

Traditional Medicinal Plants as the Potential Adjuvant, Prophylactic and Treatment Therapy for COVID-19 Disease: A Review

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Abstract

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by a severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). In an effort to combat the pandemic caused by COVID-19 disease, researchers have identified several traditional medicinal plants (TMPs) as potential adjuvant, prophylactic, and treatment for COVID-19. TMPs reported in this paper were identified based on the findings of molecular docking research and the documented traditional use of these plants for COVID-19-related symptoms, such as fever, coughing, headaches, and tiredness. Secondary metabolites with antiviral, anti-inflammatory, and immunomodulatory activity against various SARS-CoV-2 proteases were also identified from the list of South African medicinal plants. This review discusses secondary metabolites of TMPs with pharmacological benefits, which contribute to the management of COVID-19, and these include *Acacia Senegal*, *Artemisia afra*, *Aspalathus linearis*, *Clerodendrum splendens*, *Dioscorea batatas* decne, *Echinacea purpurea*, *Hypoxis hemerocallidea*, *Xysmalobium undulatum*, *Tinospora crispa*, *Sutherlandia frutescens*, and *Zingiber officinale*.

Keywords: traditional medicinal plants, COVID-19, adjuvant, antiviral, immunomodulatory

1. Introduction

Coronavirus disease 2019 (COVID-19) that caused pandemic started in December 2019 in Wuhan, China [1–3]. The novel coronavirus responsible for this respiratory disease was identified to be the member of the Coronaviridae family known to cause infections in humans called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1]. SARS-CoV-2 is reported to be found in bats, and the infections occurred in humans because of the intermediate host, the pangolin [2]. SARS-CoV-2 is the third coronavirus reported to cause the respiratory disease pandemic after severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) [2]. COVID-19 disease

spreads from human to human by respiratory droplets [4], and the symptoms include dry cough, fever, fatigue, body aches, dyspnea, chills and shivering, sputum production, diarrhea, nausea, nasal congestion, rhinorrhea, and loss of speech or movement [3, 5–7]. To date, COVID-19 is still the cause of morbidity and mortality worldwide, accounting to 409 confirmed positive cases and 5.8 million deaths between 7 and 13 February 2022 [8]. Among the African countries, South Africa (SA) reported the highest numbers of new mortality between 7 and 13 February 2022 [8].

Vaccines were quickly developed for the prevention of COVID-19 pandemic [9], but there is no specific treatment available [4] as vaccinated individuals can still contact and transmit the COVID-19 virus. COVID-19 symptom management is mainly supported with oxygen therapy, steroids, antivirals, antibiotics, and anti-inflammatory agents, including chloroquine and hydroxychloroquine [5, 6]. However, antibiotics, antiviral, and anti-inflammatory drugs are reported to be the cause of health problems due to their toxicities [6]. Africa has a long historic record on the use of traditional medicinal plants (TMPs), and phytomedicine is preferred as 80–90% of rural population rely on medicinal plants for primary healthcare [10]. Fortunately, the World Health Organization (WHO) promotes the use of traditional, complementary, and alternative medicine on condition that their efficacy, safety, and quality are scientifically reported [1, 11]. Therefore, considering the potential of TMPs as alternative and complementary conventional drugs for COVID-19 management is an important research topic during the current situation of COVID-19 pandemic [12]. Several studies were conducted on TMPs and their pharmacological activities against COVID-19 [10, 13–15], and this review is, therefore, aimed at the documentation of TMPs that can be used in adjuvant, prophylactic, and management therapy of COVID-19.

2. Potential use of TMPs in adjuvant, prophylactic, and management therapy for COVID-19 disease

TMPs have become the subject of interest in the era of COVID-19 pandemic, and various researchers have conducted studies based on selecting TMPs commonly used traditionally to treat fever, cold, and flu symptoms [13, 14]. *Echinacea purpurea* and *Zingiber officinale* were identified among TMPs with promising adjuvant symptomatic therapy [14]. A number of secondary metabolites isolated from TMPs were identified to have immunomodulatory, antiviral, and anti-inflammatory activities against SARS-CoV-2 [15]. TMPs with immunomodulatory effect could be used in COVID-19 patients as a prophylactic and treatment therapy [16]. Immunomodulation agents identified as potential therapy against infectious diseases, including COVID-19, are, among others, *Dioscorea batatas* decne, *Clerodendrum splendens*, and *Tinospora crispa* [17].

