THE SCREENING OF HERBALS AS IMMUNOMODULATORS IN THERAPEUTICS: A REVIEW

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ABSTRACT
Immune system is a network of biological structure and processes that does a remarkable job of defending the body against foreign invaders and any kind of impairment in its development or functioning leads to various disorders and dysfunctions. Researchers are going on the modulation or alteration of immune system network to repair or regain the functionality of immune system. Immunomodulation is a part of Immunotherapy that alters the immune response. This either potentiates or suppresses the response of immune system. Recently, various side effects from chemical or synthetic therapeutics came into visibility, therefore more emphasis is on the use of herbs as immunomodulatory objects as they rarely effect the in vivo environment and chances of side effects are least. Immunostimulating and immunosuppressing plant extracts have their own importance and till date many plants have been investigated for their immunomodulating properties. Searches have been going on for better agents with such activities are becoming the field of interest all over the world.

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INTRODUCTION

Immune system is a network of cells, tissues and organs that work in synchronization to protect the body from invading foreigners commonly called antigens. It is barrier to disease causing agents and if any sort of impairment in its function brings disorders and dysfunctioning of the system. Such disorders include autoimmune diseases, hypersensitivity and immunodeficiency (Lisa M. Coussens and Zena Werb)\(^1\).

Immunodeficiency disorder refers to a heterogeneous group of over 130 disorders that result from defects in immune system development and/or function. It is broadly classified as disorders of adaptive immunity (i.e., T-cell, B-cell or combined immunodeficiencies) or of innate immunity (e.g., phagocyte and complement disorders). Although the clinical manifestations are highly variable, most disorders involve at least an increased susceptibility to infection. Autoimmune diseases occur when an individual's own immune system attacks and destroys his or her healthy cells and tissues (Christine McCusker and Richard)\(^2\).

According to international union of immunological societies, more than 150 primary immunodeficiency diseases have been characterized (Geha RS, Notarangelo LD, Casanova JL et al., 2007)\(^3\).

Although scientists have learned much about the immune system and its disorders and are continuously inventing new technologies for identifying the factors that suppresses or stimulates the immune system under various circumstances. The combination of new technologies promises to reveal more about the immune response and its alteration by various factors (www.nci.nih.gov).

Immunotherapy

Immunotherapy is the treatment of diseases by inducing, enhancing or suppressing an immune response. Antibodies, vitamins, vaccines etc have been used till date in immunotherapy (Morrow JW, Sheikh NA, Clint S. et al., 2012)\(^4\).

After successful feasibility studies, net phase is to looking forward to developing a platform for Immunomodulation that will change the way of treating immune dysfunctions.

Immunomodulation

The term suggests that alteration of response from the cells of immune system. The response may be increased or suppressed. Basically it is the adjustment of an immune response to a desired level, as in immunopotentiation or immunostimulation (eg. Vaccines) immunosuppression or induction of immune response. The substances that modulate or alter the activity of immune system are called Immunomodulators. Such substances are becoming the upcoming interest as they exerts the vast applications in the field of diagnosis and treatment various diseases and disorders. Such substances may be synthetic as well as natural (Kanavos P, Sullivan R, Lewison G. et al., 2010)\(^5\).

As known, Chemical or synthetic drugs are posing various side effects on human in vivo environment as described as nephrotoxicity, hepatotoxicity, bone marrow depression, hypertension, system disturbances and various other side effects in chemical therapeutics like flu, allergic reaction, suicidal ideas, low RBC and WBC counts, low BP and sometimes its also activates latent infections. Therefore recently more emphasis is on the application of herbal medicines for the treatment (Diasio RB and LoBuglio AF et al., 1996)\(^6\).

Plants as Immunomodulators

Various plants have been claimed to possess immunomodulatory activity as they are safer, cheaper, effective and conventional (Kumar S, Gupta P, Sharma S et al., 2011)\(^7\).

