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Indian Medicinal Plants use for the Management of Covid-19: A Review Article

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ABSTRACT

The world experience the first Pandemic of this century, because of emergency of Coronavirus (COVID-19), severe acute respirators syndrome coronavirus-2 (SARS-CoV-2). From ancient time, various Indian medicinal plants have been prescribed for various disease treatment which shows Antiviral and immunomodulating activities. Thus, the aim of this review artical is to present the importance of phytomedicine against COVID 19. The main aim is to review the detailed information of COVID-19, Indian medicinal plants & their bioactive compound that possess anti-inflammatory, anti-pyretic, anti-viral and immune-modulatory property like *Ocimum sanctum, Allium sativum, Withania sommifera, Citrus limon, Allium cepa* to examine the contributions of the Ayurveda, Yoga and Naturopathy, Unani, siddha and Homeopathy (AYUSH) in managing the COVID-19 pandemic .

Keywords- COVID-19, Indian medicinal plants,SARS - CoV -2, Phytochemicals.

Introduction

On March 2010, the coronavirus disease has been started as a pandemic by the WHO has turned into the deadliest pandemic after influenza pandemic that took place in 1918. This disease was unknown before the outbreak in Wuhan, Hubai province, China in December 2019[1]. In a short period of time, the pandemic has infected millions of people of more than 200 Countries. Due to recent increase of daily cases of infection India becomes the new global epicenter of COVID pandemic [2].

As of 21 October 2022, there hase been 623893894 confirmed cases of COVID-19 including 6553936 deaths, reported by WHO The reason that it took only over two months to be declared as "Pandemic" is the interconnectedness and ever increased worldwide travel. (According to WHO report). Over the countries, plants and Herbs are used as medicines, India has been a land of medicinal plants and possesses a rich history of traditional system[3]. Indian medicinal plants and herbs are used for medicinal properties throughout the world. Medicinal plants possess several properties and are known to cure some common prevalent disease such as cough, sneezing, fever, malaria, tuberculosis, skin disorder, Gastrointestinal disorders, some viral infections etc [4]. With many developing and developed countries more than 80% of the world populations including china, India are depend on traditional and Herbal drugs as the main source of health care, and in this the major portion is occupied by Indian medicinal plants[5].

The traditional knowledge could help us to find alternatives approach for developing new antiviral drug molecules [6]. So this review article highlights the usefulness of Indian medicinal plant in the fight against COVID-19 in many ways. The paper reviews the important plant derived compounds for immediate application in alleviation of symptoms, and important secondary metabolites as candidates For anti-COVID-19 drug discovery.

Methods -

The data present in this work is based on the information obtained from the present reviews on clinical trials for COVID 19 infection and their impact on Indian medicinal plants caused by SARS-CoV-2. The information was collected from electronic databases including Google scholar, news bulletins, Pub Med, Professional bodies like WHO, World meter and using books. To get knowledge about the medicinal plants with their traditional use to treat COVID-19 affected patients. The Search data was up to December 21, 2022 and found different medicinal guidelines that provide treatment measures for COVID-19.

Data inclusion criteria include (a) Studies involving crude extract, Fraction or their preparation of plants, microorganisms or marine origins acting against COVID-19. (b) studies related to derivatives of natural products (eg. isolated compounds).(c) studies with natural product inspired synthetic derivatives acting against COVID-19.

A Brief overview of coronavirus -

Coronavirus disease 2019 (COVID-19) originated in Wuhan, Hubai province, china in December 2019 [7]. SARS was determined to be caused by SARS-CoV and emerged in a market where civets were sold [8]. Coronavirus are envelope of positive sense single-standard RNA viruses with a nucleocapsid of helical symmetry and belongs to the β-genus, Nidovirgles order of the coronaviridae family [9]. The virus encodes twenty different Proteins including four main Structural proteins (S: spike, E-envelope, M-membrane, N-nucleocapsid) [10]. (Fig-1) Coronavirus comes under the broad realm of Ribovirid[11] (Fig 2). The spike proteins of viruses bind to the angiotensin-converting enzyme 2 (ACE2) receptor present in epithelium in the nose, mouth, lungs and there by enter into the human body[12]. The viruses affect mainly the upper respiratory tract and lower respiratory tract and which include symptoms like coughing, fever and shortness of breath, it can also lead to Pneumonia, and can affect the major organ of the body like the heart, brain, kidneys and blood vessels (Fig-3) [13,14], and even cause death.

