Original Research

Potential of Malawi's medicinal plants in Covid-19 disease management: A review

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Abstract

The Coronavirus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has triggered an international pandemic that has led to significant public health problems. To date, limited evidence exists to suggest that drugs are effective against the disease. As possible treatments are being investigated, herbal medicines have shown potential for producing novel antiviral agents for the COVID-19 disease.

Aim

This review explored the potential of Malawi's traditional medicinal plants for the management of COVID-19.

Methods

The authors searched on PubMed and Google scholar for medicinal plants that are used in Malawi and published in openly available peer reviewed journals. Plants linked with antiviral treatment, anti-COVID-19 activity or COVID-19 symptoms management were targeted. These included activity against pneumonia, inflammation, cough, difficulty in breathing, pain/aches, fever, diarrhoea, rheumatism, fatigue, asthma, immunocompromised and cardiovascular diseases.

Results

11 studies were found with 306 plant species. 127 plant species had at least one COVID-19 related pharmacological activity. Of these plant species, the number of herbal entities used for each indication was: pain/aches (87), fever (2), pneumonia (9), breathing/asthma problems (5), coughing (11), diarrhoea (1), immunosuppression (8), blood issues (10), fatigue (2), heart problems (11), inflammation (8), rheumatism (10) and viral diseases (12). Thirty (30) species were used for more than one disease and *Azedarachta indica* topped the list (6 of the 13 COVID-19 related diseases). The majority of the species had phytochemicals known to have antiviral activity or mechanisms of actions linked to COVID-19 and consequent diseases' treatment pathways.

Conclusion

Medicinal plants are a promising source of compounds that can be used for drug development of COVID-19 related diseases. This review highlights potential targets for the World Health Organization and other research entities to explore in order to assist in controlling the pandemic.

Key Words: traditional medicine, herbal products, corona virus, drug development, screening

Introduction

Viruses are pathogens that cause communicable diseases like flu, AIDS and Ebola and increasing evidence shows that some viruses play a role in the disease mechanism of some non-communicable diseases like cancers, Alzheimer's disease and type 1 diabetes with high morbidity and mortality rates worldwide.[1] Most of these diseases have proved hard to cure.[2-5] Viruses cause epidemics that emerge and re-emerge and are easily transmitted to different locations due to increased global travel and rapid urbanization. Emergence of novel viruses and rapid mutation of old viruses make drug as well as vaccine development challenging and these are some of the major reasons why there has not been significant development of effective drugs or vaccines against many viruses. Notable viruses that have caused outbreaks with significant public health implications worldwide include dengue virus, influenza virus, measles virus, severe acute respiratory syndrome (SARS) virus, and West Nile virus and the recently discovered severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).[6-9] The SARS-CoV-2 is a novel virus that was discovered in 2019 in Wuhan City of Hubei Province in China and has spread rapidly throughout the world, causing serious health care burden. The virus causes a disease called COVID-19 disease that affects all populations of people, but the elderly and those with underlying medical conditions are at a higher risk of morbidity and mortality.[10] Being a novel disease caused by a novel virus, knowledge about the virus and the disease is limited and keeps on developing daily.[11]

SARS-CoV-2 is a 60 nm to 140 nm diameter, enveloped, positive sense RNA virus (11) belonging to the Coronaviruses (CoVs) that are generally enveloped viruses with single-stranded RNA genome. CoVs have the largest genomes to date among RNA viruses that range from approximately 26 to 32 kilobases. They replicate by genes encoding for viral structural proteins such as nucleocapsids (N), membranes (M), spikes (S), and envelopes (E), which play significant roles in viral integrity.[12] However, there are other commonly studied proteins that have been widely targeted

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for drug development. These include papain-like protease (PLpro), 3c-like protease (3CLpro) and spike protein[13-16].

Coronaviruses infections are well known for causing enteric, respiratory and central nervous system diseases in animals and humans.[17] The nomenclature of coronaviruses originates from spike-like projections on its surface, which gives it a shape similar to a crown when viewed under an electron microscope.[16,18] The gene sequence of SARS-CoV-2, the coronavirus responsible for COVID-19, suggests that its proteins are similar to those of South Asia Respiratory Syndrome (SARS) or Middle East Respiratory Syndrome (MERS).[19,20] Hence, drugs, compounds and medicinal plants or extracts known to inhibit these proteins in SARS and MERS could be promising leads for COVID-19 drug development.

COVID-19 is transmitted by large water droplets released by infected people (symptomatic or asymptomatic) when they cough and sneeze, and they survive in these droplets that are spread on the surfaces or individual's bodies.[21] Higher viral loads can be found in the nasal cavity than the throat.[22] People are infected by touching their nose, eyes or mouth after touching surfaces contaminated with SARS-CoV-2.[23,24] The virus enters the respiratory mucosa using angiotensin converting enzyme receptor 2 (ACE-2).[25] The virus can easily be killed by common disinfectants such as ethanol (preferably ≥ 80%), sodium hypochlorite or hydrogen peroxide.[23,24]

COVID-19 patients can be symptomatic, pre-symptomatic, or asymptomatic.[26] Common clinical features are fever, dry cough, sore throat, fatigue, headache, conjunctivitis, myalgia and breathlessness as well as loss of taste or smell.[27-29] Some patients also develop pneumonia and respiratory failure and may die within weeks. The latter scenario is associated with an extreme increase in inflammatory cytokines (cytokine storm), especially IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNFα.[30] The COVID-19 disease is also associated with complications such as acute lung injury, Acute Respiratory Distress Syndrome (ARDS), shock, and acute kidney injury.