Active secondary metabolites of these TMPs have immunomodulatory effect and can reduce cytokine production against viral infections [6]. TMPs with potential antiviral activity against SARS-CoV-2 were identified as *Artemisia afra*, *Acacia Senegal*, *Aspalthus linarias*, *Hypoxis hemerocallidea*, *Sutherlandia frutescens*, and *Xysmalobium undulatum* [15, 18, 19]. Madagascar's *Artemisia afra* was found to have inhibitory effect against SARS-CoV-2 [18]. Although the safety and dosage of this medicinal plant was determined *in vitro*, clinical studies must still be conducted to evaluate the use of this medicinal plant for COVID-19 prevention and treatment in COVID-19 patients [18]. Molecular docking research using the list of South African TMPs identified plants with

antiviral activity against SARS-CoV-2 included *Acacia Senegal*, *Aspalathus linerias*, *Hypoxis hemerocallidea*, *Sutherlandia frutescens*, and *Xysmalobium undulatum* [19].

TMPs reported in this review article target various stages in viral life cycle starting from the prevention of viral entry to the E6 cells, halting the fusion of the S protein, the inhibition of SARS-CoV-2 receptor-binding domain, the prevention of viral replication, and the transcription by targeting SARS-CoV-2 RNA-dependent RNA polymerase and major proteases [6, 15, 17, 19–25]. The diagrams in **Figure 1** show strategies for the prevention and management of COVID-19 using TMPs.

2.1 *Acacia senegal*

A. senegal (**Figure 2**), also known as white gum tree, belongs to the *Mimosoideae* family of plants and is widely distributed in Senegal, Cameroon, and Sudan [26–28]. Exotic *A. Senegal* is found in South Africa and is called siKhambophane and umKhala in isiZulu [29]. *A. senegal* is traditionally used to treat respiratory symptoms and infections, such as flu and sore throat (**Table 1**), and other conditions including, sinusitis, toothaches, stomach ulcer, colic, diarrhea, and dysentery [19, 26]. This medicinal plant has pharmacological activities, which include anti-inflammatory, antibacterial, antifungal, and antioxidant [26]. Secondary metabolites identified from *A. senegal*'s

