8. Recent advances on the ethnomedicinal plants as immunomodulatory agents

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Abstract. Modulation of immune response to alleviate diseases has long since been of interest. Recent progress on the ethnomedicinal plants as immunomodulatory agent reported from 2000 to early 2008 is reviewed. Plant extracts have been widely investigated in this time in different parts of the world for their possible immunomodulatory properties. Some of the studies demonstrated to the isolation of potential bioactive molecule. Few have been tested as herbal formulations. Several plant extracts, compounds and formulations has been patented.

Abbreviations

AIDS - Acquired immunodeficiency syndrome
CB   - Cannabinoid
CD4  - Cluster of differentiation 4
CNS  - Central nervous system
CR3  - Complement receptor 3
DNA  - Deoxyribonucleic acid
FITC - Fluorescein isothiocyanate

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1. Introduction

Immune system is a remarkably sophisticated defence system within vertebrates, to protect them from invading agents. It is able to generate varieties of cells and molecules capable of recognizing and eliminating limitless varieties of foreign and undesirable agents. Modulation of the immune system denotes to any change in the immune response that can involve induction, expression, amplification or inhibition of any part or phase of the immune response. Thus, immunomodulator is a substance used for its effect on the immune system. There are generally of two types immunomodulators based on their effects: immunosuppressants and immunostimulators. They have the ability to mount an immune response or defend against pathogens or tumors. Immunopharmacology is a comparatively new and developing branch of pharmacology aims at searching for immunomodulators. The potential uses of immunodulators in clinical medicine include the reconstitution of immune deficiency (e.g. the treatment of AIDS) and the suppression of normal or excessive immune function (e.g. the treatment of graft rejection or autoimmune disease).
Specific immunomodulators administered together with antigens known as immunological adjuvants to boost the immune response to the vaccine constituents. For instance, a plant origin saponin used in veterinary medicine. Whereas, the non-specific immunostimulators offer a generalized state of resistance to pathogens or tumors. Fungal product cyclosporin A selectively block the function of T lymphocyte and used to prevent graft rejection [1].

Medicinal plants and their active components have been shown to be an important source of immunomodulators. Thus the development of drugs for immunomodulation and antitumour activity from natural compounds has become an attractive project. Through these studies, we may not only find some promising immunomodulators, but also clarify the mechanism of clinical actions of some traditional medicines. A range of immunomodulatory agents from plants and fungi earlier has been reviewed [2, 3]. The present review will concentrate on recent developments on immunomodulatory activities of plants reported from 2000 to early 2008.

2.1. Immunomodulatory activity of crude plant extracts

2.1.1. Indian plants

Fruits of Emblica officinalis (family: Euphorbiaceae) and whole plant of Evolvulus alsinoides (family: Convolvulaceae) has been extensively used in Indian Ayurvedic medicine for varieties of medical disorders. The immunomodulatory properties of Emblica officinalis and Evolvulus alsinoides were evaluated in adjuvant induced arthritic rat model. The crude aqueous extracts of both the herbs were administered intraperitonially following a repeated treatment profile. There was a significant reduction in swelling and redness of inflamed areas in treated animals than in untreated controls. The anti-inflammatory response of both extracts was determined by lymphocyte proliferation activity and histopathological severity of synovial hyperplasia. Both extracts showed a marked reduction in inflammation and edema. At cellular level immunosuppression occurred during the early phase of the disease. There was mild synovial hyperplasia and infiltration of few mononuclear cells in treated animals. The induction of nitric oxide synthase was significantly decreased in treated animals as compared to controls. These observations suggest that both the herbal extracts caused immunosuppression. Both are as potent as dexamethasone, a traditionally used immunosuppressant for arthritis [4].

Mehrota described in vitro immunosuppressive potential of ethanolic extract of Acorus calamus rhizome. Ethanolic extract of A. calamus inhibited proliferation of mitogen (phytohaemagglutinin) and antigen (purified protein
derivative) stimulated human peripheral blood mononuclear cells (PBMCs). In addition, A. calamus extract inhibited growth of several cell lines of mouse and human origin. It also inhibited production of nitric oxide (NO), interleukin-2 (IL-2) and tumor necrosis factor-α (TNF-α). Intracytoplasmic interferon-γ (IFN-γ) and expression of cell surface markers, CD16 and HLA-DR, on human PBMC, were not affected on treatment with A. calamus extract but CD25 expression was down regulated [5].

