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

**Surbhi Bal**

**Aryan group of colleges, Rajpura, India**

**balsurbhi21@gmail.com**

**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, ailments preventive or medicinal properties. They contribute in plants colour, odour and flavour. They are present in our routine food, herbal products, dietary supplements and processed packaged food products such as cereals, protein formulations, 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 cheifly effects the chemical processes inside human 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 apects revolutionized comprising advanced analytical tools, genome mining and engineering strategies, and microbial culturing methods are answering the need for such encounters and opening up new doors of opportunities in scientific world. Consequently, growing interest in usage of natural products as preventive drugs is being fortified, in the tackling of antimicrobial resistance(5). Here, in the present chapter, recent technological developments has been summarized that are creating a new era of natural product-based drug discovery, along with highlight selected applications in recent ailments and advices about the key opportunities.

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 carcinoma progression and infectious diseases(6 ) but also for the research in other therapeutic areas, including preventive statergies for cardiovascular diseases (for example, statins) and multiple sclerosis (for instance, 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 count of [sp3 carbon atoms](https://www.nature.com/articles/s41573-020-00114-z#Glos1) and oxygen atoms but lower number of active nitrogen along with similar count of halogen atoms, higher numbers of H-bond acceptors and donors (8).These structural differences in bioactive compounds make them profitable; for instance, the higher structural 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 | Prevention of skin cancer cell progression, 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) | Promoting detoxification process 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 metastasis, metal toxicity(14) |
| Isoflavones (daidzein and genistein) | Soybeans and soy products (tofu, soy milk, edamame, etc.) | Inhibit tumor progrssion, hormones regulation and antioxidant, liver toxicity(15) |
| Isothiocyanates | Cruciferous green leafy vegetables (broccoli, cabbage, collard greens, kale, cauliflower and Brussels sprouts) | Induction of detoxification process of carcinogens, block tumor growth and acts as antioxidantive agents  (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(orange,lemons), rosemary | Prevent cancer progression, prevent inflammation and acts 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 rhizome (Ranunculaceae), barberry roots and Oregon grape root. | 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. PRACTICES USED FOR PHYTOCHEMICALS ABSTRACTION, ISOLATION, AND PURIFICATION ANALYSIS**

### **A. Abstraction of Phytochemicals Using different 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 comparable polarity to the solute will appropriately dissolve the solute. The polarity, from slightest polar to greatest polar, of a few commonly used 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 common aim of the phytochemical research, for bioactive compounds is to search most appropriate techniques that can easily screen the source material for bioactivity chief properties such as antioxidative, antibacterial, or cytotoxic, collectivly with high structural simplicity, specificity, and speed (40).



Figure 1. Phytochemicals well acknowledged effects

Figure 2. Preparation of phytochemicals/ bioactive compounds formulations

**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 comprises of combination an electrical field and a magnetic field. These are designated 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 effectiveness of the microwave extraction method such as extraction conditions including, temperature, solvent composition, and time period for extraction.

### **Ultrasonic-Assisted Extraction**

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



Figure 3. Different sources of bioactive compounds

### **B. Metods used for Isolation and Purification of Bioactive Molecules from Plants extracts**

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 extraction, separation, and purification for pure formulation preparation (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/phytochemicals compounds based on functional 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 chromatography(HPLC), electrophoresis and spectrophotometry 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 active Bioactive Molecules from crude extract**

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 of pure boctive compounds from the combination phytochemicals present in the extract. 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 including Ultraviolet-visible, Infrared (IR), Nuclear Magnetic Resonance method (NMR), and variations of mass spectroscopy. The basic principle of spectroscopy is the absorption of electromagnetic radiation by organic particles 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

**Ultraviolet(UV)-Visible Spectroscopy variation**

Ultraviolet-visible spectroscopy is one of the most widely used techniques for the aromatic molecules present in purified plant extracts as they served as dominant chromophores absorbing the UV range effectively(49). The natural phenolic compounds including different classes of anthocyanins, tannins, polymer dyes, and phenols, form strong complexes with iron can be recognized 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) method**

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 with (C–C, C=C, C≡C, C–O, C=O, O–H, and N–H) different bondings have varied vibrational frequencies (51) Fourier Transform Infrared Spectroscopy (FTIR) is a high-resolution techiques used for the identification of the chemical constituents and reveal the structural compounds. It is prompt and non-destructive method to mark herbal extracts or powders.

