ISSN: 2249- 5746
International Journal of Ayurvedic and Herbal Medicine 11:2 (2021) 3954–3996
Journal homepage: http://www.interscience.org.uk
DOI:10.31142/ijahm/v11i2.01
Impact Factor: 6.012

The Potential of Ayurvedic Medicinal Plants for Prevention and Therapeutic Treatment of Covid-19: A Review Article

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ABSTRACT: A number of pneumonia cases associated with 2019 novel coronavirus known as Covid-19 occurred in China in December 2019 and WHO declared that the coronavirus diseases as a pandemic in March 2020. The worldwide pandemic of Covid-19 affects people's health and health-related quality of life and has created a panic situation in human beings.Many researcheshave been carried out and are going to find the exact medicine to control the spread of this virus. However, there is no approved drug available today for curative treatment of this virus. Indian traditional medical science, Ayurveda, use medicinal plants or herbs known as Ayurvedic medicinal plants (AMPs) to healing illness.AMPs have several single herbs and compound medicines which care fever and respiratory diseases for many centuries. Based on our knowledge, we compile information from Handbook of AMPs and several databases which describe the potential of AMPs for prevention and therapeutic treatment of Covid-19. A total of 50 AMPs were identified as very likely to cure Covid-19 symptoms. The AMPs are well known as sources of bioactive secondary metabolites and have antioxidant, immunomodulatory, antipyretic and antiviral activities. Thiscompilation provides beneficial directionsto explore further application of AMPs in Covid-19 and other corona virus diseases prevention and therapy.

KEYWORDS: Ayurvedic medicinal plants, prevention, therapeutic, Covid-19

1. INTRODUCTION

On 31 December 2019, a novel coronavirus was eventually identified and Wuhan Municipal Health Commission reported a cluster of cases of pneumonia in Wuhan, Hubei Province of China.[1] The outbreak was declared a Public Health Emergency of International Concern on 5 January 2020. Then, WHO declared that the coronavirus diseases as a pandemic on 11 March 2020. Director General of WHO stated that "we have therefore made the assessment that Covid-19 can be characterized as a pandemic."[2] The Covid-19 pandemic, also known as the coronavirus pandemic, is an ongoing pandemic of coronavirus disease 2019 (Covid-19) caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2).[3] The coronavirus disease (Covid-19) is an infectious disease caused by a newly discovered coronavirus. The Covid-19 has much secret, continues to spread and mutate that cannot be concluded until now. This new virus is very contagious and has quickly spread globally. In one year, as of 31 December 2020, more than 83.2_million cases have been confirmed, with more than 1.8_million deaths attributed to Covid-19.[4] WHO stated, at a special meeting of

WHO leaders, that one in ten people around the world may have been infected with Covid-19.

In early January 2020, the first genome sequence of SARS-CoV-2 - the virus that causes Covid-19 - was published. The SARS-CoV-2 genome is a single-stranded positive-sense RNA of roughly 30,000 nucleotides, the A, T, C, and Gs of the genetic code.[5] Based on the finding, scientists have been worked hard to find out an effective vaccine[6] and screen a potential drug[7] to treat the virus disease. Moreover, WHO welcomes innovations around the world including repurposing drugs, traditional medicines and developing new therapies in the search for potential treatments for Covid-19. WHO recognizes that traditional, complementary and alternative medicines have many benefits and some countries such as India, China, and ASEAN counties have a long history of traditional medicines and practitioners that play an important role in providing care to societies. Ayurveda, the "science of life," or longevity, is the holistic alternative science from India, and is more than 5,000 years old.[8] Herbs or medicinal plants represent the most effective Ayurvedic approach to healing illness. Ayurvedic medicinal plants (AMPs) have several single herbs and compound medicines which care fever and respiratory diseases for many centuries in many countries in the world, especially in the South East Asia region. AMPs can manage many diseases by its preventive, curative and rehabilitative, as well as personalized medicines. There is a huge possibility to utilize AMPs for prevention and treatment of Covid-19.[9] However, a major drawback is lack of an adequate modern scientific basis. This work will compile the potential of Ayurvedic medicinal plants for Covid-19 prevention and therapeutics. This compilation will be helpful in the early development of new drugs for combat Covid-19.

2. METHODOLOGY

Based on the most common symptoms of Covid-19, we analyzed and identified traditional medicinal plants listed in Handbook of Ayurvedic Medicinal Plants (AMPs). The book describes 250 medicinal plants which are used for herbal medicines and there are about 60 medicinal plants indicated to have the virus symptoms. The scientific data of the selected plants were then searched and collected from the most authenticated and scientifically sound sources such as Google Scholar, databases include PubMed, Scopus, Research Gate, Science Direct, SciFinder, and Web of knowledge for the search terms: Covid-19 prevention and therapeutic, chemical constituents and biological activities including antioxidant activities, immunomodulatory properties, antipyretic properties and antiviral activities for the 60 selected plants. More than 300 scientific papers have been analyzed and finally we present 50 AMPs which has potential for prevention and therapeutic Covid-19 in this paper.

3. RESULTS AND DISCUSSION

3.1 Covid-19 and drug formulation: a hypothesis

Covid-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[10,11] They are spherical to pleomorphic particles, measuring between 80 and 160 nm in length. This SARS-CoV-2 isolate belong to the *β-coronavirus* genus of the Coronaviradae family which is common found in animals, either from bats, mice or domestic animals. Based on the genetic material and evolutionary evidences of the Covid-19, scientists who have studied the virus agree that it evolved naturally and transferred into humans from an animal, most likely a bat. The genome of SARS-CoV-2 has been sequenced and is similar to that of other bat coronaviruses. The virus is an enveloped single-stranded RNA virus containing a 30 kb genome (29891 nucleotides) encoding 9860 amino acids with 14 open reading frames including four major viral structure proteins: spike (S), membrane (M), envelope (E) and nucleocapsid (N) proteins.[12,13,14,15,16] One of the key features that makes SARS-CoV-2 different from the other coronaviruses is a particular "spike" protein that binds well with another protein on the outside of human cells called angiotensin-converting enzyme-2 (ACE2).[17] This enables the virus to hook into and infect a variety of human cells.

The Covid-19 is caused by a multiplicity of factors and affects different people in different ways, leading to both visible and invisible symptoms. According to WHO most infected people will develop mild to moderate illness and recover without hospitalization. The most common symptoms are fever, dry cough, and tiredness. Less common symptoms include aches and pains, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell, and a rash on skin, or discoloration of fingers or toes. The serious symptoms are difficulty breathing or shortness of breath, chest pain or pressure, and loss of speech or movement.[1]

The latest, scientists found evidences that the Covid-19 has been mutated. A mutation just means a difference, a letter change in the genome. This single character change in the viral genome - termed D614G - has been shown to increase virus infectivity in cells grown in the lab, though with no measurable impact on disease severity.[18] Although this mutation is also near systematically found with three other mutations, and all four are now found in about 80% of sequenced SARS-CoV-2 making it the most frequent set of mutations in circulation. This mutation might mean something, or it might not. The different SARS-CoV-2 strains have not yet had a major impact on the course of the pandemic - but they might in future.[19]It is a possibility that the virus will acquire mutations that changes its susceptibility to antibodies and immunity.

SARS-CoV-2 impacts the human body well beyond the lungs and shows a complex interplay with the human host that is not always correlated with its entry receptor (ACE2) expression levels.[20] In addition to pneumonia and damage to the whole immune system, COVID-19 may also result in injury to the vital organs such as heart, liver, kidney and even eye, as well as in the central nervous system and gastrointestinal tract. Many studies identified viral components (RNA, proteins) of SARS-CoV-2 in multiple organs (pharynx, trachea, lungs, blood, heart, vessels, intestines, brain, male genitals and kidneys) and body fluids (mucus, saliva, urine, cerebrospinal fluid, semen and breast milk).[20] Based on the multiple factors and complex mechanism of SARS-CoV-2 in infection human body, we hypothesis that "there is no single compound as a drug which can be used to handle the virus infection. A combination compounds is needed as a medicine to deal with Covid-19 and plants provide it." A combination of medicinal plants or herbs may act on multiple targets at the same time to provide thorough relief.This argument is supported by research findings stated that early triple antiviral therapy was safe and superior to lopinavir-ritonavir alone in alleviating symptoms and shortening the duration of viral shedding and hospital stay in patients with mild to moderate Covid-19.[7]

3.2 Scientific Evidences of Ayurvedic Medicinal Plants

Plants have been an important source of medicines for thousands of years. There is no doubt that traditional medicinal plants have a contribution to social health. Even today, the World Health Organization (WHO) estimates that up to 80 percent of people still rely mainly on traditional remedies such as herbs for their medicines. Clinical symptom-based traditional medicine practices could be beneficial to treat and prevent the infection. Ayurveda is the most ancient and applied medical doctrine of human civilization. Ayurvedic system of medicine based on medicinal plants possesses a wealth of single drug and formulations for treating various disorders. This is because of traditional medicinal plants are rich in biologically active secondary metabolites that can be used to treat various diseases, including diseases caused by viruses. Although biologists agree that herbs cannot interfere with the human gene to kill virus, they show efficacy in antiviral to reduce the harm of flu. Based on the pathophysiology and treatment of novel corona virus diseases, it has been concluded that the effective line of treatment can be the drugs having antioxidant, antiviral, immunomodulatory and antipyretic properties.[21] In classical treatise of Ayurvedic medicinal plants is mentioned a number of plants having antioxidant, immunomodulatory, antipyretic and antiviral activities. The pharmacological activities of these plants have been investigated on modern science parameters and promising results were reported. We identified fifty of Ayurvedic medicinal plants having potential for prevention and therapeutic management of various viral infections and probably Covid-19.

(1) *Abies spectabilis*

The dried leaves are useful in cases of cough, phthisis, asthma, chronic bronchitis, and catarrh of the bladder, and other pulmonary affections.[22] The plant contains bioactive components including proanthocyanidins, gallocatechin derivatives, procyanindin B1 prodelphynidin-gallocatechin polymers, prodelphynidin B4, cyclograndisolide and trans-docosanil ferulate.[23] The methanolic extract of the plant has antioxidant activity with IC_{50} value of 4.13 μg/ml, 0.20 μg/ml eq. resorcinol, 4.22 mM eq. Trolox, 3.9 μg/g eq. gallic acid in the DPPH, BR, TEAC and Folin-Ciocalteau tests, respectively.[23] The methanolic extract of *A. spectabilis* showed strong anti-influenza viral activity with IC_{50} value of 17 μg/ml and CC_{50} cytotoxicity value of >100 μg/ml.[24]

(2) *Aegle marmelos*

A decoction of the leaves is a febrifuge and expectorant; it is particularly used for asthmatic complaints. Decoction of the root bark is used in intermittent fevers.[22]*A. marmelos* contains various bioactive compounds including steroid, terpinoids, alkaloids, saponins, tannis, lignin, flavonoids,[25] aegeline, aegelenine, aegelinosides, marmelin, marmelosin, malondialdehyde, anhydromarmeline, marmelide, umbelliferone β-D-galactopyranoside, lupeol, halfordinol, butyl p-tolyl sulfide, 6-methyl-4-chromanone, butylated hydroxyanisole, imperatoin, xanthorrhizol, xanthoarnol, 1-hydroxy-5,7-dimethoxy-2-naphthalene-carboxaldehyde, 1-methyl- 2-(3'-methyl-but-2'-enyloxy)-anthraquinone.[26]

The IC_{50} value of antioxidant activity is in ranges of 37.11±3.50 to 158.99±59.46 μg/ml and 35.02±8.10 to 283.06 ± 135.80μg/ml for aqueous and ethanolic plant extracts, respectively,[25]while antioxidant activities of methanol, ethanol, water leaves extracts are 81 ± 2.064, 87 ± 1.00, and 93 ± 0.57μg/ml by DPPH radical scavenging method, respectively.[27] The IC_{50} efication value of pure compound marmelide is 62.5μg/mL against human coxsackie viruses B1-B6.[28] The antipyretic property of the plant on Brewer's yeast induced pyrexia in albino rats. The ethanolic extract, at dose of 200mg/kg body weight and 400 mg/kg body weight, produced significant reduction in elevated body temperature in a dose dependent manner.[29]This antipyretic effect of extracts is comparable to that of paracetamol (100 mg/kg body weight).

(3) *Allium cepa*

The *A. cepa* bulb is a stimulant, diuretic and expectorant. Its decoction is given in cough and stranguary.[22]*A. cepa* or anion has been found to contain quercetin, fructose, quercetin-3-glucoside, isorhamnetin-4-glucoside, xylose, galactose, glucose, mannose, organosulfur compounds, allylsulfides, flavonoids, flavenols, S-alk(en)yl cysteine sulfoxides, cycloalliin, selenium, thiosulfinates, and sulfur and seleno compounds.[30,31]The total phenolic content, flavonoid content and IC_{50} value of antioxidant activity of anionextract are found to be 39.3±0.09 mg GAE/g, 8.6±0.12 mg QE/g and 915 μg/mL, respectively,[32]whereas, the IC_{50} value of garlic essential oil are reported to be 0.5 mg/ml.[33]Onion is natural sources which are known to possess antiviral properties.[34] Organosulfur compounds like quercetin and allicin are associated with inhibition of viral infection. These chemicals can hinder virus attachment to host cell, alter transcription and translation of viral genome in host cell and also affect viral assembly. Quercetin can affect entry and attachment of enterovirus and influenza virus on host cell. This compound also has ability to inhibit RNA polymerase which is necessary for viral replication. Quercetin also inhibit process by which virus alter signalling pathway in host cell.

