**PHYTOCHEMICALS AND THEIR AMELIORATIVE POTENTIAL AGAINST COVID-19**

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**ABSTRACT**

There are several chronic ailments around the globe which needs attention of scientific community for the search of possible cure. The traditional medicinal systems are used by the mass, where healthcare system is not prevailed its availability like the remote areas, or tribal populations residing in Islands or forest regions. These medicinal system utilizes herbal formulations rich in bioactive compounds or phytochemicals also commercially available as natural products. In the present chapter, different phytochemicals has been documented following their classifications, ameliorative effects. The preparation methods of these phytochemicals has been discussed. As COVID 19 is emerging continuously in different strains and still needs research besides vaccines for the development of medication for primary treatment, some potent bioactive compounds present in Ayurveda system are also conversed as potential antiviral activities

**Keywords-** Traditional medicine, phytochemicals, Covid-19

**I. INTRODUCTION**

Phytochemicals are naturally occurring bioactive, chemical compounds derived from plants that have health stimulating, disease preventing or medicinal properties. They contribute in plants colour, odour and flavour. They are present in our routine food, herbal products, dietary supplements and processed products such as cereals, soups and beverages. They are also marketed in the form of concentrated pills, capsules, powders and tinctures such as a single vitamin substitute or in combination preparations. The consumption of these phytochemicals has been studied as an effective strategy for reducing genotoxic damage, cardiovascular diseases and cancer (1). Indian cuisine is well known for the use of spices. These spices are studied with enormous health benefits including prevention from deadly ailments including cancer (2). On consumption they influence the chemical processes inside our bodies in helpful manners. This can be confirmed by the findings from studies conducted all around the world where phytochemicals have shown potential to stimulate the immune system, prevent carcinogenesis, avert DNA damage and aid DNA repair, reduce oxidative stress, trigger apoptosis, hormone regulation and fight several other pathologies (1,2). In a study malnutrition was regarded to have a direct impact on cancer and disorders (3).

Thousands of phytochemicals/Bioactive compounds have been acknowledged so far, and scientists have only initiated to explore their promising effects(4). In recent years, several technological and scientific developments — including improved analytical tools, genome mining and engineering strategies, and microbial culturing advances — are addressing such challenges and opening up new opportunities. Consequently, interest in natural products as drug leads is being revitalized, particularly for tackling antimicrobial resistance. Here, we summarize recent technological developments that are enabling natural product-based drug discovery, highlight selected applications and discuss key opportunities.(5)

Historically, phytochemicals derived through different methods, have played a significant role in discovery of potential drugs in naturopathy that has been practised from thousands of years in Asian continent, especially for cancer and infectious diseases(6 ,) but also in other therapeutic areas, including cardiovascular diseases (for example, statins) and multiple sclerosis (for example, fingolimod)7.

These bioactive compounds offer wide range of properties as compared to chemical compounds synthetically synthesized under lab conditions, which posses both advantages and challenges for the research for future drugs. These compounds have vast scaffold range and structural complexity. These bioactive molecules are generally possess higher molecular mass, with higher number of [sp3 carbon atoms](https://www.nature.com/articles/s41573-020-00114-z#Glos1) and oxygen atoms but less nitrogen and halogen atoms, higher numbers of H-bond acceptors and donors, (8)These structural differences in bioactive compounds make them advantageous; for instance, the higher rigidity of phytochemicals showed promising outcomes studied in protein -protein interactions can be valuable in drug discovery tackling protein–protein interaction.(9)

There is a whole list of the phytochemicals classes( Table 1) which now days became a matter of scientific interest, including identification of food sources and research potential benefits mentioned thousands years back in traditional medicinal system in Asia Pacific region (Table2).There is increase in use of phytochemicals in chemoprevention and chemotherapy has been observed in research of past decade (1).

The phytochemicals/bioactive compounds/ Natural signaling pathway principally acts through modulation of cell signaling pathways in case of anti inflammatory or immnoregulatory effects, while in case of oxidative stress, the antioxidents presents come into rescue. Due to emergence of COVID 19, these phytochemicals are also being explored for antiviral activities.