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

NMR method is primarily related to the magnetic properties of the nuclei that enabled to identify the active biomolecules by identifying the variances present between the several 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)speedy and precise identification of bioactive compounds present in medicinal herbs formulations, specifically when a pure standard form is unobtainable (54). Another combination of Liquid chromatography and MS has been widely utilized for the exploration studies of phenolic compounds.

**IV. COVID 19 AND BIOACTIVE COMPOUNDS**

Since the emergence of first occurence of COVID 19 case in November 2019, in China, where it caused respiratory infection, the disease (Corona VIrus or COVID-19) blow-out worldwide as a nightmare pandemic across the globe and still continuing through emergence of 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 forms including the Omicron sub-variants such as BA.2 and BA.2.38 in Asia (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, along with addition to the present medication and preventive system treatment strategies, there is a prerequisite of long-term immunity boosting strategies to combat future pandemics. In this perspective, the ancient Ayurvedic or Unani or Chinese traditional medications can play a significant role in search of an unconventional methods 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). Asian countries like China, India, and South Korea showed significantly lower mortality rate in COVID cases because of their issued guidelines for there nationals for the usage of traditional and herbal mediciations in initial days(57)

Several bioactive molecules, chiefly the secondary metabolites, were studied recently for the prevention of COVID-19 and SARS-CoV-2 preventive potential. Among the different categories of reported high potential phytochemicals with high inhibitory activity for COVID-19 infection consists three major groups 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) differentiated on the basis of presence of quantity 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 widely utilized as herbal formulation, 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). 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 metabolic pathway of phenylpropanoid synthsis. They comprises of different bioactive compounds containing classes of phenols, phenolic acids, hydroxycinnamic acids, phenylacetic acids, phenylpropenes, quinones, coumarins, stilbenes, lignans, xanthones, neolignans, tannins, melanins, and flavonoids (61). There is number of phenolic constituents studied for their ameliorative potential against COVID-19 (figure 4).

There is a long list of different compounds among the mentioned terpenoids, alkaloids, and phenolics exhibiting strong inhibitory potential against COVID-19 and its varients (figure 5).



Figure 4. Structure of different bioactive compounds structure



Figure5.Phytochemicals/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 and its derivatives, 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 pathogenic Newcastle disease virus studied in embryonated chicken eggs, pretreated with aqueous garlic extract preparation (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 mice model, showed substantial decrease in number of inflammatory cells, eosinophils infiltration and levels of serum IgE(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 mainly the cinnamaldehyde varients along with minor constituents including eugenol, camphor, and cadinene, the plant extracts commonly prepared for herbal medications involves prime usage of cinnamon barks along with, leaf, root, and fruit, respectively on the basis of its target ailment. 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 preparation of cinnamon bark powder 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 effective (74) against the H1N1 and HSV1 virus strains by significantly decreasing the virus infectivity (75).

The bark extract preparation of Cinammon showed its immunomodulatory potential through significantly increasing the quantity of serum immunoglobulins, phagocytic index, neutrophil adhesion, and antibody titer. The bioactive molecules procyanidine polyphenols (Type A), studied in  *C. zeylanicum* bark extract exhibited high anti-inflammatory potential against edema induced by carcinogens (76). Another study also confirmed the immunomodulatory potential of Cinnamon alcoholic plant extract prepared using its bark through significantly suppressing the intracellular release of TNF-α (murine neutrophils) factors and leukocytes count (pleural fluid) as well as inhibiting the expression of TNF-α gene expression in lipopolysaccharide-stimulated human peripheral blood mononuclear cells (77).

*Curcuma longa* L. (Turmeric)

Curcuma longa l. or turmeric/haldi 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 concentrations of IgE, IgG1, mMCP-1 and Th2 proteins in serum thus showing its immunomodulatory potential(78).  There are number of studies available proving the anti-inflammatory effects of *C. longa* either alone or in combinatory formulations (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 alcoholic(ethanol) crude extracts preperations 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 is a high potential source enriched with bioactive compounds. The phenolic group of 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 studied *invitro in* human alveolar basal epithelial A549 cell line (84). There are number of molecular docking studies conducted which observed the significant antiviral potential of bioactive compounds present in crude 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 compound present in ocimum sanctum extract including, different concentrations of oleanolic acid, rosmarinic acid, ursolic acid eugenol, , linalool, carvacrol, β elemene, β caryophyllene, and 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 includes high concentration of gallic acid, along with 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.* showed significant*,* antiviral potential against 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 the structure complexibility of bioactive compounds, they exhibits enormous health benefits, with high ameliorative potential of plant-derived metabolites or bioactive compounds or natural products are gaining recognition among the scientific community. Besides, vaccine development, the preventive potential of these natural bioactive products may revolutionized the 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.