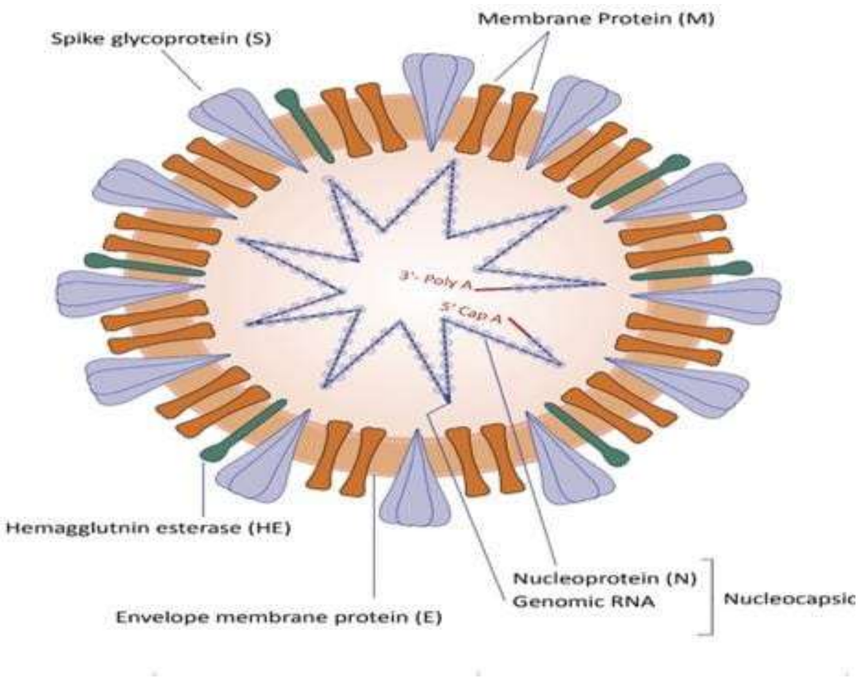

Fig -1 Schematic representation of SARS-CoV-2 structure and spike protein fragment

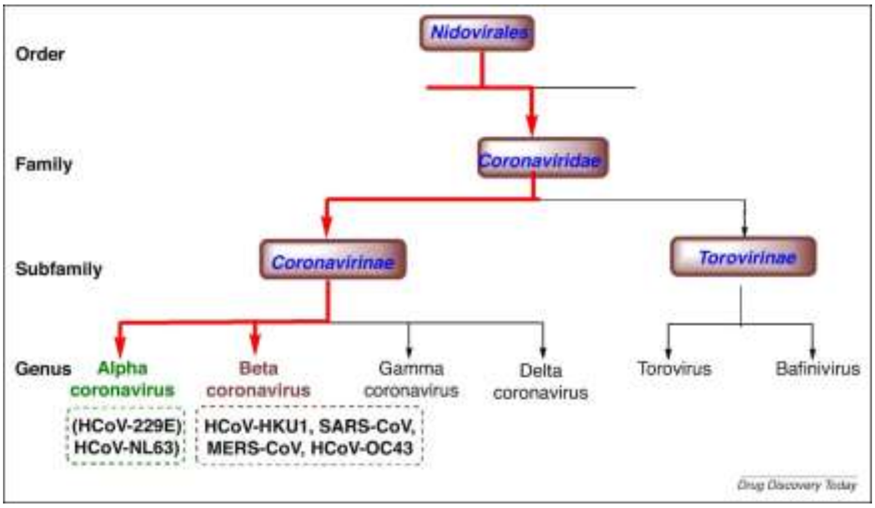

Fig. – 2. Classification of Corona virus

Pathophysiology of COVID-19

The effect of virus disturbed the normal function of cell. The virus affect ACE2 site.Virus enter in body by oral transmission and disturbed the function of ACE2 and this leads to increse bradykinin which cause the dry cough.