(4) *Allium sativum*

It is very useful in pulmonary phthisis, bronchiectasis gangrene of the lung and whooping cough.[22]A. sativum are reported to contain hundreds of phytochemicals including sulfur-containing compounds such as ajoenes (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyldithiins (2-vinyl-(4H) -1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), sulfides (diallyl disulfide, diallyl trisulfide, alliin, S-propyl-cysteine-sulfoxide, S-methyl cysteine-sulfoxide, S-alk(en)yl-l-cysteine sulfoxides, N-acetylcysteine, S-allyl-cysteine, S-ally-mercapto cysteine which are derived from alliin and others.[35] The frequent garlic intake promotes internal antioxidant activities

and reduces oxidative adverse effects either by increasing the endogenous antioxidant synthesis or reducing the production of oxidizers such as oxygen-free radical species.[36]

Garlic was found to be able to maintain the immune system homeostasis and to exhibit beneficial effects on immune cells especially through regulation of proliferation and cytokine gene expression.[37] The antiviral activity of garlic extracts has been evaluated against influenza B, human rhinovirustype 2, human cytomegalovirus (HCMV), Parainfluenza virus type 3, herpes simplex type 1 and 2,vaccinia virus, and vesicular stomatitis virus.[38] Organosulfur compounds like allicin, diallyl trisulfide and ajoene are main chemicals which impart antiviral property to garlic. It is known that allicin can pass through phospholipid membrane of cell and can further contribute in inhibiting viral multiplication.[38]

(5) *Aloe vera*

The Ayurvedic drug known as "kumara asava" is useful in general debility, cough, asthma, consumption, piles, epilepsy and colic.[22]*A. vera* contains 200 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids, which are responsible for the multifunctional activities.[39,40,41]

Ethanol extract of *A. vera* contains total phenolic content of 62.37 ± 1.34 mg gallic acid/kg, flavonoid content of 20.83 ± 0.77 mg/kg), and exhibited DPPH scavenging activity of 85.01 ± 0.52%.[42] Several ingredients in *A. vera* gel show to be effective antiviral agent. Acemannan reduces herpes simplex infection in two cultured target cell lines.[43] Lectins, fractions of *A. vera*gel, directly inhibite the cytomegalo virus proliferation in cell culture. A purified sample of *Aleo emodin* is effective against infectivity of herpes simplex virus type I and type II and it is capable of inactivating all of the viruses, including varicella zoster virus, influenza virus, and pseudo-rabies virus.[44] The anthraquinone aloin also inactivates various enveloped viruses such as herpes simplex, varicella zoster and influenza.[45] Moreover, the *A. vera* gel polysaccharide can boost the working of the macrophages in the intestines allowing the immune system to improving the activity of T-Lymphocytes by up to 50 per cent for penetrate the bad bacteria, viruses, tumor cells and various pathogens.[46,47]

(6) *Alstonia scholaris*

It is considered a good substitute for cinchona and quinine for the treatment of intermittent and remittent fevers.[22] The phytochemical screening revealed the presence of tannins, proteins, phenols and steroids in aqueous extracts of both leaf and bark of the plant.[48] The aqueous extracts of bark and leaf have antioxidant activity with IC_{50} value of 1.21 μg/mL and 2.83 μg/mL in the DPPH assay and 210 μg/mL and 523 μg/mL in the ABTS assay.[48] Alstotides show anti-viral and cell-permeable to inhibit the early phase of infectious bronchitis virus and dengue infection, in addition to their ability to inhibit-amylase.[49] The total alkaloids (TA) exhibite anti-inflammatory properties in acute respiratory disease which suggests their possible anti-inflammatory effect on influenza virus infection.[50] TA also significantly inhibite viral replication in A549 cells and U937-derived macrophages, markedly reduce cytokine and chemokine production at the mRNA and protein levels and block the activation of pattern recognition receptor (PRR)- and IFN-activated signal transduction in A549 cells.[50]

(7) *Andrographis paniculata*

The leaf juice is a household remedy for flatulence, loss of appetite, bowel complaints of children, diarrhea, dysentery, dyspepsia and general debility.[22]*A. paniculata* contains andrographolide, 14-deoxyandrographolide, 14-deoxy-12-hydroxy andrographolide, β-sitosterol, stigmasterol, chlorophyll a, 5,2'-dihydroxy-7,8-dimethoxyflavone, long chain trans-cinnamate esters, β-sitosteryl fatty acid esters, monogalactosyl diacylglycerols, lupeol, and triacylglycerols.[51]The main constituent, andrographolide exhibits significant antioxidative property with IC_{50} value of 3.2 μg/mL by DPPH method[52]and can modulate the innate and adaptive immune responses by regulating macrophage phenotypic polarization and Ag-specific antibody

production.[53]

The major active components of the plant, andrographiloids, have been extensively studied in a variety of models including human clinical trials for their therapeutic effects.[54]*A. paniculata* has been used in clinical trials of therapeutic agents including prevention of cold symptoms and the results show that andrographis significantly reduces cold symptoms.[55,56,57]*A. paniculata* was also reported to have anti HIV and immunoregulatory activities. The *A. paniculata* ethanol extract inhibited the Simian Retrovirus titer similar to the positive control Lamivudine, and it was not toxic to the A459 cell line. Low concentration (1 µg/mL) of *A. paniculata* extract could stimulated lymphocyte cell proliferation about 38% compared to the control lymphocyte cell without any treatment.[58]

Andrographolide from *A. paniculata* as a potential inhibitor of the main protease of SARS-COV-2 (Mpro) has been evaluated in silico studies. Andrographolide was docked successfully in the binding site of SARS-CoV-2 Mpro. Computational approaches also predict this molecule to have good solubility, pharmacodynamics property and target accuracy.[59]Consistently, in vitro study, andrographolide and its fluorescent derivative inhibit the main proteases of 2019-nCoV and SARS-CoV through covalent linkage.[60]Moreover, post-infection treatment of *A. paniculata* and andrographolide in SARS-CoV–2 infected Calu-3 cells significantly inhibited the production of infectious virions with the IC_{50} of 0.036 µg/mL and 0.034 µM, while the cytotoxicity profile showed the CC_{50} of >100 µg/mL and 13.2-81.5 µM, respectively, corresponding to the selectivity index over 380.[61]This study provided experimental evidence in favor of *A. paniculata* and andrographolide for further development as a monotherapy or in combination with other effective drugs against SARS-CoV–2 infection.

(8) *Argemone mexicana*

Alcoholic extract of the whole plant showed antiviral activity against Ranikhat disease virus.[22] Chemical constituents isolated from this plant belong to the class of alkaloids; besides, terpenoids, flavonoids, phenolics, long-chain aliphatic compounds, and few aromatic compounds are found to be other constituents of this plant.[62]The seeds contain 22–36% of pale yellow non-edible oil, called *argemone oil* or *katkar oil*, which contains the toxic alkaloids sanguinarine, dihydrosanguinarine, quaternary isoquinoline alkaloids, dehydrocorydalmine, jatrorrhizine, columbamine, and oxyberberine.[63]

The IC_{50} values of antioxidant activity of stem and leave methanolic extracts are 19.38 and 21.83 µg/ml by DPPH method, compared to vitamin C which has IC_{50} value of 15.6 µg/ml.[64]*A. mexicana* Linn seed powder, 100–200 mg taken twice a day, for 2 weeks shows significant effect on asthma as antiasthmatic activity.[65]*A. mexicana* stems have been studied in asthma by milk-induced leucocytosis and milk-induced eosinophilia. Methanol and aqueous extracts (50 mg/kg) showed significant decrease in leucocytes and eosinophils.[66]The benzo[*c*]phenanthridine alkaloid, (±)-6-acetonyl dihydrochelerythrine isolated from the methanolic extract of air-dried whole plants of *A. mexicana* was found to exhibit potent anti-HIV activity in H9 lymphocyte assay with EC_{50} value of 1.77 µg/ mL.[67]

(9) *Azadirachta indica*

The trees is very useful in blood disorders, consumption, eye diseases, intermediate fevers, as well as persistent low fever. It is also regarded as beneficial in malaria fever.[22] A number of compounds have been isolated from various parts of neem including nimbidin, nimbin, nimbolide, gedunin, azadirachtin, mahmoodin, (+)-gallic acid, (-)-epicatechin, catechin, gallocatechin, epigallocatechin, margolone, margolonone and isomargolonone, cyclic trisulphide and tetrasulphide, polysaccharide.[68]

Leaf aqueous extract, flower, stem bark and root bark ethanol extracts show very high free radical scavenging activity with IC_{50} value of 26.5, 27.9, 30.6, and 27.3 µg/mL, respectively.[69,70]The neem infusion successfully improves antibody titre, growth performance, and gross return at the level of 50 mL/liter of fresh drinking water.[71] In addition, neem (2 g/kg) treatment significantly enhances the antibody titres against new castle disease virus antigen.[72] While, aqueous neem bark extract (NBE) significantly blocks HSV-1 entry into cells

at concentrations ranging from 50 to 100 μg/mL.[73] Leaves extract of neem shows virucidal activity against coxsackievirus virus B-4 as suggested via virus inactivation and yield reduction assay besides interfering at an early event of its replication cycle.[74]Moreover, the neem plant has antiviral potential against bovine herpes virus type-1, poliovirus type 1, duck plague virus, dengue virus type-2, newcastle disease virus, infectious bursal disease virus, avian influenza virus, and group B coxsackie virus.[75]

(10) *Berberis aristata*

Plant extracts are as valuable as quinine in malaria fevers and useful in relieving pyrexia and checking the return of paroxysms of intermittent fevers.[22] Plant extract showed the presence of alkaloid, saponin, terpenoids, coumarin, flavonoids, tannin, glycoside and steroid.[76]The methanolic extract showed high amount of alkaloid. The major alkaloid of the plant is berberine,[77] a well-known isoquinoline.

The methanolic extract has strong antioxidant activities with IC_{50} value of 33.31 μg/ml (9.6 μg/ml for ascorbic acid as standard) determined by DPPH method and IC_{50} value of hydrogen peroxide radical scavenging activity was 60.6 μg/ml (54.23 μg/ml for ascorbic acid).[78]In an experimental autoimmune myocarditis model, berberine contributes to mitigate the cardiac damage by limiting the rise in anticardiac myosin antibodies, modulating the activity of certain STATs and blocking Th1 and Th2 cell differentiation, which play an important role in the pathogenesis of myocarditis.[78] Many clinical and experimental studies suggest that berberine has several pharmacological properties, such as immunomodulatory, antioxidative, cardioprotective, hepatoprotective, and renoprotective effects.[79]

(11) *Bombax ceiba*

The gum that excludes from the steam is an efficacious remedy for diarrhea, dysentery, hemoptysis of pulmonary tuberculosis, influenza and menorrhagia.[22] The plant has been reported to contain various phytoconstituents including mangiferin, quercetin, shamimin, shamimoside, β–sitosterol, taraxeryl acetate, lupeol, simalin a, simalin b, shamimicin, bombamalones a-d, bombaxquinone b, bombamaloside and bombasin.[80]

The methanolic extract of leaves of *B. ceiba* L possesses antioxidant properties with IC_{50} value of 84.60 μg/mL compared to that of ascorbic acid is 74.56 μg/mL.[81] Mangiferin from the methanolic extracts shows strong antioxidant activity (EC_{50} = 5.8±0.96 μg/ml or 13.74 μM) using DPPH assay.[82] The methanol extract of *B. ceiba* possessed promising immunostimulant properties.[83] The animals treated with *Bombax ceiba* methanol extract showed increase in antibody titer values 11.2 ± 0.30 and 13.1 ± 0.27 at 150 and 300 mg/kg dose and DTH reaction induced by SRBC was also found significant. It also caused increase in hematological profile, GSH, SOD, CAT activity and significantly decreased LPO levels in cyclophosphamide-induced immunosuppressed mice. In addition, the plant possesses a number of activities such as analgesic, anthelmintic, anticancer, antibacterial, antidiabetic, anti-inflammatory, hepatoprotective, immunomodulatory, cardioprotective, antiulcer, anti-diarrhoeal, antiviral, hypotensive activity,[80] proving its therapeutic usefulness in the treatment of immuno-compromised diseases and cancers.

