

## Natural Immunomodulators

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### Introduction

Immunity is the state of resistance or insusceptibility exhibited by the host towards injury caused by micro-organisms and their products. Defense against infectious disease is one of the functions. Immunity, in general, is concerned with the reaction of body against any foreign antigen. Although immunity is beneficial to host, sometimes may be harmful also leading to tissue damage and disease (hypersensitivity and autoimmune diseases). Immunity need to be modulated by stimulating the immune response to increase resistance to infection and by suppressing the immune response to treat autoimmune diseases, to prevent rejection of graft and hypersensitivity reactions. Immunity can be modulated by using immunomodulators- the agents that have the ability to boost or suppress the host defense response. Immunomodulating agents are synthetic chemotherapeutic agents or biological substances. Based on their ability to stimulate, suppress or modulate adaptive or innate immune system, they have been classified into three types.

1. Immunoadjuvants- are specific immune stimulants believed to enhance the efficacy of vaccine.

2. Immunosuppressants- are suppressors of immune response and are used for the control of pathological immune response in autoimmune diseases (to prevent and treat certain autoimmune diseases), graft rejection (to suppress rejection of transplanted organs and tissues and also to suppress graft-versus host reaction) and hypersensitivity reactions.

3. Immunostimulants- are the agents which activate or induce the mediators or components of immune system. These agents non-specifically enhance resistance to infections. They activate innate as well as adaptive immune responses. They act as immunopotentiators in healthy individuals and also act as immunotherapeutic agents in individuals with impaired immune responses. These agents are primarily responsible for non antigen dependent stimulation of granulocytes and macrophages, and enhance their functional efficiency [1-3].

A variety of available synthetic chemotherapeutic agents are highly effective but majority of them have been proved to have immunosuppressive activity and have been claimed to have many adverse effects such as pulmonary toxicity, nephrotoxicity, neurotoxicity, hepatotoxicity, gastrointestinal toxicity, growth retardation in children, cardiac toxicity, hyperglycemia, hypertension, hyperlipidemia, hyperkalemia, leucopenia,

thrombocytopenia, serum sickness and many others [2,4]. In view of these severe adverse effects, various herbal/ plant products used in traditional therapy are currently being reviewed for their immunomodulatory potentials.

The concept of modulation of immune response by using natural products obtained from plants to reduce the severity of disease has been of interest since many years and is similar to the concept of Indian alchemy (Rasayana) in Ayurveda. A variety of natural products obtained from plants/ herbs are being used as immunomodulators (immune-stimulants as well as immunosuppressors) since antiquity. Treatment of large number of diseases by modulating the immune system or function by using products obtained from plants/herbs is being practiced traditionally from ancient times [1,2,5].

In recent years, many medicinal plants have been scientifically investigated for therapeutic potentials with promising results. Many naturally occurring plant products have been claimed to have immunomodulatory activity and are being used widely in the treatment of immunological disorders. Many studies show that a variety of natural products obtained from plants have ability to enhance impaired immune system. These products have been shown to activate the components of innate immunity such as stimulation of macrophages and lymphocytes, modulate the cytokine profile and reduce the incidence of infections and stimulate the process of apoptosis. A number of studies on herbal/plant products as immunomodulator show that many of them have potential to stimulate humoral immunity (HI) or cell mediated immunity (CMI) or both as evidenced by significant increase in serum immunoglobulin (Ig) levels, and important mediators of CMI in various body fluids. Studies show that there is significant increase in the mediators of CMI such as populations of mature T cells, levels of interleukins, tumour necrosis factor-alpha (TNF- $\alpha$ ), interferons, etc. Immunostimulants have also been shown to activate humoral as well as cell mediated immune response against tumours that facilitate recognition and destruction of the tumour, and also enhance the ability of the host to tolerate damage by toxic chemicals [1,2,5,6].

### Natural Immunomodulators

These are natural products of herbal origin and are termed as phytochemicals. A large number of phytochemicals obtained from a variety of plants have potential to modulate immune response. The most common phytochemicals include:

flavonoids, flavanols, phloroglucinols, quinones, glycosides, polysaccharides, terpenoids, essential oils, various bitters, alkaloids, biopolymers, glycolipids, phenolics, macrocyclic lactones, cannabinoids, saponins, polyacetylenes, coumarins, gallic acid, lignans, artemesinin, alpha-amyrin, hexacosanol, kaempferol, vitamin C, etc. These are some of the phytochemicals known to exert various immunomodulating activities [1,2,4-8].

There are many plants which are known to have immunomodulating activities. Some of them include : *Withania somnifera*, *Acacia catechu*, *Panax ginseng*, *Allium sativum*, *Terminalia arjuna*, *Cynodon dactylon*, *Rhus toxicodendron*, *Pteridium aquilinum*, *Curcuma longa*, *Tinospora cordifolia*, *Coptis chinensis*, *Gelsemium elegans*, *Leonurus japonicas*, *Piper longum*, *Morus alba*, *Mangifera indica*, *Aloe vera*, *Azadirachta indica*, *Sophrora subprosrate*, *Jatropha curcas*, *Achillea wilhelmsii*, *Picrorhiza scrophulariiflora*, *Plantago asitica*, *Schisandra arisanensis*, *Dioscorea japonica* and lot many [1,2,4,5].

Many of these phytochemicals have been shown to modulate immune response in different ways in various in vitro and animal studies. The results of different studies are very encouraging and recommend the use of herbal formulation as immunomodulating agents for various purposes because of their potential to potentiate immune response.

Although the results of the earlier in vitro and animal studies are in favor of use of different natural products from various medicinal plants as an alternative approach to the conventional treatment, the results of systematic clinical trials using human

subjects would be more meaningful to draw more useful and concrete conclusions in future.

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