Currently, there are no approved treatment medicines in use for COVID-19 disease. The disease is being managed by prevention of transmission (face masks and washing hands with soap and water or using hand sanitizer), maintaining hydration and nutrition, controlling fever and cough, provision of oxygen and renal replacement therapy. The use of these interventions varies by availability, access, location and disease severity. Therefore, there is a need to discover, design or develop novel efficacious and cost-effective antivirals as the search for effective vaccines continues.[9]

Several approaches are being implemented to tackle COVID-19, one of which is the repurposing of widely used conventional and herbal medicines.[31] Antiviral drugs (ribavirin, lopinavir-ritonavir based on experience in SARS and MERS), combination therapy of oseltamivir, ganciclovir and lopinavir-ritonavir, and remdesivir (broad spectrum anti-RNA drug developed for Ebola) have been tested. Remdesivir, the only antiviral option showing benefit to date, has shown statistically significant improvements in time to recovery in hospitalized patients in comparison with placebo.[32] Short term therapy with low-to-moderate dose corticosteroids (such as dexamethasone) in COVID-19 ARDS, intravenous immunoglobulin therapy, arbidol (antiviral drug), interferons, hydroxychloroquine and plasma of patients recovered from COVID-19 have been trialled. Despite preliminary reports showing that dexamethasone may decrease mortality rates among critically ill patients, more evidence about its efficacy and safety, along with other agents, are needed before these treatment options are fully recommended for use.[30,33-39]

Traditional medicines, especially Chinese herbs, have been tested for use in COVID-19.[33] Aanouz *et al*., (2020) used computational techniques to evaluate the inhibition potential of compounds isolated from plants used in Morocco against COVID-19 virus. Sixty seven (67) compounds isolated from aromatic and medicinal plants were found and selected for molecular docking studies that used energy of interaction between the compound's functional groups and the corona virus (SARS-COV-2 spike protein) as one of the criteria for anti-corona virus effect. Chloroquine was used as a standard (interaction energy of -6 kcal/mol). Eleven (11) molecules showed a good interaction with the target, but the three greatest activities were for Crocin from *Crocus sativus* L. (-8.2kcal/mol), Digitoxigenin (*Nerium oleander* L., -7.2 kcal/mol) and β -Eudesmol (*Laurus nobilis* L., -7.1kcal/mol). Experimental data also showed that they had antiviral activity.[40] For example, Crocin was found *in vitro* to be an inhibitor of the replication of Herpes Simplex Virus (HSV) before and after virion entry in Vero cells, and its plant/herbal medicine source showed promise for use as an anti-HSV and anti-Human Immunodeficiency Virus (HIV) agent.[41] Derivatives of Digitoxigenin are used as antiviral and anticancer inhibitors, while β–Eudesmol has substantial antibacterial and antiviral activity.[42-43]

Zhang *et al*., (2020) executed a rational computer-based screening study aimed at identifying Chinese medical herbs and compounds with antiviral activity against respiratory infections and COVID-19. This computer-based study searched through literature for natural compounds and their respective traditional Chinese medicinal plants known to fight against MERS or SARS coronavirus. Docking studies were completed to analyse their potential for direct interaction with SARS-COV-2 protein, followed by biological activity search from literature. Thirteen (13) out of the 115 compounds found in the search of traditional Chinese medicines exhibited potential for anti-COVID-19 activity and 125 screened Chinese herbs contained 2 or more of the 13 compounds. A search for pharmacological activity showed that 26 of the 125 herbs had antiviral activity in respiratory infection, and that they regulated viral infection, immune/inflammation reactions and response to hypoxia.[44]

Hui *et al*., (2020) evaluated studies that tested the use of Chinese medicine (CM) as prophylaxis on people exposed to SARS and H1N1 influenza in clinical trials, cohort or other population studies. Results showed that the Chinese medicines performed well as prophylaxis, an effectiveness that has also been recorded in historical practice with CM.[45] During the COVID-19 epidemic, several CM products were also tested in humans for prevention of the epidemic effects and selection of the CM was based on historical use and previous experimental results in similar viral epidemics. The CM used in the studies included radix astragali (*Astragalus propinquus* Schischkin), radix glycyrrhizae (*Glycyrrhiza uralensis* Fisch. ex DC.), radix saposhnikoviae (*Saposhnikovia divaricata* (Turcz.) Schischk.), rhizoma atractylodis macrocephalae (*Atractylodes macrocephala* Koidz.), lonicerae japonicae flos (*Lonicera japonica* Thunb.) and fructus forsythia (*Forsythia suspensa* (Thunb.) Vahl.). This study revealed that historical use and previous use of the CM in similar epidemics provided clues for selection of CM use and efficacy in COVID-19.[45,46]

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Plant extracts of *Lycoris radiata* (L'Hér.) Herb., *Artemisia annua* L., *Pyrrosia lingua* (Thunb.) Farw. and *Lindera aggregata* (Sims.) Kosterm. were also evaluated and found to have anti–SARS activity after a screening exercise of hundreds of CMs.[47]

Apart from whole plant extracts, phytochemicals have been evaluated and shown potential for activity against COVID-19 disease, including Saikosaponins Types A, B2, C, and D (phytochemicals belonging to naturally occurring triterpene glycosides). For example, Saikosaponins from *Bupleurum* spp., *Heteromorpha* spp., *Scrophularia scorodonia* L. have showed antiviral activity against a human and bat corona virus HCoV-229E, that together with OC43, causes the common cold.[34,47]

Furthermore, inhibitors of SARS enzymes (nsP13 helicase and 3CL protease) have also been isolated from plants. For example, myricetin is a flavonoid polyphenolic compound that has anti-oxidant properties.[48] Scutellarein, a flavone isolated from *Scutellaria lateriflora* L., has shown activity against SARS.[35,49] Phenolic compounds isolated from *Isatis tinctoria* L., *Torreya nucifera* (L.) Siebold & Zucc. and a water extract of *Houttuynia cordata* Thunb. have also exhibited antiviral mechanisms against SARS.[50] These water extracts have been particularly known to inhibit viral 3CL protease as well as blocking viral RNA-dependent RNA-polymerase activity.[51]

Herbal-western medicine combination therapies of lopinavir/ritonavir (anti-HIV medicines), arbidol (broad-spectrum antiviral) and CM Shufeng Jiedu capsule as well as lopinavir/ritonavir and CM Shufeng Jiedu capsule have also been tested clinically. Clinical observations for both herbal-western medicine combination therapies treated patients showed that the TCMs treatments were effective in a majority of the patients that were treated with them, which showed that the TCMs can play a role in treating COVID-19. The Herbal-western medicine combination therapies were very important in the treatment of the viral pneumonia. It was found that more studies were needed to produce conclusive results on the curing capability of the combination therapies on COVID-19.[52]