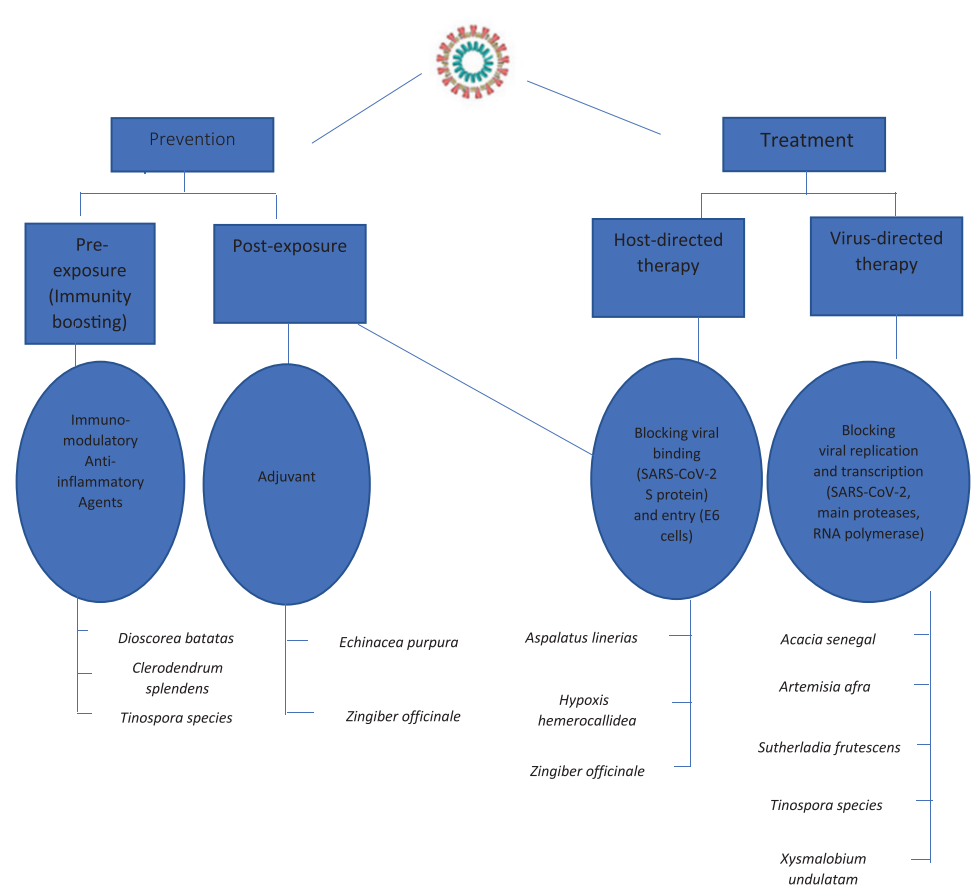


Figure 1.
Identified strategies for prevention and treatment of COVID-19 using TMPs.



Figure 2.
Acacia Senegal leaves in picture A and bark in picture B.

TMPs	Traditional uses in respiratory symptoms and diseases
<i>Acacia senegal</i>	Flu, sore throat [19]
<i>Artemisia afra</i>	Cold, cough, headache, influenza, sore throat, asthma, pneumonia [30, 31]
<i>Aspalathus linearis</i>	Asthma [32]
<i>Clerodendrum splendens</i>	Asthma, cough, [20, 33]
<i>Dioscorea batatas</i> decne	Asthma [21]
<i>Echinacea purpurea</i>	Common cold [34]
<i>Hypoxis hemerocallidea</i>	Tuberculosis [35, 36]
<i>Sutherlandia frutescens</i>	Influenza, fever [37]
<i>Tinospora</i> species	Fever [23]
<i>Xysmalobium undulatum</i>	Headache [19]
<i>Zingiber officinale</i>	Cold, cough, asthma, influenza, headache, fever, sore throat [14, 38–40]

Table 1.
Traditional uses of TMPs in respiratory symptoms and diseases.

plants extracts include glycosides, alkaloids, flavonoids, and arabic acid [15, 19, 26]. Arabic acid was determined to have a higher docking score (−5.2 kcal/mol) against 3CLpro, suggesting that *A. senegal* is a medicinal plant with antiviral activity against SARS-CoV-2 3C-like major protease (Table 2) [15, 19]. Thus, testing *A. senegal* *in vitro* might help to characterize new treatment and/or prophylactic strategies against SARS-CoV-2.

2.2 *Artemisia afra*

Artemisia afra (Figure 3), also known as African wormwood, belongs to the *Asteraceae* family [44, 45]. It is indigenous to Africa and is widely distributed in South Africa, Namibia, Zimbabwe, Kenya, Tanzania, Uganda, and Ethiopia [30, 44]. *Artemisia afra* is called Umhlonyane in Xhosa and Lengana in Sesotho [44]. It is used traditionally for the treatment of respiratory symptoms and diseases including cold, cough, headache, influenza, sore throat, asthma, and pneumonia (Table 1), and other disease conditions such as diabetes, colic, dyspepsia, bladder and kidney disorders,

TMPs	Secondary metabolites with a Adjuvant, prophylactic, and anti-COVID-19 activity
<i>Acacia senegal</i>	Arabic acid, Anti-SARS-CoV-2 3C-like major protease activity [15, 19]
<i>Artemisia afra</i>	Flavonoids, Anti-SARS-CoV-2 activity [15]
<i>Aspalathus linearis</i>	Flavonoids, quercetin, luteolin, Anti-SARS-CoV activity [41]
<i>Clerodendrum splendens</i>	Type II arabinogalactam, immuno modulatory activity [17, 20]
<i>Dioscorea batatas</i> decne	Allantoin, batatas, choline, dioscorin, diosgenin, gracillin, glycoproteins, L-arginine, mucopolysaccharides, prosapogenin, protein, polysaccharide, saponins, Immunomodulatory activity [17, 21, 22]
<i>Echinacea purpurea</i>	Chicoric acid, polysaccharide, alkanamides, immunomodulatory activity [14] and Extracts, Anti-coronavirus activity [42]
<i>Hypoxis hemerocallidea</i>	Hypoxide, Anti-SARS-CoV-2 receptor binding domain activity [19]
<i>Sutherlandia frutescens</i>	L-canavanine, Anti-SARS-CoV-2 3C-like main protease activity [19]
<i>Tinospora crispa</i>	hydroxy-5-cholen-24-oic acid, androstan-17-one, 3-ethyl-3-hydroxy-(5.alpha), camphenol, (-)-globulol, yangambin, nordazem, TMS derivative, benzene ethanamide, Anti-SARS-CoV-2 main protease activity [25]
<i>Tinospora cordifolia</i>	Amritoside, apigen-6-C-glucosyl7-O-glu-coside, 20a hydroxy ecdysone, tinosporine B, epicatechin, Anti-SARS CoV-2 main protease activity [6]
<i>Xysmalobium undulatum</i>	Uzarin, Anti-SARS-CoV-2 RNA dependent RNA polymerase activity [19]
<i>Zingiber officinale</i>	10-paradol, 8-paradol, scopoletin, 10-shogaol, 8-gingerol, 10-gingerol, Anti-SARS-CoV-2 activity [43]