**References**

1. V.Kaur,  M. Kumar,A.Kumar, K.Kaur, V.S.Dhillon, S. Kaur Pharmacotherapeutic potential of phytochemicals: Implications in cancer chemoprevention, [Biomedicine & Pharmacotherapy](https://www.sciencedirect.com/journal/biomedicine-and-pharmacotherapy), vol. 97, 2018, 564-586, https://doi.org/10.1016/j.biopha.2017.10.124
2. T. Rescigno, M.F.Tecce, A.Capasso. Protective and Restorative Effects of Nutrients and Phytochemicals. Open Biochem J. 2018 Apr 17;12:46-64. doi: 10.2174/1874091X01812010046. PMID: 29760813; PMCID: PMC5906970.
3. E. Riboli, T. Norat, Epidemiologic evidence of the protective effect of fruits and vegetables on cancer risk. *Am. J. Clin. Nutr.*;78(3)2003 Suppl.:559S–569S. doi: 10.1093/ajcn/78.3.559S.

1. J.B.,Harborne, H.Baxter, G.P. Moss.  *Phytochemical Dictionary- A Handbook of Bioactive Compounds from Plants.* Taylor & Francis; 1999.
2. Ng, C.Y.; Yen, H.; Hsiao, H.-Y.; Su, S.-C. Phytochemicals in Skin Cancer Prevention and Treatment: An Updated Review. *Int. J. Mol. Sci.*, *19*, 941. 2018<https://doi.org/10.3390/ijms19040941>
3. A.L., Harvey, R. Edrada-Ebel, R. & R.J., Quinn. The re-emergence of natural products for drug discovery in the genomics era. *Nat. Rev. Drug Discov.* **14**, 111–129 (2015).
4. M. Tintore, A., Vidal-Jordana, J & J., Sastre-Garriga,. Treatment of multiple sclerosis — success from bench to bedside. *Nat. Rev. Neurol.* **15**, 2019, 53–58 ,
5. J. Clardy & C. Walsh. Lessons from natural molecules. *Nature* **432**, 2004, 829–837.
6. A.D.G., Lawson, M., MacCoss. & J.P.,Heer, Importance of rigidity in designing small molecule drugs to tackle protein–protein interactions (PPIs) through stabilization of desired conformers. *J. Med. Chem.* **61**, 4283–4289, 2018.
7. C.J.Henrich, & J.A.Beutler. Matching the power of high throughput screening to the chemical diversity of natural products. *Nat. Prod. Rep.* **30**, 1284 ,2013
8. A.Balić , M, Mokos. Do We Utilize Our Knowledge of the Skin Protective Effects of Carotenoids Enough? Antioxidants (Basel). Jul 31;8(8):259.2019 doi: 10.3390/antiox8080259.
9. A. Ullah, S. Munir , S.L.Badshah, N.Khan, L. Ghani, B.G.,Poulson, A.H. Emwas, M. Jaremko. Important Flavonoids and Their Role as a Therapeutic Agent. Molecules. 11;25(22):5243. 2020 doi: 10.3390/molecules25225243.

13. J. Ma, R. Wang, H.Yan, R. Xu, A. Xu, J. Zhang. Protective Effects of Baicalin on Lipopolysaccharide-Induced Injury in Caenorhabditis elegans. Pharmacology. 2020;105(1-2):109-117. doi: 10.1159/000503238. Epub 2019 Oct 31..

14. S.Benvenga, H.R., Marini, A. Micali, J. Freni J, et al., Protective Effects of Myo-Inositol and Selenium on Cadmium-Induced Thyroid Toxicity in Mice. Nutrients. 2020 Apr 26;12(5):1222. doi: 10.3390/nu12051222..