Crude extract of Tinospora cordifolia contained a polyclonal B cell mitogen which enhanced immune response in mice. An arabinogalactan polysaccharide, G1-4A from the stem of Tinospora cordifolia examined to modulate induced immunosuppression. Mice pre-treated with G1-4A exhibited protection against lipopolysaccharide (LPS) induced mortality [6]. Partially purified immunomodulator, G1-4A prevented lipid peroxidation and restored the activities of superoxide dismutase and catalase enzymes. Likewise, oxidative damage, induced by peroxynitrite, was also inhibited by partially purified immunomodulator similar to selective inhibitors of reactive oxygen species (ROS) like mannitol, superoxide dismutase, sodium azide and antioxidants, GSH and vitamin C [7]. In further studies, intraperitoneal administration of alcoholic extract of Tinospora cordifolia in Dalton's lymphoma bearing mice not only augmented the basic function of macrophages such as phagocytosis, but also their antigen presenting ability and secretion of IL-1, TNF and RNI. It was also indicated that the extract slow down the tumor growth and increases the life span of tumor bearing host, thus showing its anti tumor effect through destabilizing the membrane integrity of Dalton's lymphoma cells directly or indirectly. Thus, the study demonstrated alcoholic extract of Tinospora cordifolia activated tumor associated macrophages and showed antitumor effect on the spontaneous T-cell lymphoma and may have some clinical implications [8].

Ethanolic extract of Boerhaavia diffusa, a plant used in Indian traditional system of medicine, significantly inhibited the cell proliferation [9]. Extracts of B. diffusa roots inhibited human NK cell cytotoxicity in vitro, production of nitric oxide in mouse macrophage cells, interleukin-2 and tumor necrosis factor-α (TNF-α), in human PBMCs. Whereas, intracytoplasmic interferon-γ (IFN-γ) and cell surface markers such as CD16, CD25, and HLA-DR did not get affected on treatment with B. diffusa extract and demonstrates immunosuppressive potential of B. diffusa [10].

Aqueous leaves extract of biopesticidal plant Nyctanthes arbor-tristis has been found as a potent immunomodulator [11]. The extract has been evaluated as immunorestorative or anti-immunosuppressive agent in the malathion exposed immunosuppressed mice by studying various immunological parameters (humoral, cell mediated immune, numerical values of immunocytes
and functions of phagocytes) in treated or untreated malathion-exposed mice. The results revealed that the immunological parameters which were suppressed with malathion either reverted back to normal or showed a trend towards normalcy, when treated with aqueous leaves extract of *Nyctanthes arbor-tristis* [12].

Methanol extract of *Eclipta alba* and *Centella asiatica* whole plant showed phagocytic index and antibody titer has been increased significantly. The F ratios of the phagocytic index and WBC count were also significant with a linearity in the dose-response relationship [13]. The ethanol extract of the root of the plant *Cryptolepis buchanani* caused significant stimulation of the delayed type hypersensitivity reaction and humoral antibody production in mice [14].

An aqueous extract of *Rhodiola imbricata* rhizome stimulated production of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) in human PBMCs as well as RAW 264.7 cell line. It also increased production of nitric oxide synergistically in combination with lipopolysaccharide in RAW 264.7. Furthermore, it increased the phosphorylated-IκB expression and activated the nuclear translocation of NF-κB in human PBMCs. Thus, *Rhodiola* most likely activated proinflammatory mediators via phosphorylated inhibitory κB and transcription factor NF-κB [15].

### 2.1.2. Chinese plants

Traditional herbal formulas, used to treat inflammatory arthritis in China include *Boswellia carterii* or *Boswellia serrata*. They both contain boswellic acids which have been shown to exhibit antiinflammatory and antiarthritic properties. *B. carterii* plant resin extract containing boswellic acids, where ethanol as a solvent resulted in significant cellular toxicity of TH1 cytokines (IL-2 and IFN-γ) and TH2 cytokines (IL-4 and IL-10) by murine splenocytes [16].

### 2.1.3. Asian plants

An aqueous extract (decoction) of Vietnamese plant *Crinum latifolium* L. retarded growth of 20-methylcholanthrene tumors (sarcomas) in rats. The inhibition of carcinogenesis had occurred probably due to the influence of immunomodulating and anti-tumor plant alkaloids and other biologically active components in the plant decoctions [17].