Table 2.
Secondary metabolites of TMPs with adjuvant, prophylactic, and anti-COVID-19 activity.

constipation, malaria, and rheumatism [30, 31]. *Artemisia afra* contains secondary metabolites including tannins, alkaloids, terpenoids, cardiac glycosides, and saponins [30]. Pharmacological activities of *Artemisia afra* include antioxidant, antiviral, antiplamodial, antifungal, and antibacterial [30, 31, 44]. *Artemisia afra* aqueous and ethanolic extracts, as well as teas, were shown to inhibit SARS-CoV-2 plaque formation *in vitro* [15]. The antiviral activity of this medicinal plant is reported to have been as a result of flavonoids present in *Artemisia* species (**Table 2**) [15]. The extracts showed some toxicity at higher concentrations with the selectivity index of 10, which opened a therapeutic window that is required to be further investigated in clinical trial [15]. There is still a need to prove whether *Artemisia afra* extracts can reach the serum levels required to completely inhibit the virus in COVID-19 patients.

2.3 *Aspalathus linearis*

A. linearis (**Figure 4**), also known as Rooibos in Afrikaans, belongs to the *Fabaceae* family and is an endemic South African species cultivated to produce a tea [46–48]. It is used commonly for the treatment of respiratory disease such as asthma (**Table 1**) and other diseases including cardiac arrhythmias, colic, diarrhea, and hypertension [32]. Rooibos contains flavonoids including aspalathin, isoorientin,



Figure 3.
Artemisia afra leaves.



Figure 4.
Aspalathus linearis.

isovitexin, nothofagin, orientin, quercetin, rutin, and vitexin [41]. Other present secondary metabolites include polyphenols and phenolic compounds such as dihydro-chalcones, flavonols, flavonones, and proanthocyanadins [41, 46, 47]. Rooibos has pharmacological activities including antioxidant, antiviral, immunomodulatory, anti-inflammatory, cardioprotective, and nephroprotective effects [41]. Flavonoids, quercetin, and luteolin (Table 2) present in Rooibos were found to inhibit SARS-CoV infection by preventing entry of virus into E6 cells, and luteolin acts by binding to SARS-CoV S proteins, thereby interfering with the S protein function [41]. However, more experiments must be conducted to validate the clinical relevance of Rooibos in treating COVID-19 and other respiratory diseases [41]. Although other studies have highlighted the drug interactions associated with the

Rooibos derived phytochemicals [42], more research is required in determining the safety of Rooibos in patients.

2.4 *Clerodendrum splendens*

Clerodendrum splendens (Figure 5), also known as bag flower, bleeding-heart, and glory bower in English [33, 49], belongs to the *Lamiaceae* family of plants [20]. It is distributed in tropical Africa, Southern Asia, America, and Northern Australasia [33]. *Clerodendrum splendens* is used traditionally to treat respiratory diseases such as asthma and coughs (Table 1) and other diseases including anorexia, leucoderma, leprosy, malaria, skin diseases, ulcers, uterine fibroids, wounds, burns, and sexually transmitted diseases such as syphilis and gonorrhea [20, 33]. Phytochemical constituents present in *Clerodendrum splendens* include alkaloids, cyanogenic glycosides, diterpenes, flavonoids, phenolic compounds, saponins, steroids, tannins, terpenoids, and volatile compounds [17, 20]. It has pharmacological activities including anti-bacterial, antifungal, anti-inflammatory, antiproliferative, antioxidant, and hepatoprotective [17, 20, 33]. *Clerodendrum splendens* contains a polysaccharide, type II arabinogalactan (Table 2), that has been shown to have immunomodulatory activity both *in vitro* and *in vivo* [17, 20]. Its antiproliferative activity is reported to be as a result of clerodane diterpenes and phenyl propanoids found in aerial parts this plant [17]. The methanol extract of *Clerodendrum splendens* was reported to have *in vitro* anti-inflammatory activity (Table 2) [24]. The findings reported on *Clerodendrum splendens* form the basis for further research into the efficacy and safety of this plant as potential COVID-19 treatment and anti-inflammatory agents [17, 24].