**Table 1. Different classes of phytochemicals/natural products**

|  |  |  |
| --- | --- | --- |
| **Phytochemicals classes** | **Food Source** | **Possible Benefits** |
| Carotenoids (beta-carotene, lycopene, lutein, zeaxanthin) | Red, orange and green fruits and vegetables including broccoli, carrots, cooked tomatoes, leafy greens, sweet potatoes, winter squash, apricots, cantaloupe, oranges and watermelon | Prevent skin cancer cell growth, antioxidants and improve immune response  ( 11) |
| Flavonoids (anthocyanins and quercetin) | Apples, citrus fruits, onions, soybeans and soy products (tofu, soy milk, edamame, etc.), coffee and tea | Anti-inflammatiory, anti-tumor , antioxidative  (12) |
| Indoles and Glucosinolates (sulforaphane) | Cruciferous vegetables (broccoli, cabbage, kale, cauliflower and Brussels sprouts) | Detoxification of carcinogens, hormone regulation, block carcinogens (13) |
| Inositol (phytic acid) | Bran from corn, oats, rice, rye and wheat, nuts, soybeans and soy products (tofu, soy milk, etc.) | Prevent cancer cell growth, metal toxicity(14) |
| Isoflavones (daidzein and genistein) | Soybeans and soy products (tofu, soy milk, edamame, etc.) | Inhibit tumor growth, hormones regulation and antioxidant, liver toxicity(15) |
| Isothiocyanates | Cruciferous vegetables (broccoli, cabbage, collard greens, kale, cauliflower and Brussels sprouts) | Induce detoxification of carcinogens, block tumor growth and work as antioxidants  (16) |
| Polyphenols (ellagic acid, eugenol, anethole and resveratrol) | Green tea, grapes, wine, berries, citrus fruits, apples, whole grains, spices and peanuts | Prevent cancer formation, prevent inflammation and work as antioxidants  (17) |
| Terpenes (perillyl alcohol, limonene, carnosol) | Cherries, citrus fruit peel, rosemary | Prevent cancer formation, prevent inflammation and work as antioxidants (18) |

**Table 2.Phytochemicals used in traditional Indian and Chinese medicinal system**

|  |  |  |
| --- | --- | --- |
| **Phytochemical** | **Source** | **Protective effects** |
| Acetyl-α/β-boswellic acid (α/β-ABA), | *Boswellia sacra* Flückiger-Dupiron (Burseraceae), | Anticarcinogenic, antioxidative  (19) |
| Artesunate (hemisuccinate form artemisinin) | *Artemisia annua* L. (Asteraceae | Anti inflammatory, anti tumor, antimicrobial (20) |
| Baicalein (5,6,7-trihydroxy-2phenyl-4H-1-benzopyran-4-one) | *Scutellaria baicalensis* Georgi (Lamiaceae). | Anti-inflammatory , anticarcinogenic( 21) |
| Baicalin (5,6,7-trihydroxy-2-phenyl-4H-1-benzopyran-4-one 5,6-dihydroxy-4-oxo-2phenyl-4H-1-benzopyran-7-yl-β-d-glucopyranosiduronic acid, C21H18O11) | Glucuronide derivative of baicalein | Anticarcinogenic,anti-inflammatory  (22) |
| Berberine (isoquinoline alkaloid) | *Coptis chinensis* Franch (Ranunculaceae), barberry and Oregon grape. | Gastroentertitis,anti-inflammatory(23) |
| Borneol | *Acorus calamus L. (Acoraceae)* | Anti inflammatory, antiapototic(24) |
| Chlorogenic acid(polyphenol) | Green coffee beans, cocoa, | Anticarcinogenic,anti-inflammatory (25) |
| Carvacrol | *Origanum vulgare* Linn. (Lamiaceae) | Antioxidant, anti-inflammatory (26) |
| Curcumin | *Curcuma longaL. (Zingiberaceae)* | Anticancerous, antioxidant, antiiflammatory(27) |
| Dihydrokaempferol (DHK) | *Bauhinia championii (Benth.) Benth. (Fabaceae)* | Anti-inflammatory, antioxidant(28) |
| Ellagic acid | *Fruits and vegetables* | Anticancrous, antioxidant and anti apoptotic(29) |
| Isoliquiritigenin (ISL) | *Soyabeans,licorice,and shallots* | Antioxidative, anti inflammatory(30) |
| Oxymatrine (alkaloid) | *Sophora alopecuroides* L. (Fabaceae) | Immunosupressent and anti-inflammatory(31) |
| Quercetin (3,3′,4′,5,7-pentahydroxyflavone), | Fruits and vegetables | Anticancerous, anti-inflammatory(32) |
| Rutin (quercetin-3-rhamnoglucoside | Citrus fruits | Antioxidant, anti-inflammatory(33) |
| Saikosaponins | Radix Bupleuri, *Bupleurum chinense* DC. (Apiaceae) | Antioxidant, anti-inflammatory, anti cancerous(34) |
| Tanshinone IIA (TSA) | *Salvia miltiorrhiza* Bunge (Lamiaceae) | Anti-inflammatory, anticancerous(35) |
| Tetramethyl pyrazine/ligustrazine | *Oreocome striata* | Anti inflammatory, anti carcinogenic(36) |
| Visnagin/furanacocumarin derivative | Ammi visnaga (L.) Lam. (Apiaceae) | Antioxidant, anti-inflammatory, anti carcinogenic (37) |
| Withaferin A | *Withania somnifera* (L.) Dun. (Solanaceae) | Anti-inflammatory, antioxidant (38) |