### 2.1.4. Persian plants

A group of Iranian medicinal plants *Silybum marianum, Matricaria chamomilla, Calendula officinalis, Cichorium intybus* and *Dracocephalum*
ethanolic extracts has been investigated on human peripheral blood lymphocytes and thymocytes; and on proliferative responsiveness of human lymphocytes to phytohemagglutinin. However, none of the extracts exhibited a direct mitogenic effect on human lymphocytes or thymocytes. Among the plants studied, *C. intybus*, *C. officinalis* and *D. kotschyi* showed an inhibitory effect on the proliferation of lymphocytes in the presence of PHA. Extract of *M. chamomilla* showed almost no stimulatory effect, whereas *S. marianum* displayed significant decrease in proliferation assay. In later, all the extracts except *D. kotschyi* enhanced the proliferation of lymphocytes after stimulation with the allogenic cells [18]. In a separate experiment, an aqueous extract of *Calendula Officinalis* showed in vitro human peripheral blood lymphocyte (PBL) proliferation and cytotoxic tumor cell activity [19].

Treatment of mice with the extract of *Haussknechtia elymatica* (family: Apioidae), decreased the footpad thickness indicating a dose-related inhibitory effect of H. elymatica on delayed hypersensitivity. The extract also significantly reduced the antibody titer after immunization with Sheep-RBC, human peripheral blood lymphocytes in the presence of mitogen and the production of IL-2 [20]. Amirghofran recently reported, methanolic extract of *Stachys obtusicrena* possess inhibitory effects on both cellular and humoral immune responses. *S. obtusicrena* showed a dose-related decrease in delayed type hypersensitivity and antibody responses in mice. In the in vitro study performed on the mitogen treated lymphocytes, the extract caused a dose-dependent decline in [3H]-thymidine uptake and IL-2 levels in the culture supernatants of the activated lymphocytes [21].

### 2.1.5. American plants

Native American plant *Echinacea purpurea* (family: Asteraceae), known as the purple coneflower, is a medicinal plant widely used to treat a variety of illnesses, especially common cold, respiratory infections. Several studies indicated the ability of various *Echinacea* species to activate non-specific defence mechanisms and function as an immune stimulant [22]. However, the mechanism underlying *Echinacea*-induced immunomodulation remains largely unknown. Recent findings demonstrated that *Echinacea* extracts are potent activators of natural killer (NK) cells cytotoxicity. *Echinacea* augmented the frequency of NK target conjugates and activated the programming for lysis of NK cells [23]. Hall has reported that the complex aqueous *Echinacea* extract and the isolated high molecular weight constituents (polysaccharides) from this extract have effect on cytokine expression by macrophages [24]. It was reported alkylamides from *Echinacea* modulate TNF-α mRNA expression in human monocytes/macrophages via the cannabinoid
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2.1.6. European plants

Methanol extract of a Portuguese plant *Carpobrotus edulis* (family: Aizoaceae) showed that the extract inhibit a verapamil sensitive efflux pump of mouse T cell lymphoma cell line thereby rendering these multi-drug resistant cells susceptible to anticancer drugs. It also prime THP-1 human
monocyte-derived macrophages to kill ingested *Staphylococcus aureus* and to promote the release of lymphokines associated with cellular immune functions. The extract induced the proliferation of THP-1 cells within one day of exposure to quantities normally associated with phytohaemagglutinin [29].

### 2.2. Immunomodulatory activity of plant derived compounds

#### 2.2.1. Sterols and sterolins

The phytosterols, β-sitosterol, and its glucoside (Fig. 2) enhanced the *in vitro* proliferative response of T-cells stimulated by sub-optimal concentrations of phytohaemagglutinin several fold at extremely low concentrations (femtogram level). A 100:1 (mass:mass) ratio of β-sitosterol: β-sitosterol glucoside showed higher stimulation than the individual sterols at the same concentration [30]. The mixture of the sterols (β-sitosterol) and sterolins (β-sitosterol glucoside) has the ability to enhance the cellular response of T lymphocytes both *in vitro* and *in vivo*. The mixture enhances the cytotoxic ability of natural killer (NK) cells against the target cancer cell line NK562. It has also been postulated that the sterol-sterolin mixture in a specific ratio could reinstate a balance between the TH1–TH2 cells, a delicate balance that determines the final outcome of an immune response. The same mixture inhibited the release of pro-inflammatory cytokines from endotoxin activated monocytes: interleukin-6 and tumour necrosis factor-α secretion [31]. In HIV-infected patients analysis of the CD4 cell-type (TH1 vs TH2-type) showed that those receiving the sterol-sterolin mixture maintained a favorable TH1 response, which implies that their cell-mediated response was possibly responsible for the viral control and inhibition of CD4 cell loss [32]. However, the cellular target of these molecules was not clearly described cytoplasmic receptors, gene regulation. In a different study, the total cells and eosinophils in the bronchoalveolar lavage fluid markedly decreased after β-sitosterol and lactose-β-sitosterol administration. They also mitigated the inflammation by eosinophil infiltration and mucus hypersecretion by goblet hyperplasia, inhibited the increased mRNA and protein expression of IL-4 and

