Review Article

Potential Plant Immunomodulators: A Phytotherapy Perspective for COVID-19 Infection

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Received: 10 March 2021 Revised: 21 April 2021 Accepted: 28 April 2021

Abstract

The emerging trends of pathogens like, Chikungunya virus, Hendra virus, Dengue virus, Nipah virus, SARS virus, Salmonellosis, brucellosis, Arcobacter infection, Swine flu, Campylobacter, Middle East Respiratory Syndrome, West Nile virus, SARS-Corona virus since the past 50 years and recently emergence of COVID-19 pandemic disease caused due to novel corona virus in last the month of 2019 in Wuhan city of China and outbreak to the globe and the unavailability of efficient chemotherapy and vaccines, make the whole world to find out new chemotherapy to combat with such pathogenic infectious diseases. This pandemic situation is strongly admiring the acceptance of immunomodulatory drugs as a part of routine diet as well as a drug regimen in the management and treatment of pathogenic infectious diseases. The present report contains the details of potential herbal traditional medicines which have records to been used in ethnic medicines and scientifically reported of significantly boosting the human immune system. The current article might be a good source of information for the researchers and practitioners working in the related fields.

Keywords: Immunity, pathogenic infections, phytotherapy, COVID-19

Introduction

Pathogens of human and animals are co-existing for a long time but the continuous change in environment, human lifestyle, habitat, and global scenario has altered the cellular structure of human and animal population which further, creating the risk of new diseases and enhancing the existing diseases infections are the most serious concern of human health. The last several years have seen a rise in emerging infectious pathogens like Chikungunya virus, Dengue virus, Hendra virus, Nipah virus, Salmonella, Brucella, Arcobacter, HIV, Swine flu, Campylobacter, Middle East Respiratory Syndrome, SARS-corona in humans (Jones et al., 2008). Recently, the emergence of the novel corona virus which outbreaks COVID-19 starting from China to the globe infected 43,38,658 number of the population along with 29,7119 deaths and have potentially caused a serious threat to human health and economic impacts (Woolhouse, Haydon et al. 2005). Due to a lack of efficient chemotherapy or vaccine, COVID-19 became a deadly disease throughout the globe. Affected countries have announced the lockdown and social distancing to control community spread and mortality (Zhang, Jiang et al. 2020). Several new or genetically modified pathogens had been emerged and caused mortality. The emerging trend of pathogens indicates serious emerging virus threats in future. A strong immune system can make the human body fight against pathogenic threats.

Immunity is the natural defense system of the body that works against different types of harmful diseases and infection (Calder 2013). There are two types of immune mechanism, the first one is a short-term mechanism named innate mechanism and the other one is an adaptive mechanism. Short term mechanism is the first-line defense of the body while the adaptive mechanism is known for its memory, complexity and diversity(Calder 2013). Humoral immune response and cell-mediated cytotoxic response are two subtypes of the adaptive immune system. The humoral immune response is works by B lymphocytes while the cytotoxic response works by T lymphocyte. All the working cell of the immune system are arising from bone marrow by hematopoiesis with the help of stem cells which are also derived from bone marrow. (Sharma, Kumar et al. 2017) A

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DOI:https://doi.org/10.31024/ajpp.2021.7.2.6

