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HERBAL MEDICINES AND THEIR ACTIONS ON THE IMMUNE SYSTEM: A MINI LITERATURE REVIEW

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ABSTRACT

Herbal Medicine is proving itself to be a complementary and alternative type of treatment, other than conventional medication approaches. The use of plants, roots, seeds, and other various natural resources has proven their potentially high therapeutic values and expanding healthcare treatments in a way that benefits all, especially patients with a weak immune system who may suffer from health complications, in which standard approaches no longer perform any improvement in their diagnosis or those who suffers from side effects caused by conventional drugs. The present review is mainly focused on the use of Herbal Medicine for treating a disease or preventing our immune system from breaking down by using different herbs to stabilize and regulate our immunity. Several herbal drugs have been studied and tested, proving to enhance the efficiency of immunotherapies and inhibit illness progression due to their powerful pharmacological active ingredients, which can also be combined with one another, performing an even stronger boost to our immune system and possibly fight against a disease or symptom. Since ages ago, herbs were used for healing illnesses, being unknown all the extensive benefits a single plant can provide, but at the present time, medicinal plants not only play their role to heal, but also, to regulate and treat with barely no side effect, in comparison to other chemical compounds, improving lifestyle and being a trustworthy approach all over the world.

Keywords: Herbal Medicine, Immunotherapy, Immunomodulatory.

INTRODUCTION

Everyday, we expose our bodies to many intruders and harmful pathogens, also including different chemicals available in the environment. These foreign molecules and microbes, can attempt to attack our organism, but at this very moment, the Immune System goes into action. It can be defined as a complex integrated network of cells, tissues, organs and soluble mediators, evolved to defend the organism, containing a capability of distinguishing self and non-self (based on a memory developed overtime) recognizing the possible enemy and destroying whatever threatens to enter the body, known as immune response (1). To prevent a possible unbalance of immune response and avoid a possible disorder, immunomodulatory drugs fit to perform such regulation when needed, either to enhance or suppress the immune system (2). This review is focused on plant-based drugs tested in both *in-vitro* and *in-vivo* studies, containing active components which are capable of performing powerful and alternative immunomodulatory activities through herbal medicine.

An increasing number of evidence has been collected over the past decades to find and study different pharmaceutical forms found in plant species. Their active ingredient can be found in one

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or more than one part of the plant, and also, have several different benefits, proving that medicinal plants can be a very important alternative approach in comparison to conventional medicine (3). Herbal products became even more popular over the past years, defined as a complex mixture of organic chemicals that may come from raw or processed parts of a plant, including leaves, stems, flowers, roots, fruit, bark, seeds and other parts, macerating the herb with alcohol, water, or other solvents, to obtain their concentrated extract (4). Can be found in the most various ways, in capsules, liquid extract, powdered, chopped or dried (tea) and in lotions or gels. (5). A wide selection of phytochemical components can be used to treat or prevent diseases by boosting our immune system, which can be extracted alone from a single herb, or even, for a better performance, using two or more herb components combined to yield a preferred pharmacological effect (6).

MATERIALS & METHODS

This literature review is based on scientific articles researched from reliable sources like Pubmed, Google Scholar, Scielo, Elsevier and ScienceDirect, by entering keywords related to this present work (Herbal Medicine; Immunotherapy; Immunomodulatory). Another source worth mentioning was the John Hopkins School of Medicine, ranked as one of the best universities in the United States and possessing in its website a wide selection of trustworthy facts and information. The language of the mentioned articles are mostly in English, and articles were searched within the last 26 years due to some important research worth mentioning.

DISCUSSION

A numerous selection of plants found around the globe, possesses immunomodulatory properties among other properties known to either balance or strengthen the organism's defense and response, regulating our system to support every area of our body (7). The information in this present work focuses on immunomodulatory herbal plants, also capable of possessing antiviral, antioxidant, antimicrobial or anti-inflammatory properties (Table 1).

