalia chebula* ripe fruits show potent immunomodulatory action.

***Trapa bispinosa* (Water chestnut):** Scrutinizing the role of aqueous extract of *Trapa bispinosa* as an immunomodulator in experimental animals. The objective of the present study was to scrutinize the immunomodulatory potential of aqueous extract of fruits of *T. bispinosa* (TBAE) in experimental animals. The immunomodulatory effect was assessed in rats against sheep red blood cells (SRBC) as antigen by studying cell-mediated delayed type hypersensitivity reaction (DTH), humoral immunity response and percent change in neutrophil count. Macrophage phagocytosis assay was carried out by carbon clearance method in mice. Oral administration of TBAE dose dependently increased immunostimulatory response. Delayed type hypersensitivity reaction was found to be augmented significantly ( $p < 0.05$ ) by increasing the mean foot pad thickness at 48 hr and production of circulatory antibody titre

(humoral antibody response) was significantly ( $p < 0.05$ ) increased in response to SRBC as an antigen. In addition, immunostimulation was counteracted by up regulating macrophage phagocytosis in response to carbon particles. Immunostimulatory property of TBAE further confirmed by elevated neutrophil counts significantly ( $p < 0.01$ ) compared to control values. The result of present study suggests that aqueous extract of fruits of *T. bispinosa* could stimulate the cellular and humoral response in animals and it deserves further researches to develop an immunostimulating agent among her-bal origin.

## CONCLUSION

Recently phytopharmaceutical research received much attention to develop safe and effective lead compounds with potential immunomodulatory activity. The present study was evaluated to screen out some plants with immunomodulatory activity. So, as to be used as conventional treatment to alleviate the different immunological disorders. In general plants play a significant role in the management of different diseases.

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