15. W. Lee and S.J., Kim, Protective effects of isoflavones on alcoholic liver diseases: Computational approaches to investigate the inhibition of ALDH2 with isoflavone analogues. *Front. Mol. Biosci.* 2023 .10:1147301. doi: 10.3389/fmolb.2023.1147301

16. S.N.T., Ngo, D.B. Williams. Protective Effect of Isothiocyanates from Cruciferous Vegetables on Breast Cancer: Epidemiological and Preclinical Perspectives. Anticancer Agents Med Chem. 2021;21(11):1413-1430. doi: 10.2174/1871520620666200924104550.

17. A. B. Santhakumar,  M. Battino,  J. M. Alvarez-Suarez  Dietary polyphenols: Structures, bioavailability and protective effects against atherosclerosis, c

[Food and Chemical Toxicology](https://www.sciencedirect.com/journal/food-and-chemical-toxicology),[Volume 113](https://www.sciencedirect.com/journal/food-and-chemical-toxicology/vol/113/suppl/C), March 2018, Pages 49-65<https://doi.org/10.1016/j.fct.2018.01.022>

18. J.M., Alves-Silva, M. Zuzarte,C. Marques,L. Salgueiro,H. Girao. Protective Effects of Terpenes on the Cardiovascular System: Current Advances and Future Perspectives. Curr Med Chem. 2016;23(40):4559-4600. doi: 10.2174/0929867323666160907123559. PMID: 27604093.

19. P.Y., Zhang, B. Yu, W.J. Men, R.Y. Bai, M.Y. Chen, Z.X. Wang, T. Zeng,K. Zhou. Acetyl-α-boswellic acid and acetyl-β-boswellic acid protects against caerulein-induced pancreatitis via down-regulating MAPKs in mice. Int Immunopharmacol. 86:106682.2020

20. Y. Cen, C. Liu, X.Li, Z. Yan, M. Kuang, Y.Su, X.Pan, R.Qin,X. Liu, J. Zheng, et al.. Artesunate ameliorates severe acute pancreatitis (SAP) in rats by inhibiting expression of pro-inflammatory cytokines and Toll-like receptor 4. Int Immunopharmacol. 38:252–260. 2016

21. W.L, Pu, RY, Bai., K.,Zhou, Y.F. Peng, M.Y. Zhang, M.O.,Hottiger, W.H. Li, X.M. Gao LK.. Baicalein attenuates pancreatic inflammatory injury through regulating MAPK, STAT 3 and NF-κB activation. Int Immunopharmacol. 72:204–210. 2019.

22. J. Zhen, W. Chen, Y. Liu, X. Zang. Baicalin protects against acute pancreatitis involving JNK signaling pathway via regulating miR-15a. Am J Chin Med. 49(1):147–161.2021

23. S.B.,Choi, G.S.,Bae, Jo IJ, H.J.Song, S.J. Park SJ.Effects of berberine on acute necrotizing pancreatitis and associated lung injury. Pancreas. 46(8):1046–1055.2017

24. S.Bansod, S. Chilvery , M.A.Saifi,T.J. Das,H. Tag, C. Godugu. Borneol protects against cerulein-induced oxidative stress and inflammation in acute pancreatitis mice model. Environ Toxicol. 36(4):530–539.2021.

25. A.Tarasiuk,J. Fichna.Effectiveness and therapeutic value of phytochemicals in acute pancreatitis: a review. Pancreatology. 19(4):481–487.2019

26. P. Anchi, A. Khurana,S. Bale , C. Godugu C. The role of plant-derived products in pancreatitis: experimental and clinical evidence. Phytother Res. 31(4):591–623.2017.

27. P. Siriviriyakul, T. Chingchit, N. Klaikeaw, M.Chayanupatkul,D. Werawatganon. Effects of curcumin on oxidative stress, inflammation and apoptosis in l-arginine induced acute pancreatitis in mice. Heliyon. 5(8):e02222. 2019

28. X. Liang, C. Hu ,C. Liu, K, Yu, J. Zhang J, Jia Y. Dihydrokaempferol (DHK) ameliorates severe acute pancreatitis (SAP) via Keap1/Nrf2 pathway. Life Sci. 261:118340. 2020

29. E.E. Yılmaz, Z. Bozdağ, I. Ibiloğlu, Z., Arıkanoğlu, U.C. Yazgan, I. Kaplan,M. Gümüş, S.S Atamanal. Therapeutic effects of ellagic acid on l-arginin induced acute pancreatitis. Acta Cir Bras. 31(6):396–401. 2016