The search for immunomodulating plant constituents through basic and field enquiries into the literature and practices of traditional Indian medicine is treated (Labadie RP, Vander NT, Simons JM et al., 1989)\(^8\). Immunopharmacology, a rapidly growing area of science describes the essence of Immunomodulation as pharmacological agent acting under various dose and time regimens displays an immunomodulating effect. In spite of significant advances in synthetic drug chemistry, substances of natural origin correspond more completely in view to the requirement of contemporary medicine. The action of natural substances is not foreign to the organism and the metabolism of substances excludes the generation of allergies to the level best upon treatment with medicinal plant extracts (Mukherji PK, Nema NK Bhadra S, et al., 2014)\(^9\).

Various plants which have the potential of modulating the activity of immune response are indentified from various sources in the literature.
Tamarindus indica L.,

Tamarindus is a monotypic genus and belongs to the family Leguminosae (Fabaceae). Tamarindus indica L., commonly known as Tamarind tree is one of the most important multipurpose tropical fruit tree species in the Indian subcontinent (Bhadoriya SS, Ganeshpurkar A, Narwaria J, 2011). A polysaccharide isolated and purified from Tamarindus indica showed immunomodulatory activities such as phagocytic enhancement, leukocyte migration inhibition and inhibition of cell proliferation (Sreelekha TT, Vijayakumar T, Ankanthil R, et al., 1993).

Azadirachta indica

The aim of the study by was to evaluate immunomodulatory activity of aqueous extract of Azadirachta indica flowers on humoral and cell mediated immune response to ovalbumin, phagocytic activity by carbon clearance test and cyclophosphamide induced myelosuppression. The extract was also examined for the ability to induce secretory and cellular responses in murine peritoneal macrophages in vitro. The extract showed significant increase in phagocytic index which indicates activation of reticulo endothelial system through release of the mediators. The extract also showed increase in antibody titer against the ovalbumin and protection towards the cyclophosphamide induced myelosuppression in dose dependent manner. The study, therefore, reveals that the extract holds promise as immunomodulatory agent, which acts by stimulating both specific (humoral and cell mediated immunity) and non specific immune response (cytotoxic and phagocytic activity of macrophages) (Shah AS, Gunjal MA, Juvekar AR, 2009).

Panax ginseng

Panax ginseng is one of the most commonly used Chinese medicines in China, Asia and Western countries. The beneficial effects of ginseng have been attributed to the biological activities of its constituents, the ginsenosides. Ginseng extracts and ginsenosides including Rb1, Rd, Rg1, Rg3, Rh1, Rh2, Rh3 and Rp1 have been reported to have anti-inflammatory properties in different studies related to inflammation. Ginsenosides inhibit different inducers-activated signaling protein kinases and transcription factor nuclear factor-kappaB leading to decreases in the production of cytokines and mediators of inflammation. The therapeutic potential of ginseng on TNF-α-mediated inflammatory diseases is also discussed (Davy CW Lee and Allan SY Lau, 2011).

Solanum nigrum

Solanum nigrum Linn. (Sn) commonly known as Black Nightshade is a dicot weed in the Solanaceae family. It is an African paediatric plant utilised for several ailments that are responsible for infant mortality especially feverish convulsions. In vivo experiments showed that the ratio of CD4+/CD8+ peripheral blood T-lymphocyte subpopulations were restored following the treatment of SNL-P. Furthermore, treatment with SNL-P also caused a significant increase in IFN and a remarkable decrease in IL measured by the method of ELISA. The result showed that SNL-P possess potent antitumor activity and SNL-P might exert antitumor activity via activation of different immune responses in the host rather than by directly attacking cancer cells on the U14 cervical cancer bearing mice. Thus, SNL-P could be used as an immunomodulator (F. O. Atanu et al., 2002).

