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Medicinal Plants for Potential Use in the Management of Covid-19 and other tropical diseases: A Review

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Abstract
The goal of this review is to present some medicinal plants and their antiviral properties in relation to Covid-19 and other tropical diseases.
The coronavirus disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (COVID-19). It is now well known thatsecondary plant metabolites have been used in the management of various diseases, including from diabetes, malaria, cancer and corona virus. They are adopted for used due to their accessibility and are cheap. Today's research, there are a plethora of essential medicinal plants with antiviral activity that can be utilized to treat viral infections and as a supportive treatment. Some of the limitations of medicinal plants include lack of information on their safety profiles and dosage for various ailments. Plant-based nutraceuticals can disrupt COVID-19 pathogenesis by preventing SARS-CoV-2 proliferation and entrance into host cells. Some of these antiviral medicinal plant species, such as V. amygdalina, Azadirachtaindica, Acanthaceae,Anacardiaceae, Apocynaceae, Asphodelaceae, Asteraceae, BombacaceaeCombretaceae, Cyperaceae, Fabaceae, Flacourtiaceae, Gentianaceae, Lamiaceae, MoraceaePhyllanthaceae, Piperaceae, Rosaceae, Rutaceae, Theacea, Urticaceae, Zingiberaceaeand Nigella sativa L. (Ranunculaceae), produce nutraceuticals that are useful adjuvant components in COVID-19 management.

1. Introduction
The aim of this review is to highlight several medicinal plants, their origins, features, and potential antiviral properties in relation to COVID-19.In the hunt for viable COVID-19 treatments, the World Health Organization (WHO) welcomes global breakthroughs such as repurposing medications, existing medicines, and generating new therapeutics.
Currently, viral infection has come to be the major global challenge to healthcare professionals due to uncontrolled rate of morbidity as well as mortality. A number of life-threatening viruses including human immunodeficiency virus (HIV), hepatitis virus subtype A, B, and C (HAV, HBV, and HCV), herpes simplex virus (HSV), influenza virus, and so others have been affected human health for decades. Along with these pre-existing viruses, corona virus-2 (SARS-CoV-2) has been turning into a global burden from 2019. The corona virus infection, also termed as "the novel coronavirus disease" (COVID-19) is characterized by severe acute respiratory syndrome resulting very high rate of death [71]. Unfortunately, lack of safe as well as effective antiviral drugs against these viruses has worsened the situation.
Ethnopharmacology has contributed immensely to the development of Phyto therapeutics and the discovery of new drugs [72]. In recent time, medicinal plants and their bioactive metabolites have become one of the main focuses of interest to search for effective as well as affordable drugs to cope with the current necessities [73]

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Traditional, complementary, and alternative medicine provide many benefits, according to the WHO, and traditional medicine and practitioners have a long history in Africa, where they play an essential role in delivering care to populations. Medicinal plants such as Artemisia annua are being investigated as potential COVID-19 therapies and should be thoroughly studied for efficacy and side effects. Africans have the right to use medications that have been subjected to the same rigorous testing as the rest of the world. Even though remedies are taken from conventional practice and are natural, rigorous clinical trials are required to prove their efficacy and safety.

2. Profile of Medicinal Plants

Profile of *Vernoniaamygdalina*

Kingdom: Plantae
Order: Asterales
Family: Asteraceae
Genus: Vernonia
Species: *V. amygdalina*

V. amygdalina is one of Africa's and Asia's most well-known plants. It is the most widely cultivated species of the Vernonia genus, which has over 1,000 shrub species. V. amygdalina was the most well-known species in the Asteraceae family that was researched in [1]. *V. amygdalina* does not normally produce seeds, however it is commonly grown in tropical locations and is cultivated through stem planting. This plant is generally found near drainage, commercial plantations, or forests [2]. V. amygdalina is a woody shrub that grows to a height of 2 to 10 meters and regenerates quickly after being planted. The leaves are petiolate in shape and have a bitter flavor, earning the moniker "bitter leaf." V. amygdalina is known by a variety of local names that change from nation to country. Saponins, alkaloids, tannins, and glycosides are all thought to contribute to the bitter taste. As a result, they can be used as a bittering agent and a hop substitute to control microbial contamination in beer brewing without lowering malt quality [1]. For a period of seven years, this plant can be picked twice a month. They're widely used in cuisine and traditional medicine, and their distinctive odor and bitter flavor can be lessened by washing in multiple changes of water or boiling before ingestion.

