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Review Article

IMMUNOMODULATORY PROPERTIES OF SOME HERBAL PLANTS AGAINST CANDIDA ALBICANS: A REVIEW

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ABSTRACT: Immunomodulators play a key role in immunity of each animal in this world. Almost all animals have their own system to produce different immunostimulators at different time. Various synthetic agents are being used as immunostimulators but they are associated with several side effects. Resistance to many clinically used synthetic agents has created a need to identify and developed a new generation of compounds for therapeutic u se. Many herbal plants show potent immunostimulatory property and induce cell mediated and humoral immune response. *Candida albicans* is an opportunistic human fungal pathogen that causes candidiasis. Some herbal plants are believed to act as immunostimulator which enhance the natural resistance of the body against candidiasis.

Keywords: Immunomodualtors, Immunostimulatory activity, herbal plants, *Candida albicans*

Introduction

Opportunistic infection are caused by organism that take advantage of a weakened immune system and cause disease (Toruner *et al.*, 2008) and the organism that become pathogenic when the host immune system is altered are called opportunistic pathogen.

Fungi have only emerged as significant pathogen during past few decades when they become more frequently diagnosed as opportunistic infection in immunocompromised hosts. Some species of fungi are regularly identified as cause of disease in immunocompromised host, most of the reported opportunistic fungal infections are candidiasis, aspergillosis, cryptococcosis and zygomycosis (Wanke *et al.*, 2000). Fungi cause a wide range of illness from minor skin condition to life threatning disease. They produce two kinds of infections - systemic and/or superficial. The systemic infection affects internal organs and superficial attack tissue on the surface of body. Fungi are the frequent cause of opportunistic infection. They lives as commensals in healthy individuals but they can cause disease when the immune status of host is altered (Bar *et al.*, 2012). With the increase use of antibiotics and immunosuppressive agents, fungal infection such as candidiasis becomes very common. Candidiasis is an opportunistic systemic fungal infection caused by *Candida albicans* (Gupta *et al.*, 2012. Kumar *et al.*, 2012). *Candida albicans* is an opportunistic fungal pathogen causing life threatening mucosal and systemic infection in immunocompromised humans (Hise *et al.*, 2009). Plants and its phytoconstituents can be used to treat fungal infection particularly candidiasis. Many plants have been listed having immunostimulatory effect against *Candida albicans* including *Aloe vera*, *Malaleuca alternifolia*, *Larrea divaricata*, *Glycyrrhiza glabra* etc.

Candidiasis

Fungal infections are a major cause of morbidity and mortality and there is an urgent need for the development of new antifungal agents (Coleman *et al.*, 2010). *Candida albicans* is a dimorphic fungus and it is part of human microflora. It is also an opportunistic pathogen of human body when its proliferation is not controlled by host immune system. It is one of most identified agent in nosocomial infection and is capable of invading virtually any site of host, from tissue and organs to superficial site such as skin and nails (Tournu *et al.*, 2012). *Candida* species are known as opportunistic pathogen because depending on local oral environment. It can transform from a harmless commensal to an organism causing an infection in the oral mucosa. It exists commensally in the gastrointestinal and gastro urinary tracts of healthy individuals. It causes severe disseminated and lethal infection in immunocompromised patient

such as those suffering from HIV infection or undergoing cancer chemotherapy. In the US, it constitutes the fourth most common causative agent of nosocomial blood stream infection (Rodovanoic, *et al.*, 2011).

C. albicans cause a variety of infection ranging from superficial candidiasis to life threatening invasive candidiasis (Nobuyuki et *al.*, 2012). *Candida* has a unique ability to grow in at least four kinds of forms, that is yeast like, hyphae, psuudohyphae and clamydospores. The hyphae form rather than yeast form is responsible for pathogenic character of *C. albicans*. The pathogenicity of *Candida* depends upon two major factors, one is the immune status of host and another is the virulence factor (Kabir *et al.*, 2012). The transition of Yeast to hyphal form is not only allowing immediate adaptation to changing environment condition, but also prepare the cells to subsequent steps of infection (Hube,2004).