In the search for chemotherapy for COVID-19, there are different sources of medicines, one of which is traditional medicines or medicinal plants. In the African region including Malawi, treatment options commonly stem from medicinal plants due to their abundance and untapped potential. 80% of the population in this region relies on medicinal plants as a primary health care option.[53]

Several studies have already started exploring plants for COVID-19 cure.[32,54] There may be other unexplored plants that have potential for producing a cure for the disease or addressing mild to severe symptoms. Therefore, it is important to analyse the plants that have shown potential for COVID-19 activity and study plants with similar attributes. The following section explores the literature on studies that have evaluated the efficacy of medicinal plants on SARS-CoV-2 as well as searching for plants with similar antiviral potential in Malawi. For a plant or its isolated compounds to have potential for use in COVID-19, it should be able to kill or inactivate the virus or alleviate the symptoms and complications caused by coronavirus infection.

Significance of the Study on Medicinal plants with potential for use in COVID-19 in Malawi

The WHO recommends supportive care options such as the use of supplemental oxygen through ventilators but these interventions are too expensive for most low-income countries with under resourced healthcare systems.[55,56] Furthermore, there are gaps in trained health care providers for such interventions.[57] The majority of biomedical COVID-19 treatment options available lack data to support their effectiveness.[55] Options that are showing some clinical promise have soaring prices and frequent stock outs.[58] Hence, medicinal plants may be alternatives for individuals in Malawi and other developing countries. Although there have been in-vitro studies that have shown activity for various aspects of COVID-19, there hasn't been a study completed in Malawi to assess the efficacy or toxicity of medicinal plants. Although various medicinal plants have been analysed abroad, these data cannot be extrapolated to the same species in Malawi since geographical differences have been identified in medicinal plants' composition and activity.[59] Hence, this study seeks to provide baseline data for use in the discussion of Malawi's medicinal plants use in COVID-19 treatment. Furthermore, it may confirm or refute widely-circulating arguments or fears concerning the use of medicinal plants against COVID-19. This will be achieved by the following specific objectives: To examine published ethnobotanical studies conducted in Malawi in order to identify the medicinal plants with demonstrated activity or potential for activity against COVID-19 disease. To evaluate the literature for reported pharmacological properties of medicinal plants found to have potential for use in COVID-19 disease.

Methods

The authors searched for studies on medicinal plants that are used in Malawi that met the following inclusion criteria: Published in peer reviewed journals that were openly available online between January 1994 and July 2020. Had medicinal plants reported to be found and used in Malawi by at least one ethnobotanical survey as well as being tested in a laboratory.

The plant had been linked with antiviral or anti-COVID-19 use or against the symptoms of COVID-19. The key words that were used on Google Scholar and PubMed were: Ethnobotany, ethnobotanical survey, Malawi, Malawi herbal medicine, Malawi herbalist, Malawi medicinal plant, Malawi phytochemical screening, Malawi herbals and traditional medicine. Eleven (11) studies met the inclusion criteria while over 93 studies were excluded because plants reported were not cited in the ethnobotanical surveys reported in Malawi. All plant extracts that had potential for use in COVID-19 were considered. That potential was shown by its local use on viral infections or antiviral activity (e.g., curative action against pneumonia and inflammation), COVID-19 symptoms (symptom management of cough, difficulty in breathing, pain/aches, fever, diarrhoea, rheumatism and fatigue) and risk factors (high risk comorbidities like asthma, immunocompromise and cardiovascular diseases).

For the plants that met the above criteria, further searches were conducted on Google Scholar and PubMed using key words: scientific or botanical name of the plant, phytochemicals, bioactivity and pharmacological activity to find out if there have been any laboratory studies in Malawi or any other country to evaluate their biological or pharmacological activity on COVID-19 and consequent diseases. Summaries of all the studies and plants were created using Microsoft Excel.

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Results

The literature search found a total of 11 studies.[60-70] Plant list extraction yielded 306 plant species thereafter removing species that were irrelevant or not identified by a botanist (Additional File 1: Table 1). Of these 306 medicinal plants, 127 plants were found to manage at least one of the symptoms related to COVID-19 or were found to be used for the management of viral infections (Additional File 2: Table 2). Table 3 shows a summary of the results shown in the Additional File 2.

This study revealed that 87 of 127 medicinal plants could be used for pain or aches management, and two of those for fever management (*Azadirachta indica* A. Juss. and *Pyrenacantha kaurabassana* Baill.). Pneumonia is another symptom associated with COVID-19. In this study, we found 9 medicinal plants that are used traditionally to manage pneumonia and 5 that have potential for use in managing breathing or asthma problems. Other diseases associated with COVID-19 for which we identified traditional medicines included coughing (11 plants), diarrhoea (1 plant), immunosuppression (8 plants), blood related issues (10 plants), fatigue (2 plants), heart problems (11 plants), inflammation (8 plants) and rheumatism (10 plants). COVID-19 is a viral infection and any medicinal plant used for viral diseases has potential of being tested on coronavirus. There were 12 plants found to have been used for viral infections or diseases.

Of the 127 medicinal plants with potential to manage COVID-19 related diseases or symptoms, 30 had more than one disease for which they could be used. *Azedarachta indica* topped the list with being used for 6 of the 13 COVID-19 related diseases, high risk comorbidities and symptoms followed by *Moringa oleifera* Lam. *Pyrenacantha kaurabassana* Baill. and *Sclerocarya birrea* (A. Rich.) Hochst. that could be used on 4 aspects of COVID-19. Analysis of these 30 plants revealed that they covered all types of the diseases except one; fatigue. Table 4 shows the 30 plant species and their associated benefits for COVID-19 management.