certain group of soluble extracellular proteins or glycoproteins named cytokines are the key mediator that plays an important role in the interaction between the specialized cells of the immune system. Cytokines work in the form of interleukins (ILs), interferons, and chemokines. By intermolecular cross talks, these cytokines maintain physiological stability through their secretion in all nucleated cells by the inducible response to injury (Ferreira, Borba et al. 2018). Direct interaction of different types of cells like B and T lymphocytes, T helper (Th) cells, natural killer cells and myeloid cells: Neutrophils, Basophils, Macrophage and Monocytes and by-products of synthesis which they secrete like (immunoglobins, cytokines: interleukins, interferons, colony-stimulating factors, growth factors) strongly controlled the immune response of the immune system (Cano and Lopera 2013). Innate immunity and Adaptive immunity work together for the overall protection of the body. Innate immunity is found in vertebrates, invertebrates and plants but adaptive immunity is only found in invertebrates. Innate immunity is incapable of immunological memory and bears an antigen-independent defense mechanism that is immediately activated within a few hours after the entry of pathogens (Janeway Jr, Travers et al. 2001). All cells which are involved in innate immunity are phagocytic (Neutrophils, monocytes, and macrophage), and those cells which secreting inflammatory mediators (Basophils, mast cells. Eosinophils and Natural killer cells. Inflammatory response and phagocytosis which are the two types of innate immune response are stimulated by pathogen-associated molecules named pathogen-associated immunostimulants with the help of specialized cells like neutrophils and macrophages and this process is regulated by cytokines. A group of specialized cells such as antigen-presenting cells (APCs) like dendritic cells (CDs) help to innate immune response (Borish and Steinke 2003). APCs share the processed antigen with lymphocyte and collaborate with them to elicit stimulate the immune response. Adaptive immunity involves the antigen-specific antibodies, and this immune response is regulating by T-cells and facilitated by APCs in cell-mediated immunity while B cells involved in antibody-mediated immunity. The T lymphocyte comprises the 60% to 80% of total lymphocytes and has a very high lifetime and mostly involves in killing intracellular pathogens by activating macrophage and killing those cells which are infected by the virus. These lymphocytes recognize the antigen by their primary structure while the B-lymphocyte and plasma cells recognize the antigen with the help of their spatial structure. Helper T-cells (Th) are 2/3 of the total lymphocytes and are very essential in immune response because they secrete interleukin. Interleukins are the messenger molecules that make communication easy and reliable between immune cells. Th1 secrete different types of cytokines and according to that cytokines, perform specific work that helps in the immune response. Th1 cells produce IL-2, IFN-alpha, and TNF-alpha that trigger the inflammatory reaction while Th-2 cells are responsible for producing IL-3, 4, 5 that are the important and main stimulator of Immunoglobulins A & B synthesis (Alimonti, Ball et al. 2003).The activation of B lymphocyte in antibody-mediated immunity, triggers the pleasure cells for synthesizing Immunoglobulins or memory B cells leading to immunological memory.

Medicinal herbs are the potential source of therapeutic aids worldwide since time immemorial and are a source of potentially bioactive molecules that further give rise to potent drugs for the treatment of several health problems (Khodadadi 2015). Several types of research were carried out by researchers throughout the globe to evaluate the pharmacological effects of plant drugs in enhancing human immunity and to find out the immunomodulatory bioactive principle. It is reported that deficiency of micronutrients leads to several health problems, it retains the growth of the physical and immune system (Kipkoriony Rutto and Jaja 2012). A proper balance of carbohydrates, fats, proteins, vitamins and minerals in the routine diet is very essential to maintain the health of individuals and to prevent illness. Several scientific reports reveal that amino acids, vitamins and minerals are very essential components of the immune system as they take part in several metabolic reactions in the body including the immune system, increased sensitivity of B-cells and boost cytotoxicity of T-cells towards infected and transformed cells in the body (Cherayil 2011). The significance of the rasayanas as immunomodulating agents compared to other conventional immunomodulators is that they activate the immune function without altering the other basic parameters of the body (Balasubramani, Venkatasubramanian et al. 2011). In this paper, the author highlighted the potential plant drugs which contain phytonutrients and phytoconstituents and reported in traditional literature as well as scientific reports for enhancing human immunity. The article might be beneficial for the researchers, traditional practitioners, and physicians to find a new scope in plant immunomodulatory studies and to plan the potential herbs in drug regimens for the treatment of pathogenic diseases.

Plants and derived immunomodulators

Biological products of plants have been used by human for thousands of years in pure form or also in extract form to treat different types of disease. Herbs are the basis of medicines that are used by a human being. Scientific research cleared that various herbs possess immune-stimulating properties (Khodadadi 2015). Different types

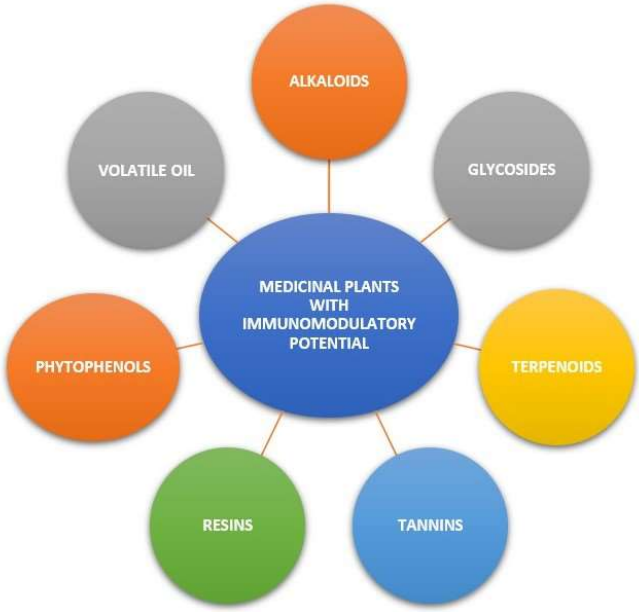

Figure. 1. Class of phytoconstituents reported to have immunomodulatory potential

