Indian Journal of Novel Drug Delivery

IJNDD

An Official Publication of Karnataka Education and Scientific Society

Review Article

Applications and Uses of Active Ingredients from Medicinal Plants

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ARTICLE DETAILS

Article history:
Received on 14 February 2014
Modified on 24 March 2014
Accepted on 03 April 2014

Keywords:
Cytokines,
Pathogen,
Ayuveda,
Medicinal Plant

ABSTRACT

The immune System is the most complex biological systems in the body. At the time of infection related to viruses, bacteria and fungi only the immune system is able to detect the pathogen by using a specific receptor to produce immediate response by the activation of immune components such as cytokines, chemokines and release of inflammatory mediators to modulate and potentiate the immune system. Modulation of immune response, as a possible prophylactic or therapeutic measure, by using various medicinal plant products has become a subject of scientific investigation. According to Ayurveda, most of the commonly used active ingredients i.e. plant derived materials (alkaloids, glycosides, proteins, lectins, polysaccharides, etc.) are extracted from Indian medicinal plants for the treatment of various ailments and have so many advantages over the conventionally used drugs, which are so expensive and known to have harmful side effects.

INTRODUCTION

Immunomodulation means that one can modulate the immune response using various substances either of natural or synthetic origin. Several types of immunomodulators have been identified, including substances isolated and purified from natural sources such as plants including microorganisms. Medicinal plants which are used for many activities and provides various alternative potential to conventional chemotherapy for a variety of diseases especially in reference to host defense mechanism. According to literature, a large number of medicinal plant products like polysaccharides, lectins, peptides and flavonoids which are used in the immune system for various *in-vitro* and *in vivo* models [1]. Now a day, the importance of medicinal plants has been increasing both for pharmaceutical industry and traditional users. Most of the countries believed or rely on traditional medicines either it is developing or under developing country. This traditional medicine involves the use of different type of organic extracts or the bioactive pure chemical constituents as shown below-

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A) Flavonoids

Flavonoids are a large family of polyphenolic compounds synthesized by plants that have a common chemical structure [2]. It is one of the largest groups of phenols and played a major role in plants i.e. color, pathogens, light and stress and also very often in epidermis of leaves and fruit skin. Several flavonoids isolated from various medicinal plants and showed some several beneficial properties. The number of flavonoids isolated from various plants is currently under investigation:-

The leaves of *Orthosiphon stamineus*, *(Family Lamiaceae*) (**Fig. 1**) are commonly used as herbal tea for diuresis, to treat rheumatoid arthritis, diabetes, oedema, eruptive fever, influenza, hepatitis, jaundice and hypertension [3]

Figure 1: *Orthosiphon stamineus*

O. *stamineus* contains several chemically active constituents such as terpenoids (diterpenes and triterpenes), polyphenols (lipophilic flavonoids and phenolic acids), and sterols [4]. Recently, six flavonoid compounds were isolated from the leaves of the medicinal plant *Orthosiphon stamineus.*

Several prenylated flavonoids isolated from the leaves and stems of *Dodonaea polyandra* (**Fig. 2**). This plant is generally used in the traditional medicine system of Northern Kaanju people of Cape York Peninsula, Queensland, Australia. The extracts of leaves and stem studied have already been studied and possess anti-inflammatory activity [5].

Figure 2: *Dodonaea polyandra*.

Dorstenia mannii (**Fig. 3**) is a plant species in the genus Dorstenia. The prenylated flavonoids from *Dorstenia mannii* (6,8-diprenyleriodictyol, dorsmanin C and dorsmanin F) were found to be potent scavengers of the stable free radical 1,1-diphenyl-2-picrylhydrazyl (DPPH), and are more potent than butylated hydroxy toluene (BHT), a common antioxidant used as a food additive and these prenylated flavonoids showed potent anti-oxidant activity as compared to the non-prenylated flavonoids, quercetin [6].

Figure 3: *Dorstenia mannii*

The number of flavonoids extracted from *Dryoathyrium boryanum* (**Fig.4**) were reported and considered as excellent antioxidants and also showed anticancer activity because of high flavonoids content in the fern [7].

Figure 4: *Dryoathyrium boryanum*

Plant phenolics, especially dietary flavonoids, are currently of major interest related to their functional properties in promoting human health. One of the medicinal plant where 13 phenolic substances and 29 extracts were prepared from finnish plant materials against number of microbes e.g. *Aspergillus niger*, *Bacillus subtilis*, *Candida albicans*, *Escherichia coli*, *etc* were studied and showed that . flavone, quercetin and naringenin were effective in inhibiting the growth of the organisms [8].