3. Several investigations on this plant have revealed that it includes flavonoids, saponins, alkaloids, tannins, phenolics, terpenes, steroidal glycosides, triterpenoids, and several forms of sesquiterpenelactones [1].These bioactive chemicals gave them antimicrobial, antimalarial, antithrombotic, antioxidant, anti-diabetic, laxative, hypoglycemia, antihelmintic, anti-inflammatory, cathartic, anticancer, antifertility, anti-fungi, antibacterial, and other pharmacological characteristics. [1,3]

Vernoniaamygdalina Bioactive Compounds Isolating and characterizing several bioactive components from *V. amygdalina* has been the subject of several investigations. Flavonoids, saponins, alkaloids, tannins, phenolics, terpenes, steroidal glycosides, triterpenoids, and numerous types of sesquiterpene lactones were isolated as a consequence of the phytochemical research.[4,5]. Sesquiterpene lactones (vernodalinol, vernolepin, vernomygdin, hydroxyvernolide, vernolide, and vernodalol) have been shown to suppress breast cancer cell development, have antitumoral and antibacterial activities, and have considerable bactericidal action against gram-positive bacteria. When tested on a murine macrophage cell line and wild chimps, isolated vernoniosides from *V. amygdalina* leaves displayed anti-inflammatory properties and were used to treat gastrointestinal disorders [4]. Antioxidant and hypolipidemic properties of flavonoids, tannins, saponins, and triterpenoids have been examined [3].In addition, the aqueous extract increased levels of surface antigen of the Hepatitis B virus (rHBsAg)-specific antibodies immunoglobulin M, immunoglobulin G sub class 1, and immunoglobulin A [6], suggesting that it could be used as an adjuvant to Hepatitis B vaccine. Ethanol, methanol, and acetone extracts have been shown to have anti-inflammatory efficacy in experimental animals by modulating levels of inflammatory cytokines and mediators, including the pro-inflammatory (prostaglandin-endoperoxide synthase 2)Nuclear factor kappa B (NFB), tumor necrosis factor-alpha (TNF-), interleukin-1, interleukin-6, interleukin-8, nitric oxide, CRP) and anti-inflammatory markers (NFB, TNF-, IL-1, IL-6, IL-8, nitric oxide, CRP) Despite the plant's purported significant effectiveness in regulating immunological and inflammatory responses, its toxicity profile is unknown. Although there was no mortality in an acute toxicity trial in animals [11], subacute administration of the aqueous extract (200 and 600 mg/kg body weight) in rats induced kidney congestion, while an ethanol extract (300 and 600 mg/kg) caused testicular toxicity [12].Despite several documented antiviral, anti-

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inflammatory, and immunomodulatory activities, there is currently insufficient direct evidence on the efficacy of V. amygdalina in COVID-19.

Profile of*Azadirachtaindica (A. indica)*

A good correlation is discovered with the outcomes of current experimental investigations, especially for inflammation-related disorders. There are also reports of a number of additional biological processes. Compounds belonging to the structural classes of limonoids, phenolics, and macromolecules are usually blamed for the effects.The evergreen tree *Azadirachtaindica* (Neem) is planted throughout the Indian subcontinent. Since antiquity, every part of the tree has been employed as a traditional medicine for treating various ailments in the home. Ayuveda, Urani, and Homeopathic medicine have all employed neem extensively. The Neem Tree is a remarkable plant that has been designated by the United Nations as the Tree of the Twenty-First Century [13]. Ancient medical writings frequently recommend extracts from the Neem tree (*A.indica*) for stomach troubles, diarrhea and intestinal infections, skin ulcers, and malaria[14].Its leaves can be used as a treatment for diabetes, eczema, and fever reduction. The roots of Neem can be used to heal ailments and repel insects, while the bark can be used to produce toothbrushes. The seed of the Neem tree contains a lot of oil. Neem oil is widely used as a pesticide, lubricant, and medicine for a range of ailments, including diabetes and tuberculosis [13,15,16]. Many biologically active substances can be isolated from neem's chemical ingredients, including alkaloids, flavonoids, triterpenoids, phenolic compounds, carotenoids, steroids, and ketones. Azadirachtin is made up of seven isomeric compounds labeled azadirachtin A-G, with azadirachtin E being the most effective [17]. Salannin, volatile oils, meliantriol, and nimbin[18] are other biologically active chemicals.Meliaazedarach Linn is a plant that has traditionally been used to cure leprosy, inflammations, and heart ailments. Its fruit extracts have ovicidal [19] and larvicidal [20] action. The leaf extracts of Meliaazedarach L. also have antiviral [21] and antifertility properties. Meliaazedarach Linn. has been well documented in Ayurveda for its therapeutic potentials. Because of its therapeutic and economic characteristics, it has been utilized in Ayurvedic medicine for more than 4000 years. This plant has long been known over the world as an insecticidal and therapeutic plant [22,23]. A close relative of neem is *Meliaazedarach L.Meliaceae* is a plant family found in India and other tropical and subtropical countries. It contains a chemical constituent that makes it a pest control candidate. It contains antibacterial, insecticidal, and nematocidal characteristics, according to reports. Antioxidant, antiviral, antiparasitic, ant lithiasis, analgesic, hematological, antimalarial, anti-inflammatory, and anti-fertility properties are also known.In vitro and in silico docking investigations shown that neem leaf extracts and phytochemicals such flavonoids and polysaccharides had direct antiviral activity against a variety of viruses, including dengue [24] and the Hepatitis C Virus. Molecular docking experiments have shown that the neem-derived chemicals nimbolin A, nimocin, and cycloartanols have the ability to bind to the SARS-CoV-2 envelope (E) and membrane (M) glycoproteins and serve as inhibitors [25].In terms of immunomodulatory effects, both neem seeds and leaves have been shown to improve immune response in animals [26,27]. Subcutaneous administration of neem seed extract increased the production of IFN- after Brucella Rev-1 immunization in mice [27]. The primary concern with investigating neem's potential for COVID-19 is its safety profile. Despite the fact that neem leaves have been used for centuries, there are no well-documented safety records.At high dosages of neem leaf extracts, some animal toxicity studies have indicated a variety of deleterious effects, including arrhythmia, hypoglycemia, and blood pressure reduction [28,29]. Human incidences of acidosis and renal damage have also been linked to the use of neem seed oil. Neem seed extracts should be avoided by pregnant women since animal research have indicated that they have abortifacienteffects [30], and human experiments have revealed that they have anti-human chorionic gonadotropin effects [30]. However, the traditional usage of neem for therapeutic purposes is mostly based on the intake of the leaves.consumed after boiling in water [31]. Due to safety concerns, studies confirming safe neem leaf doses appropriate to the formulation intended for use are required before additional efficacy research may be conducted.