of herbs having a wide range of phytochemicals like alkaloids, flavonoids, tannins, resins, glycosides, terpenes, saponins, carotenoids, plant sterols and phthalides. In all these many plants contain antioxidant compounds that are very effective against chronic disease. Those plants which are rich in flavonoids, vitamin C or carotenoids can enhance immunity. The flavonoids rich plants having anti-inflammatory action and boost the activity of lymphocytes increases phagocytosis and help in interferon production. All these phytochemicals are potent immunostimulants and boost immunity. Many immuno-boosting properties like antioxidants, anti-inflammatory, antitumor, antibacterial, antifungal and antipyretic are potently found in these phytochemicals. So, we can conclude that medicinal herbs have a great role in boosting the immunity of the body. Different phytochemical class (Jatawa, Paul et al. 2011, Sharma, Kumar et al. 2017) with immunomodulatory properties are shown in **Figure 1.**

Alkaloids

These are the organic products of natural or synthetic origin that are basic and contain one or more nitrogen atoms, normally of heterocyclic nature and process specific physiological action on human or animal body when used in small quantities. The promising families which contain alkaloids and reported as an immunomodulatory activity are – Amaryllidaceae, Apocynaceae, Berberidaceae, Euphorbiaceae, Leguminosae, Loganiaceae (Eldahshan and Abdel-Daim 2015), Liliaceae, Menispermaceae, Papaveraceae, Ranunculaceae, Rubiaceae, Rutaceae and Solanaceae (Singh, Bhalla et al. 2011). Potential alkaloids containing plant drugs are shown in **Table 1.**

Glycosides

The organic products from plant or animal sources which on enzymatic or acid hydrolysis gives one or more sugar moieties along with no sugar moieties. Sugar is called glycone and non-sugar is called aglycone. chemically they are acetyls or sugar ethers formed by interaction hydroxyl group of sugar and non-sugar moiety with the release of a water molecule. Glycosides have very good antioxidants and anti-rheumatoid properties which can be very useful. **Table 2** shows plant glycosides with the potential immunomodulatory property.

Phytophenols

Phytophenols are secondary metabolites and have structural unit C6-C3 phenylpropanoids. This has various classes of phenolics which are natural substances. A different class of phytophenols are:

Table 1. Alkaloid containing plant drugs with immunomodulatory potential

S. No.	Plant name	Botanical name (Family)	Bioactive part(s) of plant	Alkaloids	References
1	Nux vomica	*Strychnosnux-vomica* (Loganiaceae)	Leaves, seeds	Strychnine, brucine, vomicine, colubrine, pseudostrychnine and strychnicine	(Eldahshan and Abdel-Daim 2015)
2	Opium	*Papaver somniferum* (Papaveraceae)	Seeds, flowers	Morphine, codeine, heroin, narcotine, thebaine	(Mani and Dhawan 2011)
4	Cinchona	*Cinchona calisaya* (Rubiaceae)	Flowers, leaves, bark	Cinchonine, cinchonidine, quinine, quinidine	(Gachelin, Garner et al. 2017; Pradeepa,2018)
5	Tea	*Theasinesis* (Theaceae)	Leaves, leaves buds	Caffeine, theobromine, theophylline	(Di Chen, Chen et al. 2008)
6	Giloy	*Tinospora cordifolia* (Menispermaceae)	Leaves, stems,	Berberine, palmatine, tembetarine, isocolumbin	(Sharma et al., 2011)
8	Ashwagandha	*Withaniasomnifera* (Solanaceae)	Leaves, stem, flower	Withanolide, withaferin A, ergostrane, anaferine, anahygrine.	(Singh et al. 2011)
9	Black Pepper	*Piper nigum* (Piperaceae)	Seed, flower, fruit	Dipiperamide D, sabinene, phellandrene, piptigrine Piperine	(Joshi et al. 2018)