![Figure 2. β-sitosterol and β-sitosterol glucoside.](image-url)
IL-5 in the lung tissue and bronchoalveolar lavage fluid [33]. Immunomodulatory effect of a β-sitosterol glycoside, daucosterol was also observed against disseminated candidiasis caused by *Candida albicans* caused by the CD4+ TH1 immune response [34].

### 2.2.2. Cannabinoids

Advances in understanding the physiology and pharmacology of the endogenous cannabinoid system have potentiated the interest of cannabinoid receptors as potential therapeutic targets. Cannabinoids have been shown to modulate a variety of immune cell functions and have therapeutic implications on central nervous system (CNS) inflammation, chronic inflammatory conditions such as arthritis, and may be therapeutically useful in treating autoimmune conditions such as multiple sclerosis. Many of these drug effects occur through cannabinoid receptor signalling mechanisms and the modulation of cytokines and other gene products [35].

Cannabidiol and cannabis-based medicines are potential therapeutic agents. Because the immune system has been widely demonstrated to be affected by psychoactive cannabinoids, such as Δ⁹-tetrahydrocannabinol (Fig. 3). Cannabidiol significantly attenuated the elevation of IL-2, IL-4, IL-5, and IL-13 steady-state mRNA expression elicited by Ova challenge in the lungs. Plant derived immunomodulatory cannabinoids exhibited potential therapeutic utility in the treatment of allergic airway disease by inhibiting the expression of critical T cell cytokines and the associated inflammatory response [36]. *Echinacea* species with the cannabinoid (CB) receptor-binding lipophilic alkanamides are the other best known herbal cannabimimetics, which has been discussed earlier in this chapter.

![Figure 3. Cannabidiol and Δ⁹-tetrahydrocannabinol.](image-url)
2.2.3. Polysaccharides

Polysaccharides from plants have been the subject of study for a very long time mainly for their physical properties and industrial use based on these properties. Over the last 20 years there has been an ever increasing interest in the biological activity of biomolecules has led to new sources for interesting bioactive plant polysaccharides [37]. Botanical polysaccharides exhibit a number of beneficial therapeutic properties, and it is thought that the mechanisms involved in these effects are due to the modulation of innate immunity and, more specifically, macrophage function. Furthermore, botanical and microbial polysaccharides bind to common surface receptors and induce similar immunomodulatory responses in macrophages, suggesting that evolutionarily conserved polysaccharide structural features are shared between these organisms. Thus, the evaluation of botanical polysaccharides provides a unique opportunity for the discovery of novel therapeutic agents and adjuvants that exhibit beneficial immunomodulatory properties [38].

The immunomodulatory effects of the polysaccharide of *Cistanche Deserticola* have been evaluated by *in vitro* proliferation of murine thymus lymphocytes by MTT method. The enhancing effect of polysaccharide on murine thymus lymphocyte proliferation was related to its promotion on thymus intracellular Ca\(^{2+}\) delivering [39]. High molecular weight substances were isolated from *Salicornia herbacea*, which has been used to treat a variety of diseases including cancers in traditional oriental remedy. The active components of the extract have been described as polysaccharides, which not only activate monocytic cells strongly, but also induce differentiation of monocytic cells into macrophages [40].

2.2.4. Alkaloids

Plant bis-benzylisoquinoline alkaloid tetrandrine is active purified compound from dried tuberous root of the creeper *Stephania tetrandra*, is a potent immunomodulator used to treat rheumatic disorders, silicosis and hypertension in mainland China [41]. Tetrandrine effectively suppressed cytokine production and proliferation of CD28-costimulated T cells [42]. Recently, tetrandrine downregulated IκBα kinases- IκBα -NF-κB signalling pathway in human peripheral blood T cell. Compared to four tetrandrine analogs (tetrandrine, dauricine, berbamine and hemandezine; Fig. 4.), dauricine appeared as the most potent inhibition on CD28 but not on H\(_2\)O\(_2\)-induced NF-κB DNA-binding activities [41, 43]. Recent studies showed tetrandrine might modulate lipopolysaccharide induced microglial activation by inhibiting the NF-κB-mediated release of inflammatory factors [44].
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Figure 4. Alkaloid immunomodulators.