**II. TECHNIQUES USED FOR PHYTOCHEMICALS EXTRACTION, ISOLATION, AND PURIFICATION ANALYSIS**

### **A. Extraction of Phytochemicals Using Solvents**

There are several classes of phytochemicals, which becomes the basis of identification of different methods for isolation of different classes of phytochemicals. In solvent based process polarity is primarily considered (like dissolves like), followed by stability of the properties, for instances phenolic compounds has antioxidant properties, in case of walnut methanol is more effective solvent then ethanol (39). A solvent of similar polarity to the solute will properly dissolve the solute. The polarity, from least polar to most polar, of a few common solvents is as follows: Hexane < Chloroform < Ethylacetate < Acetone < Methanol < Water. Plant extracts are usually prepared and then stored I dry powdered forms, which later used for further analysis.

For the preparation of plant extracts different plant parts are used such as roots, shoots, fruits, leaf and stem(figure 1and2). After proper washing and sterilization, dried and homogenized for further processing, before selecting the plant of interest, a vast knowledge about its status must be considered as endangered species are prohibited for such methods, along with it in case of some particular plants, permission of certain organizations is mandatory as some are part of asthetic beleifs. The goal when searching for bioactive compounds is to find an appropriate method that can screen the source material for bioactivity such as antioxidant, antibacterial, or cytotoxicity, combined with simplicity, specificity, and speed (40).



Figure 1. Phytochemicals well acknowledged effects

Figure 2 preparation of phytochemicals/ bioactive compounds

**Microwave-Assisted Extraction (MAE)**

This method of extraction involves usage of electromagnetic radiation ( 300 MHz to 300 GHz ) consisting of both electric and magnetic fields for isolation of phytochemicals from various plant parts of fruits and vegetables . These electromagnetic waves consist of both an electrical field and a magnetic field. These are described as two perpendicular fields. The advanced methods are identified which in lesser extraction time prevents the loss of natural antioxidant properties such as stability and also use less amount of solvent(41). There are some factors which affects the efficiency of the microwave extraction such as extraction temperature, solvent composition, and extraction time.

### **Ultrasonic-Assisted Extraction**

It has been used widely for the preparation of plant extract e compounds from plant materials (43). Ultrasound is used to disrupt plant cell walls in a homogenized plant sample with suitable solvent(ultrasonic bath) with controlled temperature and time which helps improve the solvent’s ability to penetrate the cells and obtain a higher extraction yield. The drawback of the method is lower yield besides this it is a green technology that also protects the environment from production of toxic substances Tabaraki et al. 44



Figure 3. Different sources of bioactive compounds

### **B. Techniques of Isolation and Purification of Bioactive Molecules from Plants**

Purification and isolation of phytochemicals from plant extracts is a dynamic process that has undergone new development in past decade (45). These modern methods lead to development of several bioassays for isolation, separation, and purification on the other (figure3)