Table 2. Glycoside containing plant with immunomodulatory properties

S. No.	Plant name	Botanical name (Family)	Bioactive part(s) of plant	Glycosides	References
1	Digitalis	*Digitalis purpurea* (Plantaginaceae)	Flower	Purpurea glycoside A, gitoxin, digoxin, digitoxin	(Boericke 1927)
2	Dioscorea	*Dioscorea deltoid* (Dioscorea)	Tubers, flower	Diosgenin	(Niyas 2015)
3	Ginseng	*Panax ginseng* (Araliaceae)	Roots	Ginsenosides, panaxosides	(Kim 2018) (Leung and Wong, 2013; Jakaria et al. 2019)
4	Citrus	*Citrus limon* (Rutaceae)	Fruits	Limonene, citral, beta-pinene, sabinene	(Mannucci, Calapai et al. 2018)
5	Milk Thistle	*Silybusmarianum* (Asteraceae)	Flowers	Glycosides, fiber, hesperitin	(Mulrow et al. 2000)
6	Aloe vera	*Aloe barbadensis* (Asphodelaceae/Liliaceae)	Leaves	Carboxypeptidase Aloe-emodin, Aloetic acid, barbaloin, anthranol	(Surjushe et al. 2008)

- Flavonoids: Anthocyanidins
- Phenolic acid: a) Hydroxybenzoic acid: para Hydroxybenzoic acid b) Hydroxy cinnamic acid: Ferulic acid
- Tannins: a) Phthalic tannins: Ellagitannins

b) Catechin type tannins: Acertannin

- Stilbenes: Resveratrol

Phytophenols are components of plants and have various and specific benefits and known for anti-inflammatory and antioxidant characters. **Table 3** shows Phytophenols with the potential immunomodulatory property.

Resins

Resins are the secondary metabolites. Resins are collected by giving artificial injury to plants. On artificial injury, plants secrete resins in response to protect the plant. Resins are viscous compound that becomes harden over some time but softens on melting. Resins do not soluble in water and not react with water. This special property makes it available for sustained release medicament formulation and for preparing many excipients in the pharmaceutical dosage forms. They are amorphous mixtures of essential oils, carboxylic acids, and oxygenated products of terpenes. They are translucent or transparent solid, semi-solid or liquid substances having many carbon atoms. Most resins are heavier than water. They are soluble in alcohol, volatile oil, fixed oils, chloral hydrate and benzene and ether (non-polar organic solvent). The classification resin depends upon the constituents of the resin, they are classified as ester resin, acid resin and resin alcohols. The homogenous mixtures of resins and oils are called oleoresins. The homogenous mixtures of volatile oil, gum, and a resin called oleo-gum resin. The benzoic and cinnamic acid-containing resin is called balsam. The major source of resins is *Canada balsam, Protium copal Hymenaeacourbaril* having the major chemical constituents such tannic acid, D- lysinol, diaminodiphenylsulfone. Resin with immunomodulatory effects is mentioned in **Table 4.**

Table 3. Plants with phytophenols as immunumodulators

S. No.	Plant name	Botanical name (Family)	Bioactive part(s) of plant	Phytophenol	References
1	Orange	*CitrusAurantium* (Rutaceae)	Juice Peel fruits	Vitamin C, polyphenols, Phytochemicals, antioxidant, linalool	(Heng et al., 2020)
2	Tangerene	*Citrus Reticula* (Rutaceae)	Juice Peel fruits	Vitamin C, Carotenoids, Polyphenols	Hirsch, 1959
3	Japanese knotweed	*Reynoutria japonica* (Polygonaceae)	Roots, seed, Flower, stem	Vitamin C ,Resveratrol, Quercetin	
4	Chamomile	*Matricaria recutita* (Asteraceae)	Leaves, flower	Bisabolol, Chamazuiene, Apigenin, Matricin	
5	Neem	Azadirachta indica (Meliaceae)	Leaves,bark Stem,fruit	Orcidch et al., 2017	Kumar and Navaratnam, 2013 Alzohairy, 2016.
6	Onion	Allium Cepa	Roots,Leaves	Srivastava et al., 2010	Borah and Banik, 2018