Bradykinin also known as chemical mediator which prevent breakdown of a natural chemical in the body and which cause swelling, may contribute to the development of angioedema in lungs & disturbed the function of alveoli [16].

T cell mediated responses against coronaviruses have been previously reviewed [17]. SARS CoV can also bind to dentritic cell specific intercellular adhesion molecule -3- -grabbing non-integrin (DC-SIGN) and lDC-SIGN related protein in addition to ACE-2 [18,19,20] CD8+ T cells are primary cytotoxic T cells . Severe patients also showed pathological cytotoxic T cells derived fromCD8+ T cells [21]. These cytotoxic T cells can killl virus but contibute lung injury [22].

Fig – 3 COVID-19 affects the major organs of the body

Some Plants Species and Bioactive Metabolites Used For the Treatment of Viral Infection

Plant name	Common name	Family	Parts used	Active compound	Effective against virus	Reference
Gymnanthemum amygdalinum	Bitter leaf	Asteraceae	Leaf, stem	Flavonoids, phenolic compound, ergosterol, oleic acid	HIV/AIDS, Retrovirus, covid	23
Withania somnifera	Ashwagandh	Solanaceae	Root, leaf	Flavonoids, alkaloids, fatty acid and phenolic compound	IBDV, HSV-1, HSV-2	24
Ocimum tenufloruml	Tulasi, basil	Lamiaceae	Leaf, seed	Caffeic acid, luteolin, apigenin, eugenol, limonene	Virions carrying diverse envelopes	25
Curcuma longa	Turmeric	Zingiberaceae	Rhizome	Alkaloids, steroids, saponins, glycosies, curcumene, curcone		26
Zingiber officinale	Ginger	Zingiberaceae	Rhizome	Gingerol, zingiberol, zingerone, alphcurcumene	Rhin ovirus IB, SARS-COV	27
Azadirachta Indica	Neem	Meliaceae	Leaves, root, bark stem bark	Deacetyl-3-cinnamoyi-azadirachtin	Newcastle disease virus(NOV), hepatitis virus	28
Origanam vulgare	Oregano	Lamiaceae	Essential oil	Thymol	Herpes simplex virus type-1 (HSU-1)	29
Allium cepa L.	Onion	Amaryllidacea e	Balbs	Flavonoids,sulfur-compounds s-propyl crystcinesulfoide, cycloallin	Influenza A virus, Newcastle disease virus(NDV)	30
Melissa officinalis	Lemon balm	Lamiaceae	Whole plant	Monolerpenaldehydecitral	Avian influenza virus (AIV)	31

Phyllanthus emblica L	Amla, Indion gooseberry	Leiothrichidae	Fruits	Tannins, flavonoids, saponins, terpenoids	HIV	32
Mentha piperita L	Peppermint	Lamiaceae	Leaf	Methanol, limonene, caryophyllene and pinene	Syncytial virus (RSV)	33
Allium sativum	Garlic	Amaryllidaceae	Root, leaves	Allicin, alliln, diallyl sulfide	Influenza A & B, HIV, HSV-1, viral pneumonia, rhinovirus	34
Morua alba L.	White mulberry toot	Moraceae	Root	Kuwanon S, mulberroside C, cyclomorusin, hydroperoxide	HSV-1, FMD virus	35
Nigella sativa L.	Black seed black caraway	Ranuncalaceae	Seed	Steroids, tannins, flavonoids, coumarin, glycosides, saponins	Murine cytomegalovirus (MCMV)	36,37
Glycyrrhiza uralensis fish	Licorice	Fabaceae	Root	Echinatin	HIV, RSV, HSV, SARS-COV	38
Ajuga bracleasa wall, ex benth	Bugleweed	lamiaceae	Whole plant	20-Hydroxyecdysone	Cytotoxic, phytotoxic, antioxidant	39
Hypericum connoum lam	St john's wort	Hypericaceae	Flowers	Amentoflavone, hyperoside, guaijaverine, luteoforol	HSV,HIV, inflenza	40
Panax ginseng	Ginseng	Panax	Root extract	Ginseng called ginsenosides	RSV, herpes viruses, hepatitis A	41