Emblica officinalis

A study was done by on the immunomodulatory properties of fruit extracts of Amla in immuno-compromised rats, with the emphasis on lymphocytes, using chromium (VI) as an immunosuppressive agent. Amla relieved the immunosuppressive effects of Cr on lymphocyte proliferation and even restored the IL-2 and γ-IFN production considerably (M Sai Ram, D Neetu, B Yogesh, et al., 2002).

Evolvulus alsinoides

In a study it was revealed that methanolic extract of Evolvulus alsinoides herb possessed profound antihypertensive activity in adrenaline induced hypertensive model. Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were measured in normal rats with respective before and after drug treatment using tail-cuff apparatus with BIOPAC. Induction of SBP and DBP as well as % inhibition in SBP and DBP were measured which indicated antihypertensive action of methanolic extract of Evolvulus alsinoides herb which was compared with disease control group and with propranolol, nifedipine and enalapril (Joshi US, Ganatra TH, Desai RTB, et al., 2012).
Centella asiatica

Centella asiatica (CA) has been used for treatment of various illnesses, focused on the influence of extracts of Centella asiatica on cell mediated and humoral immune responses. In human peripheral blood mononuclear cells (PBMCs), CA (water extract) significantly increased proliferation and the production of IL-2 and TNF-α. In contrast, an ethanol extract of CA inhibited human PBMC mitogenesis and the production of IL-2 and TNF-α. BALB/c mice treated with CA extracts showed higher responses to both primary and secondary antibodies against BSA when compared with non-treated group. Only the secondary antibody response was increased in RN extract-treated mice. The present study revealed immunomodulating activity of CA extracts with regard to both non-specific cellular and humoral immune responses (Punturee K, Christopher P, Kasinrerk W, et al., 2005)16.

Tinospora cordifolia

The active principles of Tinospora cordifolia, a traditional Indian plant were found to possess anticomplementary and immunomodulatory activities. Syringin (TC-4) and cordiol (TC-7) inhibited the in vitro immunohaemolysis of antibody-coated sheep erythrocytes by guinea pig serum. The reduced immunohaemolysis was found to be due to inhibition of the C3-convertase of the classical complement pathway. However, higher concentrations showed constant inhibitory effects. The compounds also gave rise to significant increases in IgG antibodies in serum. Humoral and cell-mediated immunity were also dose-dependently enhanced. Macrophage activation was reported for cordioside (TC-2), cordiofolioside A (TC-5) and cordiol (TC-7) and this activation was more pronounced with increasing incubation times (Kapil A and Sharma S, 1997)17.

Withania somnifera

The aqueous suspension of Withania somnifera root powder was investigated for their in vivo and in vitro immunomodulatory properties. W. somnifera showed potent inhibitory activity towards the complement system, mitogen induced lymphocyte proliferation and delayed-type hypersensitivity reaction. Administration of W. somnifera root powder did not have a significant effect on humoral immune response in rats. The results report immunosuppressive effect of W. somnifera root powder, thus it could be a candidate for developing as an immunosuppressive drug for the inflammatory diseases (Rasool M, and Varalakshmi P, 2006)18.

Aloe barbadensis

The scientists have characterized a new immunostimulatory polysaccharide called Aloeride from commercial aloe vera (Aloe barbadensis) juice. Aloeride increased NF-kappa B directed luciferase expression in THP-1 human monocytes to levels 50% of those observed by maximal concentrations (10 μg/mL) of LPS. Aloeride induced the expression of the mRNAs encoding IL-1β and TNF-α to levels equal to those observed in cells maximally activated by LPS. Acemannan, the major carbohydrate component from aloe, used in the macrophage assay resulted in negligible NF-kappa B activation. Analysis of acemannan and Aloeride using size-exclusion chromatography suggests that the low activity of acemannan is due to trace amounts of Aloeride. Although Aloeride comprises only 0.015% of the aloe juice dry weight, its potency for macrophage activation accounts fully for the activity of the crude juice (Pugh N, Ross SA, ElSohly MA, et al., 2001)19.

REFERENCES