Table 4. Resins with immunomodulatory effect

S. No.	Plant name	Botanical name (Family)	Bioactive part(s) of plant	Resins	References
1	Colophony	*Pinuspalustris* (Pinaceae)	Pines Fruits	Resin acid (abietic acid), resene, mixture of dyhydrobietic acid and dehydroabietic acid.	(Sadhar, Founds et al. 1994)
2	Asafoetida	*Ferules asafoetida Linn* (Umbelliferae)	Roots Dried latex (gum)	Volatile oil, gum, resin. Resin (notannol, asaresinotannol, umbellic acid and umbelliferone).	(Mahendra and Bisht 2012)
3	Myrrh	*Commiphoraobyssinica Engles* (Burseraceae)	Resinous exudate	Volatile oil, resin, gum, bitter principle. volatile oil (eugenol, m-cresol, cumin aldehyde).	(Khalil, Fikry et al. 2020), (Cao, Wei et al. 2019)
4	Turmeric (Haridra)	*Curcuma longa* (Zingiberaceae)	Rhizome Roots	curcumin Volatile oil, resin and zinzgiberaceous starch grains. Volatile oil (d-alpha-phellandene, d-sabinene, cineol, borneol, zingiberene, and sesquiterpenes	(Prasad and Aggarwal 2011)
5	Male Fern	*Dryopterisfilix-mas(Linn*) (Dryopteridaceae)	Roots Dried rhizomes	Derivative of phloroglucinol and butyric acid	(Schott 2002)
6	Cinnamon	*Cinnamomum verum* (Lauraceae)	Barks	Eugenol, cinnamic acid, cinnamate, cinnamaldehyde	(Feldman and Bauer 2008),(Ulbric, Seamon et al. 2011)

Tannins

Tannins are secondary plant metabolites that are water-soluble phenolic compounds. Their molecular weight is ranging from 500 to 3000. Tannins have the property of combining with cellulose, proteins, gelatin, and pectin and form an insoluble complex. Their chemical structures varied so can act as potential metal ion chelating agent, biological antioxidant or relying on its concentration, as a complexing agent. In low concentration, it acts as a complexing agent and in high concentration act as a precipitating agent. Tannins are classified into two main groups: Hydrosable tannins and Condensed tannins. Hydrosable tannins: Gallotannins, ellagitannins and complex tannins (sugar derivatives-gallic acid, glucose and ellagic derivatives) Condensed tannins: Procyanidins. Tannin containing plants with immunomodulatory activity containing are shown in **Table 5.**

Terpenoids

Terpenes are secondary metabolites, and they are produced with the help of enzymatic resections of primary metabolites (amino acids, sugars, vitamins). Terpenes are the biggest class of secondary metabolites and normally having 5 carbon isoprene (C5H8) units which are connected in thousands of ways. Simply, terpenes are hydrocarbons but terpenoids are modified terpenes having different functional groups and oxidized methyl group moved or removed at different positions. Terpenoids are divided into Hemiterpene (1 isoprene unit): C_5H_8; Monoterpene (2 isoprene unit): $C_{10}H_{16}$; Sesquiterpene (3 isoprene unit): $C_{15}H_{24}$; Diterpene (4 isoprene unit): $C_{20}H_{32}$; Sesterpene (5 isoprene unit): $C_{25}H_{40}$; Triterpene (6 isoprene unit): $C_{30}H_{48}$. Terpenoids containing immunomodulatory plants drugs are shown in **Table 6.**

Table 5. Plant containing Tannin having immunomodulatory action

S. No.	Plant name	Botanical name (Family)	Bioactive part(s) of plant	Tannin	References
1	Green tea	*Camellia sinensis* (Theaceae)	Leaves, Buds, Flower Barks	Xanthine derivatives such as caffeine, theophylline, theobromine, and the glutamate derivatives theamine.	Chacko, Thambi et al. 2010; Katiyar, Ahmad et al. 2000
2	Grapes	*Vitis vinifera* (Vitaceae)	Fruits Juice	Tartaric acid, malic acid, citric acid, and amino acids.	Yadav, Jain et al. 2009; Percival and West 2013
3	Strawberry	*Fragaria X ananassa* (Rosaceae)	Fruits, Flower	p-Hydroxy-Benzoic acid, Palmitic acid, Palmitolic acid and Pantothenic acid.	Liberal, Francisco et al. 2014; Basu, Nguyen et al. 2014
4	Basil	*Ocimum basilicum* (Lamiaceae)	Leaves	Methyl chavicol, methyl eugenol, linalool, limonene, cis-ocimene and citronellol.	Jamshidi and Cohen 2017; Malav, Pandey et al. 2015; Bhateja and Arora 2012; Al-Maskari, Hanif et al. 2012
5	Coffee	*Coffea Arabica* (Rubiaceae)	Seeds, Beans	Caffeine, Chlorogenic acid, diterpenes and trigonelline.	Higdon and Frei 2006; Poole, Kennedy et al. 2017
6	Amla	*Embilica officinalis* (Euphobiaceae)	Dried or fresh fruits	Vitamin C, gallic acid, ellagic acid, chebllagic acid	Grover, Deswal et al. 2015;Annapurna 2012