30. X. Liu,Q Zhu,M Zhang,T Yin, R. Xu, W Xiao, Wu J, Deng B, Gao X, Gong W, et al.. Isoliquiritigenin ameliorates acute pancreatitis in mice via inhibition of oxidative stress and modulation of the Nrf2/HO-1 pathway. Oxid Med Cell Longev. 2018:7161592. 2018

31. Z. Zhang, Q, Liu, H. Zang,Q Shao,T Sun T. Oxymatrine protects against l-arginine-induced acute pancreatitis and intestine injury involving Th1/Th17 cytokines and MAPK/NF-κB signalling. Pharm Biol. 57(1):595–603,2019

32. B. Sheng, L.Zhao,X. Zang, J.Zhen,Y. Liu, W. Bian, W. Chen W.Quercetin inhibits caerulein-induced acute pancreatitis through regulating miR-216b by targeting MAP2K6 and NEAT1. Inflammopharmacology. 29(2):549–559.2021

33. F.F., Abreu, A.C.,Souza, S.A.,Teixeira SA, Soares AG, Teixeira DF, Soares RC, Santana MT, Lauton Santos S, Costa SK, Muscara MN, et al.. 2. Elucidating the role of oxidative stress in the therapeutic effect of rutin on experimental acute pancreatitis. Free Radic Res. 50(12):1350–1360.2016

34. P.Feng, Y. Xu, B.Tong, X.Tong, Y. Bian, S. Zhao, H. Shen H. Saikosaponin a attenuates hyperlipidemic pancreatitis in rats via the PPAR-gamma/NF-kappaB signaling pathway. Exp Ther Med. 19:1203–1212.2019

35.L. Chen, Y.Chen, H. Yun, Z. Jianli. Tetramethylpyrazine (TMP) protects rats against acute pancreatitis through NF-κB pathway. Bioengineered. 10(1):172–181. 2019.

36. W. Chen, C. Yuan, Y. Lu, Q. Zhu Q, X.Ma, W Xiao, et al.. 2020. Tanshinone IIA protects against acute pancreatitis in mice by inhibiting oxidative stress via the Nrf2/ROS pathway. Oxid Med Cell Longev. 2020:5390482. 2020.

37.L. P. Pasari, A. Khurana, P. Anchi, M, Aslam Saifi, S. Annaldas, C. Godugu C.Visnagin attenuates acute pancreatitis via Nrf2/NFκB pathway and abrogates associated multiple organ dysfunction. Biomed Pharmacother. 112:108629. 2019.

38.V.L.Tiruveedi,S. Bale. A, Khurana, C. Godugu C. Withaferin A, a novel compound of Indian ginseng (Withania somnifera), ameliorates cerulein-induced acute pancreatitis: possible role of oxidative stress and inflammation. Phytother Res. 32(12):2586–2596. (2018).

39.A. Altemimi, D.A.,Lightfoot, M. Kinsel, D.G. Watson. Employing response surface methodology for the optimization of ultrasound assisted extraction of lutein and β-carotene from spinach. Molecules. 2015;20:6611–6625. doi: 10.3390/molecules20046611.

40.S. M, Tsubaki, Sakamoto, J. Azuma. Microwave-assisted extraction of phenolic compounds from tea residues under autohydrolytic conditions. *Food Chem.*2000;123:1255–1258. doi: 10.1016/j.foodchem.2010.05.088.

41.O.J., Williams, G.S.V., Raghavan, V. Orsat,J. Dai., Microwave-assisted extraction of capsaicinoids from capsicum fruit. *J. Food Biochem.*2004;28:113–122. doi: 10.1111/j.1745-4514.2004.tb00059.x

42.R. Tabaraki, A., Nateghi A. Optimization of ultrasonic-assisted extraction of natural antioxidants from rice bran using response surface methodology. *Ultrason. Sonochem.*2011;18:1279–1286. doi: 10.1016/j.ultsonch.2011.05.004.

43.A., Altemimi., D.A, Lightfoot., M. Kinsel, D.G.. Employing response surface methodology for the optimization of ultrasound assisted extraction of lutein and β-carotene from spinach. *Molecules.*2015;20:6611–6625. doi: 10.3390/molecules20046611.

44.H. Sarajlija,N., Čkelj, D., Novotni, G., Mršić., M., Ćurić, M., Brncic , D, CuriC. Preparation of flaxseed for lignan determination by gas chromatography-mass spectrometry method. *Czech J. Food Sci.*2012;30:45–52.