The oral cavity is a primary target for opportunistic infection particularly oral candidiasis caused by *Candida albicans* (Peters, 2010). Candidiasis infection has steadily increased over the past 30 years. Infections caused by *Candida albicans include* thrush, vulvar rash, vaginitis, conjunctivitis and infection of nails (Kumar *et al*., 2012). It is generally associated with predisposing factors such as use of immunosuppressive agents, and antibiotics (Janqueira, 2012). Candidiasis in humans has become the third or fourth leading cause of blood stream infection, and at least 40% affected individuals will die of this disease. It is estimated that 60,000-70,000 cases of disseminated candidiasis occurs per year in the US alone, and associated health care costs are $2-4 billion/year (Xin *et al*., 2012). Vulvovaginal candidiasis affect 75% of normal healthy women's at least once during their reproductive years. Factors contributing to the development of disease include antibiotic, high estrogen contraceptive use, hormone replacement therapy and uncontrolled diabetes mellitus (Zeng *et al*., 2011). Treatment of this infection has continued to be problematic because of the potential toxicity of traditional antifungal agents against host cell (Williams and Lewis, 2011).

Induction of immune response

The immune system is designed to protect the host from invading pathogen and to eliminate disease. Activation of immune system by non

self antigen or self antigen is generally believed to require processing of the antigen by the phagocytic cells such as macrophage, monocytes or related cells. There are two type of immune response in the human body, innate and adaptive immune response. Immune system is a part of body to detect pathogen by using specific receptor to produce immediate response by the activation of immune cells (Kumar *et al*., 2012). The most important component of immune system in the initial stage of the defense is phagocytosis. Phagocytic cells include neutrophils, eosinophils, macrophage and monocytes that recognize foreign substances and invading microorganism.

These cells engulf and destroy the foreign substances with their intracellular killing mechanism. When the immune system fails, the next level of defense is provided by B cells and T cells (Ranjith *et al*., 2008). The innate immune system provides the principle protection against disseminated candidiasis. The Polymorphonuclear Leukocytes are primary component of host innate immune defense against *Candida albicans*. The receptor present in leukocytes utilized in fungal or microbial recognition. The receptors mediate the migration of leukocytes to the site of infection and adhesion to microorganism with subsequent phagocytosis (Soloviev *et al*., 2011). Neutrophils are also important for the control of systemic fungal infection. The fungal cell wall composed of multiple layer of carbohydrate including mannose, Beta glucan and chitin. These components are recognized by receptors to activate the host immune system. The suppression of immune system allows opportunistic pathogen to overwhelm the host to cause secondary infection (Patil *et al*., 2010).

Role of Herbal Plants as Immunostimulator

Immunomodulation is the regulation and modulation of immunity either by enhancing or by reducing the immune response. Modulation of immune response involved induction, expression or amplification of immune response**.** The modulation in immune system resulting in enhancement of immune reaction is called immunostimulation. There are two main categories of immunostimulator, one is specific which provide antigen specificity like vaccine or any antigen and other is non -specific which act irrespective of antigen specificity like adjuvant (Kumar *et al*., 2011). Immunomodulation modulate immunity using various substance either of natural or

synthetic origin. An immunomodulator is a substance which suppresses or modulates the component of immune system including innate or adaptive immunity of the immune response (Kumar *et al*., 2012). Immunomodulators are capable of interacting with the immune system to up regulate or down regulate specific aspects of host response. They play their role in maintaining the immune system by increasing T cell immunity, stimulating the natural killer cells and interferon production as well as inducing specific cytokine production by activating targeting cells (Yeap *et al*., 2011).

One of the most important sources of immunostimulator which are being explored extensively currently comes from plant derived substances (Table 1) (Yeap *et al*., 2011). A large population of India uses plants for its healing, preventive, curative and much therapeutic property together with immunostimulatory property (Archana *et al*., 2011). Certain medicinal plants promote positive health and maintain organic resistance against infection by re-establishing body equilibrium. Many polysaccharides isolated from higher plants are considered to be biological response modifier and enhance various immune responses, like complement activation, proliferation of lymphocytes and stimulation of macrophages. Plant flavonoids also used as immunostimulator, which is important for growth, development and immunity (Mahiuddin and Shaikh, 2010). Various synthetic agents are used as immunostimulative agent such as levamisole, thalidomide, but there are various side effects of these agents such as nephrotoxicity, hepatotoxicity, bone marrow depression, gastrointestinal disturbance and so on. Because of the side effects associated with synthetic agents and as plants are safer, much more effective and cheaper, conventional immunomodulator plants can be explored (Kumar *et al.*, 2011). There are number of plants that have been reported to have immunostimulatory activity against many pathogens. Some of the herbal plants having immunostimulatory activity against *Candida albicans* are shown in Table 2.