2.5 *Dioscorea batatas* decne

D. batatas decne (Figure 6), commonly called Chinese yam [50, 51], belongs to the *Dioscoreaceae* family of plants [21, 52]. *Dioscoreaceae* plant species are widely distributed in West Africa, Southeast Asia, and Tropical America [52]. *D. batatas* decne is used traditionally for the treatment of respiratory disease such as



Figure 5.
Clerodendrum splendens leaves and flowers.

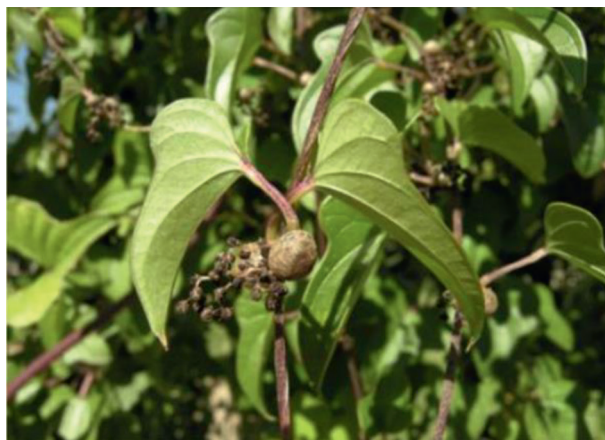


Figure 6.
Dioscorea batatas decne leaves and fruits.

asthma (**Table 1**) and other conditions including, abscesses, cancer, inflammation, hypertension, ulcer, chronic diarrhea, and diabetes [21]. It has antioxidant and anti-inflammatory activities [22, 50]. *D. batatas decne* contains various active components, such as allantoin, batatasins, choline, dioscorin, diosgenin, gracilin, glycoproteins, L-arginine, mucopolysaccharides, prosapogenin, protein, polysaccharides, and sapogenins (**Table 2**) with immunomodulation effects when orally administered [17, 21, 22]. The immunomodulatory activity of tuber protein and dioscorin occurs through the activation of TLR4-induced macrophage due to the stimulation of signaling molecules such as NF- κ B, JNK, p38, and ERK, and by TNF- α and IL-6 cytokines expression [17, 21, 22]. The immunomodulation effect of tuber extract on inflamed and normal skin was reported to be due to the enhancement of granulocyte-macrophage colony-stimulating factor promoter [17]. The tuber extract of *D. batatas* was found to be the potent inhibitor of SARS-CoV (**Table 2**) at concentrations between 25 and 200 μ g/mL [53].

2.6 *Echinacea purpurea*

E. purpurea (**Figure 7**), also known as Eastern Purple Coneflower, belongs to the *Asteraceae* family [54–56]. It is native to eastern North America [55]. *E. purpurea* is used for the treatment of respiratory conditions such as common cold (**Table 1**) and other conditions including pain, cancer, toothache, seizures, arthritis, and skin disorders [14, 34, 54]. *E. purpurea* has been approved by the European Medicine Agency Herbal Medicinal Product Committee to be used as prophylactic therapy for the maximum of 10 days for immunostimulation and to prevent cold and other respiratory infections [14]. Pharmacological activities of *E. purpurea* include antiviral, antioxidant, antibacterial, immunomodulatory, antitumor, and anti-inflammatory [54, 55]. *E. purpurea* contains phytochemicals such as alkamides, betaine, phenolic compounds, polysaccharides, lipoproteins, saponins, sesquiterpenes, and polyacetylene [55]. *Echinacea* species exerts a soothing effect and could be useful in the relief of respiratory symptoms and common cold [14]. The immunomodulatory activity of *E. purpurea* was reported to be as a result of chicoric acid, polysaccharide, and alkamides (**Table 2**) in a rat study [14]. The use of *Echinacea*