45. I.E.,Popova, C., Hal, A., Kubátová. Determination of lignans in flaxseed using liquid chromatography with time-of-flight mass spectrometry. *J. Chromatogr. A.*2009;1216:217–229. doi: 10.1016/j.chroma.2008.11.063.

46. Z., Zhang, X. Pang, D.Xuewu, Z., Ji., Y. Jiang. Role of peroxidase in anthocyanin degradation in litchi fruit pericarp. *Food Chem.*2005;90:47–52. doi: 10.1016/j.foodchem.2004.03.023

47. M., Urbano, M.D., Luque de Castro, P.M., Pérez, J., García-Olmo, M.A., Gómez-Nieto Ultraviolet–visible spectroscopy and pattern recognition methods for differentiation and classification of wines. *Food Chem.*2006;97:166–175. doi: 10.1016/j.foodchem.2005.05.001.

48.W. Kemp.  *Organic Spectroscopy.* Macmillan Press Ltd.; London, UK: 1991. Infrared spectroscopy; pp. 19–56.

49. W. Kemp. Energy and electromagnetic spectrum. In: Kemp W., editor. *Organic Spectroscopy.* Macmillan Press; London, UK: 1991. pp. 1–7.

50.A., Cherkaoui, J. Hibbs, S., Emonet, M.,Tangomo M., Girard M., Francois P., Schrenzel J. Comparison of two matrix-assisted laser desorption ionization-time of flight mass spectrometry methods with conventional phenotypic identification for routine identification of bacteria to the species level. *J. Clin. Microbiol.*2010;48:1169–1175. doi: 10.1128/JCM.01881-09.

51.H.D.Beckey   *4–Qualitative Analyses with the Fi Mass Spectrometer.* Pergamon; Bergama, Turkey:

52.S.R.Jeon., J. Kang J. W., Ang L., Lee H. W., Lee M. S., Kim T. H. Complementary and alternative medicine (CAM) interventions for COVID-19: An overview of systematic reviews. *Integr. Med. Res.*2022;11:1–9. doi: 10.1016/j.imr.2022.100842.

53. S., Ahmad, S. Zahiruddin, B. Parveen, P. Basist, A. Parveen, R Gaurav, M, Ahmad. Indian medicinal plants and formulations and their potential against COVID-19 – preclinical and clinical research. *Front. Pharmacol.*2021;11:1–34. doi: 10.3389/fphar.2020.578970.

54. K., Xu,H. Cai, Y. Shen, Q., Ni., Y., Chen, Hu S., Li J., Wang H., Yu L., et al. Management of corona virus disease-19 (COVID-19): The Zhejiang Experience. *J. Zhejiang. Univ. Med. Sci.*2020;49:147–157. doi: 10.3785/j.issn.1008-9292.2020.02.02.

55. H., Lu. Drug treatment options for the 2019-new coronavirus (2019-nCoV) *Biosci. Trends.*2020;14:69–71. doi: 10.5582/bst.2020.01020.

56. Y., Jin. H., Cai L., Cheng Z. S., Cheng H., Deng T., Fan Y. P., et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (19-nCoV) infected pneumonia (standard version) *Mil. Med. Res.*2020;7:1–23. doi: 10.1186/s40779-020-0233-6.

57. D.,Sruthi and C., Jayabaskaran, C. in Biotechnological Approaches to Enhance Plant Secondary Metabolites: Recent Trends and Future Prospects (Shahnawaz, M., ed.) CRC Press, Taylor & Francis, FL., pp. 1-17.2021

58.J., Huang, G., Tao, Liu J., Cai J., Huang Z., Chen J. X. Current prevention of COVID-19: Natural products and herbal medicine. *Front. Pharmacol.*2020;11:1–18. doi: 10.3389/fphar.2020.588508.

59. B., Benarba, A., Pandiella. Medicinal plants as sources of active molecules against COVID-19. *Front. Pharmacol.*2020;11:1–16. doi: 10.3389/fphar.2020.01189.

60. J.Y., Park J., Kim., H., Kim Y. M., Jeong H. J., Kim D. W., Park K. H., et al. Tanshinones as selective and slow-binding inhibitors for SARS-CoV cysteine proteases. *Bioorg. Med. Chem.*2012;20:5928–5935. doi: 10.1016/j.bmc.2012.07.038.