(12) *Boswellia serrata*

The gum resin that exudes from the trunk is prescribed in chronic lung diseases, diarrhea, dysentery and pulmonary diseases.[22] Qualitative phytochemical study of this plant extract indicates the presence of tannin, pentosans, lignin, holocellulose, β-sitosterol, and both volatile and non-volatile oils. The volatile oils of resin such as cadinene, eleneol, gereniol, linalool, β-pinene, phenols, terpenyl acetate, bornyl acetate etc and non votalie oils like diterpene alcohol serratol, α- and β-amyrin and eight triterpenic acids, viz., boswellic acid.[84] *B. serrata* leaf methanolic extract has strong antioxidant activity with IC_{50} value of 54.06 μg/ml compared to ascorbic acid with IC50 value of 26.02 μg/ml.[85]Boswellic acids, a mixture of pentacyclic triterpene acids obtained from *B. serrata*, have been investigated for their effect on cell mediated and humoral components of

the immune system and the immunotoxicological potential.[86]*B. serrata* gum resin extract has been examined and showed antiviral activity against CHIKV, vesicular stomatitis virus vector particles and viral infections. The extract blocked entry of CHIKV Env-pseudotyped lentiviral vectors and inhibited CHIKV infection *in vitro,* indicating a broad antiviral activity.[87]*B. serrata* proved to be one such agent that has exhibited efficacy against various chronic diseases like arthritis, diabetes, asthma, cancer, inflammatory bowel disease, Parkinson's disease, Alzheimer's, etc. The molecular targets attributed to its wide range of biological activities include transcription factors, kinases, enzymes, receptors, growth factors, etc.[88]

(13) *Caesalpinia crista*

Seeds and root bark are very useful in simple, continued and intermittent fevers, asthma and colic.[22]*C. crista* contains favonoids, tannins, proteins, alkaloids, carbohydrates reducing sugars, phytosterols, saponins, coumarins, triterpenoids, furano-cassane-diterpenes, nor-cassane diterpenes, neo-cassane diterpenes and many other bioactive compounds.[89]

The methanolic plant extract has 50.23 ± 0.003 mg/mL gallic acid equivalent phenolic content and 106.83 ± 0.0003 mg/mL quercetin equivalent flavonoid content.[90]Antioxidant activity of the extract expressed as IC_{50} values is 0.44 ± 0.1 mg/ml, 24.9 ± 0.98 µg/ml, 33.72 ± 0.85 µg/ml, 61.13 ± 3.24 µg/mL and 170.51 ± 4.68 µg/mL for hydroxyl, superoxide, nitric oxide, singlet oxygen and hypochlorous acid, respectively.[90]The extract isalso potent iron chelator with IC_{50} = 279.85 ± 4.72 μg/mL.Aqueous, ethanol and methanol extracts of *C. crista* showed complete inhibition on paramyxovirus while showing highly significant inhibitory activity on orthomyxovirus.[91,92]Ethanol and aqueous extracts of *C. crista* seeds have antipyretic or fever reduction effects on experimental animals.[93] The ethanol extract also showed antipyretic activity comparable to that of paracetamol, the standard drug.

(14) *Calotropis procera*

Tincture of *C. procera* leaves is used in intermittent fevers and powders of flowers are prescribed in cold, cough, asthma and indigestion.[22] The plant are well known for its ability to produce large quantities of latex, which is a milky liquid consisting of several biologically active compounds, including proteins, amino acids, carbohydrates, lipids, vitamins, alkaloids, resins, tannins and terpenes, anthocyanins, proteolytic enzymes, cardenolides, cardioactive glycosides, triterpenoids, flavonoids, flavonoids quercetin, saponins and resins.[94,95,96]

The inhibitory concentration (IC_{50}) of the methanolic extract and the lyophilized latex is 110.25 µg/ml and 0.060 µg/ml, respectively. These suggest a potent antioxidant activity of *C. procera* plant species.[97] The ethanolic extract of root bark of *C. procera* stimulates defense system by modulating several immunological parameters and can be complementary medicine for the management of immunodeficiency disorders.[98]The plant has anti-inflammatory, anti-nociceptive, analgesic, anti-proliferative, nociceptive, spasmogenic, carminative, anti-dearrhoeal, hepatoprotective and other biological activities.[94]

(15) *Cedrus deodara*

The bark is good remedy in remittent and intermittent fevers, diarrhea and dysentery.[22] The plant contains (-)-matairesinol, (-)-nortrachelogenin, a dibenzyl butyrolactollignan,[99]α- himachalene, β-himachalene,[100] himachalol, allohimachalol, himadarol, isocentdarol and centdarol.[101] The pine needle essential oil scavenges 76.84% to 97.33% of DPPH radicals and its SC_{50} (0.53 ± 0.21 µg/mL) is lower than that (1.75 ± 0.69 µg/mL) of vitamin C.[102] Moreover, protocatechuic acid and 2R,3R-dihydromyricetin isolated from pine needles of *C. deodara* show very strong antioxidant activities with IC_{50} value of 16,7 + 0.9 and 5.6 + 0.2 µM respectively, compared to cuercetin as standard with IC_{50} value of 6.3 ± 0.1 µM.[103]

The volatile oil of *C. deodara* wood, administered orally at doses of 50 and 100 mg/kg, significantly inhibited neutrophil adhesion to nylon fibers, indicating inhibition of process of margination in the blood vessels.[104] It

also significantly inhibited Type III hypersensitivity reaction, i.e. Arthus reaction induced by methylated bovine serum albumin, and Type IV, i.e. delayed type hypersensitivity reaction induced by sheep erythrocytes and oxazolone, indicating an inhibitory effect on humoral and cell-mediated immune responses.[104]

(16) *Cinnamomum camphora*

It is good in typhus, confluent smallpox, all fevers, eruption of the typhoid class, also in whooping cough, spasmodic asthma, and chronic bronchitis.[22] The main constituents of *C. camphora* leaves essentialoil are *D*-camphor (40.54%), linalool (22.92%), cineole (11.26%), and 3,7,11-trimethyl-3-hydroxy-6,10-dodecadien-1-yl acetate (4.50%).[105] The main components of essential oil of barks are D-camphor (51.3%), 1,8-cineole (4.3%), α-terpineol (3.8%), and 3-methyl-2-butenoic acid, oct-3-en-2-yl ester (3.1%), while the main constituents of essestial oil of fruits are safrole (29.0%), D-camphor (28.1%), linalool (12.8%), and 1,8-cineole (5.3%).[106]

The essential oil distilled from the wood yields the active ingredient (1R)-(+)-camphor. Camphor exhibits a number of biological properties such as insecticidal, antimicrobial, antiviral, anticoccidial, anti-nociceptive, anticancer and antitussive activities, in addition to its use as a skin penetration enhancer.[107]Antioxidant activity ofbutanol and ethyl acetate of *C. camphora* extractsexpressed as IC_{50} values are 14 and 15 μg/ml, respectively.[108] The methanol extract, hexane and ethyl acetate fractions of *C. camphora* significantly block the production of interleukin (IL)-1β, IL-6 and the tumor necrosis factor (TNF)-α from RAW264.7 cells stimulated by lipopolysaccharide (LPS) up to 20-70%, inhibit nitric oxide (NO) production in LPS/interferon (IFN)-γ-activated macrophages by 65% and strongly suppress the prostaglandin E2 (PGE2) production in LPS/IFN-γ-activated macrophages up to 70%.[108] It is interesting to note that hexane, butanol and ethyl acetate extracts (100 μg/ml) also inhibit the functional activation of β1-integrins (CD29) assessed by U937 homotypic aggregation up to 70–80%.[108] These data suggest that the anti-inflammatory actions of *Cinnamomum camphora* may be due to the modulation of cytokine, NO and PGE2 production and oxidative stress.[108]

(17) *Costus speciosus*

The root is useful in catarrhal fevers, coughs dyspepsia and worms.[22] The plant contains diosgenin, 5α-stigmast-9(11)-en-3β-ol, sitosterol-β-D-glucoside, dioscin, prosapogenins A and B of dioscin, gracillin, quinones, α-tocopherol, tricontanoic acids, curcumin, tricontanol, aliphatic hydroxyl ketones, triterpenes, starch mucilage, oxa-acids, fatty acids, abscisic acid and corticosteroids, tigogenin and diosgenin.[109]

The IC_{50} values of anti-oxidant activities of petroleum ether, cyclohexane, benzene, ethyl acetate, chloroform, acetone, methanol and aqueous extracts are in the range of 2.42 ±0.05 and 15.30±0.1 μg/ml, while ascorbic acid as standard gives IC_{50} value of 16.14±0.20 μg/ml.[110] Butanolic fraction of rhizome extract of *C. speciosus* shows immunomodulatory activity. Both at low doses and high doses the rhizome extract elevated serum Ig level and phagocytic index, DTH reaction, HA titer in dose dependant manner i.e. the effect at higher dose (200 mg/kg BW) were found to be highly significant than lower dose (100 mg/kg BW) which produce less significant effects.[111] Anti-viral activity of *C. speciosus* leaves methanolic extract has also been evaluated *in vitro* through haemagglutination and anti-haemolysis of human RBCs methods. It was found that the extract has binding affinity to the receptors of erythrocytes and prevents agglutination. In addition, the methanolic extract showed concentration dependent anti-haemolysis of RBCs. As the concentration increases anti-haemolysis activity of extract increases and it was to be 83.33% at 10 mg/ml of concentration.[112]

(18) *Curcuma longa*

The rhizomes are used in catarrhal cough and intermittent fever.[22] More than 235 compounds, primarily phenolic compounds and terpenoids were identified from the turmeric, including diarylheptanoids and diarylpentanoids, phenylpropene and other phenolic compounds, monoterpenes, sesquiterpenes, diterpenes, triterpenoids, sterols and some alkaloidal compounds.[113] Antioxidant compounds from *C. longa* are

bisabolone-9-one, 4-methyllene-5-hydroxybisabola-2,10-diene-9-one, turmeronol B, 5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-1-hepten-3-one, 3-hydroxy-1,7-bis(4-hydroxyphenyl)-6-hepten-1,5-dione, cyclobisdemethoxycurcumin, bisdemethoxycurcumin, demethoxycurcumin and curcumin.[114] The methanolic extract of *C. longa* contains high concentrations of phenolic compounds (157.4 mg gallic acid equivalent/g extract) and flavonoids (1089.5 mg rutin equivalent/g extract). It shows significantly higher DPPH radical-scavenging activity (IC_{50} = 26.4 μg/mL).[114] The IC_{50} for DPPH radical-scavenging activity is 18 μM and hydroxyl radical-scavenging activity was 1.5 μM for curcumin.[114]

Curcumin, an active ingredient present in *C. longa* indicated the immunostimulatory activity. It increased the circulating antibody titre against sheep red blood cells.[115] It has been demonstrated that curcumin has a wide range of antiviral activity against different viruses.[116] Curcumin was found to be an inhibitor of HIV-1 and HIV-2 protease with IC_{50} of 100 μM and 250 μM, respectively. The study of curcumin and its bioconjugates against variety of viruses including parainfluenza virus type 3 (PIV-3), feline infectious peritonitis virus (FIPV), vesicular stomatitis virus (VSV), herpes simplex virus (HSV), flock house virus (FHV) and respiratory syncytial virus (RSV) assessed by MTT test showed the potent antiviral activity. Moreover, bioconjugates of curcumin, di-*O* tryptophanylphenylalanine curcumin and di-*O*-decanoyl curcumin revealed remarkable antiviral activity against VSV and FIPV/FHV with EC_{50} values of 0.011 μM and 0.029 μM, respectively. Curcumin also showed anti-influenza activity against influenza viruses PR8, H1N1, and H6N1. The results showed more than 90% reduction in virus yield in cell culture using 30 μM of curcumin. The plaque reduction test elicited the approximate EC_{50} of 0.47 μM for curcumin against influenza viruses.[117] In H1N1 and also H6N1 subtypes, the inhibition of haemagglutinin interaction reflected the direct effect of curcumin on infectivity of viral particles. *In vitro* study of curcumin and its derivatives, namely, gallium-curcumin and Cu-curcumin, exhibited remarkable antiviral activity against herpes simplex virus type 1 (HSV-1) in cell culture with IC_{50} values of 33.0 μg/mL, 13.9 μg/mL and 23.1 μg/mL, respectively.[118] The potential antiviral effects of curcumin can be helpful for researchers to further investigate the potency of curcumin against the new emerging Covid-19 infection. The ability of curcumin to modulate a wide range of molecular targets makes it a suitable candidate for the management of coronavirus infection.[119]

(19) *Curcuma zedoaria*

The rhizome decoction is a household remedy for fever, cold, cough and bronchitis.[22] Phytochemical studies of all crude extracts showed the presence of terpeniods, alkaloids, saponins, flavanoids, glycosides and carbohydrates, phenolic, tannins and phytosterols etc.[120] The major compounds of the white turmeric oil are camphor, isobornyl alcohol, borneol, furanodiene, furanodienone, 1,8-cineole, camphene, β-pinene, 2-nonanon and germacrene-D.[121]

C. zedoaria extract shows potent antioxidant activity. The concentration of 100 μg/ml of ethanolic, ethyl acetate and water extracts of the rhizome exhibits 85.41, 97.9 and 98.95 % inhibition of DPPH free radicals, respectively.[120]Polysaccharide fraction of C. zedoaria at dose 300 mg/kg bw has potency to be developed as immunomodulator.[122] In vitro studies found that the antiviral effect of compound of *C. zedoaria* volatile oil on H5N1 avian influenza virus (AIV) cell line was effective via mechanisms including virus killing, virus inhibiting, the prevention of the virus spread, and the treatment of the virus-related injury in MDCK. In vivo studies indicated that compound of *Curcuma zedoaria* volatile oil prolonged the mean survival days of the chickens, showing significant preventive effect in the chickens.[123]