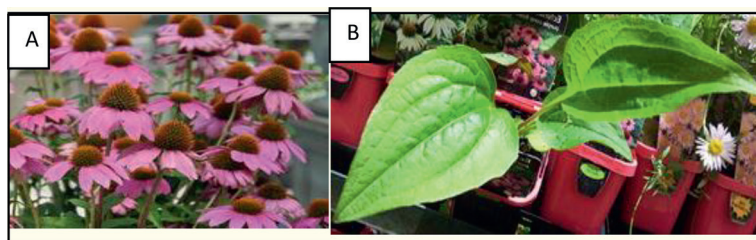


Figure 7.
Echinacea purpurea. (A) Flowers and (B) leaves.

for supplementation is reported to decrease the duration of acute respiratory tract infections and the severity of the disease [57]. The extract of *E. purpurea* (L.) Moench has shown direct antiviral activity against coronaviruses, and the preliminary published findings on human clinical trials covering antiviral activity of *Echinacea* against SARS-CoV-2 further support the use of this plant species against this particular coronavirus [58].

2.7 *Hypoxis hemerocallidea*

Hypoxis hemerocallidea (Figure 8), also known as African Potato, belongs to the *Hypoxidaceae* family [35, 36, 59]. It is called inkomfe in Zulu and Lotsane in Tswana [60]. *Hypoxis hemerocallidea* is widely distributed in Southern Africa including, South Africa, Lesotho, Mozambique, and Zimbabwe and is also found in East Africa [36]. It is used traditionally to treat HIV/acquired immunodeficiency syndrome, arthritis, diabetes mellitus, testicular tumors, cancers, infertility, urinary infection, cardiovascular diseases, and respiratory disease such as tuberculosis (Table 1) [35, 36]. *Hypoxis hemerocallidea* contain phytochemicals, such as sterols, sterolins, norlignan, daucosterol, and rooperol, responsible for its therapeutic benefits [35]. Hypoxide is the main glycoside isolated from *Hypoxis* species [36]. Molecular docking analysis identified hypoxide (Table 2) as a potent inhibitor of SARS-CoV-2 receptor-binding domain with the docking score of -6.9 kcal/mol [19]. The study conducted on rats has demonstrated that *Hypoxis hemerocallidea* has the ability to impair kidney function. There is a need for more *in vitro* and *in vivo* research on the toxicity, safety, and efficacy of *Hypoxis hemerocallidea* [61].

2.8 *Sutherlandia frutescens*

Sutherlandia frutescens (Figure 9), also known as cancer bush, belongs to *Fabaceae* family of plants [6, 62]. It is an indigenous medicinal plant commonly used in South Africa to treat respiratory symptoms and disease such as fever and influenza (Table 1) and other diseases including cancers, diabetes, kidney and liver problems, rheumatism, depression, wounds, hemorrhoids, gonorrhea, urinary tract infections, and back pain [37]. Various *Sutherlandia* formulations are available in pharmacies and herbal shops and include capsules and tablets, gels, creams, liquid extracts, and ointments [37]. *S. frutescens* has been scientifically reported to have anticancer, antidiabetic, and anti-HIV properties [37, 62]. It has phytochemical constituents including sutherlandioside A, B, C and D, D-pinitol, gamma (γ) aminobutyric acid, and L-canavanine responsible for its biological



Figure 8.
Hypoxis hemerocallidea leaves.

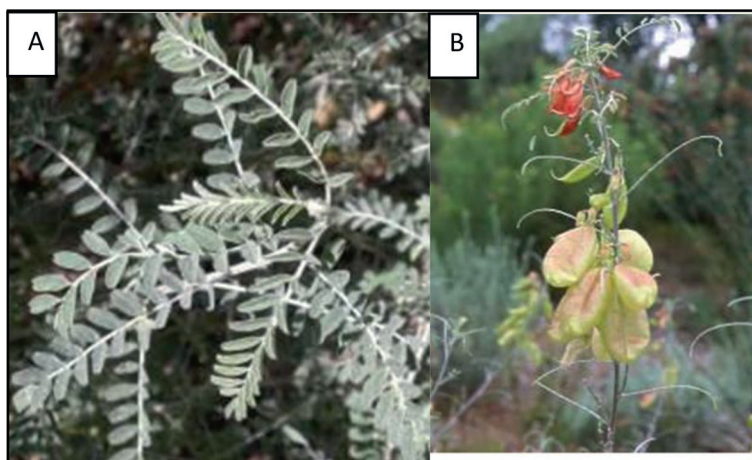


Figure 9.
Sutherlandia frutescens. (A) Leaves and (B) flowers.

activities [37]. The results of molecular docking analysis identified L-canavanine (**Table 2**) present in *S. frutescens* as a potential inhibitor of SARS-CoV-2 3C-like main protease [19]. The results of a randomized, double-blind, placebo-controlled trial of *Sutherlandia* leaf powder in healthy adults revealed that 800 mg/day of *Sutherlandia* leaf powder capsules were safe for consumption twice per day for three months in healthy adults [63].