Table 1 - Medicinal Plants and their actions on the Immune system:

Name of Plant	Family	Region	Effects	References
E. purpurea *E. angustifolia* *E. pallida*	Asteraceae	North America	Immunomodulatory Anti-inflammatory Antivital Antimicrobial	Sharifi-Rad et al., 2018 Barrett et al., 2003
Panax ginseng	Araliaceae	Asia	Immunomodulatory Anti-inflammatory	Liu et al., 2021
Curcuma longa	Zingiberaceae	Asia	Immunomodulatory Antioxidant Anti-inflammatory	Ganjali et al., 2014 Sahebkar et al., 2015 Panahi et al., 2012
Astragalus membranaceus	Fabaceae	China Mongolia Korea	Immunomodulatory Antioxidant Anti-inflammatory Anti-cancer Antiviral	Yang et al., 2005 Yu et al., 2009 Qin et al., 2012 Shen et al., 2008 Zhu et al., 2009
Morinda citrifolia	Rubiaceae	Asia USA (Hawaii) Australia	Immunomodulatory Anti-inflammatory	West et al., 2009 Hirazumi et al., 1999
Sambucus nigra	Adoxaceae	Europe	Immunomodulatory Anti-inflammatory Antiviral	Vlachojannis et al., 2010 Knudsen et al., 2015 Santin et al., 2022
Tinospora cordifolia	Menispermaceae	Indian subcontinent	Immunomodulatory Antioxidant Antimicrobial Hepatoprotective Neuroprotective	Maurya et al., 1996 Ilaiyaraja et al., 2011 Bonvicini et al., 2014 Kavitha et al., 2011 Kosaraju et al., 2014
Ficus carica	Moraceae	Mediterranean	Immunomodulatory Antioxidant Anti-tumor	Du et al., 2018 Yang et al., 2009 Chen et al., 2015

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Echinacea

Echinacea (*E. purpurea, E. angustifolia, E. pallida*) of Asteraceae family, which can be found in North America, are the three most commonly used species for medical purposes (8). Its active compounds can be extracted from different parts of the plant (leaf, flower, seed or root) (9) but preparations may vary depending on the chosen species and the part of the plant used. Also, its effects depend on the extraction protocol followed (10). These three main species have traditionally been roluted as "anti-infective" agents, but overtime, evidence has proven them to be powerful immunomodulatory, anti-inflammatory, antiviral and antimicrobial plants (11). Echinacea is famous for its immunostimulant properties (12) acting on a weakened and unbalanced immune system to restore health. Used to treat and prevent respiratory infections (13) reducing inflammation and also treating common cold and sore throat.

Ginseng

Ginseng (*Panax ginseng*) belongs to the Araliaceae family, most commonly found in Asia (14) has been used for over 2000 years all around the world, due to its powerful pharmacological active ingredients (vitamins, minerals, amino acid, polysaccharides and many others) which can help treat and protect many diseases (15). It contains various benefits, among them aging, cancer, cardiovascular system (16), anxiety, neurological disorders (17) and diabetes (18), but mainly, acting on immune-regulatory function and inflammation (19). Can be extracted and isolated from the root, but also from its stem and leaves. One of the main benefits *P. ginseng* can provide, is the modulation of the immune system (20) due to the stimulative proliferation of lymphocytes. Ginsenosides is one of the many components found in Ginseng and improves cellular immune function, therefore, studies considered a *P. ginseng* as a very safe herb, rarely inducing side effects or drug interactions (21), boosting our immune system and helping to control diseases.

Turmeric

Turmeric (*Curcuma longa*) belongs to the Zingiberaceae family, originating from Asia. Can be considered as a small tropical tree, extracting from its roots and rhizomes of the plant. Turmeric has been used for centuries due to its pharmacological properties (22). Popularly known as a culinary spice, as curcuminoids provides its yellow color and both curcuminoids and curcumin being the main components of Turmeric (23). Traditionally used to treat indigestion, throat infections, rheumatism, common cold, sinusitis and liver ailments (24), as well as topically to heal wounds or treat skin ulcers (25). Curcimin is considered a powerful immunomodulatory agent, capable of modifying immune cell activity and down-regulating pro-inflammatory cytokines (26), also possessing antioxidant (27) and anti-inflammatory effects (28), according to recent studies. Evidence both *in vitro* and *in vivo* has also proven its effective therapeutic values in many diseases such as cancer (29), cardiometabolic diseases, pulmonary and liver diseases (30), anxiety and depression (31).