Brief description of some of the plants recommended for COVID-19

1) *Gymnanthemum amygdalinum*

- **Family**- Asteraceae
- **Genus** - vernonia
- **Botanical name** - vernonia amygdalina
- **Common name** - Bitter Leaf, South African Leaf [42]
- **Chemical constituents** - Hexadecanoic acid, oleic acid, ergosterol Flavonoids. and phenolic compounds [43]
- **Pharmacological principles** - oxalate, phytates Anti-COVID 19 activity, antimicrobial, terpens , anticancer , anti-allergic, antibacterial, steroid , antifungal, antipyretic , tannins ,antioxidant properties. [44,45]
- **Parts used** - Leaf , stem
- **Therapeutic uses** - Headache, fever, diarrhoea and cough [46].

Vernonia amygdalina is mostly found in Asia and high tropical Africa countries. It shows immune-inducing effects as an adjunct to vaccines. Aqueous extracts of G- amygdalina showed positive effects in inducing a humanimmune response by increasing the level of CD4+ and white blood cells [47]It has ability to increase the number of CD4+ counts, and showed an adjuvant to antiretroviral therapy in HIV patients. Currently, there is a lack of measurable evidence on the efficacy of this plant in COVID-19 patients to have good immunomodulatory, antiviral and anti-inflammatory effect [48].

2) *Withania somnifera*

- **Scientific Name** -Ashwagandha
- **Family**- solanaceae
- **Chemical constituents**- steroidal, alkaloids , Saponins, glycosides and volatile oil. Sitoindosides, withaferin A, withanolide A to Y, withasomniferin A [49].
- **Pharmacological Principle** ANTI-COVID-19 activity, Antimicrobial, Anti bacterial, Antioxidant, Anti -malarial, neuroprotective, Adaptogenic, Anti -diabetic [50, 51].
- **Parts used** - Root leaf, Alkali

- **Therapeutic uses**- fitigue, weakness, tumors, dyspnoea, insomnia, stress anxiety, infection etc. [52, 53]

In the current study, withaniasomnifera having a drug-like activity and used potent resource against COVID-19 which have highest affinity with active site residues of the SARS-COV-2 [54].

Withania somnifera may be candidate against the good COVID-19 [55].

3) *Ocimum tenuiflorum* L.

- **Scientific Name**- Holy Basil
- **Common Name** - Basil, Tulasi
- **Family**- Labiatae, Lamiaceae
- **Chemical constituents** - Bornylacetate, candinene, eugenol, eugenol methyl ether, methyl chavicol , limonene [56].
- **Pharmacological principle** -Tulsinol (A,B,C,D,E), Antiviral, Antifungal,Antibacterial, Adaptogenic , Hypoglycaemic, Antispaspasmodic, GI disorder [57,58]
- **Parts used** - Leaf, root, seed
- **Therapeutic uses** - fever, viral hepatitis, toxic disorders, dyspnoea, cough, worms.[59]

A recent study reported that

Ocimum sanctum effective in the managpamummemt of COVID-19. Basil leavel of sanctum contains chronic acid which is a caffeic acid derivatized with tartaric acid. The main phenolic compound found in both leaves and stems was Rasmarinic acid [60].

4) *Curcuma longa* L.

- **Common Name** - turmeric
- **Family**- Zingiberaceae
- **Chemical constituents** - carcamene, curcumenone, curcone. cineole, Curzevenone, eugenol, procurcumenol, epiprocureumenol,Curcuminoids [61].
- **Pharmacological principle** -Antibacterial, Antioxidant, Antiinflammatory,Antihistamine, Antiseptic, hypocholesterolenic, hydrochologogue[62].
- **Parts used** - Rhizome
- **Therapeutic uses** - Bronchitis, Respiratory illness, Bronchial asthma, tropical eosinophilia, diabetes, Anaemia, jaundice, skin disease relieve toxicity [63].