2.9 *Tinospora* species

Tinospora crispa (**Figure 10A**) is also known as Seruntum in Malaysia, Brotawali in Indonesia, Makabuhay in Philippines, Boraphet in Thailand, Da ye ruanjinteng in China, Banndol Pech in Cambodia, Golonchi in Bangladesh, and Lyann span Zeb kayenn in Martinique island [23, 64]. *Tinospora cordifolia* (**Figure 10B and C**), also known as heart leaved Moonseed plant in English, Giloy in Hindi, and Guduchi in Sanskrit [65]. *Tinospora* species belongs to the family Menispermaceae [23, 65, 66]. *Tinospora crispa* is found in South East Asia and the Pacific [23, 66], and *Tinospora cordifolia* is found throughout India and certain parts in China [65]. Traditionally, *Tinospora* species are used to treat respiratory diseases and symptoms such as fever (**Table 1**) and other conditions including muscle pain, immune system associated inflammatory disorders, rheumatism, muscle pain, diabetes, and abdominal pain, septicemia, scabies, and ulcer-related disorders, hypertension, jaundice, paralysis, skin disease, leprosy, flatulence, dyspepsia, and diarrhea [6, 23, 66]. Phytochemical constituents of *Tinospora crispa* include alkaloids, flavonoids, furanoditerpenes, lignans, lactones, and steroids [66]. *Tinospora crispa* has pharmacological activity including antioxidant [23]. Active constituents such as boldine, cardioside, eicosenoic acid, quercetin, magnoflorin, and syringin are reported to have the antioxidant potential higher than that of ascorbic acid [23]. The same constituents are also reported to have the ability to increase the expression of IL-6, IL-8, and INF-g, thereby activating the immune system [17]. *Tinospora cordifolia* contains secondary metabolites including folioside A, tinocordiside, magnoflorine, and syringin with immunomodulatory activity [6]. The results of the molecular docking study on *Tinospora crispa* have revealed nine potential anti-SARS-CoV-2 lead molecules, namely, imidazolid-4-ne, 2-imino-1-(4-methoxy-6-dimethylamino-1,3,5-triazin-2-yl), spiro [4, 8] dec-6-en-1-ol, 2,6,10,10-tetramethyl, 3.beta-hydroxy-5-cholen-24-oic acid, androstan-17-one, 3-ethyl-3-hydroxy-(5.alpha), camphenol, (–)-Globulol, yangambin, nordazem, TMS derivative, and benzeneethanamide (**Table 2**). Three of these molecules have demonstrated some biological activity, which led to further optimization and drug development research for COVID-19 disease [25]. Molecular docking analysis also revealed that *Tinospora cordifolia* contains bioactive compounds, including amritoside, 20a hydroxy ecdysone, apigen-6-C-glucosyl-7-O-glucoside, tinosporine B, and epicatechin (**Table 2**), with promising anti-SARS CoV-2 main protease activity [6]. The acute toxicity study conducted on rats has revealed that the ethanol extract of *Tinospora crispa* stem is not toxic and did not cause animal

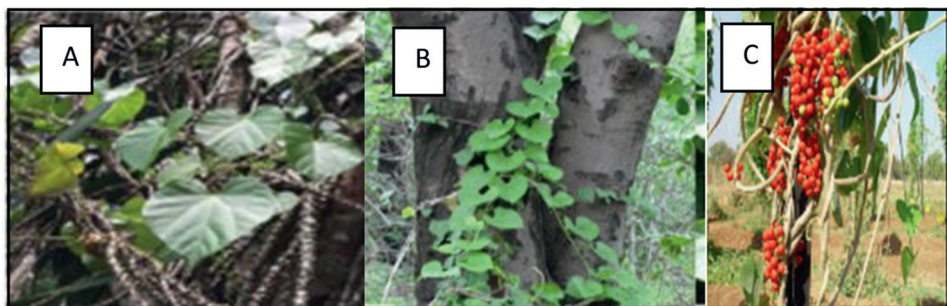


Figure 10.
(A) *Tinospora crispa*. (B) and (C) *Tinospora cordifolia*.

death at a dose of 4.0 g/kg of body weight (g/kg BW). However, six-month chronic toxicity study has reported hepatic and renal toxicities of the ethanol extract at a dose of 9.26 g/kg BW/day [64].