Aloe vera

Aloe vera is a species of succulent plant that probably originated in northern Africa. Aloe vera is a stemless or very short-stem succulent plant growing to 60–100 cm (24–39 in) tall, spreading by offsets. Natural products are important resources in traditional medicine and have been long used for prevention and treatment of many diseases

(Farahnejad *et al.*, 2011). *Aloe vera* is a medicinal plant with anti-inflammatory, antimicrobial, antidiabitic and immune boosting properties (Fani and Kohanteb, 2012) (Fig.1).

Figure: 1 *Aloe vera*

The botanical name of *Aloe vera* is Aloe barbadinsis Miller and belongs to Liliaceae family. It grows mainly in dry region of Africa, Asia, Europe and America. In India it is found in Rajasthan, Gujarat, Maharashtra and Tamil Nadu (Surjush *et al.*, 2008). The gel of *aloe vera* species contain immunomodultory polysaccharides, such as acetylated mannan, glucomannan and galactogalacturan. Acemannan is mixture of various polymer chain of β (1,4) linked acetylated galactomannan. The immunomodulatory activity of orally administered *aloe vera* gel has been examined in *C. albicans* infection. The acemannan, which present in aloe gel, mediates its activity through activation of macrophage. The activated macrophage with acemannan enhance phagocytic and candidicidal activities. Oral administration of *aloe vera* gel significantly reduced the fungal trouble in kidney and spleen (Im *et al.*, 2010).

Malaleuca alternifolia

Melaleuca alternifolia is native to Australia family Myrtaceae known for its natural soothing and cleansing properties. The species are shrubs and trees are 6.6–98 ft tall, often with flaky, exfoliating bark. The leaves are evergreen, alternately arranged, ovate to lanceolate, 1–25 cm (0.39–9.8 in) long and 0.5–7 cm (0.20–2.8 in) broad, with an entire margin, dark green to grey-green in colour. The essential oil of *M. alternifolia* also known as Tea tree oil is widely used as antimicrobial, anti-inflammatory and anti cancer agent (Fig. 2) (Hammer *et al.*, 2006). Tea tree oil is obtained by steam distillation from Malaleuca *alternifolia*. It contains several components such as monoterpenes, sesqluiterpnes and related alcohols. Tea tree oil show efficacy in the treatment of oral candidiasis and it may be effective in the treatment of vaginal candidiasis (Hammer *et al.*, 2004). Terpinen-4-ol is the major tea tree oil component and has shown strong antimicrobial and anti inflammatory properties (Mondella *et al.*,

2006). Tea tree oil inhibits the respiration of Candida species due to membrane disruption. It denatures proteins and disrupts the structure and function of normal cellular membrane which cause cytoplasmic leakage, cell lysis and death. Oral epithelial cells produce pro-inflammatory IL-8 response to Candida *albicans*. *Candida albicans* infection of human oral epithelial cells induce the expression of chemokines IL-8 and cytokine granulocyte macrophage colony stimutating factor(GM-CSF) and it moderate induction of IL-1β and TNF-α. It leads to chemo attraction of polymorphonuclear leucocytes to the site of which results in reduced growth of pathogen (George *et al.,* 2010).