There are some factors that should be considered during isolation and purification methods as sometimes they hinder the separation process of bioactive compounds such as the plant part used for extraction as few parts has number of debris and toxic chemicals as well for instance usage of seeds for bioactive compounds isolation as these naturally consists of certain inhibitors used by plants as defense mechanisms (46). Different solvents are used to prepare different formulations of bioactive compounds based on their chemical and physical properties. Generally chromatography methods are widely used for the isolation and purification of bioactive compounds. Different types of chromatography techniques used for bioactive compounds separation including HPLC (High Pressure Liquid Chromatography), which is technically advanced instrument which fastens the purification process with high accuracy.

Developed instruments such as (HPLC) accelerate the process of purification of the bioactive molecule. Different varieties of spectroscopic techniques like UV-visible, Infrared (IR), Nuclear Magnetic Resonance (NMR), and mass spectroscopy can identify the purified compounds (47).

### **C. Purification of the Bioactive Molecule**

The prepared plant extracts contains several bioactive molecules which further processed for the preparation of commercial nutraceuticals in the form of serums, tablets and other powder forms. Paper thin-layer and column chromatographic methods are used widely used because of their ease to use, economically and availability of wide range of solvents and stationary phase(48) Mostly Silica, alumina, cellulose, and polyamide materials are used for separation the phytochemicals. Plant materials extracts include combination of complex phytochemicals, which makes a good separation process difficult(44). After the isolation, identification of the bioactive compound structure is must to analyse its further usage

### **III. Structural identification of the Bioactive Molecules**

As the crude plant extracts contains several bioactive compounds along with debris which is after purification step removed, with a filtrate remaining with bioactive compounds. The filtrate further processing involves identification of constituents for the preparation of pure bioactive compounds using different spectroscopic methods such as UV-visible, Infrared (IR), Nuclear Magnetic Resonance (NMR), and mass spectroscopy. The basic principle of spectroscopy is the absorption of electromagnetic radiation by an organic molecule that produces different spectra on the basis of its structure ( bonds of the molecule), based on the spectra different constituting chemical compounds are identified. Based on the structure of different phytochemicals different spectroscopies are used

**UV-Visible Spectroscopy**

Ultraviolet-visible spectroscopy is used for the aromatic molecules present in purified plant extracts as they served as powerful chromophores absorbs the UV range(49). The natural phenolic compounds including anthocyanins, tannins, polymer dyes, and phenols form complexes with iron can be identified through ultraviolet/visible (UV-Vis) spectroscopy (34). Moreover, it also provides information about the total phenolic contents in a short time period with high sensitivity(50)

### **Infrared Spectroscopy(IR)**

Besides identification of phenolic contents, structure identification is must for furher replication and commercial production of the phytochemicals which is possible through IR spectroscopy which based on the principal of vibrational changes caused by the different bonds present in the bioactive compounds (C–C, C=C, C≡C, C–O, C=O, O–H, and N–H) have diverse vibrational frequencies (51) Fourier Transform Infrared Spectroscopy (FTIR) is a high-resolution analytical method used for the identification of the chemical constituents and reveal the structural compounds. It is rapid and non-destructive method to fingerprint herbal extracts or powders.

### **Nuclear Magnetic Resonance Spectroscopy (NMR)**

NMR method is primarily related to the magnetic properties of the nuclei that enabled to study biomolecules by identifying the differences between the various magnetic nuclei of different bioactive compounds in a mixture, and thereby providing a distinct image of nuclei positions with demonstration of atoms are present in compound.(52)

### **Mass Spectrometry (MS)**

### The bioactive molecules identified from crude extract were isolated and purified by chromatography and identification through spectroscopy which provides (53)rapid and accurate identification of chemical compounds in medicinal herbs, especially when a pure standard is unavailable (54). Another combination of Liquid chromatography and MS has been extensively used for the analysis of phenolic compounds.