(20) *Dillenia indica*

Juice of the fruit is used as a cooling beverage in fevers and as cough mixture.[22]*D. indica* contains glycoside, flavonoids, triterpenoids, steroids, saponins and reducing sugar. Various chemical constituents like 3, 5, 7-trihydroxy-3', 4'-dimethoxy flavone (dillenetin), botulin, betulinic acid, β-sitosterol and stigmasterol are found in *D. indica*.[124,125]

Higher amount of phenolic content in the methanolic extract contributes to its superior *in vitro* antioxidant property. The IC_{50}values for DPPH, hydroxyl, oxygen, nitric oxide and reductive ability of the methanolic extract are 31.25, 51.82, 51.44, 39.73 and 40.18μg/ml respectively.[126]Major chemical compounds betulin (pentacyclic triterpenoid) and betulinic acid show wide spectrum of pharmacological activities like anti-HIV, anti-inflammatory, anti-cancer, anti-malarial, anti-diabetic, anti-proliferation, anti-diarrhoeal, antiimplantation, cytotoxic, wound healing and hair waving activity.[127]

(21) *Dolichos biflorus*

The seed is useful in bronchitis and asthma.[22]Phytochemical analysis showed that the extract of *D. biflorus* contains alkaloids, flavonoids, carbohydrates, proteins, and tannins, which may contribute to its anti-inflammatory and antioxidant activity. *D. biflorus* has high sterol content including cholesterol, 24-α-methylcholest-5-en-3-β-ol, 24-β-methylcholest-5-en-3-β-ol, 24-α-ethylcholest-5-en-3-β-ol, 24-α-ethylcholesta-5,22-diene-3-β-ol, isofucosterol, 24-methylene-25- methylcholesterol, β-sitosterol, stigmasterol, 24-ethyl-5-α-cholest-7-en-3-β-ol[9] and 24-ethyl-5-α-cholest-7, 22-diene-3-β-ol, 24-ethyl-5α-cholest-9(11)ene-3-β-ol and a triterpene, lupeol.[128,129]

The phenolic and flavonoid contents of plant extract (100 mg) are 44.67 ± 0.004 mg/ml gallic acid equivalent and 72.0 ± 0.008 mg/ml quercetin equivalent respectively.[130]The extract was found tobe an antioxidant with a trolox equivalent antioxidant capacity (TEAC) value of 0.28 ± 0.006. The IC_{50} values for hydroxyl, superoxide, nitric oxide and hypochlorous acid of the extract are 184.55 ± 7.08, 114.14 ± 6.85, 74.77 ± 1.73 and 287.9 ± 8.56 μg/ml, respectively. The extract shows moderate inhibition of lipid peroxidation with IC_{50} 128.63 ± 3.44μg/ml.[130]

Pharmacological studies on methanolic seeds' extract shown that seeds extract of *D. biflorus* exhibited mild analgesic activity, the result is (84.6±6.68) at dose 300mg/kg.[131] While the seed extract exhibited remarkable diuretic activity, the values at 300 mg/kg is (1.33±0.13) and at 500 mg/kg is (2.66±0.31) which are highly significant as compared to drug Lasix (20 mg/kg) having result (2.38±0.23). Anti-inflammatory effects of crude extract obtained at 0.06mg/kg and 01mg/kg were (26.6±2.96) and (36±1.67) respectively. While the value for aspirin as standard drug (300mg/kg) was (17.44±1.59).[131]Another study showed that *D. biflorus* exhibited anti-inflammatory and antioxidant properties in an acute inflammatory model.[132] A dose of 50 mg/kg *D. biflorus* methanol extract showed 73% inhibition of paw edema at the 3rd hour. The result was comparable to the effect produced by the standard anti-inflammatory drug Voveran (20 mg/kg).[132]

(22) *Elettaria cardamomum*

The seeds are very useful in asthma and bronchitis.[22] The phenolic content of ethanolic extract was 84.19 ± 4.64 mg/100g dry extract.[133] The major components of the essential oil areα-ionone, eucalyptol, santolina alcohol, 3.7-dimethyl-1,6-octadiene-3-ol, (Z)-3.7-dimethyl-2,6-octadiene-1-ol,3-ol, (E)-cinnamaldehyde, terpinen-4-ol, 3,7,11-trimethyl-1,6,10-dodecatrien-3-ol, 1-methyl-1-(4-methyl-5-oxy-cy) acetic acid.[134]

The total phenolic content, scavenging of DPPH and inhibition of linoleic acid arefound to be 27.75-126.35 mg gallic acid equivalent g^{-1} dry weight, 46-91% at 5 μg/ml of extract concentration and 34-83%, respectively.[135] The green cardamom components extracted with 1 N acidified methanol also shows strong anti-mutagenic activity (81.01%). *E. cardamomum* exert immunomodulatory roles and antitumor activities, and hence they manifest themselves as natural agents that can promote the maintenance of a healthy immune system. *E. cardamomum* constituents can probably be used as potential therapeutic tools to regulate inflammatory responses and prevent/attenuate carcinogenesis.[136]

(23) *Euphorbia hirta*

Decoction of the plant is given in bronchial affections and asthma.[22] Crude aqueous, methanolic and ethanolic leaves extracts have phenolic content of 275.64±2.45, 285.41±3.00, and 291.74±2.46 mg of GAE/g and

flavonoid contents of 26.37±0.37, 32.29±6.30, and 40.32±1.67 mg of QE/g, respectively.[137]*E. hirta* contains a number of active constituents including afzelin (I), quercitrin (II), myricitrin (III), rutin (IV), quercitin (V), euphorbin-A (VI), euphorbin-B (VII), euphorbin-C (VIII), euphorbin-D (IX), 2,4,6-tri-*O*-galloyl-β-D-glucose, 1,3,4,6-tetra-*O*-galloyl-β-D-glucose, kaempferol, gallic acid, protocatechuic acid, β-amyrin, 24-methylenecycloartenol, β-sitosterol, heptacosane, *n*-nonacosane, shikmic acid, tinyatoxin, choline, camphol, and quercitol derivatives containing rhamnose and chtolphenolic acid.[138]

The leaves of *E. hirta* possess antioxidant property with the IC_{50} value of aqueous, ethanol and methanol extracts is 7.07±0.06 2.81±0.04 μg/mL and 4.34±0.04 μg/mL, respectively, whereas that of the standard, ascorbic acid exhibits 2.13±0.02 μg/mL determined by DPPH method.[139] The ethanol extract of *E. hirta* showed a dose-dependent shift on neutrophils in *in vitro* phagocytosis. Also intraperitoneal injection of *E. hirta* was found to stimulate macrophages as evident from the increase in phagocytic index when compared with control using carbon clearance assay. *E. hirta* was found to be immunostimulatory at concentrations ranging from 0.98 to 500 μg/ml, but at concentrations below 0.98 μg/ml the plant exerted an immunosuppressive activity.[139]The plant may be a promising initiative towards drug development in the cue of immunomodulatory agents in future.

The antiretroviral effects of extracts of *E. hirta* against SIVmac251, HIV-1 and HIV-2 viruses have been evaluated with bioassay methods.[140] A dose-dependent inhibition of reverse transcriptase was observed on HIV-1, HIV-2 and SIV_{mac251}, with IC_{50} values (inhibitory concentration for 50% yield reduction) of 38, 22 and 177 μg/ml, respectively. High antiretroviral activity was recorded for aqueous and methanolic (50%) extracts, with IC_{50} values of 9 μg/ml and 5 μg/ml, respectively.

(24) *Evolvulus alsinoides*

The whole plant in the form of decoction or infusion is used in fever, nervous debility and loss of memory. Leaves made into cigarettes are smoked in chronic bronchitis and asthma.[22] Total phenolic contents of various *E. alsinoides* extracts obtained by using different polarity solvents range from 1686 ± 1.527 to 1255 ± 0.020 mg GAE/100 of dry weight.[141] The plant contains piperine, octodeconoic acids, hexadecanoic acid, squalene, scopoletin, umbelliferone, scopolin and 2-methyl-1,2,3,4-butanetetrol, cis-α-necrodol, 2-butoxyethanol, benzyl alcohol, γ-butyrolactone, hexan-1-ol, γ-nonalactone, α-methyl-γ-butyrolactone, dimethyl sulfone and an irregular monoterpene with a cyclopentane skeleton, which is very unusual in the plant kingdom.[142,143,144]

The methanol extracts display significantly higher DPPH· scavenging activity with IC_{50} value of 0.095 mg/ml compared to the standard antioxidant, BHT, with IC_{50}value of 0.026 mg/ml.[141]The EC_{50} values for ethanolic and aqueous ethanolic extracts are 196.08±2.16 μg/ml and 307.66±1.72 μg/ml for DPPH assay, and 460.20±0.632 μg/ml and 483.49±1.13 μg/ml for hydrogen peroxide assay.[145]The immunomodulatory properties of *E.alsinoides* have been evaluated in adjuvant induced arthritic (AIA) rat model.[146] The *E.alsinoides* extract showed a marked reduction in inflammation and edema. At cellular level immunosuppression occurred during the early phase of the disease. There was mild synovial hyperplasia and infiltration of few mononuclear cells in *E.alsinoides* treated animals. The induction of nitric oxide synthase (NOS) was significantly decreased in treated animals as compared to controls.The methanol extract of *showed strong antiviral activity* against Herpes simplex virus (HSV) and mouse corona virus (MCV, the surrogate for human SARS virus) at a concentration as low as 0.4 μg/mL.[147]

(25) *Gymnema sylvestre*

A decoction of the leaves is given in fever and cough.[22] Besides gymnemic acids and gymnemasins,[148] some compounds are isolated and their structures are elucidated as conduritol A, stigmasterol, lupeol, stigmasterol-3-*O*-β-D-glucoside, sodium salt of 22α-hydroxy-longispinogenin-3-*O*-β-D-glucopyranosyl-(1→3)-β-*D*-glucurono-pyranosyl-28-*O*-α-*L*-rhamnopyranoside, oleanolic acid-3-*O*-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside, and sodium salt of 22α-hydroxy-longispinogenin 3-*O*-β-D-glucuronopyranosyl-28-*O*-α-L-

rhamnopyranoside from *G. sylvestre*.[149]

G. sylvestre extracts shows significant antioxidant activity where DPPH inhibition is at the level of 87.3% and hydroxyl free radical inhibition was 59.8%.[150]The ethanol extract of this plant was observed to improve immunosuppressed condition induced by cyclophosphamide in Albino Rats. The plant extract significantly improved haemagglutination titer, phagocytic activity and decreased paw edema, when compared with cyclophosphamide treated control.[151]*In vitro* immunomodulatory activity of the methanolic leaf extract (1-200μg/ml) showed significant enhancement in NO and ROS generation in macrophages and in proliferation of lymphocytes in dose dependent manner.[152] EC_{50} value was 3.10, 3.75 and 2.68 μg/ml for NBT reduction, nitrite release and lymphoproliferation, respectively. Potential effect was observed at 100 μg/ml in NO and ROS generation in macrophages and 20 μg/ml in lymphocyte proliferation. *G. sylvestre* leaf extract stimulates macrophage reactivity, increasing the level of activity even higher when combined with phorbol myristate acetate or lipopolysaccharide. Moreover, gymnemic acid A and B isolated from *G. sylvestre* showed anti influenza virus activity *in vitro* study with good and moderate inhibition.[153]

(26) *Hyoscymus niger*

The plant is prescribed in spasmodic cough, asthma, and other diseases.[22] The plant contains hyoscine, hyoscyamine, anisodine, anisodamine, aesculetin, coumarin, kaempferol, quercetin, rutin, cuscohygrine, chlorogenic acid, linoleic acid, myristic acid, oleic acid, stearic acid, pyridine, trimethylamine, b-sitosterol, grossamide, cannabisin D and G, daucosterol, N-*trans*-feruloyltyramine, 1-O-octadecanoyl glycerol, 1-O-(9Z,12Z-octadecadienoyl) glycerol, 1-O-(9Z,12Z-octadecadienoyl)-3-O-(9Z-octadecenoyl), vanillic acid, calystegines and anolides.[154]

The total phenolic content of *H. niger* determined by Folin-Ciocalteu method is 583.33±0.4 GAE mg/g of dry extract.[155] The methanolic extracts of *H. niger* shows antioxidant activity (IC_{50} = 1.64 μg/ml) compared to α-tocopherol (IC_{50} = 0.60 μg/ml), which is used as the positive control.[156]The result of the antipyretic study showed that oral administration of methanolic extract of seeds of *H. niger* at 800 mg/kg after 22 h of treatment caused a significant decrease in temperature (Pb 0.01) while, after 23 h a very significant inhibition (Pb 0.001) was noticed. The antipyretic effect of 800 mg/kg methanolic extractwas comparable with that of paracetamol (150 mg/kg, oral) between 22 to 23 h after treatment.[157]The metanolic extract of *H. niger* exhibited cytotoxicity and anti-influenza viral activity with the CC_{50} value of 50 mg/mg and the IC_{50} value of 40 mg/mg.[158]