Figure: 2 *Malaleuca alternifolia*

Larrea divaricata

Larrea Divaricata is an evergreen shrub growing to 1 to 3 meters (3.3 to 9.8 ft) tall (Fig. 3). *Larrea divaricata* Cav. is a plant which belongs to Zygophyllaceae family (Turner *et al*., 2011) and widely used in medicines to treat tumor infection and inflammatory disease (Davicino et *al., 2007*). It distributed in the west of America and widely in Argentina (Divicino *et al*., 2011). *Larrea divaricata* immunomodulatory effects. Fraction (F1) which obtained from *Larrea divaricata* is able to induce the activation of innate immune response. Phagocytes such as neutrophils and macrophage prevent the systemic candidiasis. The activated macrophage leads to the release of several key mediators. These cells are able to kill Candida by internalization and fusion of phagosome with lysosome. TNF-α is critical in the host defense against candidiasis. F1 increase TNF-α concentration which triggers a protective response to infection (Martino et *al*., 2011). F1 show effects on cytotoxic protein levels, apoptosis, phagocytosis, reactive oxygen species production and liposomal activity. F1 increase macrophage yeast phagocytosis, reactive oxygen species and NO production. F1 induce a state of pre activation of macrophage, which make more effective response against *Candida albicans* (Martino *et al.,* 2012).

Figure: 3 *Larrea divaricata*

Glycyrrhiza glabra

The liquorices plant is a legume (related to beans and peas) that is native to southern Europe and parts of Asia *Liquorices* grows best in deep valleys, well-drained soils, with full sun, and is harvested in the autumn, two to three years after planting. *Glycyrrhiza glabra* is a medicinal plant commonly known as licorice, sweet wood, mulahatti and yastimadhu (Fig. 4).

Liquorice or licorice is the root of *Glycyrrhiza glabra* from which a somewhat sweet flavor can be extracted. It belongs to Fabaceae family and cultivated in UK, USA, Italy, China and Nourthern India (Vispute and Khopade, 2011). The roots of *Glycyrrhiza glabra* contain Glycyrrhizin (GR), which is a saponin glycoside that is 60 times sweeter than cane sugar. Glycyrrhizin involved in the decrease of IgG and IgA which play an important role in hypersensitive mechanism (Rohsan *et al*., 2012). Non specific immune response expressed by activation of polymorphonuclear neutrophils and macrophage which involved in the resistance to early phase infection with *Candida albicans.* A major influence i n host resistance against *Candida albicans* infection is a type 1 T cells associated cellular response. Type 1 T lymphocytes produce type 1 cytokines. These cytokines are able to activate and enhance the killing activities of effector cells targeted to cells infected with *Candida albicans*. GR an active component reduced the susceptibility of thermally injured mice to *Candida albicans* infection. It protects the injured mice by inhibiting type 2 cytokines production from burn associated type 2 T cells. The production of type 2 cytokines regulated by GR through the induction of CD4 T cells inhibiting the production of type 2 cytokine by burn associated type 1 cells (Utsunomiya *et al.,* 1999).

Figure: 4 *Glycyrrhiza glabra*

Table 1. Immunostimulatory property of some herbal plants

S. No	Plants	Phytoconstituent	Immunostimulatory	Reference
1.	*Aloe vera*	Acemannan	Help in antibody production	Im *et al.*, 2012
2.	*Allium sativam*	Protein	Stimulate T cell and IL-2 production	Archana *et al.*, 2011
3.	*Aesculus indica*	Crude extract	Stimulate cell mediated immunity	Bibi *et al.*, 2011
4.	*Angelica gigas*	Angelan	Selectively modulate cytokines	Hashemi and Davoodi, 2012
5.	*Asparagus racemosus*	Alcoholic extract	Inhibit ochre toxin A induced suppression of IL-1and TFN-α	Archana *et al.*, 2011
6.	*Azadirachta Indica*	Oil	Stimulate cytokines,activate immune system	Faal *et al.*, 2012
7.	*Baliospermum montanum*	Aqueous extract	Stimulate cell mediated immune System by increasing function of neutrophils	Mali *et al.*, 2008
8.	*Caparis zeylanica*	Ethyl acetate fraction	humoral and cellular arm of immune system	Agarwal *et al.*, 2010
9.	*Chlorophytum borivilianum*	Extract	Improve humoral and cell mediated immunity	Thakur *et al.*, 2006
10.	*Curcuma longa*	curcumin	Show anti inflammatory and anti tumour activity	Megraj *et al.*, 2011
11.	*Emblica officinalis*	Fruit	Immunostimulatory effect on lymphocyte function	Sharma *et al.*, 2000
12.	*Ficus benghalensis*	Extract	Stimulate cell and antibody mediated immune response	Patil and patil *et al.*, 2010
13.	*Gymnema sylvestre*	Tannin	Anti inflammatory activity	Gupta *et al.*, 2010
14.	*Magnifera indica*	magniferin	Cell & humoral mediated activation of B and T cell	Archana *et al.*, 2011
15.	*Nyctanthes arbortristis*	Lipids	Enhance humoral and Macrophage activity	Agarwal and Singh, 1999
16.	*Ocimum sanctum*	steroids	Inhibit tumor development in mice	Archana *et al.*, 2011
17.	*Panax ginseng*	Glucopyranoside	Enhance production of cytokine	Archana *et al.*, 2011
18.	*Phylanthus emblica*	Vitamin C	Enhance NK cells activity against tumor	Archana *et al.*, 2011
19.	*Ricinus communis*	Tannins	Increased the phagocytic function of Neutrophils	Kumar *et al.*, 2011
20.	*Sipunculus nudus*	Polysaccharides (SNP)	Increase bone marrow cellularity	Zang and Dai *et al.*, 2011
21.	*Tinospora cordifolia*	Polysaccharides	Immunomodulatory property	Sharma *et al.*, 2012
22.	*Tricosanthes dioica*	Extract	Enhance production of RBCs,WBCs & Heamoglobin	Bhadoriyal and Mandoriyal
23.	*Urena lobata*	Methanolic extract	Increase phagocytic function of neutrophils	Rinku *et al.*, 2011
24.	*Withania somnifera*	Root	Inhibit tumor development, enhance spleen colony, colony forming unit	Megraj *et al.*, 2011