Alcoholic extract of the fruits of well known spice (black pepper) *Piper longum* and its component alkaloid piperine exhibited immunomodulatory and antitumor activity to Dalton's lymphoma ascites cells and Ehrlich ascites carcinoma (EAC) cells. *Piper longum* extract and piperine increased the total WBC count, number of plaque forming cells, and bone marrow cellularity and α-esterase cells [45].

Chronic rejection after solid organ transplantation is the major cause of graft failure in the first postoperative year. The pathogenesis of this process remains poorly understood. To a rat model of cardiac transplantation the effect of retransplantation has been compared with the immunomodulatory effect of cyclosporin A and sinomenine, an alkaloid extract from the Chinese medical plant *Sinomenium acutum*. Treatment with either cyclosporin A or sinomenine prevented progression of vascular changes including myointimal proliferation, whereas combination therapy resulted in long-term graft survival and absence of the lesions mentioned above [46].
2.2.5. Flavonoids

Eupalitin-3-O-β-D-galactopyranoside (Fig. 5) purified from the ethanolic extract of *Boerhaavia diffusa* root inhibited phytohemagglutinin stimulated proliferation of peripheral blood mononuclear cells, two-way MLR and natural killer cell, as well as lipopolysaccharide induced NO production by RAW 264.7. It further inhibited production of phytohemagglutinin stimulated IL-2 at the protein and mRNA transcript levels; lipopolysaccharide stimulated TNF-α production in human peripheral blood mononuclear cells. It blocked the activation of DNA binding of nuclear factor-κB and AP-1, two major transcription factors centrally involved in expression of the IL-2 and IL-2R gene, which are necessary for T cell activation and proliferation. On the other hand, eupalitin showed little activity on the above experiments [47].

The extract of *Apium graveolens* var. dulce contained apiin as the major constituent (1.12%, wt./wt., of the ext.). The extract and apiin showed significant inhibitory activity on nitrite (NO) production *in vitro* and iNOS expression in LPS-activated J774.A1 cells. The findings suggested the properties of the extract *in vivo* were due to reduction of iNOS enzyme expression [48]. *Bidens pilosa* is an ethnical medicine for bacterial infection or immune modulation in Asia, America and Africa. Flavonoid, centaurein and its aglycone, centaureidin has been isolated from the butanol subfraction of *Bidens pilosa*. The study suggested that centaurein regulated IFN-γ transcription as an immunomodulator, probably via NFAT and NFκB in T cells [49].

![Figure 5. Flavonoid immunomodulators.](image-url)
2.2.6. Lectin

A plant lectin from *Viscum album* has been previously shown to increase the number and cytotoxic activity of natural killer cells and to induce antitumor activity in animal models. Lectin-sugar interactions on the cell surface of immunocompetent cells can induce cytokine gene expression and protein synthesis [50]. Recently, plant lectin *Viscum album* agglutinin-I also demonstrated interesting potential therapeutic properties and immunomodulatory activities. Lectin alters mitochondrial transmembrane potential and increases intracellular levels of reactive oxygen species [51].

2.2.7. Glycoprotein

Immunomodulatory effect of a C3 binding glycoprotein has been isolated from the parasitic plant *Cuscuta europea*. The glycoprotein showed a dose-dependent *in vivo* immunostimulation against mice immunized with sheep red blood cells. The *in vitro* stimulation was assessed by an increase in the number of hemolytic plaque forming cells and hemagglutination titers [52]. Later studies demonstrated that C3 binding glycoprotein induced proinflammatory and immunoregulatory cytokine production, in the highest degree IL-12, followed by IL-6 and in lower degree TNF-α. IL-12 quantity was significantly increased in glycoprotein stimulated cultures in comparison with LPS, PHA and PWM stimulated PBMC. The authors suggested that a part of the mechanism of action of C3 binding glycoprotein is mediated through NF-κB signal transduction pathway [53].