(27) *Hyssopus officinalis*

The leaves in the form of syrup of infusion are useful in hysteria and colic, cough, asthma, sore throat and chronic bronchitis.[22]The plant contains quercetin, apigenin, luteolin, diosmin and acacetin.[159]The oil isolated from *H. officinalis* contains 20 compounds representing 99.97% of the oil where the main components were linalool, 1,8-cineole, limonene, β-caryophyllene, β-pinene α-pinene, myrtenylacetate, camphor, germacrene, spathulenol.[160] The total phenol content of the water, n-butanol and ethylacetate extracts are 200, 246 and 51 mgGAE/g determined by the Folin–Ciocalteau method.[161]

The IC_{50} values of antioxidant activities of apigenin 7-*O*-β-D-glucuronide, ethylacetate, *n*-butanol and water extracts determined by DPPH radical scavenging assay are 116, 103, 25 35.6 μg/ml, respectively.[162]The methanolic extracts, subsequent to ether, chloroform and chloroform-ethanol extractions of dried leaves of *H. officinalis*, showed very strong anti-HIV (Human Immunodeficiency Virus) activity as measured by inhibition of HIV reverse transcriptase, p17 and p24 antigen expression and syncytia formation probably due to caffeic acid and it may be useful in the treatment of patients with acquired immunodeficiency syndrome (AIDS).[162] In another study shown that a polysaccharide from *H. officinalis* aqueous extract showed anti-HIV activity against HIV-1 in HUT78 T cell line as demonstrated by the inhibition of syncytia formation and HIV-1 p24 antigen.[163]

(28) *Justicia adhatoda*

It is a well-known drug in Ayurvedic medicine and is recommended in bronchitis, asthma, fever, jaundice and consumption. The leaves and roots are antispasmodic and efficacious in cough. Root is given in malarial fevers and diseases of the respiratory system.[22]Some important bioactive compounds are essential oil, betaine, steroids and quinazoline alkaloids including vasicine, vasicinone, vasicinol, adhatodine, adhatonine, adhvasinone, anisotine and hydroxypeganine.[164]The phytochemical analysis shows that phenols, tannins, alkaloids, anthraquinone, saponins, flavonoids and reducing sugars are present in the leaves of *J. adhatoda*.[165,166] The most studied chemical component is a bitter quinazoline alkaloid, vasicine which is present in the leaves, roots and flowers. Besides vasicine, the leaves contain several alkaloids (vasicinone, vasicinol, adhatodine, adhatonine, adhvasinone, anisotine and hydroxypeganine), betaine, steroids and alkanes.[166]

J. adhatoda leaf extracts including ethanol, chloroform, and aqueous against chemically induce oxidative radicals.[167]Among the extracts, EtOH extract reveals a highest AO potential (86.5 ± 0.25) at 250 g in assays of DPPH, NO radical (48.35 ± 0.16), hydroxyl radical (38.75 ± 0.12), and TAA (78 ± 0.45) than rest of the extracts. *In-vitro* study *J. adhatoda* extracts showed anti-viral activity against herpes simplex virus.[168]The methanolic extract at 10mg/ml significantly inhibited formation of plaques in Vero cells infected with 100 pfu of HSV1 and 2 by 100%. Similarly, the aqueous extract at 10mg/ml inhibited the plaque formation by 100% and 86% for HSV1 and 2. Moreover, the aqueous extracts at concentrations of 10mg/ml and 5mg/ml reduced the hemagglutination (HA) to 33% and 16.67%, respectively, in the simultaneous assay. While the methanolic extract showed 100% reduction in HA in the simultaneous and post treatment assays at the concentration of 10mg/ml.[169] These results suggest that the plant extracts have potent anti-viral agents against herpes simplex viruses and strong anti-influenza virus activity that can be exploited for development of an alternative remedy for HSV infections and may be used as viral prophylaxis.

(29) *Linum usitatissimum*

Infusion of the seeds known as linseed tea is given internally as a demulcent and expectorant drink in cold, cough and bronchial affections.[22]The plant is a rich source of nutritive and bioactive compounds. Phytochemical screening tests shown that *L. usitatissimum* extracts contain terpenoids, steroids, tannins, saponins, anthocyanins, emodins, alkaloids, glycosides, flavonoids, and phenolic compounds.[170] The methanolic and butanolic extracts of the plant contain total phenolic compounds of 47.01±5.40 and 43.33±2.77 μg gallic acid equivalents/g of extract, respectively and flavonoids of 30.89±0.09 and 29.55±0.15 μg Quercetin equivalents/g of extract, respectively.[171] The *L. usitatissimum* oil is primarily in the form of triacylglycerides with a fatty acid profile typically including linolenic (52%), linoleic (17%), oleic (20%), palmitic (6%), and stearic (4%) acids.[172]

Aqueous methanol (70%) extract of the plant exhibits inhibition level of 62.10% with IC_{50} value of 55.74 mg/ml.[170]*L. usitatissimum* fixed oil (LUFO) has immunomodulatory activity by its ability to reduce granuloma formation in the subcutaneous cotton pellet implantation model.[173] The LUFO produced a dose-dependent reduction injoint swelling and circulating TNF-α levels in both preventive and curative protocols of arthritis induced by complete Freund's adjuvant (CFA). Expression of TNF-R1 and Interleukin (IL) 6 proteins in the arthritic paw was also significantly reduced in the LUFO-treated animals. In the cotton pellet induced granuloma model, LUFO treatment significantly reduced the dry granuloma weight as compared with the control group. While, ether insoluble phenolic components of *n*-butanol fraction (EPC-BF) of flaxseed modulates immune response in rat by reducing cell-mediated immune response at lower dose which could be due to the presence of both immunostimulant and immunosuppressant phenols.[174] Moreover, cyclolinopeptide A (CLA), a cyclic nonapeptide from *L. usitatissimum* seed, possesses strong immunosuppressive and antimalarial activity along with the ability to inhibit cholate uptake into hepatocytes.[175] The fixed oil of *L.*

usitatissimum inhibited PGE2-, leukotriene-, histamine-, bradykinin-induced inflammation, arachidonic acid-induced inflammation, and showed antipyretic activity comparable to aspirin.[176]

(30) *Madhuca longifolia*

The flowers are given in bronchitis, cough and are considered useful in piles.[22] The qualitative phytochemical analysis indicates the presence of various phytoconstituents such as alkaloids, sapogenins, steroids, flavonoids and glycosides saponins, tannins, triterpenoids except gums and fixed oils in the methanolic and aqueous extract of *M. longifolia* leave.[177,178] Several bioactive constituents have been isolated and identified in the leaves of *Madhuca* like sitosterol, quercetin, 3-*O*-L-rhamnoside, stigmasterol, *n*-hexacosanol, *n*-octacosanol, carotene, myricitin, erthrodiol, β-*D*-glucoside, β-sitosterol, 3-β-caproxyolcan-2-en-28-ol, 3-galactoside, 3-O-arabinoside, and xanthophylls.[179]

Leaves and barks of *M. longifolia* extracts show considerable antioxidant activity with IC_{50} values of61.83 μg/ml and 66.34μg/ml, respectively, by DPPH method compared to ascorbic acid as standard with IC_{50} value of 45.738μg/ml.[180]*M. longifolia* showed immunomodulatory activity. Methanolic extract of bark of *M. longifolia* has been administered orally at doses of 50, 100 and 150 mg/kg/day to healthy mice and the assessment of immunomodulatory activity was carried out by testing the humoral (antibody titre) and cellular (foot pad swelling) immune responses to the antigenic challenge by sheep RBCs. The extract significantly suppressed the cellular immunity by decreasing the footpad thickness response to sheep RBCs in sensitized mice. With a dose of 100 and 150 mg/kg/day the DTH response was 7.66 ± 2.75 and 6.41 ± 1.21 respectively in comparison to corresponding value of 14.50 ± 2.38 for untreated control group.[181]In addition, the ethanolic extract of *M. longifolia* at a dose of 100 and 200 mg/kg body weight has been studied for its immune modulatory activity on albino mice. The significant increase in antibody titre value and DTH response was observed as a sign of its stimulating effect on humoral and cell mediated immunity respectively. Consequently, the *M. longifolia* with the significant immunostimulatory activity on both the specific and non-specific immune mechanisms holds great promises for being used as an immunomodulating agent.[182]Methanolic extract of *M. longifolia* also showed significant antipyretic activity in yeast induced Swiss albino rats administered in a dose of 250 mg/kg body weight.[183]

(31) *Mimusops elengi*

The plant is considered useful in consumptive cough, bronchitis and other diseases.[22]Steam distillation of bark sample yields 0.18% of volatile oil with major constituents are alpha cadinol, tau muurolol, hexadecanoic acid, diisobutyl phthalate, octadecadienoic acid, and phenyl propyl gallate. The bark contains taraxerone, taraxerol, betulinic acid and spinasterol, sodium salt of betulinic acid and ursolic acid, fatty acid esters of alpha-spinasterol, and triterpenoids such as farnan-2-one-3 betaol (mimusopfarnanol), farnan-3-one, and olean-18-en-2-one-3-ol and lup-20 (29)-en-3 beta-ol, 3β-hydroxy-lup-20(29)-ene-23, 28-dioic acid, beta amyrin, and lupeol.[184]

The IC_{50} value of the methanol leaves extract is 43.26μg/ml while the IC_{50} value of the reference standard ascorbic acid is 58.92 μg/ml determined by DPPH method.[185]The immunostimulatory activities on specific and non-specific immunity methanolic extract of bark of *M. elengi* Linn (MEMEL) were studied by carbon clearance test (CCT), haemagglutination antibody (HA) and delayed type hypersensitivity, using sheep red blood cells (SRBC) as the antigen and the MEMEL possesses potential for augmenting immune activity by cellular and humoral-mediated mechanisms.[186]Ethanol extract (70%) of *M. elengi* Linn. bark has an antiinflammatory, analgesic and antipyretic activity.[187]The ethanol leaves extract of *M. elengi* has strong anti-HIV-1 IN activity with an IC_{50} value of 62.1μg/mL. This mixture of gallocatechin and epigallocatechin isolated from the ethanol extract showed satisfactory anti-HIV-1 IN activity with an IC_{50} value of 35.0μM.[188]

(32) *Moringa oleifera*

It is used as a cardiac stimulant in asthma, cough and similar disorders. The fresh root of a young tree is given in intermittent fevers.[22] The multiple biological activities are attributed to the presence of functional bioactive compounds, such as carotenoids, tocopherols (α, γ, δ), phenolic acids, flavonoids, alkaloids, phytosterols, folate, polyunsaturated fatty acids, natural sugars, vitamins, minerals, and organic acids.[189,190] Its stem contains alkaloids (moringine and moringinine), 4-hydroxymellein, octacosanoic acid, and β-sitosterol.[191]

The methanol extract of *M. oleifera* shows free radical scavenging activity with IC_{50} value of 49.30 μg/mL in DPPH assay and 11.73 μg/mL in ABTS assay compared to trolox as standard with IC_{50} 5.89 μg/mL in DPPH assay and 3.06 μg/mL in ABTS assay.[192]The immunomodulatory activity of aqueous extract of *M. oleifera* Lam. leaf has been studied and the extract has immunostimulant activity and the low dose (0,1 μg/ml) can increase the cell number of CD4+ and CD8+, while high dose (10 μg/ml) significantly increase B220+ cells compared to the control.[193]The ethanolic leaf extract of *M. oleifera* exhibited significant antipyretic activity at 100, 200, and 400 mg/kg.[194]Extract of the seeds showed protection against asthma as investigated in various models; the proposed mechanism for this effect was a direct bronchodilator effect combined with anti-inflammatory and antimicrobial actions[195] and inhibition of immediate hypersensitive reaction.[196]*M. oleifera* was reported to possess antiviral activity against foot and mouth disease virus at concentration ranges of 12–100μg/ml and 50–300μg/ml.[197]Aqueous extract, methanolic extract and petroleum ether extract of *M. oleifera* leaf shown active against HIV lentiviral vector and inhibited early events of viral replication with EC_{50} values of 7.17, 7.72 and 7.59 μg/ ml, respectively.[198] Crude ethanolic extract of M. oleifera leaves attenuated the activity of HSV-1, specifically with EC_{50} value of 100 ± 5.3 μg/ml.[199]The water leaves extract of the plant showed antiviral activity against HBV with EC_{50} values of 60 μg/ml.[200]The ethanolic and methanolic leaves extracts of the plant showed antiviral activity against EBV with EC_{50} values of 32.5 and 35.3 μg/ml, respectively.[201]

(33) *Myristica fragrans*

Powder is used as a sedative, anodyne antispasmodic in ashma, colic, neuralgia, menorrhagia, dysmenorrhea, spasmodic cough and lumbago.[22]The seed extract contains secondary metabolites such as alkaloids, flavonoids, saponins, tannins, phenols, anthraquinones, cardiac glycosides, coumarins, anthocyanin, chalcones, emodins, and triterpenoids.[202]The main component of the seed is myristicin.The stem bark contains licarin A, licarin B, odoratisol A, elemicin, fragransin B1, raphidecursinol B, lignan surinamensin, and grandisin.[203]