Table2. Some herbal plants and their immunostimulatory properties against *Candida albicans*

S. No	Plants	Phytoconstit-uent	Immunostimulatory	Reference
1.	*Aloe vera*	Acemannan	Enhance Phagocytic and candidicidal activity	Im *et al.*, 2012
2.	*Glycyyrhiza glabra*	Glycyyrhizin	Protect thermally injured mice from *Candida albicans*	Utsunomiya *et al.*, 1999
3.	*Larrea divaricata*	Fraction	Induce an activation state of macrophage	Martino *et al.*, 2011
4.	*Malaleuca alternifolia*	Oil	Treatment of candidiasis	Hammer *et al.*, 2004
5.	*Matricaria chanomilla*	Extract	Enhance total WBCs count	Ghonime *et al.*, 2011
6.	*Nycthanthes arbortristis*	Extract	Enhance humoral and DTH macrophage	Agarwal and Singh, *et al.*, 1999
7.	*Nigella sativa*	Thymoquinin-e	Enhance T cell and NK cell mediated immune response	Saleem *et al.*, 2005
8.	*Silence nocturna*	extract	Enhance total WBCs and bone marrow cellularity	Ghonime *et al.*, 2011

Conclusion

As a consequence of increasing demand for herbal drug treatment of various diseases, plant drugs from Ayurvedic system are being explored globally. Many organisms which cause damage to human health exhibit drug resistance due to inadequate use of antibiotics. Various natural and synthetic agents are used as immunostimulative agent but there are various side effects of these agents. Thus, there is a need for discovery of new agents from natural sources including plants. Medicinal plants can provide an alternative to conventional chemotherapy for a variety of disease, especially when host defense mechanism has to be altered. There is a need to evaluate several medicinal plants for their immunomodulatory property which are still unrevealed. Thus there is an urgent need to check the efficacy, safety and translational guidelines for a potent herb to be use as a safe and effective immunostimulator.

REFERENCES

Agarwal S S, Singh V K. (1999). Immunomodulators: A review of Studies on Indian medicinal plants and synthetic peptides. PINSA. 3:179-204.

Agarwal S S, Khadase S C, Talele G S. (2010). Studies on immunomodulatory activity of *Capparis zeylonica* leaf extract. International Journal of Pharmaceutical Science and Nanotechnology. 3:887-892.

Archana, Jatawa S, Paui R, Tiwari A. (2011). A review on immunostimulatory plants: A rich source of NaturalI mmunomodulator. International J ournal of Pharmacology.7:198-205.

Bar E, Gladiator A, Bastidus S, Roschitzki B, Acha-Orbea H, Oxenius A, LeibundGut L S. (2012). A novel Th cell epitope on *Candida albicans* mediates protection from fungal infection. J immonol. 188(11):5636-43.