Thymus vulgaris (*Family Lamiaceae*) is a species of flowering plant in the mint, native to southern Europe from the western Mediterranean to southern Italy. The crude extracts from locally grown *Thymus vulgaris* showed high concentration of flavonoids and it could be used as antibiotics for different curable and uncurable diseases [9].

Figure 5: *Thymus vulgaris*

B) Polysaccharides

Polysaccharides isolated from various medicinal plants, mushrooms, lichens, algae etc and contained a number of prophylactic and therapeutic properties which is beneficial for anti-tumour activity, immunomodulation, wound healing and other therapeutic effects. The number of polysaccharides isolated from various medicinal plants is still under investigation:-

Polysaccharides contains galactose, galacturonic acid, and mannose isolated from *Porana volubilis,* (**Fig. 6**) and reported as the first natural

nonsulfated polysaccharide from higher plants with anticoagulant activity, which may be considered as a new source of compounds with action on coagulation and thrombosis [10].

Figure 6: *Porana volubilis*

Water and water–ethanol soluble polysaccharide materials were isolated from the leaves of popular Malian medicinal plants *Trichilia emetica* (**Fig.7**) and *Opilia celtidifolia* and fruits of *Crossopteryx febrifuga* and showed significant antitussive activity [11]. Some of the. pectic polysaccharides strain i.e. BP-II, Oc50A1.I.A and CC1P1 isolated from the Malian medicinal plants like B*iophytum petersianum, Cola cordifolia* and *Opilia celtidifolia,* respectively, are able to protect against *Streptococcus pneumoniae* infection in mice [12].

Figure 7: *Trichilia emetica*

Maytenus ilicifolia (**Fig. 8**) is one of the important medicinal plants which played an important role in the anti-ulcer effect. Its leaves are used in homemade and industrial medicines for effective treatment of stomach ulcers e.g. Significantly inhibited ethanol-induced gastric lesions in rats, and suggest that it has a protective anti-ulcer effect [13].

An α-d-glucan novel polysaccharide, non toxic which is isolated and characterized from the medicinal plant *Tinospora cordifolia* (**Fig. 9**) and it is composed of (1→4) linked back bone and (1→6) linked branches with a molecular mass of > 550 kDa and exhibiting unique immune stimulating properties.

Figure 8: *Maytenus ilicifolia*

The cytokine profile of this novel polysaccharide increased the Th1 pathway of T helper cell differentiation essential for cell mediated immunity. The water solubility, high molecular mass, activation of B and T lymphocytes including NK cells, complement activation, Th1 pathway-associated cytokine profile and absence of oxidative stress confer important immunoprotective potential to this novel α-d-glucan [14].

Figure 9: *Tinospora cardifolia*

Several polysaccharides have been isolated from the leaves of *Arctium lappa* (**Fig. 10)**, *Aloe-barbadensis*, *Althaea-officinalis* var. *robusta*, *Plantago lanceolata*, aerial parts and roots of *Rudbeckia fulgida*, stems of *Mahonia aquifolium*, and peach-tree (*Prunus persica*) gum exudates. Out of these, these polysaccharides has the ability to inhibit peroxidation of soyabean lecithin liposomes by OH radicals [15].

Figure 10: *Arctium lappa*

C) Alkaloids

Alkaloids are derived from various plant sources, these are generally basic and contained one or more nitrogen atoms and have a marked physiological action on man or other animals. The first structure of alkaloid Coniine was established and in the twentieth century, alkaloids featured strongly in the search for plant drugs with anticancer activity. One of the example of alkaloid e.g. *Catharanthus* which has given both the activities i.e. anti-cancer and anti-viral activity. Due to these activities, researchers focused on alkaloids are currently under investigation:-

Cissampelos sympodialis (*Menispermaceae*), plant used in Brazilian folk medicine for the treatment of respiratory allergies. In this plant, there is a tendency to decrease antigen specific IgE levels and enhanced CD4 and CD8 T cell population in mice. These properties showed the immunoregulatory effect of the plant [16].

Diterpenoid alkaloid i.e. Bullatine A of the genus *Aconitum*, possesses antirheumatic, antiinflammatory and antinociceptive effects [17].