2.10 *Xysmalobium undulatum*

Xysmalobium undulatum (**Figure 11**) also known as Uzara wild cotton and milk bush, belongs to the family *Apocynaceae* [67–70]. Genus *Xysmalobium* is endemic to Africa and there are about 18 plant species occurring in SA [67]. Uzara is used traditionally to treat respiratory symptoms such as headaches (**Table 1**) and other disease conditions including, diarrhea, stomach cramps, afterbirth cramps, dysmenorrhea, wounds, sores, abscesses, and hysteria and has a diuretic effect [68]. Uzarin and its isomers allouzarin, xysmalorin, and alloxysmalorin are the main compounds isolated from Uzara [67]. Pharmacological activities of Uzara include antidiarrheal and antidepressant [68]. Uzarin (**Table 2**) was identified as the potential inhibitor of SARS-CoV-2 RNA-dependent RNA polymerase, and it showed favorable docking score of -3.5 kcal/mol in a molecular docking study conducted from the list of South African TMPs [19].

2.11 *Zingiber officinale*

Z. officinale (**Figure 12**), also known as Ginger, belongs to the *Zingiberaceae* family which comprises of close to two hundred species [38, 71]. *Z. officinale* is used for the treatment of respiratory symptoms and diseases including common cold, cough,



Figure 11.
Xysmalobium undulatum leaves and flowers.



Figure 12.
Zingiber officinale whole plant showing roots, stem, and leaves.

asthma, influenza, headaches, sore throats, and fever (**Table 1**) and other diseases such as arthritis, rheumatism, nausea, flatulence, muscular aches, pains, cramps, constipation, hypertension, dementia, infectious diseases, helminthiasis, colic, and diarrhea [14, 38–40]. It has pharmacological activities including immunomodulatory, antitumorigenic, anti-inflammatory, antiapoptotic, antihyperglycemic, antilipidemic, antiemetic, antipyretic, antioxidant, antibacterial, and analgesic [38–40]. Active compounds in ginger include phenolic and terpene compounds, and phenolic compounds in ginger include gingerols, paradols and shogaols, and paradols [39]. The profile and chemistry of *Z. officinale* makes it a perfect anti-inflammatory therapy in the context of upper respiratory affections [39]. Molecular docking *in silico* studies suggested that phytochemical compounds, such as 10-Paradol, 8-Paradol, Scopoletin, 10-Shogaol, 8-Gingerol, and 10-Gingerol, in *Z. officinale* (**Table 2**) have potential in reducing viral load and detaching of SARS-CoV-2 in the nasal passages [43].

Future aspects include the extraction of the medicinal plants listed in **Table 1**, the isolation of pure compounds as well as their fingerprinting and identification, and the confirmation of their mechanisms of action [72]. Further testing of extracts in animal models and investigations of effective and safe dosages, route administration, drug administration intervals, pharmacokinetics, and mechanisms of action are required before the use of medicinal plants discussed in this review can be advocated to be used for COVID-19 patients [7].

3. Conclusions

The current review has summarized TMPs commonly used in the treatment of respiratory symptoms and diseases, which possess potential adjuvant, prophylactic, and therapeutic properties against SARS-CoV-2 including *Acacia Senegal*, *Artemisia afra*, *Aspalathus linearis*, *Clerodendrum splendens*, *D. batatas* decne, *E. purpurea*, *Hypoxis hemerocallidea*, *Xysmalobium undulatum*, *Tinospora crispa*, *Sutherlandia frutescens*, and *Z. officinale*. Secondary metabolites present in selected TMPs are responsible for the pharmacological activities of these medicinal plants. TMPs identified by molecular docking analysis should be investigated experimentally as potential SARS-CoV-2 treatment. Further studies are warranted to isolate and test secondary metabolites with inhibitory properties against SARS-CoV-2. Safety and efficacy profiles of these TMPs must be explored *in vitro* and *in vivo*. Animal studies and human clinical trials are required for further testing of these TMPs before recommendations to use in COVID-19 patients.

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Conflict of interest

The authors declare no conflict of interest.

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