**IV. COVID 19 AND BIOACTIVE COMPOUNDS**

Since the emergence of first case of COVID 19 in November 2019, in China, where it caused respiratory infection, the disease (Corona VIrus or COVID-19) spread worldwide as a nightmare pandemic across the globe and continues till today through new variants. As a result, vaccine development became a prime target which is successfully implemented as well. However, the fear is still there as it is s still affecting people through modulating it forms and appearing with different the Omicron sub-variants BA.2 and BA.2.38 in India, while the BA.4 and BA.5 sub variants are also observed in other parts of the world. Moreover, countries with lower economies with poor healthcare system are still suffering for the assess of primary treatments (51). Therefore, in addition to the existing medication system treatment strategies, there is a need of long-term immunity boosting strategies to prevent future pandemics. In this context, the ancient Ayurvedic or Unani or Chinese traditional medications can play a significant role in search of an alternative solution for COVID-19 treatment. The phytochemicals or Bioactive compounds present in traditional herbs still serving as a treatment for 80% of the world’s population for their common health issues and severe ailments as well.(56) These high potential herbs with thousands of bioactive compounds is well recognized and acknowledged by China during the initial days of COVID-19 (56). Lianhuaqingwen and Shufeng Jiedu). Countries like China, India, and South Korea showed significantly lower mortality rate in COVID cases because of their issued guidelines for there citizen on the use of traditional and herbal medicines in Initial days(57)

Several bioactive molecules, chiefly the secondary metabolites, were studied recently for the prevention of COVID-19 and SARS-CoV-2 inhibitory potential. Among the different categories of reported high potential phytochemicals against COVID-19 infection consists three major classes of plant secondary metabolites viz., terpenoids, alkaloids, and phenolics (Figure3)

**Terpanoids**

Terpenes are considered as the largest group of plant secondary metabolites (isoprene (C5H8) derivatives), which are synthesized through the isoprenoid or the mevalonate pathway with Acetyl-CoA precursor. There are different classes of terpene (hemiterpenes, monoterpenes, sesquiterpenes, diterpenes, sesterterpenes, triterpenes, tetraterpenes, and polyterpenes) on the basis of number of isoprene units present in the structure. These have great significance and therapeutic usage against several ailments (60). For instance, **Diterpenoids, isolated from** Torreya nucifera  and Ferruginol showed potential inhibition against Covid 19, where as the terpenoid derivative 22-hydroxyhopan-3-one and 6-oxoisoiguesterin along with (10-hydroxyusambarensine, cryptoquindoline were showed strong protective effect against SARS-CoV-2 (61).Tanshinones are diterpenes Salvia miltiorrhiza  (62). **Saponins isolated from** Aesculus turbinata seed that has been used as herbal medicine, have been studied (EC50 6.0 µM) (63). **Withanone derived from**  Withania somnifera(Ashwagandha), also showed promising effects against Covid19 in molecular docking (64).

Alkaloids are metabolically active,cyclic compounds with well acknowledged therapeutic, nutritional, toxicological,potential which leads to the several studies to find their effects against Covid 19([60](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9937517/#CR8)). For instance, Cepharanthine(tetrandrine ) derived from plant Stephania tetrandra showed significant effect against the SARS-CoV-2 NSP12-NSP8 (65)

Phenolics, a abundant plant secondary metabolites (8000 ) found around the globe that made its research for therapeutic potential for Covid. These are phenylalanine derivatives which are produced through the phenylpropanoid pathway. They include variety of bioactive compounds including phenols, phenolic acids, hydroxycinnamic acids, phenylacetic acids, phenylpropenes, quinones, coumarins, stilbenes, lignans, xanthones, neolignans, tannins, melanins, and flavonoids (61). The following sections discuss the phenolic constituents studied for their effectiveness to protect from COVID-19. (figure4)

The list of compounds among the mentioned terpenoids, alkaloids, and phenolics potentially effective in COVID-19(figure 5)



Figure- 4Structure of different bioactive compounds



Figure. 5Phytochemicals/Bioactive compounds with ameliorative potential against COVID 19