The main constituent of curcuma longa is curcumin, which neutralize the entry of SARS-CoV-2 viral protein. The binding to curcumin to RBD site of viral protein prolong with the viral attachment sites of ACE 2 receptor[64]. In India due to the uptake of curcumin the immunity and protective defence against COVID-19 infections boosted in many hospitalized Patients. So, the Curcumin considere of preventive heab in the inhibition of transmission of COVID-19 [65,66] .

5) *Zingiber officinale*

- **Common Name** - Ginger
- **Family** - zingiberaceae Chemical constituents- flavonoid, Alpha curcamene, citral, citronellol, gingerol, zingibevrenes, zingiberol, zingerone, gingerols, gingerenone A etc [67].
- **Pharmacological principle** - Anticancer Antibacterial, Antihistaminic, Antioxidant, Antiinflammatory Hypoglycaemic, bioavailability enhancer, Hypolipidemic [68].
- **Parts used** -Rhizome
- **Therapeutic uses** - Fever, dyspnoe,cough, heart ailments, reduced appetite, diarrhoea, blotted abdomen, bleeding disease, Anaemia [69].

Ginger is used a common triditional medicinal plant having many therapeutic properties. The phytocompound 6-gingerol obtained from ginger is an main candidate for drug discovery against. COVID-19, it proved to have the highest binding affinity with multiple target of SARS-CoV-2 [70].

6) *Azadirachta indica*

- **Common Name** - Neem tree, Margosa tree
- **Family** - Mediaceae
- **Chemical constituents**- Azadirachtin, Nimbin, NimbondialNimbidin, sitosterol, Margosinolide, laminoids, terpene [71]

- **Pharmacological principles**- Antimicrobial, Immunostimulant,anti-inflammatory, Antiarthritic, Antidiabetic [72] .
- **Parts used**- Root bark, stem bark, Leaves
- **Therapeutic uses** -Fever, skin disease, cough, alleviater toxicity, diabetes[73]

Neem extract having many therapeutic activities. The important phytochemicals in neem are limonoids and terpene [74]. In studied it is found that the bioactive compound present in neem such as Azadiradione, Epiazadiradione, Nimbione are the potential inhibitor of COVID-19 [75].

7) *Cymbopogon jwarancusa* (Jones) Schult

- **Common Name** - cetronella, lemon grass
- **Family**- Poaceae
- **Chemical constituents** - Piperitone, borneol, cadinene, camphene, champhor, farnesene, geraniol, alpha and beta pinene [76].
- **Pharmacological principle** - Diaphoretic, stimulant, Antioxidant, Antirheumatic, blood purifier, carminative, diuretic, lithontriptic, emmenagogue [77].
- **Parts used** - whole plant
- **Therapeutic uses** - Fever, gout, rheumatism, skin disease, blood disease, vomiting [78].

Safety and Regulatory aspects of using Phytomedicine -

This paper highlights the important of phytotherapeutic agents against COVID-19. The action mechanism of plant extracts rich in bioactive compounds an are potential against SARS-CoV-2. That ensuring all safety regulations in the clinical trials to treat or prevent COVID-19 viral infections. Therefore safety aspects must be taken into consideration. untested use of pure compounds is not recommended, and these compounds should first go through the proper testing of Safety and efficacy. For example Food & Drug Admisitration (FDA) provides guidlines for safe use of natural drug products [79].

There is a wrong perception that herbal drugs are fully safe and free from any side effects. There are some toxic constituents in many plants. But as compare to synthetic compound natural products and plant-based compounds shown lesser toxicity. However, to avoid side effects of the unregulated use of natural compounds, safety regulation on the use of products is important [80] . So, the regulatory authorities should work for regulating herbal products and using them as drug candidates for treating COVID-19.

Conclusion -

India has always known for its rich biological varities of plants, which found from Himalayas to the marine. The herbal medicine is a main platform for answering COVID-19 virus management. The secondary metabolites of many plants shows results against viruses. The phytochemicals serve as phytotherapeutic agents against the Coronaviruses. Medicinal plants can interfare with COVID-19 Pathogenesis by Inhibiting SARS-CoV-2 replication and avoid entry to its host cells. some plants effective in the prevention and supportive management of COVID-19 through boosting the immune system. The proper use of the Indian medicinal plants against COVID-19 reduce the risks of infection.

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