61. C.Y., Wu, Jan J. T., Ma S. H., Kuo C. J., Juan H. F., Cheng Y. S. E., et al. Small molecules targeting severe acute respiratory syndrome human coronavirus. *Proc. Natl. Acad. Sci. USA.*2004;101:10012–10017. doi: 10.1073/pnas.0403596101.

62. Z.,Ruan, C.,Liu,Y., Guo Y., He Z., Huang X., Jia X., et al. SARS-CoV-2 and SARS-CoV: virtual screening of potential inhibitors targeting RNA-dependent RNA polymerase activity (NSP12) *J. Med. Virol.*2020;93:389–400. doi: 10.1002/jmv.26222.

63.,R., Kamel, and N. A.,El-Shinnawy, N. A. Immunomodulatory effect of garlic oil extract on Schistosoma mansoni infected mice. *Asian Pac. J. Trop. Med.* 8 (12), 999–1005. 2015., doi:10.1016/j.apjtm.2015.11.016

64.T., Arify, S.,Jaisree, K., Manimaran,S., Valavan, and A.Sundaresan. Antiviral effects of garlic (allium sativum) and nilavembu (andrographis paniculata) against velogenic strain of newcastle disease virus- an in ovo study. *Int. J. Livest. Res.* 8 (5), 157.2018. doi:10.5455/ijlr.20170814051902

65.M., Rasool, and P., Varalakshmi, P. Immunomodulatory role of Withania somnifera root powder on experimental induced inflammation: an *in vivo* and *in vitro* study. *Vasc. Pharmacol.*44 (6), 406–410. 2006.,doi:10.1016/j.vph.2006.01.015

66. C.C.,.Hsieh, W.H. Peng, H.H.,Tseng, Liang, S. Y., Chen, L. J., and Tsai, J. C. .The protective role of garlic on allergen-induced airway inflammation in mice. *Am. J. Chin. Med.* 47 (5), 1099–1112. 2019.,doi:10.1142/S0192415X19500563

67. A. Brochot, A., Guilbot, L.,Haddioui., and C., Roques, C. . Antibacterial, antifungal, and antiviral effects of three essential oil blends. *Microbiologyopen* 6 (4), 2017., e00459. doi:10.1002/mbo3.459

68.S.,Vetal, S.L.Bodhankar,V., Mohan, and P.A., Thakurdesai. Anti-inflammatory and anti-arthritic activity of type-A procyanidine polyphenols from bark of Cinnamomum zeylanicum in rats. *Food Sci. Hum. Wellness* 2 (2), 59–67. 2013. doi:10.1016/j.fshw.2013.03.003

69. S.R.,Niphade, M., Asad, G.K., Chandrakala, E., Toppo, and P., Deshmukh, P. Immunomodulatory activity of Cinnamomum zeylanicum bark. *Pharm. Biol.* 47 (12), 2009, 1168–1173. doi:10.3109/13880200903019234

70. K., Joshi, S., Awte, P., Bhatnagar, S., Walunj, R., Gupta, S., Joshi, et al. Cinnamomum zeylanicum extract inhibits proinflammatory cytokine TNFµ: *in vitro* and *in vivo* studies. *Res. Pharmaceut. Biotechnol.* 2, 014–021. 2010., doi:10.5897/RPB.9000004

71.R., Mustafa, and E., Blumenthal. Immunomodulatory effects of turmeric: proliferation of spleen cells in mice. *J. Immunoassay Immunochem.* 38 (2), 140–146. 2017. doi:10.1080/15321819.2016.1227835

72.M.Ichsyani, A., Ridhanya, M., Risanti, H., Desti, R., Ceria,, D.H., Putri, et al. Antiviral effects of Curcuma longa L. against dengue virus *in vitro* and *in vivo*. *IOP Conf. Ser. Earth Environ. Sci.*101, 012005. 2017., doi:10.1088/1755-1315/101/1/012005

73. B., Sornpet, T., Potha, Y., Tragoolpua, and K., Pringproa, Antiviral activity of five Asian medicinal pant crude extracts against highly pathogenic H5N1 avian influenza virus. *Asian Pac. J. Trop. Med.* 10 (9), 871–876. 2017., doi:10.1016/j.apjtm.2017.08.010

74. H.S., Shin, H.J., See, S.Y., Jung,., D.W,Choi, D.A., Kwon, M.J., Bae, et al. Turmeric (Curcuma longa) attenuates food allergy symptoms by regulating type 1/type 2 helper T cells (Th1/Th2) balance in a mouse model of food allergy. *J. Ethnopharmacol.* 175, 21–29. 2015doi:10.1016/j.jep.2015.08.038