Astragalus

Astragalus (*Astragalus membranaceus*) of the Fabaceae family, mainly grown in China, Mongolia and Korea, has been involved in several studies and proven to possess several benefits (32). The main applications for this herb are Immunomodulation (33), Anti-oxidative (34), Anti-inflammatory actions (35), Anti-cancer actions (36) and antiviral activity (37). Its dried roots contain a wide amount of active compounds, which may vary based on the region they were grown or the period they were first harvested (38), and also, can be combined with other herbs for better performance. Can assist in immunodeficiency disorder treatments, relieving the adverse effects caused by conventional drug treatments by enhancing the immune system (39), ie, used as a tonic to enhance the body's defenses (40) by increasing the number of stem-cells in bone marrow, facilitating their development into active immune cells.

Noni

Noni (*Morinda citrifolia*), from the Rubiaceae family, considered as a small tree grown in Asia, USA (Hawaii) and Australia (41), has been used for over 2000 years due to its curative and preventive properties capable of managing many diseases (42). The whole plant can be used to obtain its extracts (leaf, bark, fruit, root and stem). Lots of evidence was collected to indicate that Noni is able to treat and prevent various infections by stimulating the immune system (43) due to the active compounds present in this plant, capable of enhancing the immune response by influencing components of the immune system, suppressing inflammation (44) and tissue damage in ulcerative colitis with minimal side effects (45) among other various benefits.

Black Elderberry

Elderberry (*Sambucus nigra*) from the Adoxaceae family originated from Europe possess great pharmacological properties known to modulate specific and nonspecific immune defense and reduce inflammatory status (46). This plant contains many active compounds which have become popular for its immune system function boost (47) and antiviral effects (48). Extract from *S. nigra* flowers also proved to perform anti-inflammatory effects by modulating the production of inflammatory mediators (49) and relaxing both vascular and non-vascular smooth muscle tissue. Studies mention its traditional use for cold and flu symptoms but actual evidence mentions significant effects on reducing duration and severity of upper respiratory symptoms due to viral infections as well (50).

Guduchi

Guduchi (*Tinospora cordifolia*) belongs to the Menispermaceae family originated from the Indian subcontinent (51). Its leaves are heart-shaped and *in-vivo* and *in-vitro* studies identified phytochemical activities in different *T. cordifolia* extracts (ethanolic,

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methanolic and aqueous) and fractions from its aerial parts, stem, leaf or fruit, that yields to immunomodulatory activities (52), antioxidant activity (53), antimicrobial activity (54), hepatoprotective effects (55) and neuroprotective potential (56). Immunostimulatory proteins known as gudichi immunomodulatory protein (ImP) were also found in its dry as well fresh T.cordifolia stem powder (57). Most of the clinical studies involving this herb, concludes that its use is safe and poses minimal risk with regard to herb-drug interaction potential (58).

Common Fig

Fig (*Ficus carica*) from the Moraceae family planted in tropical and temperate regions (Mediterranean) (59), is rich in flavonoids, phenolics and polysaccharide. F. carica's polysaccharide is the major bioactive compound isolated from this plant, which contains potent antioxidant activity (60), anti-tumor properties (61) and mainly, immunoregulation function (62). Further studies are still needed to prove its anti-inflammatory properties, but it's already proven its beneficial effects on reshaping gut microbiome and treating colitis symptoms in induced-colitis in vivo tests (63) as well.

CONCLUSION

With the growing number of incidence and susceptibility to acute and chronic diseases, there has been an increase in interest on the use of active herbal compounds to promote disease prevention and resilience, possibly because herbal formulations and phytochemicals could generate profound advances, with safety and effectiveness. Nowadays, we may take advantage of the relatively nontoxic nature and immunomodulating properties of herbal medicinal or enhance energy levels, immunity, longevity and general health. In this current review, several medicinal plants were mentioned (both popular and lesser-known plants) due to their powerful medicinal benefits to somehow regulate and strengthen human's immune system according to *in vivo* and *in vitro* evidence based on their active ingredients. Although toxicity and drug interactions are considered low risk and safe in most of the plants mentioned, professional support is essential when using these herbal medicines.

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