Biscoclaurine [18] alkaloid i.e. Cepharanthine isolated from *Stephania cepharantha* Hayata and has been shown to have anti-inflammatory, anti-allergic, and immunomodulatory activities *in vivo.*

D) Lectins

These cell-agglutinating and sugar-specific proteins have been named lectins. These are widely distributed in plants and to some extent also in invertebrates. In 1970s, few lectins have been isolated and are extremely useful tools for the detection of carbohydrates on cell surfaces, in particular for the isolation and characterization of glycoproteins. In recent years, number of lectins have been isolated from plants, animals as well as micro-organisms and also established the hundreds of structures. Consequently, it is considered that lectins function as recognition molecules in cell–molecule and cell–cell interactions in a variety of biological systems.

On the basis of recent studies in biochemistry, molecular cloning and related to structural analysis, mostly all known plant lectins can be classified into seven families of structurally and evolutionarily-related proteins [19], and most of these divided into four groups of evolutionarily related proteins: legume lectins, chitin-binding lectins, monocot mannose-binding lectins and type 2 ribosome inactivating proteins, among which monocot mannose-binding lectins is more popular and attracted to most of the pharmaceutical companies because of their great application values in biological and biomedical research; such as in the isolation of mannose containing glyconjugates, and their potent inhibitory effect on animal and human retroviruses, including HIV [20]. In addition, most monocot mannose binding lectins which played an important role in the plant's defense against different kinds of plant-eating organisms; which is due to their recognition of high-mannose type glycans of plant predators [21-26]. Up to now, monocot mannose binding lectins have been cloned from seven families of angiosperms including *Amaryllidaceae, Alliaceae, Orchidaceae, Liliaceae, Iridaceae* and *Bromeliaceae* [27-29], among which lectins from Amaryllidaceae species have been extensively studied [27-31]. However, little is known about the possible origin and molecular evolution of the carbohydrate-binding domains of plant lectins from modern flowering plants with little gene sequence information about plant lectins outside higher flowering plants [32]. Until now, there have been no reports on molecular cloning of lectin genes from gymnosperms, including family *Taxaceae*, therefore the molecular evolution relationship of the plant lectins between flowering plants and gymnosperms is unclear.

E) Therapeutic proteins

Now a days, pharmaceutical industries is largely dependent on the production of relatively small organic molecules i.e. antibiotics, analgesics etc for the treatment of bacterial or viral diseases. Recently, researchers focused on larger and complex proteins as therapeutic agents. Since proteins played an important role in immunology and there are so many therapeutic uses in preventing and curing diseases. One of the examples of therapeutic protein i.e. Insulin a small peptide is used for the treatment of diabetes. In addition, the antigens are proteins used in vaccination to induce the immune response. On the other hand, the use of proteins from plants means a lower cost of production and easier expansion for large-volume production than cell culture systems [33]. Inspite of large investment in cell culture facilities, plant protein production systems can be expanded simply by growing and harvesting additional plants. However, about 50 percent of the total cost of production is in extraction and purification of the proteins, which is required in cell culture facilities.

Protein antigens isolated from various pathogens have been expressed in plants and is able to induce the immune responses resulting in protection against intracellular or extracellular diseases in humans. Plant derived protein as antigen used as *vaccines* have been produced against *Vibrio cholerae*, *E. coli*, hepatitis B virus, rabies virus, rotavirus and respiratory syncytial virus.

In plant virus particles expressing multiple antigens from various pathogens have been useful as vaccines against pulmonary infections of *Pseudomonas aeruginosa*, opportunistic infections of *Staphylococcus aureus*, malaria, HIV and hepatitis B virus.. A company in California has developed a virus-based system in tobacco to produce personalized vaccines against cancer.

Plants have been used and tested as production systems for different range of therapeutic proteins to be used either directly in foods or after purification [33]. Expression in plants of milk proteins such as lactoferrin and beta-casein may contribute the therapeutic values of these proteins to other food products. Expression of thioredoxin in most of the foods such as cereal grains would increase the digestibility of proteins and thereby reduce their allergenicity.

CONCLUSION

There are a number of medicinal plants which is generally used for the enhancement of the body's immune response to fight against intracellular or extracellular pathogens. In contrast, a large number of proteins, polysaccharides, lectins and flavonoids extracted from the plants are coming in to the market by proper clinical trials.

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