Profile of *Nigella sativa L.*

is a plant that belongs to the *Nigella* genus (*Ranunculaceae*)*N. sativa* (Nigeria sativa) is often known as black cumin or black seeds, is a spicy, medicinal herb that is well-known for its culinary purposes and has long been prized in traditional

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medicine.Black cumin is grown in Egypt, Iran, Greece, Syria, Albania, Turkey, Saudi Arabia, India, and Pakistan, and is native to a large range of the eastern Mediterranean, northern Africa, the Indian subcontinent, and Southwest Asia. As a panacea, black cumin has been used in traditional medicine to treat a variety of ailments and conditions, including asthma, bronchitis, rheumatism, headache, back pain, anorexia, amenorrhea, paralysis, inflammation, mental debility, dermatitis, and hypertension, to name a few [32].The wide range of medicinal properties of *N. sativa* seeds, including antioxidant, anti-inflammatory, immunomodulatory, anticancer, neuroprotective, antimicrobial, antihypertensive, cardioprotective, antidiabetic, gastroprotective, and nephroprotective and hepatoprotective properties, are largely responsible for these traditional uses [33]. Thymoquinone (TQ), thymohydroquinone, thymol, carvacrol, nigellidine, nigellicine, and -hederin are largely responsible for the pharmacological actions and therapeutic benefits of black cumin seed, notably its essential oil [34].Black cumin has a high food value, despite its lack of attention in scientific literature, because it includes a sufficient amount of protein and fat, as well as a significant number of important fatty acids, amino acids, vitamins, and minerals [35]. Black cumin's active phytochemicals and critical nutrients both contribute to the human body's immunity and well-being, making this culinary plant a significant source of nutraceuticals.*N. sativa* (black cumin) seed was one of the medicinal plants with the most published positive evidence, according to our evidence summaries. Ethanolic extracts of *N. sativa* seeds showed antiviral effects in hepatitis C patients, reducing viral load, alpha fetoprotein, and improving liver function indicators [36. N. sativa seed oil showed antiviral and immunomodulatory actions against cytomegalovirus in animal experiments, lowering viral loads to undetectable levels. It can also boost the immune response by boosting CD3 and CD4 levels, as well as increasing the release of interferon-gamma (IFN-) from natural killer T cells and macrophages.In cell investigations, ethanolic extracts of N. sativa seeds inhibited the propagation of the coronavirus MHVA59 (mouse hepatitis virus-A59) by downregulating gene expression of different leukocyte transient receptor proteins (TRP) such TRPA1, TRPC4, TRPM6, TRPM7, TRPM8, and TRPV4 genes [38]. *N. sativa* has been utilized for a variety of purposes in the past, including respiratory illnesses like asthma [39]. The advantages of supplementing with *N. sativa*in a clinical experiment, it was also found to be effective in reducing asthmatic symptoms, which is assumed to be attributable in part to the anti-hypersensitivity and maybe anti-inflammatory characteristics [40]. Three distinct review publications have found that N. sativa has immunomodulatory and anti-inflammatory properties based on preclinical and clinical research. The immunomodulatory effects of *N. sativa* and its bioactive component thymoquinone have been described in respiratory illnesses, particularly those of infectious origin. Thymoquinone increases the survival of antigen-activated CD8+ cells in vitro, indicating the possibility for adoptive T-cell therapies [40].The ability of N. sativa to modify B cell-mediated immune responses while regulating the Th1/Th2 ratio to augment T cell-mediated immunity responses deserves more research. This action could be used in conjunction with possible vaccine candidates to help mediate a meaningful and long-lasting immune response after vaccination, which is one of the key problems with current COVID-19 vaccine candidates in development. Long-term (up to three months) ingestion of N. sativa seeds at 3 g/day in humans showed no significant detrimental effects on liver or kidney function. However, thymoquinone should be used with caution because animal toxicity tests at high doses of 2–3 g/kg resulted in hypoglycemia and hepatic enzyme abnormalities.