M. fragrans shows middle level of antioxidant activity with the IC_{50} value of 68.43 μg/ml in DPPH free radical scavenging assessment.[204]The immunomodulatory and radiomodifying properties of lignans present in the aqueous extract of fresh nutmeg mace in mammalian splenocytes have been satudied. The macelignans inhibited the proliferation of splenocytes in response to polyclonal T cell mitogen concanavalin A and protected splenocytes against radiation-induced intracellular ROS production in a dose dependent manner.[205]

The extracts from *M. fragrans* Houtt seeds (160 μg/ml) inhibited 90% of human rotavirus recognized as the major agents of diarrhea in infants and young children.[206]

(34) *Nyctanthes arbor-tristis*

Fresh leaf juice is a mild cholagogue and a safe purgative for infants. It is given with honey in chronic and bilious fevers.[22] Phytochemical analysis of the various dried leaves extracts of *N. arbor-tristis* showed the present of alkaloids, phytosterols, phenolics, tannins, flavonoids, glycosides and saponins.[207]The essential oil of *N. arbortristis* contains 1-octanol, phytol, bis (2-ethylhexyl) phthalate, and eucarvone, methyl palmitate, methyl anthranilate and hexahydrofarnesyl acetone in small quantities.[208] Chloroform extract of FAME contains palmitic acid, alfa-linolenic acid and oleic acid as major fatty acids in leaf.[209]

The antioxidant capacity of ethyl acetate flower extract is 30.11±1.77 mg of AAE/g dray weight of plant material and the IC_{50}values is 23.98±1.05 μg/mL.[210]The antiproliferative activity was carried out by MTT

assay by employing different human cancer cell lines. The lowest IC_{50}value of 24.56 ± 6.63 μg/mL was observed against Colo 205 cell line.[210] The aqueous extract of *N. arbor-tristis* flowers showed immunomodulatory activity with particular reference to splenocytes proliferation and induction of cytokines.[211] Humoral and cell-mediated immunostimulant activity of the flower extract seems to be mediated through splenocytes proliferation and increased production of cytokines, especially IL-2 and IL-6. The water-soluble portion of an ethanol extract of the leaves exhibited significant aspirin-like antinociceptive activity.[212] It was also found to possess antipyretic activity against brewer's yeast-induced pyrexia in rats.[212] The extract also produced gastric ulcers following oral administration for six consecutive days in rats.[212] The ethanolic extracts, various fractions and two pure compounds isolated from the plant *N. arbortris* have been tested against Encephalomyocarditis Virus (EMCV) and Semliki Forest Virus (SFV).[213] Pronounced in vitro virus inhibitory activity was observed with the ethanolic and n-butanol fractions as well as with the pure compounds arbortristoside A and arbortristoside C. In addition, ethanolic extracts and n-butanol fraction protected EMCV infected mice to the extent of 40 and 60% respectively against SFV at a daily dose of 125 mg/kg body weight.

(35) *Ocimum sanctum*

Fresh leaves cure chronic fever. With honey and ginger juice, it is a good expectorant, useful in cough, bronchitis, and children's fever.[22] More than 60 chemical compounds have been reported from *O. sanctum*, including phenolics, flavonoids, phenyl propanoids, neolignans, coumarins, terpenoids, fatty acid derivatives, essential oil, fixed oil, and steroids.[214] The volatile oil contains eugenol, bornyl acetate, camphor, ethyl cyclohexenal ketone, α-selinene, β- pinene, *n*-butyl benzoate, α-pinene, β-guaiene, α-thujene, bicyclogermacene, β-gurjunene, borneol, α-camphene, myrcene, α-terpineol, limonene, eucalyptol and other constituents in trace amount.[215]

The methanol extract of O. sanctum showed very high DPPH free radicals scavenging activities with an IC_{50} value of 11 µg/mL.[216]The immunomodulatory activity of aqueous leaf extract of *Ocimum sanctum* (ALEOS) by *in-vitro* and *in-vivo* methods has been evaluated in Wistar strain rats and the results showed that the plant *Ocimum sanctum* was found to be a better herb for immunomodulatory activity.[217]The antipyretic activity of the extracts of *Ocimum sanctum* on brewer's yeast induced fever in experimental rats has been investigated and the result shown that the antipyretic effect of *Ocimum sanctum* is dose dependent.[218]The antiviral activity of ethanolic extract of *O. sanctum* against H_1N_1pdm virus was assessed in MDCK cells through different virus inhibition assays.[219] The CC_{50} value of *O. sanctum* ethanolic extract was 726.2±3.1 µg/ml implying very low toxicity. A dose dependent inhibition was observed against 10, 5, 1 and 0.1 multiplicity of infection (MOI) of the virus with IC_{50} values 55.5±0.9, 54.1±1.4, 44.7±0.7 and 38.6±2.2 µg/ml respectively.

(36) *Papaver somniferum*

It is used in diarrhea, dysentery and cough. Syrup of codeine phosphate is popular in cough and in bronchitis and useful in respiratory diseases.[22] More than 30 alkaloids have been isolated from *P. somniferum*. The major alkaloids are morphine (4-21%), noscapine (4-8%), codeine (0.8-2.5%), papaverine (0.5-2.5%), and thebaine (0.5-2%).[220] The essential oil of *P. somniferum* obtained by hydrodistillation method consists of tridecanoic, myristic, palmitic, steraric, oleic, linoleic, linolenic, eicasadienoic, eicasatrienoic saturated and unsaturated oil.[221]

The antioxidant properties characterized by IC_{50} values is 35.1 to 157.6 µg/mL for DPPH radical, 138.5 to 306.3 µg/mL for ABTS radical scavenging.[222] The FRAP values varied from 59.75 to 1348.71 mM $FeSO_4$/g extract.[222] Opioid compounds modulate both innate and acquired immune responses and opioid receptors participate in the function of the cells of the immune system.[223] The plant showed anti-HIV activity. Chloroform and butanol extracts of *P. somniferum* seeds with concentration of 7.5 and 15 mg/ml extract resulted in inhibition of 44.2 and 41.7%.[224]The plant has also been used against respiratory diseases. Opiate drugs have long been known to exert effects on the respiratory system. These include reducing the respiratory

response to CO_2, hypoxia, inspiratory flow-resistive loading and exercise, with overdoses being capable of producing respiratory depression. Opioid receptors from various areas of the CNS and the cardio-respiratory systems seem responsible for the mediation of the mechanisms of their antidyspnoeic effects.[225] Triple effects of opioids such as treating dyspnoea, inhibiting the cytokine storm and disrupting lysosomal acidification with effects on both the viral infectious cycle and on the host's response to the infection, morphine could potentially be exploited in Covid-19.[225]

(37) *Peganum harmala*

The seeds in the form of powder are given in the treatment of intermittent and remittent fevers. The drug is useful in chronic malaria. Its decoction is a good anodyne in asthma.[22]The commonly known phytochemical compounds are alkaloids, flavonoids and anthraquinones. The plant is rich in indole alkaloids and type β-carboline alkaloids contain up to 2 - 7% total alkaloids including harmaline, harmine, harmalol, harmol and tetrahydroharmine.[226,227]Vasicine and vasicinone are quinazoline alkaloids that found in the plant. The aerial parts of *P. harmala* contain flavonoids, including acacetin and glycoflavone. Two anthraquinones from the seeds are peganone 1 and peganone 2.[228] In addition, a total of 105 compounds were identified in the essential oil seed, the main components being oxygenated monoterpenes and oxygenated sesquiterpenes and eugenol.[229] Total phenolic content of aqueous, ethanol and aqueous-ethanol extract are 348.82±2.79, 318.41±28.49, and 329.09±27.48 mg Gallic acid/g dry weight.[230]DPPH method specifies an IC_{50} equal to 112.96 µg/mL, 35.83 µ/mL and 107.91 µg/mL respectively for leaf, seeds and alkaloids extracts. Standard ascorbic acid shows IC_{50} value of 4.24 µg/ml.[231]Seed extracts are potent reversible and competitive inhibitors of human monoamine oxidase (MAO-A) with an IC_{50} of 27 mg/l whereas root extracts strongly inhibits MAO-A with an IC_{50} of 159 mg/l.[227] The potent inhibition of MAO-A by seed and root extracts of *P. harmala* should contribute to the psychopharmacological and toxicological effects of this plant and could be the basis for its purported antidepressant actions.

Preliminary study showed that the ethanolic seeds extract of *P. harmala* and its total alkaloids have an antiviral activity against influenza A/Puerto Rico/8/34 (H1N1; PR8) virus.[232] The crude extract of *P. harmala* seed and its total alkaloids showed the best inhibitory effect against influenza A virus replication in MDCK cells using MTT assay, $TCID_{50}$ method and hemagglutination assay. The IC_{50} of crude extract and total alkaloid influenza virus were 9.87 (CI95%: 7.3-11.3) and 5.8 (CI95%: 3.7-8.9) µg/ml with SI value of 12.45 and 23.1 respectively. In comparison, The IC_{50} and CC_{50} of oseltamivir were 539.4 (CI95%: 378.9- 768.5) and 0.873 (CI95%: 0.55-1.37) µmol with SI value of 617.8. The extract inhibited viral RNA replication and viral polymerase activity but did not effect on hemagglutination inhibition and virucidal activity. This *in vitro* antiviral activity is most probably associated with inhibiting viral RNA transcription.[232]

(38) *Picrorhiza kurroa*

The plant has beneficial results in the management of bronchial asthma.[22]*P. kurroa* contains iridoids such as picroside-I and II as major bioactive compounds, pikuroside, veronicoside, phenol glycosides, a number of cucurbitacin glycosides and 4-hydroxyl-3 methoxyacetophenone.[233,234] Hydroalcoholic fraction of *P. kurroa* contains iridoid glucosides such as picroside I, picroside II, picroside III, picroside IV, kutkoside, pikuroside and flavonoids like apocynin and vanillic acid.[235] Butanol extract of the stems of *P. kurroa* contains bis-iridoid glycosides, saungmaygaosides A-D, and iridoid glycosides.[236]

P. kurroa exhibits DPPH radical scavenging and metal chelating activities with IC_{50} of 75.16±3.2 and 55.5±4.8 µg/mL and also shows potent reducing power and total antioxidant activities.[235]The extract inhibits macromolecule damage such as H_2O_2 induced plasmid DNA damage and AAPH induced oxidation of bovine serum albumin and lipid peroxidation of rat hepatic tissues.[235] A 50% ethanolic extract of *P. kurroa* leaves was found to stimulate the cell-mediated and humoral components of the immune system as well as phagocytosis in experimental animals.[237] Methanolic extracts of *P. kurroa* rhizome in Wister rats at 260

mg/kg as well as 520 mg/kg exhibited highly significant analgesic and antipyretic activity by oral dose for analgesic and rectal dose for antipyretic effects.[238] Compounds saungmaygaoside D, sylvestroside IV dimethyl acetal, and sweroside showed potent inhibitors with effective doses of 5 and 10 μM, respectively, without showing any notable cytotoxicities in anti-Viral protein R (Vpr) activity using TREx-HeLa-Vpr cells.[236] Extracts of *P. kurroa* plants also have potent antiviral action against both DNA and RNA-based viruses.[239]

(39) *Piper longum*

It is given with honey in doses of 5 to 10 gr for indigestion, dyspepsia, flatulent colic, cough, chronic bronchitis, chest affection and in asthma.[22]*P. longum* contains a large number of alkaloids and related compounds. The most abundant is piperine, together with methyl piperine, iperonaline, piperettine, asarinine, pellitorine, piperundecalidine, piperlongumine, piperlonguminine, refractomide A, pregumidiene, brachystamide, brachystamide-A, brachystine, pipercide, piperderidine, longamide, pirrolidine, pyrrolidine, (*R*)-(-)-turmerone, (+)-aphanamol I, demethoxycurcumin, guineesine, pipericide, 2*E*,4*E*-dienamide, piperlonguminine, methyl piperate and other compounds.[240,241,242]

P. longum showed anti-oxidant activity by DPPH scavenging method. It has been found that at 50 mg mL^{-1} concentration petroleum ether extract and piperine exerts 74.12 and 72.13% of inhibition.[243] Alcoholic extract of the fruits and its component piperine have been studied for their immunomodulatory activity.[244] Administration of *Piper longum* extract and piperine increased the total white blood cell (WBC) count to 142.8 and 138.9%, respectively, in Balb/c mice. Piperine also exhibits significant analgesic and antipyretic activities without ulcerogenic effects and the results were comparable with indomethacin which was used as standard drug for reference.[245]*Piper longum* in methanolic extract showed higher anti-viral activity against Human para influenza virus on HeLa cell line.[246] Cytotoxicity assay of *P. longum* treatment showed significant dose-dependent inhibition of growth of HeLa cells at IC_{50} values of 46.24, 33.43 and 38.49μg/ml at 24, 48 and 72 hours of incubation respectively. In addition, *P. longum* in methanolic extract showed 100% of inhibition at 240 mg/ml.