Pharmacological effects of the plants

The 30 plants with activity against one or more aspects of COVID-19 were considered more user-friendly since one entity can be used for multiple purposes. This may lead to a decreased incidence of toxicity and interactions. However, it should also be pointed out that the use of medicinal plants potentially leads to the administration of multiple active compounds (drug promiscuity), and is dangerous as it risks drug resistance and adverse events from unknown drug-drug interactions. Some of the components therein would be administered to the patient in suboptimal doses and others in overdoses, with chances of drug resistance and toxicity.[71]

On the other hand, documented evidence exists that suggests that the use of more than one medicinal plant (polyherbalism) improves the efficacy of the products as well as convenience for patients during administration (dose and frequency). Research also suggests that combining medicinal plants with more than one pharmacological effect can provide even greater benefit.[72] Therefore, the 30 plants with multiple COVID-19 activities were evaluated further using literature review to determine if any studies had been completed to scientifically confirm their traditional ethnobotanical uses. Table 5 shows a summary of studies done so far on the plants. The table shows that the majority of the medicinal plants had phytochemicals linked to several of their COVID-19 symptoms alleviation capabilities and had demonstrated some mechanism of action related to COVID-19 treatment pathways. A few medicinal plants had no studies conducted to confirm their use.

Discussion

This study has demonstrated that there are multiple medicinal plants in Malawi that are being used for disease state management (Additional File 1: Table 1) and that several of these diseases are symptoms associated with COVID-19 (Additional File 2: Table 2). According to the World Health Organization (WHO), patients with mild COVID-19 are recommended to be treated with medicines that manage the presenting symptoms.[55]

The WHO acknowledges that traditional medicines may be sources of new therapies in the search for potential treatments for COVID-19. This is based on the historical integration of medicinal plants into primary healthcare in many areas of the world and on phytochemicals serving as precursor molecules for several commonly used biomedical drugs.[55] This study was completed as a way of supplementing in the search for therapies for COVID-19 since initial selection of potential plant species for plant-derived lead compounds or medicines stems from ethnobotanical surveys. Since the disease is novel, we could not identify a novel medicinal entity with clinically significant SARS-COV-2 activity. However, plants targeting other viruses and associated symptoms might be repurposed in a similar fashion to various conventional medicines.[73] However, the WHO warns against the use of traditional medicines without evaluating them first for efficacy, toxicity, and safety. Although WHO recognizes that traditional, complementary and alternative medicines show beneficial effects, and that Africa has a long history of traditional medicine use, medicinal plants can also be toxic and medicinal plants' efficacy may vary due to differences in geographical locations.[55,59,73]

The majority of the 30 medicinal plants identified contained known phytochemicals (Table 4 and 5). The review of the pharmacological effects of the plants confirms why they have potential for testing in the management of COVID-19 patient symptoms and eliminating the virus. The results, for example on *Azadrachta indica,* are consistent with the results reported by Roy and Bhattacharyya (2020), Shanmuga (2020), as well as Shanmuga *et al*., (2020) that also showed the potential of this plant in review, computational work, and clinical case study respectively.[74-76] Furthermore, the study results are similar to those of Li *et al* who describe the Shufeng Jiedu Capsule/Granule (SFJD) containing eight medicinal herbs in China that is reported to have antiviral, antibacterial, antitumor, and anti-inflammatory activities, and have effective protection against lung injury and neuronal loss achieved through enhancement of autophagy and apoptosis reduction in rats with allergic rhinitis.[77] It is also reported to improve *Pseudomonas aeruginosa*-induced upper respiratory tract infection by acting on various targets, particularly ERK phosphorylation. When combined with oseltamivir treatment, SFJD reduced IAV-induced airway inflammation and pulmonary virus titres. This suggests that SFJD may be used for the prevention and treatment of infectious diseases by regulating various signal pathways.[77]

This study can assist WHO's efforts to select traditional medicine products that can be investigated for clinical efficacy and safety in COVID-19. The WHO has historically supported clinical trials of traditional medicine products.

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Through these previous WHO trials, 89 products have been given market authorisation in 14 countries after meeting international and national requirements for registration. Furthermore, 43 products were included in national essential medicines lists for diseases including malaria, opportunistic infections related to HIV, diabetes, sickle cell disease and hypertension.[55] This report recommends that the medicinal plants identified be evaluated as potential sources of COVID-19 management remedies and be prioritized for inclusion in clinical and analytical studies for antiviral activity or management of COVID-19 disease.

Conclusions

Coronaviruses have been in existence for decades and novel strains will continue to emerge. Efforts to find viable, safe and effective treatments in drug discovery pipelines are continuing and will adapt in response to evolving strains. From various community practices across the world, natural products have played a significant role in managing coronavirus related diseases to varying extents. As the aetiology of COVID-19 disease is studied further at the molecular and enzyme levels, a narrower selection can be made for potential hits and leads effective against the disease. Natural products, including plant products, are undoubtedly a promising source of compounds in drug development for possible drug leads and vaccines. It is recommended that multidisciplinary approaches are used to study active phytochemicals with regard to identifying suitable compounds that can be used as they are or developed into possible treatments against Covid-19 and other related coronavirus diseases.

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Table 1: List of Medicinal Plants that were included in the study