Profile of Acanthaceae

Mangrove plant *Acanthus ilicifolius L.*, which belongs to the Acanthaceae family, has many therapeutic qualities, including anti-inflammatory, antioxidant, and hepatoprotective actions. Strong antiviral action against the hepatitis B virus is displayed by this medicinal herb. According to a study using a duck model, an alcoholic extract of the entire plant can lower the viral load by interfering with DNA replication, albeit the precise mechanism was not well understood [41]. The genus Andrographispaniculata (*Burm.f.)*Nees is a member of the Acanthaceae family. It has outstanding anti-human immunodeficiency virus neutralizing properties (HIV). This plant contains andrographolide, a phytochemical with antiviral activity against the herpes simplex virus (HSV), HIV, flaviviruses, and pestiviruses [42]. This substance prevented HIV from altering the cell cycle, which raised CD4+ lymphocyte counts in HIV-1-infected individuals [43]. Additionally, this bioactive substance has been linked to reports of suppression of

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HSV-I viral envelope glycoproteins D and C expression [44]. According to a different study, andrographolide (5 g/ml) and an ethanolic extract of *A. paniculata* (25 g/ml) significantly reduced the production of the Epstein-Barr virus (EBV) lytic proteins Rta, Zta, and EA-D during the viral lytic cycle in P3HR1 cells [45]. Andrographolide is not harmful to P3HR1 cells at a concentration of less than 5 g/ml, according to this study. This substance is now undergoing a clinical trial (phase-IV) to treat bronchitis.

Profile of Anacardiaceae

Mangiferaindica L. is one of the most widely grown fruit trees and is regarded as the supreme fruit. It is a member of the Anacardiaceae family. Antioxidants and other nutritive macromolecules are abundant in this fruit. The plant extract's effectiveness against the influenza virus has been documented. In addition, it includes a bioactive substance called mangiferin that may be effective in preventing HSV-I replication and counteracting the cytopathic effects of HIV [46].

Profile of Apocynaceae

Folk medicine typically uses *Alstoniascholaris (L.) R. Br*., a plant of the Apocynaceae family, to treat colds, coughs, asthma, and chronic obstructive pulmonary disease (COPD). Total alkaloids from this plant have exceptional anti-inflammatory and antiviral properties. The entire amount of alkaloids found in this plant were found to be effective in combating IAV, according to a study. The inhibition of viral replication (in A549 cells and U937-derived macrophages), the reduction of cytokine and chemokine production at the mRNA and protein levels, the interference with the activation of pattern recognition receptor (PRR)- and IFN-activated signal transduction are all components of the mechanism underlying this antiviral activity (in A549 cells). Along with this, the lethal PR8 mouse model showed an increase in survival rate and a decrease in viral titer [47].

*Calotropisgigantea (L.)*Dryand, commonly known as milk weed, is a significant member of the Apocynaceae family and may be found in Bangladesh's Bandarban, Chattogram, Cox's Bazar, Khagrachari, that Rangamati. Two phenolic compounds, 6′-O-vanilloyltachioside and 6′-O-vanilloylisotachioside, as well as (+)-pinoresinol 4-O-(6″-O-vanilloyl)—d-glucopyranoside, have been identified from the plant's latex. Among these, the lignin glycoside (IC50 value of 13.4-39.8 g/ml) proved effective against H1N1 strains of both subtypes A and B. The viral ribonucleoprotein nuclear export was inhibited, and the NF-B pathway was also inhibited, all without interfering with the virus's ability to activate the Raf/MEK/ERK pathway [48].

Profile of Asphodelaceae

The *Asphodelaceae* family includes the well-known medical plant *Aloe vera (L.)*Burm.f., which is virtually ubiquitous in Bangladesh. Inhibitory activity of A. vera gel (0.2–5%) on HSV-I proliferation in Vero cell line has been documented. This investigation has shown that the topical gel treatment for oral HSV-I infection is efficient [49]. According to an in vitro investigation, treatment with an ethanolic extract of A. vera greatly lowers IAV replication while also inhibiting the production of the viral proteins hemagglutinin (HA), matrix protein 1 (M1), and matrix protein 2 (M2) (M1, M2, and HA). Many strong antiviral bioactive substances were discovered, including quercetin, catechin hydrate, and kaempferol, which have blocked IAV (H1N1 or H3N2)-induced autophagy and M2 activation. M2 protein expression and the production of viral mRNA. In addition to this, an in silico docking simulation investigation revealed that these bioactive substances have a higher binding affinity (for the M2 protein) than known M2 protein inhibitors. Because there are no effective medical treatment options now available, the COVID-19 pandemic has recently caused burden throughout the world. Quercetin is currently the subject of a clinical investigation to treat the infection's symptoms and as a preventative measure. Additionally, 9-dihydroxyl-2-O-(z)-cinnamoyl-7-methoxy-aloesin, aloeresin, and feralolide have been found in A. vera, and in an in-silico study, they demonstrated the potential to block the major protease (3CLpro) responsible for the replication of SARS-CoV-2. Due to its greater binding affinity to 3CLpro and drug ability (in accordance with Lipinski's rule of five), this study also showed that feralolide may be one of the best options for the creation of a potential drug for COVID-19 infection [50].