Bhandoriyal S S, Mandoriyal N. (2012). Immunomodulatory effect of *Tricosanthes dioica Roxb*. Asian Pacific Journal of Tropical Biomedicines. 5985-5987.

Bibi Y, Nisa S, Chaudhary F M, Zia M. (2011). Antibacterial activity of some selected medicinal plants of Pakistan. BMC Complementary and alternative medicine. 11:1-7.

Coleman J J, Okoli I, Tegos G P, Holson E B, Wagner F F, Hamblin M R, Mylonakis E. (2010). Characterization of plantderived saponins naturalproducts against *Candida albicans*. ACS Chem. Biol. 5(3); 321-332.

Davicino R, Matter A, Casals Y, Porporatto C, Correa SG, Micalizzi B. (2007). *In vivo* immunomodulator effects of aqueous extract of *Larrea divaricata Cav*. Immunonopharmacol Immunotoxicol.29 (3-4):351-366.

Divicino R, Martino R, Anesini C. (2011). *Larrea divaricata* Cav: Scientific evidence showing its beneficial effects and its wide potential application. BLACPMA.10(2):92-103.

Faal T J, Hussain A A, Faraj M K, Al-Ramahy A K. (2012). The immunomodulatory effect of

Neem (*Azadirachta indica*) seed aqueous, ethanolic extract and *Candida albicans* cell wall mannoproteins on immune response in mice vaccinated with Brucella Rev-1. The Iraqi J Vet Med.36. (1):120-127.

Fani M, Kohanteb J. (2012). Inhibitory activity of *Aloe vera* gel on some clinically isolated cariogenic and periodontopathic bacteria. Journal of Oral Science.54:15-21.

Farahnejad Z, Ghazanfari T, Yaraee R. (2011). Immunomodulatory effects of *Aloe vera* and its fraction on response of macrophage against *Candida albicans*. Immunnopharmacology and Immunotoxicology. 33(4):676-681.

George S. (2010). Candidiosis management: antigungal, cytotoxic and immunomodulatory properties of tea tree oil and its derivative components. M.Sc. Thesis Univ of Glasrow. 1-111.

Ghonime M, Eldomany R, Abdolaziz A, Soliman H. (2011). Evaluation of immunomodulatory effect of three herbal plants growing in Egypt. Immunopharmacology and Immunotoxicology. 33:141-145.

Gupta S, Satishkumar M N, Duraiswamy B, Das S, Chhajed M. (2012). Potential herbs and its phytoconstituents against fungal infection: A Systematic Review. World Journal of Pharmaceutical Research. 1(1):1-20.

Hammer K A, Carson C F, Riley T V. (2004). Antifungal effects of *Malaleuca alternifolia* (tea tree) oil and its component on *Candida albicans, Candida glabrata* and *Saccromyces cerevisiae*. Journal of American Chemotherapy. 53:1081-1085.

Hammer K A, Carson C F, Riley T V, Nielson J B. (2006). A review of the toxicity of *Malaleuca alternifolia* (tea tree) oil. Food and Chemical Toxicology. 44(5):616-625.

Hashemi S R, Davoodi H. (2012). Herbal plants as new immune stimulator in Poultry industry: A review. Asian Journal of animal and Veterinary Advances. 7(2):105-116.

Hise A G, Tomalka J, Ganesan S, Patel K, Hall B A, Brown G D, Fitzgerald K A. (2009). An essential role for NLRPs inflammasome in host defense against the human fungal pathogen *Candida albicans*. Cell Host

and Microbe. 5(2):487-497.

Hube B. (2004). From commensal to pathogen: stage and tissue specific gene expression of *Candida albicans*. Current opinion in microbiology. 7(4):336-341.

Im S A, Lee Y R, Lee Y H, Lee M K, Park Y I, Lee S, Kim K, Lee C K. (2010). *In vivo* evidence of the immunomodulatory activity of orally administered *Aloe vera* gel. Arch Pharm Res. 33(3):451-456.

Jauqueira J C. (2012). Model host for study of oral candidiasis. Adv Exp Med Biol. 7(10):95-105.