Abrus precatorius	*Cissus zombensis* Gilg and Brandt	*Grewia bicolor*
Acacia adenocalyx	*Clerodendrum glabrum*	*Grewia flavescens*
Acacia amythethophylla	*Cocculus hirsutus*	*Grewia inaequilatera*
Acacia nilotica	*Coffea swynnertonii*	*Grewia micrantha*
Acacia sieberana	*Colocasia esculenta* (L.) Schott	*Grewia stolzii*
Acacia sp.	*Combretum apiculatum*	*Habenaria* sp.
Acalypha chirindica	*Combretum fragrans*	*Heteromorpha trifoliata*
Acalypha villicaulis	*Combretum microphyllum*	*Hibiscus cannabinus* L.
Adenia gummifera (Harv.) Harms	*Combretum mossambicense*	*Hippocratea parviflora*
Aeschynomene abyssinica	*Commiphora mossambicensis*	*Holarrhena pubescens*
Aframomum angustifolium	*Cordyla africana*	*Hymenocardia acida* Tul.
Afzelia quanzensis Welw.	*Crinum macowanii* Baker	*Hymenodictyon floribundum*
Ageratum houstonia (compsitae)	*Crossopteryx febrifuga*	*Hymenodictyon parvifolium*
Albizia harveyi	*Cryptolepis obtusa*	*Hypoxis villosa* L.f.
Albuca abyssinica Jacq.	*Cucumis hirsutus* Sond.	*Indigofera emarginella*
Algae spp.	*Cyphostemma* ssp.	*Inula glomerata*
Allium sativum	*Cyphostemma junceum*	*Jateorhiza bukobensis*
Allophylus chaunostachys	(Webb) Desc. ex Wild	*jatropha curcas*
Aloe swynnertonii	& R.B. Drumm.	*Julbernardia globiflora*
Aloe vera	*Cyphostemma setosum*	*Kaempferia rosea* Schweinf. ex
Ampelocissus africana	*Cyphostemma zombense*	Baker
Ampelocissus obtusata (Welw. ex	*Dalbergia melanoxylon*	*Khaya nyasica* or *Khaya*
Baker) Planch.	*Dalbergia nitidula*	*anthotheca*
Annona senegalensis	*Dalbergiella nyassae*	*Kigelia africana*
Anthospermum spec.	*Dichrostachys cinerea*	*Kirkia acuminata*
Apodytes dimidiata	*Dicoma anomala*	*Lagenaria sphaerica*
Aristolochia hockii	*Dioscorea bulbifera* L.	*Lannea discolor*
Asparagus setaceus	*Dioscorea dumetorum* (Kunth) Pax	*Lannea edulis*
Azadirachta indica	*Dioscorea esculenta* (Lour.)	*Lecaniodiscus fraxinifolius*
Azanza garckeana	Burkill	*Ledebouria cordifolia* (Baker)
Azadiracht indica	*Dioscorea odoratissima* Pax	Stedje & Thulin
Bauhinia petersiana	*Dioscorea zanzibarensis* Pax	*Ledebouria revoluta* (L.f.) Jessop
Bauhinia thonningii	*Diospyros kirkii*	*Leersia hexandra*
Berberis holstii	*Diospyros zombensis*	*Leonotis nepetifolia*
Bersama abyssinica	*Diplorhynchus condylocarpon*	*Maerua parvifolia*
Boophone disticha (L.f.)	*Disa* sp.	*Mangifera indica*
Borassus aethiopum	*Dolichos kilimandscharicus*	*Manihot glaziovii* Müll. Arg.
Boscia salicifolia Oliv	*Dolichos trinervatus* Baker	*Margaritaria discoidea* or
Brachystegia allenii Hutch. &	*Dombeya acutangula*	*Phyllanthus discoideus*
Burtt Davy	*Dychrostachys cinerea*	*Markhamia obtusifolia*
Bruneodia microcephala (Del.)	*Ehretia amoena*	Maunkhalambo
Bridelia cathartica G. Bertol.	*Ehretia divaricata*	*Maytenus heterophylla* or
Byrsocarpus orientalis (Baill.)	*Ehretia obtusifolia*	*Gymnosporia buxifolia*
Bak.	*Ekebergia benguelensis* Welw. ex	*Maytenus senegalensis* or *G.*
Calotropis procera	*Elephantorrhiza goetzei*	*senegalensis*
Canthium glaucum ssp.	*Elytraria lyrata*	*Melia azedarach*
Carica papaya	*Eminia antennulifera* (Baker) Taub	*Momordica foetida* Schumach &
Cassia abbreviata	*Eriospermum abyssinicum* Baker	Thonn.
Cassipourea mollis	*Erythrophleum suaveolens*	*Mondia whitei*
Cassytha filiformis L.	*Euphorbia hirta*	*Monodora junodii*
Catunaregam spinosa	*Euphorbia matabelensis*	*Moringa oleifera*
Cissus aristolochiifolia Planch	*Ficus capensis* Thunb.	*Mucuna poggei* Taub.
Cissus cornifolia	*Ficus kirkii* Hutch.	*Multidentia crassa*
Cissus faucicola	*Ficus natalensis*	*Musa paradisiaca* L.
Cissus integrifolia	*Ficus sycomorus*	*Neorautanenia mitis* (A.Rich.)
Cissus quadrangularis	*Flacourtia indica*	Verdc.
Cissus rubiginosa (Welw.ex	*Fluggea virosa*	*Nidorella auriculata*
Baker) Planch	*Gladiolus dalenii* Van Geel	*Nymphaea caerulea* Savigny
Cissus sp.	*Gloriosa superba* L. *goetzei*	*Terminalia kaiseriana*

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Table 1 Cont....

Cissus votundifolia	*Gonatopus boivinii* (Decne.) Engl.	*Terminalia mollis*
Ocimum americanum	*Raphionacme welwitschii* Schltr. & Rendle	*Terminalia sericea*
Olax dissitiflora	*Rhus longipes*	*Terminalia stenostachya*
Olax obtusifolia	*Rhus natalensis*	*Tragia brevipes*
Oldfieldia dactylophylla	*Ricinus communis*	*Tricalysia coriacea*
Ormocarpum kirkii	*Rothmannia fischeri*	*Tricalysia* spp.
Ozoroa reticulata	*Rytigynia adenodonta* or *Rytigynia reticulata*	*Trichillia emetica*
Paederia bojerana	*Rytigynia monantha*	*Trichodesma zeylanicum*
Parinari excelsa	*Sclerocarya birrea*	*Tricliceras longepedunculatum*
Passiflora edulis	*Sclerocarya caffra*	*Turraea floribunda*
Paulozia mixta	*Searsia tenuinervis*	*Turraea nilotica*
Pericopsis angolensis	*Securidaca longepedunculata*	*Tylosema fassoglensis* (Kotschy ex Schweinf.) Torre & Hillc.
Phelinus gilvus	*Senna siamea* or *Cassia siamea*	*Vangueria infausta*
Philenoptera capassa	*Smilax anceps*	*Vernonia adoensis*
Philenoptera violacea	*Solanum anguivii*	*Vernonia colorata*
Phyllanthus ovalifolius	*Solanum pandurtforme*	*Vigna radiata*
Phyllanthus reticulatus	*Sphaeranthes angolensis*	*Vigna subterranean*
Piliostigma thonningii	*Sphenostylis emarginata*	*Vitex doniana*
Plectranthus esculentus N.E. Br	*Steganotaenia araliacea*	*Vitex mombassae*
Popowia obovata or *Friesodielsia obovata*	*Sterculia quinqueloba*	*Vitex payos*
Portulaca oleracea L.	*Stereospermum kunthianum*	*Xeroderris stuhlmannii* (Taub.) Mendonca & EP Sousa.
Pouzolzia mixta	*Strophanthus kombe*	*Ximenia americana* L.
Protea petiolaris	*Strychnos madagascariensis*	*Ximenia caffra*
Pseudarthria hookeri	*Stylochiton puberulus* N.E.Br.	*Zanha africana*
Pseudolachnostylis maprouneifolia	*Tabernaemontana elegans*	*Zingiber officinale*
Psidium guajava	*Tacca leontopetaloides*	*Ziziphus abyssinica*
Psorospermum febrifugum	*Tamarindus indica*	
Pterocarpus angolesis	*Tephrosia vogeli*	
Pterocarpus brenanii		
Pupalia lappacea		
Pyrenacantha kaurabassana		