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Profile of Asteraceae

The sole member of the *Asteraceae* family with considerable antiviral properties is *Ecliptaprostrata L*. The cultivators in Bangladesh view this precious medicinal plant, which grows profusely in vacant fields, as weed. This plant, also known as kalokeshi, is used as a traditional remedy to cure blood-borne hepatitis and snake bites. This plant contains coumestan, a phytosterol that has been shown to have good inhibitory effect against the NS5B protein of HCV. For the replication of viral RNA, this protein is necessary [51]. This substance and its analogues may therefore be used as a starting point for the creation of brand-new HCV replication inhibitors.

Profile of Bombacaceae

The plant *Bombaxceiba L.*, which belongs to the Bombacaceae family, is widely distributed in Bangladesh. Because it makes cotton from blossoms, it is also known as the cotton tree. The cis-coumaroyl-connected flavonoid glycoside kaempferol-3-O-(6″-O-E-p-coumaroyl)—d-glucopyranoside is produced in this plant's flower. It has been shown that this flavonoid glycoside inhibits the respiratory syncytial virus (RSV) [52]. Additionally, a computer simulation study found that Kaempferol-3-O-(6″-O-E-p-coumaroyl)-d-glucopyranoside inhibits the SARS-CoV-2 ORF 3a protein. The expression of a cation-selective channel that controls the viral release mechanism depends on this protein.

Profile of Combretaceae

An Asian species of the Combretaceae family called Anogeissusacuminata (Roxb. ex DC.) Wall. exGuillem. &Perr. is found in Bangladesh's Bandarban, Chattogram, Cox's Bazar, Khagrachari, and Rangamati regions. Anolignan A and Anolignan B, two dibenzylbutadienelignans produced by this plant, were found to significantly block the HIV-I reverse transcriptase (RT) enzyme. Additionally, both phytocompounds had a synergistic effect on this enzyme [53].

Profile of Cyperaceae

Cyperusrotundus L., a member of the *Cyperaceae* family, is thought to be a bothersome and financially detrimental weed that can be found in practically all Bangladeshi croplands. Unexpectedly, this plant has a wide range of therapeutic benefits, including antidiarrheal, antioxidant, anti-inflammatory, antimutagenic, antiperiodic, anticonvulsant, anti-saturated, antipyretic, antifungal, antidiabetic, antimalarial, antilipidemic, antibacterial, antiviral, anti-tumoral, cardioprotective, and wound-healing properties. According to a study, this plant's rhizomes' essential oil exhibits inhibitory effect against HAV, HSV-I, and CVB. The two main bioactive components from this essential oil were discovered as humulene epoxide and caryophyllene oxide [54].

A promising candidate for the development of a topical therapeutic drug to treat HSV-I-caused recurrent infection has been reported to possess extremely powerful inhibitory activity against HSV-I. In addition, an in-silico study showed that humulene epoxide has exceptional affinity for four target proteins, including spike glycoprotein, papain-like protease (PLpro), 3-chymotrypsin-like protease (3CLpro), and RNA-dependent RNA polymerase (RdRp), which are essential for controlling the lifecycle of SARS-CoV-2.

Profile of Fabaceae

A plant belonging to the Fabaceae family called *Albiziaprocera (Roxb.)*Benth. can be found in Bangladesh's Chittagong, Chittagong Hill Tracts, Cox's Bazar, and Dhaka-Mymensingh Sal forests. The bark of this well-known traditional medicinal plant is used to treat stomachaches, haemorrhages, and rheumatism [55]. IAV is resistant to this plant's powerful antiviral effects. A study found that the integrase enzyme of IVA was inhibited by ethanolic, ethyl acetate, aqueous, and hexane-chloroform extracts of the bark of A. procera, with IC50 values of 19.5, 19.1, 21.3, and >100 g/ml, respectively. The bark of this plant contains two important chemicals, (+)-catechin and protocatechuic acid. Protocatechuic acid had a negligible impact compared to (+)-catenin's significant action against IAV intergase (IC50 value: 46.3 M). According to an in silico docking research, protocatechuic acid binds to Thr66, His67, Glu152, Asn155, and Lys159 while (+)-catechin interacts with Thr66, Gly148, and Glu152 in the core domain of the integrase enzyme [56].

4. Another significant member of the Fabaceae family and well-known medicinal plant known as "flame of the forest" is *Buteamonospermic (Lam.)*Taub (local name: Palash). This plant has a wide range of therapeutic benefits in Ayurvedic,

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Unani, and homoeopathic medicine. Scientific research, however, found that aqueous extracts of this plant's bark, flowers, fruit, leaves, and roots significantly inhibited EV-71 (BrCr). This plant's blossom yielded a flavone glycoside known as 5,7-dihydroxy-3,6,4-trimethoxy flavone-7-O-L xylopyranosyl (13)-O-L arabinopyranosyl-(14)-O-D galactopyranoside, which had strong antiviral activity.