**V. Commonly used Indian plants with ameliorative potential against Covid 19**

Indian Ayurveda system is one of the worlds well acknowledged ancient medicinal system, consisting of remedies against chronic ailments. These remedies often consist of combination of different plant extracts enriched in bioactive compounds, the plants utilized in preparing the plant extracts also been utilized in every Indian household routine food preparation and around the globe in some traditional medicinal practices. This also explains contribution of diet in the lower mortality rate during Covid wave observed in Asian Continent as compared to rest of the world, with high health infrastructure. There are some herbs which came into limelight during pandemic and research is still continued for their therapeutic potential

*Allium sativum* L. (Garlic)

*A. sativum*  or Garlic is one of the famous ingredient of common Indian households and also known for its pungent smell, it contains diverse range of bioactive chemicals, mainly includes allicin, alliin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, ajoene, and S-allyl-cysteine. In traditional medicine garlic oil is used for muscular pains, arthritus and raw garlic for boosting metabolism, as it also generates heart burn in excess consumption its consumed in the form of pickles during winter and usage decreases during summers. There is number studies has been conducted to study the ameliorative properties of garlic extract, it showed promising results by decreasing levels of serum proteins(TNF-ɑ, ICAM-1 and immunoglobulins(IgG & IgM)), thus proven role in enhancing immunity(66). Thus, emergence of new strains of Covid 19 scientist also began to study garlic antiviral properties, explored earlier , for instance aqueous garlix extract found to be preventive against the Newcastle disease virus in embryonated chicken eggs Pre-treated with aqueous garlic extract(67).  In another study, conducted by Rasool et al., (68,)*A. sativum* also found effective against avian influenza virus H9N2 on Vero cells (69). Its also studied as immunobooster in invivo studies conducted in rodent model, showed significant decrease in inflammatory cell count, eosinophil infiltration and serum IgE modulation (70).

*Cinnamomum verum* J.Presl. (Cinnamon) or *Cinnamomum zeylanicum*Blume

Cinnamon or commonly known as dalchini in Indian households, is a major constituent of desserts as well as savoury dishes to enhance flavour, in Ayurveda system it is either consumed in powder form ( generally mixed with other herbs) or in the form of water extract for the treatment of digestive, respiratory and circulatory system related ailments. It is also used in case of joints pains, also nowadays for the obesity treatments (71). The major bioactive compounds present includes Cinnamaldehyde, eugenol, camphor, and cadinene, the plant extract can be prepared using cinnamon bark, leaf, root, and fruit, respectively. The bark extract showed immunomodulatory effects by increasing the levels of serum immunoglobulins in case of inflammation(72), Similarly in another study conducted by Joshi et al., (73) alcoholic extract of cinnamon bark found to supress the TNF-ɑ and leucocyte count in vivo. The well acknowledged immunomodulatory effects makes it’s a potential candidate for antiviral properties as well studied against Newcastle virus in chickens, the oil and powder extract of cinnamon exhibited immunostimulatory effects against the virus, In another study it is also found protective (74) against H1N1 and HSV1 viruses by significantly reducing in virus infectivity viruses (75).

Its bark extract exhibited immunomodulatory activity and significantly increased serum immunoglobulins, phagocytic index, neutrophil adhesion, and antibody titer. Procyanidine polyphenols (Type A) extracted from *C. zeylanicum* bark showed anti-inflammatory potential in edema induced by carrageenan (76). Alcoholic extract of bark suppressed intracellular release of TNF-α (murine neutrophils) and leukocytes (pleural fluid) as well as inhibition of TNF-α gene expression in lipopolysaccharide-stimulated human peripheral blood mononuclear cells (77).

*Curcuma longa* L. (Turmeric)

Curcuma longa l. or turmeric is being utilized in Indian cuisine as natural food colour, but also as a common immune boosting drink (Turmeric milk, also gaining popularity in western world as Turmeric Latte). Turmeric powder has been also used in covering minor cuts and injuries from the ancient time. The chief bioactive compound found in Turmeric is Curcumin, which is categorized under group of phenolic compounds known as curcuminoids, about hundred types of curcuminoids has been isolated and studied, out of which more then half present in turmeric alone. The plant extract of turmeric in various studies showed antiallergic effects, by significantly reducing the levels of IgE, IgG1, mMCP-1 and Th2 proteins thus proving immunomodulatory effects(78).  There are number of studies available showing anti-inflammatory effects of *C. longa* either alone or in combination (79). In case of antiviral effects, the aqueous extract found to be protective against dengue virus both invivo and invitro (80). Another study conducted by sornpet et al. , water and ethanolic crude extracts of turmeric showed positive outcomes against H5N1 through upregulating TNF-α and IFN-β mRNA expression, by inhibiting viral replication (81).