(40) *Rheum emodi*

The tuber is very useful in chronic bronchitis, chronic fever, asthma and coryza.[22] The main chemical constituents are emodin, aloe-emodin, physcion, chrysophanol, rhein, emodin glycoside chrysophanol glycoside such as sulfemodin, revandchinone-1, revandchinone-2, revandchinone-3, revandchinone-4, 6-methyl-rhein and 6-methyl aloe-emodin.[247]

The extract of *R. emodi* possesses antioxidant activity. *In vitro* evaluation the antioxidant potential of methanolic crude extract is the highest (IC_{50}18.28mg/mL), followed by ethyl acetate crude extract (IC_{50}19.37mg/mL) and chloroform extract (IC_{50}20.27mg/mL) in DPPH radical scavenging activity.[248]The ethyl acetate extract of *R. emodi* rhizome has been shown to possess immuno-enhancing activity on cell lines. The effect is believed to be because of a dose-dependent increase in the release of nitric oxide and cytokine TNF-α, IL-12 and a decrease in IL-10 by RAW 264.7 in macrophage cell lines in the presence of extract alone.[249]Emodin, one of the main phytoconstituents, found to block both the binding of SARS-CoV S protein to ACE2 and the infectivity of S protein-pseudotyped retrovirus to Vero E6 cells. These findings suggested that emodin was a novel anti-SARS-CoV compound and might be considered as a potential lead therapeutic agent in the treatment of SARS.[250]

(41) *Rhus succedanea*

The galls are useful in cough, phthisis, asthma, fever and condition of the respiratory tract.[22] Phytochemical screening showed the presence of carbohydrates, protein, alkaloids, phenols, flavonoids, terpenoids and anthraquenones.[251] Bioactive constituents from *R. succedanea* include amentoflavone, agathisfla-vone, robustaflavone, hinokiflavone, volkensiflavone, volkensiflavone hexamethyl ether, rhusflavanone,

rhusflavanone hexaacetate, succedaneaflavanone, and succedaneaflavanonehexa acetate.[252]

Aqueous extract of *R. succedanea* galls showed remarkable and concentration dependent free radical scavenging activity comparable to that of standard ascorbic acid in the studied models. $IC_{50}$was found to be 27.33μg/ml and 32.63μg/ml in DPPH assay and NO scavenging assay respectively.[253]Biflavonoid compounds of *R. succedanea* demonstrated activity against HIV-1 reverse transcriptase (RT), with IC_{50} values in the range of 65-236 microM. In addition, morelloflavone compound of *R. succedanea* demonstrated significant antiviral activity against HIV-1 (strain LAV-1) in phytohemagglutinin-stimulated primary human peripheral blood mononuclear cells at an EC_{50} value of 6.9 μM and a selectivity index value of approximately 10.[254]Another study showed that biflavonoids as well as their methyl ethers and acetates of *R. succedanea* have antiviral activities against a number of viruses including respiratory viruses (influenza A, influenza B, respiratory syncy-tial, parainfluenza type 3, adenovirus type 5, and measles) and herpes viruses (HSV-1, HSV-2, HCMV, and VZV).[252]

(42) *Salvadora persica*

In the form of a decoction, it is given in asthma and cough.[22] The chemical constituents are N-benzylbenzamide, decane, stigmasterol, 9-desoxo-9-x-acetoxy-3,8,12-tri-O-acetylingol, β-sitosterol, 2,6-dimethyl-N-(2-methyl-α-phenylbenzyl)aniline, spiculesporic acid, homo-γ-linolenic acid, methyl hexadecanoate, benzeneacetonitrile, 4-aminocarbonyl-5-fluoro-1-α-D-ribofuranosyl-imidazole, and benzylisothiocyanate.[255]

Sulphur-containing imidazoline alkaloid persicaline isolated from *S. persica* shows a promising antioxidant activity with IC_{50} 0.1, 0.08, and 0.09 μM in the three assays - DPPH, superoxide anion and nitric oxide radicals scavenging assays, respectively, comparable to ascorbic acid.[256]Immunomodulator properties of water and alcohol extracts have been done by observing Specific Phagositosis Activity (SPA) and Index Phagositosis (IP) of mice peritonium macrophage cells level induced by *S. epidermidis* bacteria.[257] Water extract enhance SPA and IP at the level of 57.7 and 76.1%, while alcohol extract enhance 82,7% and 90,2% compare to negative control, respectively. The efective of SPAand IP of the tested extracts as imunostimulant is in low dose (0-100 μg), but administration of extract in higher doses (100-1000 μg) indicatedimunorestoration tendency, especially on water extract.[257]*S. persica* inhibites the replication of HSV-1 in baby hamster kidney cells as well as the cytolytic activity of cell free virus. Topical application of *S. persica* on the skin of mice infected with HSV-1 reduces the development of cutaneous lesions and the viral titers in the skin and ganglia are also reduced.[258]

(43) *Solanum indicum*

The plant is useful in asthma, dry cough, difficult parturition and chronic febrile affection.[22] Various phytoconstituents from the plant has been reported, which includes phytoconstituents steroidal saponins, steroidal glycoside, sesquiterpenoids, sesquiterpenoids, hydroxycoumarins, phenolic compounds, coumarins, coumarinolignoids alkaloids, saponin, fatty acid,glycerides of the oil, polysachharide, and triterpenes.[259]

Ethanolic and aqueous extracts of berries from *S. indicum* have been investigated for its antioxidant activity using *in vitro* DPPH scavenging assay and β-carotene/linoleate model system.[260] The IC_{50} values for ethanolic and aqueous extracts are 10.17 ± 0.6) and 21.83 ± 0.84 % for DPPH assay compared to ascorbic acid (3.0 ± 0.4 %) as standard. While, antioxidant activities of ethanolic and aqueous extracts of *S. indicum* fruits by using β-carotene-linoleic acid method are37.22 ± 1.3 and 29.07 ± 1.5 % compared to BHA (46.86 ± 0.1 %) as standard.The methanol extract of dried fruits of *S. indicum* has been evaluated for its analgesic, anti-inflammatory, antipyretic and central nervous system(CNS) depressant activity. The crude methanol extract exhibited statistically significant analgesic, anti-inflammatory, antipyretic, and CNS depressant activity on the established animal models.[261] Experimental evidences lead to the hypothesis that methanol extract of *S. indicum* Linn. fruit possesses pharmacological activity which satisfies the claim of traditional medicinal uses.

(44) *Solanum surattense*

The plant is useful in fever, cough and asthma. A fine powder of the fruits of this plant mixed with honey is very useful for chronic cough in children. A decoction of the root with that of *Tinospora cordifolia* is used as tonic in fever and cough.[22]*S. surattense* contains bioactive compounds including solanocarpine, solamorgine, solanocarpidine, caffeic acid, coumarins (esculentin and aesculin), steroids (carpesterol, campesterol, daucosterol, stigmasterol, cycloortanol and cholesterol),triterpinins and sapogenin (lupeol and diosgenine), solosodine, β-sitosterol, diosgenin, cyclocartanol, cycloartinol, sitosterol, stigmasterol, campsterol, sitosteryl glucoside, solamargine, β-solamargine, linoleic acid, oleic acid, palmitic, steric and arachidonic acid.[262]

The plant extract exhibited remarkable antioxidant activity at all test doses in a dose-dependent manner with IC_{50} value of 55μg/ml.[263]Methanol extracts of fruits of *S. xanthocarpum* showed pronounced immunoprotective activity by increasing the depleted levels of total WBC count and RBC, % Hb, and % neutrophils adhesionat a dose of 100mg/kg body weight.[264,265]The fruit extract of *S. surattense* has been reported to possess anti-reverse transcriptase (RT) activity. Acetone extracts at 0.6 μg/ml concentration exhibited 20% of RT inhibition, whereas extracts at 6 μg/ml, benzene exhibited 25% followed by hexane (20%) and chloroform (15%).[266] In search of safe and effective medicine from the plants to cure asthma, *S. surattense* considered as the right choice, because of long usage in Ayurveda and siddha as effective to cure respiratory disorders.[267] Anti-asthmatic efficiency studies on *S. surattense* flower extracts revealed that the presence of anti-histamine and mast cell stabilizing efficiency.

(45) *Swertia chirata*

It is well-reputed drug for intermittent fevers. It is given in the form of infusion or tincture in bronchial asthma.[22]The plant has a wide spectrum of pharmacological properties. The wide-range biological activities of *S. chirita* are attributed to the presence of a diverse group of pharmacologically bioactive compounds belonging to different classes such as xanthones and their derivatives, lignans, alkaloids, flavonoids, terpenoids, iridoids, secoiridoids, and other compounds such as chiratin, ophelicacid, palmitic acid, oleicacid, and stearic acid.[268]The pharmacological efficacy of *S.chirata* has been partly attributed to the biological activity of major phytoconstituents including amarogentin, swertiamarin, mangiferin, swerchirin, sweroside, amaroswerin, and gentiopicrin.[269]

Various methanolic extracts showed significant antioxidant activity. The IC_{50} value of the DPPH method is in the range of 74.3 ± 3.4 to 85.77 ± 2.49 %.[270] The methanolic extract of *S. chirata* showed dose related decrease in primary and secondary antibody response and Delayed type hypersensitivity (DTH) response with the maximum decrease at 200 mg kg^{-1} b wt (primary antibody response-5.41±0.24, secondary antibody response-5.39±0.19 and DTH response-0.62±0.05) on Swiss albino mice.[271] It also showed dose dependent decrease in the production of T lymphocytes (CD3 and CD19) and Th 1 cytokines (IL-2, IFN-γ and IL-4). The maximum decrease in the production of CD3, CD19, IL-2, IFN-γ and IL-4 was 33.66, 19.70, 31.12, 35.09 and 14.63% at 200 mg kg^{-1} b wt.[271] The results revealed that *S. chirata* showed significant decrease in the production of CD3 and IFN-γ.[271] The aqueous extract has been evaluated for its antipyretic potential on Brewer's yeastinduced pyrexia in albino rats and Typhoid-Paratyphoid A, B vaccine induced Hyperexia in rabbits. In both models, the extract, at dose of 200 mg kg^{-1} body wt. and 400 mg kg^{-1} body weight, produced significant reduction in elevated body temperature in a dose dependent manner.[272] The antipyretic effect of the extract was comparable to that of paracetamol (150 mg kg^{-1} body weight, p.o.), a standard antipyretic agent. *S. chirata* plant crude extract (1 gm/mL) at 1:64 dilution inhibited HSV-1, plaque formation at more than 70% level.[273]

(46) *Taxus baccata*

In the form of tincture, it is used as antispasmodic and given in asthma.[22]The major compounds, approximately 30% of the total alkaloid fraction from *Taxus baccata* consist of a mixture of compounds called "taxine", which contains the main alkaloids taxine B and isotaxine B and is responsible for the toxicity of the yew plant

have been isolated in yields of 1.2% dry wt.Alkaloids taxoids paclitaxel (taxol A), 10-deacetyltaxol,baccatin III, 10-deacetylbaccatin III, cephalomannine (taxol B), and 3,5-dimethoxyphenol; the alkaloidal diterpenoids monoacetyltaxine, taxine B, monohydroxydiacetyltaxine, triacetyltaxine, and monohy-droxytriacetyltaxine have been determined in yew tree.[274]The predominant volatile constituents of *T. bacata* leaves are 1-octen-3-ol, 1-hexanol, (E)-2-hexen-1-ol, caryophyllene oxide and hexahydrofarnesyl acetone.[275]

The extracts of the leaves and seed cones of *T. baccata* have been analyzed for antioxidant activity by DPPH scavenging activity method. The IC_{50} value for acetone extract is 25.24±1.2 and 81.43±1.98 µg/ml for leaves and seed cones, respectively.[276]Among plant-derived natural products, paclitaxel ($C_{47}H_{51}NO_{14}$), which was first isolated from the bark of the Pacific yew *Taxus brevifolia*, also known commercially as taxol, is a chemotherapeutic diterpenoid drug that exhibits potent anticancer activity.[277]Paclitaxel exhibited inhibitory activity to a certain extent after viral invasion of the cells. At a paclitaxel concentration of 20µg/mL, the inhibition of HIV-1 pseudovirus reached about 66%.[278]

(47) *Tinospora cordifolia*

The plant is commonly used in bronchitis. In cough and chronic fever the juice of the fresh plant is administered in doses of 56 to 112 ml with long pepper and honey.[22] The chemical constituents of *T. cordifolia* belong to different classes such as terpenoids, alkaloids, glycosides, steroids, phenolics, and aliphatic. Terpenoids found in *T. cordifolia* are tinosporide, furanolactone diterpene, furanolactone clerodane diterpene, furanoid diterpene, tinosporaside, ecdysterone makisterone and several glucosides isolated as poly acetate, phenylpropene disaccharides cordifolioside A, B and C, cordifoliside D and E, tinocordioside, cordioside, palmatosides C and F, sesquiterpene glucoside tinocordifolioside, sesquiterpene tinocordifolin.[278]Alkaloids in *T. cordifolia* are (S)-tinosporine, (S)-magnoflorine, (S)-berberine, (S)-choline, (S)-jatrorrhizine, (S)-1,2-substituted pyrrolidine, alkaloids, viz. jatrorrhizine, palmatine, beberine, tembeterine, choline.[279]