Profile of Flacourtiaceae

A member of the family *Flacourtiaceae*, *Flacourtiaindica (Burm.f.)Merr*. is a tropical species with a wide geographic range that includes Bangladesh. It is a type of wild fruit that can be eaten and is used by practitioners of traditional medicine to treat snakebite. There have been reports of this medicinal plant's inhibitory effect against the dengue (DENV) and chikungunya (CHIKV) viruses. This plant's stem bark's ethyl acetate extract has been shown to suppress CHIKV. Additionally, isolated substances such as flacourtosides A and E, betulinic acid 3-caffeate (IC50 = 0.85 0.1 M), and scolochinenoside D (IC50 values 10 M) have been shown to have considerable inhibitory effect against DENV RNA polymerase enzyme [57].

Profile of Gentianaceae

Swertiaangustifolia var.pulchella (D. Don) Burkill, a member of the Gentianaceae family and a native of Bangladesh, is primarily found in mountainous areas. It is a common Ayurvedic herb used to treat diabetes and malaria. Additionally, local people utilize this herb as a traditional remedy for hepatitis, inflammation, and digestive issues. This herb's crude extract has been shown to have anti-HSV-I action [57]. In an anti-HBV experiment using HepG 2.2.15 cells line, (+)-cycloolivil-4′-O-d-glucopyranoside, a new bioactive chemical, reduced the production of HBsAg and HBeAg (IC50 values: 0.31 0.045 mM and 0.77 0.076 mM, respectively) as well as HBV DNA replication (IC50 value: 0.29 0.034

Profile of Lamiaceae

The *Lamiaceae* family, which includes the vast genus Ocimum, is recognized as "the medical plant for any ailment" and is widely distributed throughout Bangladesh. This genus' species have a wide range of therapeutic benefits, and they have been used as traditional remedies for centuries. The largest source of antiviral phytocompounds is actually the genus [58]. Ocimumtenuiflorum L., *Ocimumbasilicum L.*, *Ocimumgratissimum L.*, *Ocimumcampechianum Mill.*, *Ocimumamericanum L.*, *OcimumafricanumLour.*, *OcimumforsskaoliiBenth.*, and *Ocimumcarnosum (Spreng.)* Link & Otto ex Benth. are eight species of this genus that are found in Bangladesh O. tenuiflorum, also referred to as "basil or holy basil," is regarded as a sacred plant in Hinduism. In Bangladesh, this therapeutic plant can be found in practically every backyard. It produces a number of bioactive antiviral chemicals that have the ability to suppress HSV-I and II, including ursolic acid, eugenol, 1,8-cineole, and rosmarinic acid. O. basilicum, often known as sweet basil, includes substances that have been shown to be effective against HIV-I, HSV, ADV-3, 8, 11, HVB, EV, and CV, including 1,8-cineole, camphor, thymol, eugenol, eugenol epoxide, apigenin, linalool, and ursolicacid [58]. An aromatic plant called O. gratissimum is also referred to as African basil. Eugenol and thymol are two alcohols found in this basil leaf's essential oil. HSV-I and II replication is prevented by eugenol, but not by thymol. 1,8-cineole and -caryophyllene, which both suppress the infectious bronchitis virus (IBV) and destroy the HSV-I virion, have been isolated from O. campechianum [58]. O. americanum, often known as American basil, is an essential oil-producing medicinal plant that may be found in Bangladesh. The essential oils that were extracted from this herb are rosmarinic acid and oleanolic acid. Rosmarinic acid inhibits the internal ribosome entry site of EV-71 while oleanolic acid inhibits the HIV-I protease [58]. Caffeic acid, which is produced by O. africanum, prevents HSV-I from replicating. Additionally, linalool, which exhibits anti-ADV-11 action, has been extracted from the essential oil of this medicinal plant. Wild Amazonian basil, or O. forsskaolii, generates ursolic acid, which has anti-HCV properties. O. carnosum also demonstrated anti-HSV-I and II activity. due to presence of trans-anethole which inhibits multiplication of HSV-I and II [58][59].

Profile of Moraceae

Ficusreligiosa L., a member of the *Moraceae* family, is used in ancient Ayurvedic and Unani treatments to treat cough, wheezing, and asthma as well as gonorrhea and genital ulcers, which are sexually transmitted illnesses. This medicinal herb

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demonstrates a wide range of antiviral properties. A study showed that an ethanolic extract of the bark of F. religiosa suppressed Human Rhinoviruses (HRV) by interfering with the late steps of the replicative cycle (EC50 value: 5.52 g/ml). Aqueous extract demonstrated inhibitory effect against respiratory syncytial virus (RSV) by partial inactivation as well as inhibiting attachment to host cells (EC50 value: 2.23-4.37 g/ml) [60]. According to a different investigation, bark extracts in both aqueous and chloroform were effective against HSV-II and acyclovir-resistant strains. The underlying mechanism of the chloroform extract reduced the attachment and penetration of the virus to the host cell membrane along with the production of viral offspring, in contrast to the aqueous extract's immediate suppression of viral activity.