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Table 2: List of Medicinal Plants that were evaluated further for Pharmacological and Physicochemical Properties

Abrus precatorious	*Dicoma anomala* Sond.
Acacia macrothyrsa	*Dicoma kirkii*
Acalypha chirindica	*Dioscorea bulbifera* L.
Aerva lanata	*Diplorhynchus condylocarpon*
Aeschynomene abyssinica	*Dolichos kilimandscharicus*
Aeschynomene nyassana	*Dolichos trinervatus* Baker
Afzelia quanzensis	*Ectadiopsis oblongifolia*
Ageratum houstonia (compositae)	*Ehretia amoena* Klotzschi
Albizia zimmermanii	*Ehretia divaricata*
Albuca abyssinica Jacq.	*Ehretia obtusifolia*
Algae spp.	*Elephantorrhiza goetzei*
Allium sativum	*Eriosperman abyssinicum* Baker
Aloe spp.	*Erythrophleum suaveolens*
Aloe swynnertonii	*Fagara chalybea*
Aloe vera	*Ficus capensis*
Ampelocissus Africana (Lour.) Merr.	*Flacourtia indica*
Annona senegalensis	*Fluggea virosa, Securinega virosa*
Azanza garckeana	*Gonatopus boivinii* (Decne.) Engl.
Azadarachta indica	*Grewia micrantha*
Bauhinia thonningii	*Heteromorpha arborascens*
Berberis holstii	*Holarrhena pubescens*
Boophone disticha (L.f.)	*Hymenocardia acida*
Brachystegia utilis	*Hypoxis villosa* L.f.
Breonadia microcephala	*Ipomoea tenuirostris*
Bridelia micrantha	*Jatropha curcas*
Burkea africana	*Kaempferia rosea* Schweinf. ex Baker
Capsicum frutescens	*Kigelia africana*
Carica papaya	*Lannea edulis*
Carissa edulis	*Lotus* sp.
Cassia abbreviata	*Markhamia obtusifolia*
Ceiba pentandra	*Melia azedarach*
Cissampelos mucronata	*Momordica foetida* Schumach & Thonn.
Cissus quadrangularis	*Moringa oleifera*
Cissus rubiginosa (Welw.ex Baker) Planch.	*Mucuna poggei* Taub.
Cissus zombensis (Baker) Gilg & M. Brandt	*Multidentia crassa*
Combretum microphyllum	*Musa paradisiaca*
Corchorus trilocularis	*Neorautanenia mitis* (A.Rich.) Verdc.
Cordyla africana	*Nidorella auricalata*
Crinum macowanii Baker	*Oldfieldia dactylophylla*
Croton megalobotrys	*Parinari excelsa* Sabine
Cussonia arborea	*Pericopsis angolensis*
Cyphostema spp.	*Phelinus gilvus*
Cyphostemma juncosum (Webb)	*Phyllanthus reticulatus*
Dalbergia nyassae, Swartzia madagascariensis	*Piliostigma thonningii*

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Table 2 Cont....

Dichrostachys cinerea	*Pseudolachnostylis maprouneifolia*
Psorospermum febrifugum	*Tricalysia coriacea*
Pterocarpus angolensis	*Tricalysia* spp.
Pyrenacantha kaurabassana Baill.	*Trichillia emetica*
Rauvolfia caffra	*Trichodesma zeylanicum*
Rhus longipes	*Turraea floribunda*
Rothmannia fischeri	*Turraea nilotica*
Schrebera trichocloclada	*Tylosema fassoglensis* (Kotschy ex Schweinf.)
Sclerocarya birrea	Torre & Hillc.
Searsia tenuinervis	*Uapaca kirkiana*
Senna petersiana	*Vernonia corolata*
Senna sengueana	*Vigna radiata*
Sphaeranthes angolensis	*Vitex mombassae*
Steganotaenia araliacea	*Xeroderris stuhlmannii* (Taub.) Mendonca &
Strychnos innocua	EP Sousa.
Tabernaemontana elegans	*Ximenia americana*
Tacca leontopetaloides (L.) Kuntze	*Ximenia caffra*
Tephrosia vogeli	*Xylopia perviflora*
Terminalia sericea	*Zanha africana*
Thunbergia spp.	*Zingiber officinale*

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Table 3: Number of plants found to be used for each of the COVID-19 related diseases or symptoms

Variable	Frequency n=306	Percentage
Cough	11	3.59
Pneumonia	9	2.94
Breath/Asthma	5	1.63
Pain/Aches	87	28.43
Fever	2	0.65
Diarrhoea	1	0.33
Immunity	8	2.61
Blood	10	3.27
Fatigue	2	0.65
Heart	11	3.95
Viral Activity	12	3.92
Inflammation	8	2.61
Rheumatism	10	3.27

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Table 4: Medicinal plants used on more than one COVID-19 related disease