Table 6. Terpenoid plant with immunomodulatory activity

S. No.	Plant name	Botanical name (Family)	Bioactive part(s) of plant	Terpenoids	References
1	Caraway	*Carum carvi Linn.* (Apiaceae)	Seeds Fruits	Carvone, limonene, acetaldehyde, furfural carveole, pinene, thujone, camphene, phellandrene.	(Kazemipoor and Cordell 2015),(Johri 2011)
2	Spearmint (peppermint)	*Mentha spicata* (Lamiaceae)	Fresh or dried Leaves	Carvone, cis-carveol, limonene, 1,8 cineol, cis-dihydrocarvone, carvyl acetate and cis-sabinene hydrate.	(Balakrishnan 2015)
3	Olive	*Olea europaea* (Oleaceae)	Ripe fruits Leaves Woods	Oleuropein, hydroxytyrosol, luteolin, rutin, caffeic acid, polyphenols, and flavonoids	(Hashmi, Khan et al. 2015)
4	Apple	*Malus domestica* (Rosaceae)	Fruits Juice	ursolic acid, Vitamins and Minerals	(Boyer and Liu 2004)
5	Orange	*Citrus X sinensis* (Rutaceae)	Fruits Peel Juice	Organic acids(citric,malic,and ascorbic acid), sugars(Sucrose, glucose), phenolic compounds and limonene.	(Milind and Dev 2012)

Volatile Oil

Volatile oils are known as an essential oil because it is responsible for the essence and odor of the plant. Volatile oils are a mixture of different types of terpenes like simple hydrocarbon terpenes, sesquiterpenes, polyterpenes and their oxygenated derivatives. The volatile oil obtained from various parts of the plant and evaporates on exposure in the air at ordinary temperature. The fresh volatile oils are colorless liquids, but few are amorphous or crystalline solid. On exposure to the air and the sunlight for a long time, volatile oil becomes darker in colour. So, that's why volatile oils always are stored in tightly closed, amber-colored bottles in a cool and dry place. Volatile oils are strongly soluble in alcohol, ether, and most of the organic solvents while slightly soluble in water. It is easily smeared on paper and gives a translucent strain which disappearing as the oil volatilizes. Volatile oils are classified as: Hydrocarbon: Turpentine oil, Alcohol: Peppermint oil, Pudina, Sandalwood oil, Aldehydes: Cymbopogon sp., Lemongrass oil, Cinnamon, Cassia and Saffron. Ketone: Camphor, Caraway and Dill, Jatamansi, Fennel, Phenols: Clove, Ajowan, Tulsi, Phenolic ether: Nutmeg, Calamus, Oxides: Eucalyptus, Cardamom and Chenopodiumoil, S Esters: Valerian, Rosemary oil, Garlic, Gaultheria oil. Potential volatile oils containing plant drugs are shown in **Table 7.**

Mode of action of immunomodulators

Many neurodegenerative diseases are persistent and are troublesome, one of the major cause for problems are free radicals like superoxide anion, singlet oxygen, hydroxyl radical and hydrogen peroxide which can induce mutations in the body as well as brain and can lead to disorders and