Another group of antiviral medicinal plant species can be found in the Artocarpus genus. The species of this genus that exhibit antiviral action include Artocarpus integer (Thunb.) Merr.,Artocarpusheterophyllus Lam., Artocarpuscamansi Blanco, and Artocarpusaltilis (Parkinson ex F.A.Zorn) Fosberg. Rotavirus (human rotavirus, HCR3 strain, and simian rotavirus, SA11) action against A. integer has been observed. Another study found that the leaves of A. heterophyllus exhibited considerable anti-HCV activity in dichloromethane extract (IC50 value: 1.5 0.6 g/ml) without significant toxicity, but the leaves of A. altilis and A. camansi exhibited only moderate anti-HCV activity (IC50 value: 0.6 g/ml). had IC50 values of 6.5 0.3 and 9.7 1.1 g/ml, respectively, which indicated moderate anti-HCV activity. The direct virucidal activity (inhibition of viral entry), inhibition of RNA replication, and increased concentrations of viral protein production were synergistic effects that contributed to A. heterophyllies' powerful anti-HCV efficacy.

Profile of Phyllanthaceae

A medicinal plant called Phyllanthus*niruri L.*, which belongs to the *Phyllanthaceae* family, is found in Bangladesh and is traditionally used to treat edema, constipation, helminthiasis, dysentery, diarrhea, and discomfort. Additionally, this herb has antiviral properties. HBV and woodchuck hepatitis virus (WHV) endogenous DNA polymerase has been shown to be inhibited by an aqueous extract of the entire plant [61]. According to another study, *P. niruri'*sethanolic extract possesses anti-HCV action (IC50 value: 4.14 g/ml). In addition, it demonstrated synergistic action (4-fold) with the well-known medication simeprevir, an inhibitor of the NS3 protease. In an in silico molecular docking study, phyllanthin and hypophyllantin from this plant were found to bind to the protein 4GAG, which is necessary for the entry of HCV into host cells.

Profile of Piperaceae

A non-toxic and edible grass from the *Poaceae* family known as durva grass or Bermuda grass is *Cynodondactylon L*. It is widespread in Bangladesh's rural areas and is used as an emmenagogue, alexipharmic, laxative, expectorant, emetic, coolant, and many other things. This herb has a strong antiviral impact against the bovine coronavirus (BCoV), which blocks the protease enzyme. This viral strain can be employed as a dietary COVID-19 intervention since it shares several characteristics with SARS-CoV and SARS-CoV-2 [63].

Profile of Rosaceae

Cabbage rose, Rosa centifolia L., is a member of the Rosaceae family of flowering plants that may be found in Bangladesh. This plant's leaves have antiviral properties. R. centifolia L. leaf methanolic extract exhibited anti-HIV efficacy [64].

Profile of Rutaceae

Aeglemarmelos (L.) Corrêa, a food-producing plant that belongs to the *Rutaceae* family, is widespread throughout Bangladesh. It is sometimes referred to as stone apple, wood apple, or bale. Due to its antidiarrheal, antibacterial, antiviral, radioprotective, anticancer, chemo preventive, antipyretic, ulcer-healing, antigenotoxic, diuretic, antifertility, and anti-inflammatory characteristics, several portions of this plant are utilized in Ayurveda. Seselin, a bioactive substance produced by this plant, has efficacy against several SARS-CoV-2 targets. Seselin has the potential to be an inhibitor of the receptors, according to an in silico molecular docking research. Protein from SARS-CoV-2S (binding energy: 6.6 kcal/mol), the primary protease of COVID-19 (6.9 kcal/mol), and the main protease free enzyme of SARS-CoV-2 (2019-nCoV) (6.7 kcal/mol) [66].

5. This family contains several plants that produce citrus fruits, including the sequentially known as lemon, orange, and grapefruit *Citrus limon*

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*(L.)*Osbeck, *Citrus sinensis (L.)*Osbeck, and *Citrus paradisiMacfad*. They are all excellent sources of vitamin C, which increases immunity and speeds COVID-19 recovery. There have been reports of essential oils with HAV inhibiting potential that were isolated from the fruits of several medicinal herbs. Hesperidin and luteolin, two potent antiviral substances, have been identified from C. sinensis fruit. Hesperidin was found to be effective at inhibiting spike protein and Mpro, which modify immature proteins (pp1a and ppa1b) to the complex and functional one to advance SARS-CoV-2 replication. Additionally, an in-silico assay for luteolin revealed that it inhibits the ACE2 receptor (both AT1 and AT2 subtypes) and the RdRp enzyme.

Profile of Theaceae

The tea plant, *Camellia sinensis (L.)*Kuntze, is a member of the *Theaceae* family and is also referred to as green tea, which is the most consumed beverage globally. This plant is grown in two ecologically distinct regions in Bangladesh, including the Surma valley in greater Sylhet and the Halda valley in Chittagong [67]. Epigallocatechin-3-gallate (EGCG), epicatechingallate (ECG), and epicatechin (EC) have been identified as the unique antiviral bioactive components from the leaves of this plant. EGCG has been linked to a variety of unexpected and unusual antiviral actions. It attaches to proteins on the surface of the virion and prevents HSV-I from adhering to the host cells' heparansulphate. It prevents HBV from expressing its antigen and synthesizing RNA and DNA. HCV, IAV, murine cytomegalovirus (mCMV), vesicular stomatitis virus (VSV), and reovirus are among the viruses that it has broad-spectrum antiviral activity against. In addition to this, EGCG demonstrated the ability to suppress the production of the HIV p24 antigen, hence inhibiting HIV reverse transcriptase. The HIV-I viral particle has been demonstrated to have a damaging effect. It also prevents HIV-I from adhering to the surface of the host cell. Furthermore, EGCG also prevents the growth of DENV, Japanese encephalitis virus (JEV), tick-borne encephalitis virus (TBEV), Zika virus (ZIKV), CHIKV, EV-71, and rotaviruses.