Species name	Cough	Pneumonia	Breath/ Asthma	Pain/ Aches	Fever	Diarrhoea	Immune system boosters	Blood	Fatigue	Heart	Viral	Inflammation	Rheumatism	Number of COVID-related diseases/ symptoms
Azadrachta indica A. Juss.	Yes (f)			Yes (f) Yes (k)	Yes (f)		Yes (g)	Yes (f)			Yes (f)			6
Azanza garckeana (F.Hoffm.) Exell & Hillc.				Yes (i)			Yes (c)							2
Berberis holstii Engl.	Yes (b)	Yes (b)												2
Carica papaya L.				Yes (i)						Yes (g)				2
Combretum microphyllum Klotzsch	Yes (c)	Yes (c)		Yes (c)										3
Cyphostemma junceum (Baker) Desc. ex Wild & R.B. Drumm.								Yes (e)				Yes (e)	Yes (e)	3
Dicoma anomala Sond.	Yes (e)			Yes (e)									Yes (e)	3
Dolichos kilimandscharicus Taub.											Yes (e)		Yes (e)	2
Elephantorrhiza goetzei (Harms) Harms				Yes (e)		Yes (e)								2

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Table 4 Cont....

Eriospermum abyssinicum Baker										Yes (e)		Yes (e)		2
Flacourtia indica (Burm. f.) Merr.				Yes (i)							Yes (g)			2
Hypoxis villosa L.f.				Yes (e)			Yes (e)				Yes (e)			3
Kigelia africana (Lam.) Benth.				Yes (k)						Yes (g)				2
Moringa oleifera Lam.				Yes (f)			Yes (g)			Yes (f) Yes (g) Yes (g)		Yes (f)		4
Mucuna poggei Taub.	Yes (e)		Yes (e)							Yes (g)				3
Neorautanenia mitis (A. Rich.) Verdc.				Yes (c)							Yes (e)			2
Oldfieldia dactylophylla (Welw. ex Oliv.) J. Léonard	Yes (d)	Yes (d)		Yes (d)										3
Pericopsis angolensis (Baker) Meeuwen			Yes (g)	Yes (i)										2
Piliostigma thonningii (Schum.) Milne-Redh.				Yes (g)				Yes (c)						2
Pyrenacantha kaurabassana Baill.				Yes (e)	Yes (e)					Yes (e)			Yes (e)	4

Table 4 Cont....

Sclerocarya birrea (A. Rich.) Hochst.				Yes (f)				Yes (f)			Yes (f)	Yes (f)		4
Tabernaemontana elegans Stapf				Yes(c)									Yes (c)	2
Tacca leontopetaloides (L.) Kuntze				Yes (e)							Yes (e)		Yes (e)	3
Tephrosia vogelii Hook. f.											Yes (f)	Yes (f)		2
Terminalia sericea Burc. ex DC.			Yes (g)	Yes (i)										2
Trichilia emetica Vahl		Yes (f)		Yes (f)				Yes (f)						3
Xeroderris stuhlmannii (Taub.) Mendonca & Sousa								Yes (c)				Yes (c)		2
Zanha africana (Radlk.) Exell			Yes (g)	Yes (c) Yes (g)										2
Zingiber officinale Roscoe							Yes (g)			Yes (g)				2
Total	**6**	**4**	**4**	**22**	**2**	**1**	**5**	**6**		**8**	**8**	**6**	**6**	

Table 5: Literature Reported Pharmacological properties of medicinal plants with potential for use in COVID-19 disease

Plant species	Cited Uses in Ethnobotanical survey(indicated in the excel sheet)	Lab study done in Malawi on the plant	Phytochemicals available	Mechanism studies of the plants studied	COVID-19 related tests/Studies
Azadrachta indica A. Juss.	Cough, pain/aches, fever, blood, immunity, viral infections.	None	Alkaloids, flavonoids, triterpenoids, phenolic compounds, carotenoids, steroids and ketones. Glycosides, Reducing Sugar, Tannins, Saponins, Polysaccharides, Phytosterols, Phenols Azadirachtin.[78-79]	Cough, asthma, antiviral activity, antidiarrheal, anti-inflammatory, antipain, immunity response, fever. Suppression of viral replication; anti-oxidant activity; induce a cell-mediated and humoral immune response; maintaining normal immune homeostasis by upregulating type 1 response; Th1 type immune responses; antibody production against viruses; increases $CD4^+$ cell levels; induce dendritic cell maturation; macrophage-mediated antigen presentation.[74,80-84]	Case report, Review, Computational study.[74-76]
Azanza garckeana (F.Hoffm.) Exell & Hillc.	Protect from illness.	Antimalarial Activity.[85] Nutritional value.[63]	Amino acids, alkaloids, ascorbic acid, carotenoids, flavonoids, glucosides, phenols, lipids, tannins and saponins.[86]	Antibacterial, antifungal, antihyperglycemic, antimalarial, anti-oxidant and iron absorption activities.[86]	None.

Table 5 Cont....

Berberis holstii Engl.	Cough, pneumonia.	None.	Total phenols, tannins, flavonoid, saponins, alkaloids.[87-88]	Antidiabetic activity, antioxidants, antimicrobial, analgesic, anti-inflammatory, anti-arthritic and wound healing.[87,89]	None.
Carica papaya L.	Pain/aches, heart problems.	None.	Flavonoids, other phenolic compounds polysaccharides, glycosides, enzymes, flavonoids, lectins, saponins, vitamins, steroids.	Anti-inflammatory, immunomodulatory, analgesic, Nephroprotective, hepatoprotective, hypoglycaemic, hypolipidemic, antisickling. membrane-stabilizing properties and protect blood cells against stress-induced destruction.[90-94]	None.
Combretum microphyllum Klotzsch	Pain/aches.	None.	Triterpenes, flavonoids, lignans, amino acids, alkaloids.[95,96]	Anti-oxidant, antimutagenic, anti-oxidant, antiplatelet, anticoagulant, antinecrotic, antitumour, antinephrotoxic, antihepatotoxic, anti-inflammatory, anti-nociceptive, anticholinesterase, antidiabetic, anti-asthmatic, antimicrobial and anti-insecticidal activities.[97]	None.
Cyphostemma junceum (Baker) Desc. ex Wild & R.B. Drumm.	Blood, inflammation, rheumatism.	None.	None.	None.	None.
Dicoma anomala Sond.	Headache, cough, Pains in Stomach, fever, Rheumatism.	None.	Acatylenic compounds, phenols, flavonoids, phytosterols, saponins, sesquiterpenes, tannins and triterpenes.[98]	Anthelmintic, anticancer, antihyperglycemic, anti-inflammatory, antimicrobial, antioxidant, antiplasmodial and hepatoprotective activities.[98]	None.