2.3. Herbal formulations as immunomodulators

The increased neopterin production and tryptophan degradation in stimulated peripheral blood mononuclear cells was found to be significantly suppressed by several plant extracts, e.g., *Uncaria tomentosa*, *Hypericum perforatum*, green and black tea from *Camellia sinensis* and by the Tibetan herbal remedy PADMA 28. The plant compounds down-regulated TH1-type immune response by reducing the expression of the cytokine IFN-γ [3].

Peanut allergy is potentially life threatening and there is no curative therapy for this disorder. FAHF-2 is a Chinese herbal formula completely eliminated anaphylaxis in mice allergic to peanut challenged as long as 5 weeks post therapy. This result was associated with down regulation of TH2 responses [54].

The immunomodulatory activities of Triphala, an Indian Ayurvedic formulation of three plants (*Terminalia chebula*, *Terminalia belerica* and
Emblica officinalis) were assessed by testing the various neutrophil functions like adherence, phagocytosis (phagocytic index and avidity index and nitro blue tetrazolium) reduction in albino rats. Oral administration of Triphala stimulated the neutrophil functions in the immunized rats. Stress induced suppression in the neutrophil functions were also significantly prevented by Triphala [55].

2.4. Patented immunomodulators

Polysaccharides

Extracellular polysaccharides of Aphanothece halophytica has been patented for regulating immunity and treating and/or preventing pulmonitis [56]. A polysaccharide fraction (0.1-20%), extracted from callus plant tissue of Ungernia species was evaluated for its antimutagenic, immunomodulating, and antitumor activities. Per oral administration of the polysaccharide fraction at a daily dose during 20-30 days to mice enhanced effectiveness and safety of treatment [57].

Gulvel is extensively used in Ayurveda as a single or polyherbal formulation. Several plants of genus Tinospora such as T. cordifolia, T. malabarica, etc., are well known by this name. A process for the preparation of an immunomodulator from the above plants has been described. A branched polysaccharide, arabinogalactan was selectively precipitated from the polar extracts in aqueous medium by methanol. The active polysaccharide was further purified by high-performance gel permeation chromatography. It is polyclonally mitogenic to β-cells, and augments antibody response as well as enhances T-cell responses to model antigens [58].

Coumarinolignoids

A novel pharmaceutical composition consisting of a combination of three coumarinolignoids isolated from the seeds of the plant Cleome viscosa has been described to modulate humoral and cell mediated immune response [59].

Polyphenols

Polyphenols are useful for prophylactic and therapeutic treatment of allergy. Apple polyphenol containing ~50% proanthocyanidin significantly promoted interferon-γ formation later and inhibited IL-5 and IL-10 in ovalbumin-immunized murine spleen cells [60].
Stilbenoids

Extraction of pharmaceutically active stilbene derivatives (e.g., resveratrols, ε-viniferin, viniferin derivatives, hopeaphenol, and Ampelopsin A) with immunomodulating activity from spermatophyte plants has been reported [61].

Herbal formulation

An immunomodulator for the prevention and the treatment of AIDS comprises Cordyceps plants (such as Cordyceps militaris L., Brazil Cordyceps, and FENG Cordyceps), Radix Glycyrrhizae, Rhizoma Atractylodis Macrocephalae, Radix Angelicae Sinensis, Rhizoma Coptidis, Radix Aconiti Lateralis Preparata, Minor Decoction of Bupleurum, and AZT. This composition can maintain or improve the immunologic function of patients [62].

Fve proteins and peptides

The Fve protein (i.e., a protein from the golden needle mushroom Flammulina velutipes) upregulated expression of TH1/TC1 cytokines such as interferon-γ and tumor necrosis factor-α; whereas down regulated expression of TH2/TC2 cytokines such as IL-4 and IL-13. In addition, it upregulated expression of T regulatory cell cytokines IL-10 and transforming growth factor-β. Furthermore, Fve proteins exhibited the following properties hemagglutination, lymphocyte aggregation, and lymphoproliferation. This peptide may be used as an immunomodulator, as an adjuvant, either alone or as a fusion protein with an antigen or allergen [63].

3. Conclusions

Immunomodulation using medicinal plants can provide an alternative to conventional chemotherapy for a variety of diseases, especially when host defence mechanism has to be activated under the conditions of impaired immune response or when a selective immunosuppression is desired in situations like autoimmune disorders. There is great potential for the discovery of more specific immunomodulators which mimic or antagonize the biological effects of cytokines and interleukins, and the refinement of assays for these mediators will create specific and sensitive screens. Natural remedies should be revisited as important sources of novel ligands capable of targeting specific cellular receptors.
References