Kabir M A, Hussain M S, Ahmad Z. (2012). *Candida albicans*; a model organis m for studying fungal pathogen. ISRN Microbiology. 1-15.

Kumar A, Singh V, Ghosh S. (2011). an experimental evaluation of *in vitro* immunomodulatory activity of isolated compound of *Ricinus communis* on

human neutrophils. IJGP. 5(3):201-204.

Kumar A U, Manjunath C, Thaminzhmani T, Kiran Y R, Brahmaiah Y. (2012). A review on immunomodulatory a ct i vit y plants. Indian Journal of New Drug Delivery. 4(2): 7864-7887.

Kumar S, Gupta P, Sharma S, Kumar D. (2011). A review on Immunostimulatory plants. Journal of Chinese Integrative Medicine. 9(2):117-128.

Kumar S N, SiJi J V, Nambisan B, Mohandas C. (2012). Antifungal activity of Stilbenes against *Candida albicans* by Time Kill Assay. IJPSR. 3(6):1790-1794.

Kumar S V, Kumar P S, Dudhe R, Kumar N. (2011). Immunomodulatory effects of some traditional medicinal plants. J Chem Pharm Res. 3(1):675-684.

Mahiunddin, Shaikh. (2010). Recent advance on ethanomedicinal plants as immunomodulator agent. Ethnomedicine. 227-244.

Mali R G, Wadikar R R. (2008). *Baliospermum montanum* (*Danti*): Ethnobotany, Phytochemistry and Pharmacology- A review. Int J Green Pharm. 2(4):194-199.

Martino, Renzo F, Davicino, Roberto C, Mattar, Maria A, Sasso, Corina V, Casali, Yolanda A, Alonso, Rosario, Anesini, Claudia, Correa, Silvia G, Micalizzi, Blas. (2012). Macrophage activation by a purified fraction, free of

nordihydroguaiaretic acid (NDGA), from Larrea *divaricata Cav*. As a potential novel therapy against *Candida albicans*. Immunopharmacology and Immunotoxicology. 34(6):975-982.

Martino R F, Divicino R C, Mattar M A, Casali Y A, Correa S G, Micalizzi B. (2011). *Larrea divaricata Cav.* enhance the innate immune response during the systemic infection by *Candida albicans*. African Journal of Microbiology Research. 5(7):753-761.

Megraj K V K, Koneri R, Balaraman R, Kandhavelu M. (2011). Biological activities of some Indian medicinal plants. Journal of Advanced Pharmacy Education and Research.1:12-25.

Mondella F, Bernardis F D, Girolamo A, Cassone A, Salvatore G.(2006). *In vivo* activity of Terpinen-4-ol, the main bioactive component of *Malaleuca alternifolia* Cheel (tea tree) oil against azole-susceptible and resistance human pathogenic Candida species. BMC Infect.Dis. 3(6):158.

Nobuyunki S, Kobayashi H, Suzuki S. (2012). Immunochemistry of pathogenic yeast, *Candida species* focusing on mannan. Proce Jpn Acad Ser B Phys Biol Sci.88 (6):250-265.

Patil V V, Patil V R. (2010). *Ficus bengalensis Linn*- A review. International Journal of Pharma and Bio science. 1(2):1-11.

Patil J K, Jalalpure S S, Hamid S, Ahirrao R A. (2010). In vivo Immunomodulatory activity of extract of *Bauhinia vareigata Linn* stem bark on human neutrophils. Iranian Journal of Pharmacology and Therpeutics. 9:41-46.

Peters B M, Zhu J, Fidel P L, Jr, Mark A, Scheper, Hackett W, Shaye S E, Rizk A J. (2010). Protection of the oral mucosa by salivary Histatin-5 against *Candida albicans* in an *Ex vivo* Murine model of oral infection. FEMS Yeast Res. 10(5):597-604.

Ranjith M S, Ranjitsingh A J A, Shankar G, Vijayalaksmi G S, Deepa K, Sindhu H S. (2008). Enhanced phagocytosis and antibody production by *Tinospora cordifolia*- A new dimension in immunomodulation. African Journal of Biotechnology. (2):81-85.

Rodovanoic I, Mullick A, Gros P. (2011). Genetic control of susceptibility of infection with *Candida albicans* in mice. PLoS ONE.