Ethanolic stem extract of *T. cordifolia* has phenol content of 66.28 ± 0.82 mg/g and showed the antioxidant activity of 56.35% using DPPH free radical scavenging method.[280] The formulation of *T. cordifolia* tablet showed potent antioxidant activity and inhibitory concentration (IC_{50}) at 5 µg/ml as compared to standard drug ascorbic acid.[281]Compounds isolated from ethyl acetate, water fractions and hot water extract of *T. cordifolia* exhibited significant immunomodulatory activity with significant enhancement in phagocytic activity and increase in nitric oxide and reactive oxygen species generation at concentration 0.1-2.5 µg/ml.[282]The anti-pyretic activity of two *T. cordifolia* formulations (900 and 1800 mg/kg) in albino rats against yeast induced pyrexia has been investigated. Both the *T. cordifolia* samples including vehicle significantly attenuated the raise in temperature after three hours of yeast injection. After 6 and 9 hours of yeast injection also both the *T. cordifolia* samples attenuated the raise in temperature in a highly significant manner in comparison to both yeast control and vehicle control groups. This result shows that both the *T. cordifolia* formulations having significant anti-pyretic activity.[283]

T. cordifolia extract has been shown to demonstrate a decrease in the recurrent resistance of HIV virus thus improving the therapeutic outcome.[284] Anti-HIV effects of TCE was revealed by reduction in eosinophil count, stimulation of B lymphocytes, macrophages and polymorphonuclear leucocytes and hemoglobin percentage thus, revealing its promising role of application in management of the disease. The root extract of *T. cordifolia* affects the immune system of HIV positive patient.[285] The stem extract of *T. cordifolia* reduces the ability of eosinophil count, stimulation of B lymphocytes, macrophages, level of hemoglobin, and polymorphonuclear leucocytes.[286]The methanol and ethyl acetate (80:20) extract of *T.cordifolia* inhibits the growth of HSV by 61.43% at $10TCID_{50}$.[287]

(48) *Vitis vinifera*

Grapes are used in chronic bronchitis, in cough and fevers.[22] Grapes are rich in polyphenols; 90–95% of grape polyphenols exist in the seeds and skin. The major constituents of grape are epicatechingallate, procyanidin

dimers, trimers, tetramers, catechin, epicatechin, gallic acid, procyanidin pentamers, hexamers, and heptamers and their gallates, resveratrol, phenolics, flavonoids, and anthocyanins.[288]The plant contains vitamin C (6.25 mg ascorbic acid/100g) and anthocyanin (131mg/100g). A total of one hundred twenty nine compounds (forty two phenolic acids and their derivatives, twenty three flavan-3-ols, twenty one flavanols, five stilbenes and thirty eight anthocyanins) were identified in the plant extracts.[289]

The plant extract has strong antioxidant activity.[290]Regarding the phenolic compounds of the grapes, *trans*-resveratrol showed the strongest correlation with antioxidant activity. Grape reduces nitric oxide, prostaglandin E2, expression of nuclear factor κB and other pro-inflammatory cytokines like IL (Interleukin)-1β, IL-6, IL-8, and tumor necrosis factor-α. It also elevates anti-inflammatory mediators and expression of peroxisome proliferator-activated receptor-γ. According to these studies, grape probably has effects on the immune and endocrine factors involved in threatened miscarriage.[291]

The chloroform fraction of *V. vinifera* aqueous extract showed a promising effect against *Herpes simplex* virus type-1 (HSV-1) and *Parainfluenza* viruses (PIV).[292]Moreover, the effect of commercial grape seed extract (GSE), gravinol-S, on the infectivity of human enteric virus surrogates (feline calicivirus, FCV-F9; murine norovirus, MNV-1; and bacteriophage MS2) and hepatitis A virus (HAV; strain HM175) has been evaluated.[293] GSE at concentrations of 0.5, 1, and 2 mg/ml was individually mixed with equal volumes of each virus at titers of ~7 log10 PFU/ml or ~5 log10 PFU/ml and incubated for 2 h at room temperature or 37°C. The infectivity of the recovered viruses after triplicate treatments was evaluated by standardized plaque assays. At high titers (~7 log10 PFU/ml), FCV-F9 was significantly reduced by 3.64, 4.10, and 4.61 log10 PFU/ml; MNV-1 by 0.82, 1.35, and 1.73 log10 PFU/ml; MS2 by 1.13, 1.43, and 1.60 log10 PFU/ml; and HAV by 1.81, 2.66, and 3.20 log10 PFU/ml after treatment at 37°C with 0.25, 0.50, and 1 mg/ml GSE, respectively in a dose-dependent manner. GSE treatment of low titers (~5 log10 PFU/ml) at 37°C also showed viral reductions. Room-temperature treatments with GSE caused significant reduction of the four viruses, with higher reduction for low-titer FCV-F9, MNV-1, and HAV compared to high titers.[293]

(49) *Zingiber officinale*

Ginger (*Zingiber officinale*) is extremely valuable in the bowels unattended by fevers for cold, cough, asthma, dyspepsia and indigestion.[22]Ginger contains several compounds among which a mixture of zingerone, gingerol, zingiberene, β-sesquiphellandrene, shogaol, bisabolene (α-form); β-phellandrene, farnesene, 1,4-cineol, citral, camphene, 6-paradol, curcumene, terpineol (α-form), borneol, β-elemene, zingiberenol, limonene, geraniol, and linalool.[294] Other constituents include capsaicin, gingediol, galanolactone, gingesulfonic acid, galactosylglycerols, gingerglycolipids, diarylheptanoids, neral, monoacyldi-vitamins, and phytosterols. Ginger contains up to 3% of a fragrant essential oil and the main constituents are sesquiterpenoids, with zingiberene as the main component.[294]Otherimportant constituents present in the volatile oil are the mono and sesquiterpenes, camphene, β-sesquiphellandrene, β-bisabolene, α-farmesene, curcumene, cineole, citral, terpineol, terpenes, borneol, β-elemene, zingiberenol, limonene, geraniol, zingiberol and linalool. The nonvolatile phenylpropanoid-derived compounds, particularly gingerols, shogaols, paradols, and zingerone are responsible of the pungent taste of ginger.[294]Ginger shows to be comparatively as effective as ascorbic acid as an antioxidant agent.[295]The total phenol content of the alcohol extract is 870.1 mg/g dry extract. DPPH radical scavenging reached 90.1% and the IC_{50} concentration for inhibition of DPPH is 0.64 μg/ml. The ginger extract inhibited the hydroxyl radicals 79.6% at 37 ^{o}C and 74.8% at 80 ^{o}C, which show a higher antioxidant activity than quercetin. The IC_{50} concentration for inhibiting OH radicalsat 37 ^{o}C is lower than that at 80 ^{o}C - 1.90 and 2.78 lμ/ml, respectively.

Ginger exhibited a concentration- and time-dependent cytotoxic effect against protoscoleces and cyst wall and was more effective than the [6]-gingerol.[296] Other study showed that ginger essential oil recovered the humoral immune response in immunosuppressed mice.[297]The rhizome extracts of *Z. officinale* have high potential to

treat Chikungunya virus (CHIKV).[298] Maximum non-toxic dose (MNTD) of *Z. officinale* plant extract was found 62.5 µg/ml. During anti-chikungunya experimentation, cell viability increased to 51.05% and 35.10%, when Vero cells were pre-treated with MNTD and half of MNTD of *Z. officinale* extract respectively.Moreover, a lyophilized juice extract from *Zingiber officinale* at different concentrations (5, 25, 50, 75, 100, 150 and 200µg/ml) have been tested *in vitro* as anti-hepatitis C virus (anti-HCV) using the hepatocellular carcinoma HepG2 cell line infected with HCV. The inhibitory dose was found to be effective at 100µg/ml.[299]

Fresh ginger dose-dependently inhibited HRSV-induced plaque formation in both HEp-2 and A549 celllines. Incontrast, dried ginger did not show any dose-dependent inhibition.[300]Fresh ginger at 300 mg/ml concentration decreased the plaque counts to19.7% (A549) and 27.0% (HEp-2) of that of the controlgroup. In addition, fresh ginger at 300 mg/ml decreased the plaque formation to 12.9% on A549 cellswhen given before viralinoculation.Moreover, fresh ginger dose-dependently inhibited viral attachment and internalization. Fresh ginger of high concentration could stimulate mucosal cells to secrete Interferon-b (IFN-b) that possibly contributed to counter acting viral infection.

(50) *Zizyphus vulgaris*

Syrup of dried*Z. vulgaris*fruits is used for bronchitis. The fruit is sweet or sour, good in chronic bronchitis and fever.[22]The plants contain active principles including saponin compounds, jujuboside A and B, flavonoid components and flavone-C-glycosides such as swertisin, spinosin, 6-sinapoylspinosin, 6-feruloylspinosin, ρ-coumaroylspinosin, cyclopeptide alkaloids sanjoinine A (frangufoline), B, D, F, G1 and sanjoinenine, and other compounds such as nuciferine, nornuciferine, norisocorydine, N-methylasimilobine, caaverine, sanjoinine-K, steroid triterpene, botulin, ziziphusine, jajubogenin, mucilage, vitamin C, proteins, sugar and ziziphique acid.[301]

Anti-oxidative capabilities of *Z. vulgaris* have been evaluated by determining its effect on cell membrane of hepatocytes and red blood cell hemolysis.[302] The inhibitory effects of *Z. vulgaris* ethanolic and aqueous extracts on hemolysis of RBC are 67% at a concentration of 10 µg/ml.Betulinic acid, a pentacyclic triterpene isolated from *Z. vulgaris* tree, showed the anti-influenza viral activity at a concentration of 50 µM without a significant cytotoxicity in influenza A/PR/8 virus infected A549 cells.[303] Also, betulinic acid significantly attenuated pulmonary pathology including increased necrosis, numbers of inflammatory cells and pulmonary edema induced by influenza A/PR/8 virus infection compared with vehicle- or oseltamivir-treated mice *in vivo* model. The down-regulation of IFN-γ level is critical for innate and adaptive immunity in viral infection after treating of betulinic acid in mouse lung. Based on the obtained results, it is suggested that betulinic acid can be the potential therapeutic agent for virus infection via anti-inflammatory activity.[303]

Based on all the scientific findingsabove, it can be fairly conclude that Ayurvedic medicinal plants naturally provide a variety of antioxidant, immununomodulatory, antipyretic and other biological active compounds so that they have a great potential for prevention and therapeutic treatment of Covid-19. Most Ayurvedic formulations are polyherbal drugs extracted from two or more plants to get the maximum effect based on empirical knowledge. The formulation can be fresh extracts, juices, syrups, tinctures, decoctions, teas, tablets or pills. Polyherbal combinations have proven more effective than single herbs. These constituents are combined accurately, in such a way that formula is balanced and reproducible. One or two of the plants in these combinations will be active and the others will play a supporting role. The supporting herbs will each have different actions, acting as catalysts to help proper absorption, transportation, and to reduce toxicity. If and ideal combination is delivered, then the result can be excellent, but such outcomes are based on thorough plant knowledge.[304] Moreover, bioavailability of Ayurvedic herbal drugs can depend on chemical complexity of the herbs due to synergetic and antagonistic action of the constituents in promoting absorption, hydrophobic properties determining the ability to cross luminal wall, gut microflora, and hepatic activity of the individual

and chemical modifications of the herbal constituents.[305]

Recent research shows that combining plants of varying potency enhances their effect, both when compared to individual plant use and also to the sum of their individual effect. This phenomenon is known as synergy. Some pharmacological actions, from the active constituents of some herbs, have proven to be significant only when potentiated by those of other plants, but are not evident when used alone.[306] Two mechanisms have been proposed for these actions: pharmacokinetic synergy and pharmacodynamic synergy.[307]Covid-19 infection involvesmany factors and crucial mechanisms, leading to both visible and invisible symptoms, and a combination of herbs are needed to cure it.

4. CONCLUSION

The Covid-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus infects the human body through the respiratory tract causing damage to the immune system by involving a complex mechanism and results in damage to vital organs. A drug combination is needed to deal with Covid-19 and plants provide it.Plants are the largest reservoir of bioactive secondary metabolites which contribute in the management of different diseases.They possess a wealth of single drug and formulation for treating various diseases. According to scientific finding, Ayurvedic medicinal plants possess a number of activities such as antioxidant activity, immunomodulatory activity, antipyretic properties, antiviral activity and other biological activities proving its potential for prevention and therapeutic usefulness in the treatment of Covid-19.A total of 50 Ayurvedic medicinal plants are identified as very likely to appeal to Covid-19. Many phytochemicals such as terpenoids, steroids, flavonoids, alkaloids, tannins and saponins in the plants materials are responsible for their activities. This information provides a basis for further research and development of clinical applications of Ayurvedic medicinal plants for the treatment of newly emerged corona virus.

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