Profile of Urticaceae

The sole member of the *Urticaceae* family that demonstrates antiviral action is Boehmerianivea L. It grows in Bangladesh's Bandarban, Khagrachari, and Rangamati regions and has historically been used to stop miscarriages, encourage pus discharge from wounds, and treat infections. According to a study, the root's ethanolic extract has anti-HBV action. The author's proposed mechanism might entail a potential suppression of HBsAg and HBV DNA expression [68].

Profile of Zingiberaceae

Ginger, the actual Roscoe is a member of the *Zingiberaceae* family, which includes ginger, a popular cooking spice grown in Bangladesh. Because of its anti-arthritis, anti-inflammatory, antidiabetic, antibacterial, antifungal, and anticancer characteristics, this herb's rhizome has been employed in Ayurveda since ancient times. This herb's rhizome's freeze-dried powdered extract shown anti-HCV and anti-CHIKV properties. Gingeronone A and 6-gingerol, two active metabolites found in Z. officinale's rhizome have been shown in molecular docking experiments to have anti-SARS-CoV-2 action. Additionally, viral proteases, RNA binding protein, and Spike protein interact with 6-gingerol to suppress SARS CoV-2 [69]. Gingeronone A, on the other hand, blocks major protease (6LU7) and SARS-CoV-2 ORF8 (7JTL)

Another plant of the Zingiberaceae family with many therapeutic benefits is Curcuma longa L. It is grown in Bangladesh and is also a spice that is used in cooking. Rheumatoid arthritis, chronic anterior uveitis, conjunctivitis, skin cancer, chicken pox, small pox, wound healing, urinary tract infection, and malignancies are all treated with it as herbal medicine. This plant's rhizome has anti-HBV action when extracted in water. By blocking the HBV enhancer, I and X promoter through the p53 protein, it prevented HBx gene transcription [70]. This plant generates curcumin, which has a variety of pharmacological effects. It blocks various pathways to stop HIV, DENV, CHIKV, ZIKV, VSV, IAV, RSV, EV71, and Kaposi's sarcoma-associated herpesvirus. Additionally, a randomized controlled trial demonstrated the efficiency of curcumin for COVID-19 pre-exposure prophylaxis. This preventative effect may be brought on by (a) a variety of antiviral mechanisms of action (direct interaction with viral membrane proteins, disruption of viral envelope, inhibition of viral protease, and induction of host antiviral response by enhancing immunity) against a

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variety of enveloped viruses (as SARS-CoV-2 is a enveloped virus) (b) severe pneumonia protection (by focusing on the NF-B, IL-6 trans signal, and HMGB1 pathways); (c) safety and tolerability in both healthy and ill human patients.

Limitations

Plant metabolites have a variety of therapeutic uses. They may have a synergistic impact, leading to better treatment results. Along with these benefits, there are a number of obstacles to be addressed in the drug discovery process. The plant metabolites' draggability is the main barrier. The most important elements influencing a chemical generated from plants' drug ability are its pharmacokinetic ADME (absorption, distribution, metabolism, and elimination) properties. Fortunately, the development of new drug delivery systems and nanotechnologies raises the possibility of creating medications from plant metabolites. Numerous plant metabolites have already been developed as inventive medication delivery methods. . Obtaining and authenticating plant materials, using high-throughput screening bioassays, scaling up bioactive lead compounds, and complexity are other upcoming hurdles. Metabolite of plants new delivery method Andrographolide Self-Nano dispersion, self-microemulsion, nanoparticle, inclusion complex, and microsphere Acid oleanolic Nanoparticle, self-nano emulsion, self-microemulsion, and nanosuspensionQuercetin Nano emulsion, self-nano emulsion, mixed micelle, nanocrystal, nanoparticle, phytosomeas well as nanosuspension Solid dispersion, mixed micelle, micro pellet, phytosome, and self-microemulsion are some of the different apigenin delivery methods. Curcumin Mixed micelle, co-polymeric micelle, exosome, self-nano emulsion, self-microemulsion, solid dispersion, and nanoparticle O/W, oil-in-water; W/O/W, water-in-oil-in-water Additionally, it happens that the toxicities of plant metabolites are not taken into account in laboratory tests that are carried out for clinical trials. Because the isolation, purification, and bioassay of pure plant-derived chemicals are so difficult, time-consuming, and labor-intensive, it is frustrating when medication development fails during the clinical trial phases.

3. Conclusion

Finally, the three medicinal plants (*V. amygdalina, A. indica, and N. sativa*) studied here showed pleiotropic properties that could give a multimodal approach to COVID-19 management via antiviral, anti-inflammatory, and immunomodulatory actions. Although more research is needed to validate its pharmacological effects on covid-19, it is promising.

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