6(4):1790-1794.

Rinku M, Prasanth V V, Parthasarathy G. (2011). Immunomodulatory activity of methanolic extract of *Urena lobata Linn*. International Journal of Pharmacology. 7(1).

Roshan A, Verma N K, Kumar C S, Chandra V, Singh D P, Panday M K. (2012). phytochemical constituent, pharmacological activities and medicinal use through the millennia of Glycyrrhiza *glabra Linn*: A review. International Research Journal of Pharmacy. 3(8):45-55.

Salem M L. (2005). Immunomodulatory and therapeutic properties of *Nigelle sativa* seed. International Immunopharmacology. 5(13-14):1749-1770.

Sharma A, Sharma M K, Kumar M. (2000). Molecular role of *Emblica officinalis* fruit extract against arsenic induced oxidative stress in Swiss albino mice. Chemico- Biological interaction. 71(1):193-200.

Sharma U, Singh B, Saini R, Verma P K, Kumar N, Bala M, Kulkarni R, Bhaleao S. (2012). Polysaccharide enriched immunomodulatory fraction from *Tinospora cordifolia*. Indian Journal of Exp Biol. 50:612-617.

Soloview D A, Jawhara S, Fonzi W A. (2011). Regulation of innate immune response to *Candida albicans infection* by αMβ2 1p infection. Infact Immun. 79(4):1546-1558.

Surjush A, Yasana R, Saple D G. (2008). *Aloe vera*: A short review. Indian J Dermatol. 53(4):163-166.

Thakur M, Bhargava S, Dixit V K. (2007). Immunomodulatotry activity of Chlorophytum borivilianum Sant. F. CAM. 4(4):419-423.

Toruner M, Loftus E V, Harmsen W S, Zinsmeister A R, Orenstein R, Sandborn W J, Colombel J F, Egan L J. (2008). Risk factor for opportunistic infection in patient with inflammatory Bowel disease. Gastroenterology. 134:929-936.

Tournu H, Dijck P V. (2012). *Candida* biofilms and the host models and new concept for Eradiation. International journal of Microbiology. 1-16.

Turner S, Division R, Alonso R, Ferraro G, Filip R, Anesini C. (2011). Potential use of low NDGA L a r r e a *d i v a r i c a t a* *e x t r a c t* a s antioxidant in f oods. Rev. Peru. Biol.18 (2):159-164

Utsunomiya T, Kobayashi M, Herndon D N, Pollard R B, Suzuki F. (1999). Effects of *Glycyyrhizin*, an active component of Licorice roots, on *Candida albicans* infection in thermally injured mice. Clin Exp Immunol.116 (2):291-298.

Vispute S, Khopade A. (2011). *Glycyriza glabra*: A Review. International Journal of Pharma and Bio Science. 2(3):42-51.

Wanke B, Lazera M S, Nucci M. (2000). Fungal infection in Immunocompromised host. Mem Inst Oswaldo. 95(1):153-158.

Williams D, Lewis M. (2011). Pathogenesis and treatment of oral candidiasis. Journal of Oral Microbiology. 3:1-18.

Xin H, Cartmell J, Bailey J J, Dziadek S, Bundle D R, Cutler J E. (2012). Self adjuvanting glycopeptides conjugate vaccine against Disseminated Candidiasis. PLoS ONE. 7(4):1-14.

Yeap S K, Omar A R, Ho W Y, Ben B K, Ali A M, Alitheen N B. (2011). Immunomodulatory effect of *Rhaphidophora korthalsii* on mice spenocyte, thymocyte and bone marrow cell proliferation and cytokine expression. African Journal of Biotechnology. 10(52):10744-1075.

Zang C X, Dai Z R. (2011). Immunomodulatory activities on macrophage of a polysaccharide from *Sipunculus nudus L*. Food and chemical Toxicology. 49(4):2961-2967.

Zeng H, Tian J, Zheng Y, Ban X, Zeng J, Mao Y, Wang Y. (2011). *In vitro* and *In vivo* activities of essential oil from the seeds of *Anethum graveolens L*. against *Candida spp*. Evidence Based Complementary and Alternative Medicine. Article ID 659704, 8 pages.

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