Table 7. Volatile oil containing plant drugs with immunomodulatory potential

S. No.	Plant name	Botanical name (Family)	Bioactive part(s) of plant	Volatile oil constituents	References
1	Ginger (Zinziber)	*Zingiber officinale* (Zingiberaceae)	Rhizomes	Volatile oil (Camphene, phellandrene, zingiberene, zingiverol, eucalyptol, citral, borneol and linalool.	Mashhadi, Ghiasvand et al. 2013; Bode and Dong 2011; Ingle, Verma et al. 2013
2	Garlic	*Allium Sativum* (Amaryllidaceae)	Ripe bulb	Organosulfur compounds such as allicin, diallyl disulphide, S-allyl cysteine &diallyl trisulphide.	Imo and Za'aku
3	Peppermint	*Mentha pipertia* (Lamiaceae)	Fresh or dried Leaves	Menthol, menthone, menthyl acetate, 1,8-cineole, limonene, beta-pinene and beta-caryophyllene.	Balakrishnan 2015
4	Eucalyptus	*Eucalyptus globules* (Myrtaceae)	Leaves, Bark, Fruits Wood	1,8-cineol and alpha-pinene.	Shao, Yin et al. 2020
5	Clove	*Eugenia caryophyllus* (Myrtaceae)	Flower buds	Phenylpropanoids such as carvacrol, thymol, eugenol and cinnamaldehyde	Batiha, Alkazmi et al. 2020; Hussain, Rahman et al.)
6	Lemongrass	*Cymbopogon citrates* (Poaceae/Gramineae)	Grass oil	z-citral, borneol, estragole, limonene, pipertone, citronellal	Shah, Shri et al. 2011

sometimes damage to DNA (More and Pai 2011). Some of the alkaloids are beneficial in cancer like Vincristine, Vinblastine obtained from Catharanthus roseus and Camptothecin from Camptothecaacumunatal. Rhizomes of Glorisa superba contain Colchicine which is also alkaloid. Vincristine stops mitosis at the metaphase, and this stops growth and new cell formation. Cinchonine, Quinine obtained from cinchona bark of Cinchona calisaya and its species is also important antimalarial and can be administered in Pregnancy.

Mechanism of Glycosides

Enhance production of IL 1 and TNF alpha from macrophages Glycosides can inhibit Na-K pump and affect the transport of sodium and potassium in and out of membranes. Digitalis is a popular cardiac glycoside and increases the force of contraction of cardiac muscles by binding to Na/K/ATPase of myocardial fibers to inhibit the same, but this is slow action and eventually reduces potassium levels in cells which can be corrected by giving potassium ions in form of i.v. infusion of by Coconut water or lemon which are rich in potassium.

Mechanism of Phytophenols

Flavonoids are antioxidants and relieve free radicals from the body. They stimulate T cells and B cells. Flavonoids also keep the cardiovascular and digestive system healthy by antioxidant activity(Lobo, Patil et al. 2010). They are used as fruits and rich in citrus fruits and also in curry leaves, in addition to these benefits they are also antitumor, anti-rheumatoid antihypertensive, anti-gout and antihyperlipidemic. (Sinha, Sharma et al. 2010, Santilli, Piotrowska et al. 2013)

Mechanism of Resin

Resins are fully loaded with minerals and vitamins that help the body to fight against infections and boost the immune system. Dried fruit save us from fevers, infections and many types of illness because of having anti-inflammatory and antibacterial properties.(Mukherjee, Nema et al. 2014)

Mechanism of terpenoids

The terpenes that are found in citrus fruits having the capacity for enhancing the immunity. They possess anti-inflammatory, antioxidant, anti-stress and have diseases-preventing properties. Terpenes like carvone, limonene, perillic acid, glycyrrhizic acid and nomilin (Kuttan, Pratheeshkumar et al. 2011). These terpenes which are found in Fennel, Apple, Lemon, Orange, Olive tree are responsible for activating the immune system without affecting other parameters of the body. Scientific studies show that terpenoids can enhance the total count of WBC by doing enhancement in bone marrow circularity.

Mechanism of volatile oil

Essential oils are very helpful in boosting my immunity; they are very effective in eradicating those bacteria and virus that are responsible for many harmful diseases. They work by directly fortify the immune response. They are capable to do this because of their specific immune-strengthening properties like antibacterial and antiviral (Yang et al., 2019).

Conclusion and recommendations

The emerging trends of pathogenic infections since the past 50 years has created a challenge among the researchers, practitioners, and the Governments of developed and developing countries to combat the microbial threat and economy situation raised by the new pathogenic or genetically modified microbial strains. Recent emergence of COVID-19 pandemic disease caused due to novel corona virus strongly admire the acceptance of immunomodulatory drugs as a part of routine diet as well as a drug regimen in the management and treatment of pathogenic infectious diseases. Through this paper we have attempted to enlist most commonly used medicinal herbs and plants which are not only work as an immunomodulator but also helpful to fight from various diseases and infections. The source of information may be utilised by general public for maintaining immunity in day-to-day life. The present review might be a good source of information for the researchers and practitioners too working in the related fields.

Conflict of interest

The author declares no conflict of interest.

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