75. S.Y.,Lee, S.S., Cho, Y.C., Li, C.S., Bae, K.M., Park, and D.H., Park, Anti-inflammatory effect of curcuma longa and allium hookeri Co-treatment via NF-κB and COX-2 pathways. *Sci. Rep.* 10 (1), 5718. 2020. doi:10.1038/s41598-020-62749-7

76. S., Liang, X., Li, X., Ma, A., Li, Y., Wang, M.J.T., Reaney, et al. A flaxseed heteropolysaccharide stimulates immune responses and inhibits hepatitis B virus. *Int. J. Biol. Macromol.* 136, 230–240.2019. doi:10.1016/j.ijbiomac.2019.06.076

77.A.H., Palla, N.A.,Khan, S.,. Bashir, N., Ur-Rehman, J., Iqbal, and A.H., Gilani, A. H. Pharmacological basis for the medicinal use of Linum usitatissimum (Flaxseed) in infectious and non-infectious diarrhea. *J. Ethnopharmacol.* 160, 61–68. 2015. doi:10.1016/j.jep.2014.11.030

78.D.M., Kasote, A.A., Zanwar, S.T., Devkar, M.V., Hegde,and K.K Deshmukh, Immunomodulatory activity of ether insoluble phenolic components of n-butanol fraction (EPC-BF) of flaxseed in rat. *Asian Pac. J. Trop. Biomed.* 2 (2), 2012., S623–S626. doi:10.1016/S2221-1691(12)60285-8

79. B.Salim, and M., Noureddine, M.. Identification of compounds from nigella sativa as new potential inhibitors of 2019 novel coronasvirus (Covid-19): molecular docking study. 2020. chemRxiv:10.26434/chemrxiv.12055716.v1.

80.A.A.,Alshatwi, . Bioactivity-guided identification to delineate the immunomodulatory effects of methanolic extract of Nigella sativa seed on human peripheral blood mononuclear cells. *Chin. J. Integr. Med.* (Epub ahead of print). 2014,doi:10.1007/s11655-013-1534-3

81.A.E., Koshak, N., Yousif, B.L., Fiebich, E.A.,, Koshak, and M. Heinrich, M. Comparative immunomodulatory activity of Nigella sativa L. preparations on proinflammatory mediators: a focus on asthma. *Front. Pharmacol.* 9, 2018., 1075. doi:10.3389/fphar.2018.01075

82 S.,Ghoke, R. Sood, N. Kumar, A.K., Pateriya, S., Bhatia, A. Mishra, A., Evaluation of antiviral activity of Ocimum sanctum and Acacia arabica leaves extracts against H9N2 virus using embryonated chicken egg model. *BMC Complementary Altern. Med.* 18 (1), 2018, 174. doi:10.1186/s12906-018-2238-1

83. G.,Bhalla, S. Kaur,J. R. Kaur, and P. Raina, P. Antileishmanial and immunomodulatory potential of Ocimum sanctum Linn. and Cocos nucifera Linn. in murine visceral leishmaniasis. *J. Parasit. Dis.* 41 (1), 2017, 76–85. doi:10.1007/s12639-016-0753-x

84.K.Soni, T. Lawal, S. Wicks,U. Patel, and G. Mahady. Boswellia serrata and Ocimum sanctum extracts reduce inflammation in an ova-induced asthma model of BALB/c mice. *Planta Med.* 81 (11), 2015 B4.. doi:10.1055/s-0035-1556201

85.S.K.,Bandyopadhyay, A. Chatterjee, A., and S.Chattopadhyay, S Biphasic effect of Phyllanthus emblica L. extract on NSAID-induced ulcer: an antioxidative trail weaved with immunomodulatory effect. *Evidence Based Complementary Altern. Med.* 2011, 1–13. 2011, doi:10.1155/2011/146808

86. Y., Xiang, Y., Pei, C. Qu, Lai, Z., Ren, Z., Yang, K., et al.  *In vitro* anti-herpes simplex virus activity of 1,2,4,6-tetra-O-galloyl- β-D-glucose from Phyllanthus emblica L. (Euphorbiaceae). *Phyther. Res* 25 (7), 2011, 975–982..doi:10.1002/ptr.3368