*Linum usitatissimum* L. (Flax Seed)

Flaxseed (Linum usitatissimum L.) or Alsi, has gained worldwide acknowledgment in past decade as a healthy food found beneficial in weight loss dietary programs because of its nutritional richness and high fibre content, thus it’s a rich source of bioactive compounds as well. The phenolic compounds present in flax seed showed immunomodulatory effects through significant decrease in T cells thus modulating the cell mediated immune response in studies in vivo (81). The hetropolysacchrides present in flax seed showed antiviral activity by inhibiting expression of viral antigen and also inhibiting viral replication (82).

*Nigella sativa* L. (Black Cumin)

Nigella sativa's or Black cumin or jeera, is also a prominent ingredient of Indian food preperations. It is consumed raw or in powder dry roasted form for digestive disorders in Ayurveda, nowadays it is also an ingredient of commercial herbal formulations. The main chemical composition includes different bioactive compounds present in cumin are thymoquinone, dithymoquinone, and dihydrothymoquinone. Among these, thymoquinone is the major bioactive compound. The alcohol extract of cumin seeds showed immunomodulatory effects by affecting the lymphocytes proliferation(83). The oil extract of cumin seeds has been found to exhibit anticarcinogenic effects in human alveolar basal epithelial A549 cells (84). The molecular docking studies have been observed antiviral potential of bioactive compounds of cumin extract(85).

*Ocimum sanctum* L. (Tulsi)

Ocimum sanctum or holy basil or Tulsi is a popular plant that has deeper aesthetic value, it is worshipped in Hindu religion. The usage of tulsi leafs or droplets of tulsi extract (modern formulation) is a popular common household treatment in India for cold and cough. There are several bioactive chemicals present in ocimum sanctum including, oleanolic acid, rosmarinic acid, ursolic acid eugenol, , linalool, carvacrol, β elemene, β caryophyllene, germacrene. The extract of O.sanctum has been studied invitro in HL-60 cells, where it showed significant decrease in inflammation of lung cells (85). In another study, Bhalla et al., observed immunomodulatory potential of leaf extract with reduction in number of infected liver cells with heightened immune response(86). The antiviral properties of  *Ocimum sanctum extract has been studied*  in H9N2 viruses, where significant reduction of viral multiplication was observed.

*Phyllanthus emblica* L. (Amla)

Phyllanthus emblica L or Amla or Indian gooseberry is a rich source of antioxidants, and advertised constituent of many skin, hair care products and toothpaste. It is bitter in taste when consumed raw but tastes sweeter afterwards due to reaction with salivary amylase. It is also known for high content of vitamin C. The quantification study through HPLC, the major bioactive compounds recognized are gallic acid, ascorbic acid, ellagic acid, rutin, quercetin, and catechol. The plant extract has been reported as antitoxic agent against chromium induced genotoxicity in lymphocytes by significantly increasing levels of of IL-2 and INFγ (88). It also showed immunostimulatory effects by proliferating splenocytes, reducing inflammation(85). Amla extraxt in a study conducted by Xiang et al., antiviral potential was observed HSV virus, by preventing viral penetration and replication by inhibiting gene expression of virus(86).

**VI. CONCLUSION**

Medicinal plants and their therapeutical potential has been recognized as ‘traditional medicine’ and still being used as potential remedies for several health issues in countries with low economy. Highly populated countries still recommend traditional medication as a primary method I areas where is lack of health care infrastructure. Due to their structure complexibility and enormous health benefits, the high-value plant-derived metabolites or bioactive compounds or natural products are gaining recognition among the scientific community. Besides, vaccine development, the ameliorative potential of these natural products may lead to the emergence of new traditional medication development strategies against new emerging strains of SARS-CoV-2, which can be easily available in native countries for a fast, economical and reliable treatments.

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