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Table 5 Cont....

Dolichos kilimandscharicus Taub.	Shingles, rheumatism, new castle disease in chicken and rheumatism.	None.	None.	None.	None.
Elephantorrhiza goetzei (Harms) Harms	Pain/aches Diarrhoea.	None.	Phenolic compounds, coumarins, flavonoids, saponins, stilbenoids, tannins and triterpenoids.[86]	Antibacterial, antifungal, antiviral, anthelmintic, antioxidant.[86]	None.
Eriospermum abyssinicum Baker	Heart, Inflammation.	None.	None	None.	None.
Flacourtia indica (Burm. f.) Merr.	Pain/aches, Viral infections.	None.	Flavonoids Saponins Tannins Terpenoids Phenols Alkaloids Steroids Pholabatannins Anthroqinones Cardiac glycosides Coumerins Reducing sugars.[99]	Antimicrobial, antiviral, antifungal properties, anti-oxidant, anti-inflammatory.[99]	None.
Hypoxis villosa L.f.	Pain/aches, Immunity, Viral infections.	None.	None.	None.	None.

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Table 5 Cont....

Kigelia africana (Lam.) Benth.	Pain/aches, Heart.	None.	Iridoids, flavonoids, kigelinone, isopinnatal, dehydro-∝-lapachol, p-coumaric acid, kigelinone, isopinnatal, iridoids, ferulic acid, palmitic acid and verminoside.[100]	Antiprotozoal, antibacterial, antifungal, analgesic, anti-inflammatory, antidiarhoea, andidiabetic, antiprotozoal, anti-inflammatory, analgesic, anticancer, antidiarrhoeal, anti-ulcer.[101]	None.
Moringa oleifera Lam.	Pain/aches, Immunity, Heart, Inflammation.	None	Alkaloids (moringine and moringinine), pterygospermin, triterpenoids, saponins and tannins.[102,103]	Anesthetic, antinociceptive, antispasmodic, diuretic, anti-urolithiatic, anti-ulcer, hypotensive, cardioprotective, antihelmentic, hypolipidemic, anti-atherosclerotic, hepatoprotective, wound healing, antifungal, antibacterial, antitrypanosomal, hypoglycemic, and anti-AIDS outcomes.[102,103]	None.
Mucuna poggei Taub.	Cough, Heart. Breathe/asthma.	None.	Balsams, tannins, triterpenoids, saponins, alkaloids, terpenoids, carbohydrates.[104]	Anti-inflammatory and anticancer properties.[104]	None.
Neorautanenia mitis (A. Rich.) Verdc.	Pain.	None.	Saponin glycosides, flavonoids, tannins and alkaloids.[105]	Acaricidal and insecticidal activities, cytotoxicity, antimicrobial and antinociceptive activities, antidiarrheal.[106]	
Oldfieldia dactylophylla (Welw. ex Oliv.) J. Léonard	Pneumonia, coughing, pain.	None.	None.	None.	None.
Pericopsis angolensis (Baker) Meeuwen	Breathe/asthma,	None.	None.	None.	None.

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Table 5 Cont....

	Pain.				
Piliostigma thonningii (Schum.) Milne-Redh.	Nose bleeds, (fever, respiratory ailments, Malaria.	None.	Flavonoids, tannins, kaurane diterpenes, alkaloids, carbohydrates, saponins, terpenes, and volatile oils.[107]	Antilipidemic, antibacterial, antihelminthic, anti-inflammatory, anthelmintic, analgesic, antipyretic, antidiabetic, anti-oxidant and antilipidemic activities.[107]	None.
Pyrenacantha kaurabassana Baill.	Breathe/asthma Fever, Heart, Rheumatism.	None.	Xanthose.[108]	Anti-HIV.[108]	None.
Sclerocarya birrea (A. Rich.) Hochst.		None.	Polyphenols, tannins, coumarins, fl avonoids, triterpenoids, phytosterols.[109-110]	Antidiarrhoeal, antidiabetic, anti-inflammatory, antimicrobial, antiplasmodial, antihypertensive, anticonvulsant, antinociceptive and anti-oxidant, astringent, antihyperglycemic, anti-atherogenic, antiviral.[109-110]	None.
Tabernaemontana elegans Stapf	backache and rheumatism.	None.	Alkaloids.[111]	Antibacterial activity.[111]	None.
Tacca leontopetaloides (L.) Kuntze	Yellow fever, stomachache, rheumastism.	None.	Flavonoids, steroids, and tannins, taccalonolide, flavones, isoflavones, anthocyanins, coumarins, catechins, and carotenoids.[112]	Anticancer, anti-oxidant.[112]	None.

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Table 5 Cont....

Tephrosia vogelii Hook. f.	Viral, Inflammation.	None.	Rotenoids, flavones, flavonones, tephrosin, rotenone, dequelin terpenoids, flavonoids, tannins, saponins, and phlobatannins.[113,114]	Anti-oxidant, antimicrobial, antivirus, and anticancer.[114]	None.
Terminalia sericea Burc. ex DC.	Breathe/asthma, Pain/aches.	None.	Saponins, lignin, steroids, glycosides, phenolic acids, amino acids, terpenoids, tannins, flavonoids, lignans, phenols and glycosides and anthraquinones.[44,115,116,117]	Antibacterial, anti-HIV, antifungal, lipolytic activity, anti-inflammatory activity, hypoglycemic activity, anti-mutagenic activity, acetyl-cholinesterase effect, antioxidant activity, wound healing, anticancer, anti-neurodegenerative, anti-parasitic activity, antidiabetic.[44,115,116,117]	None.
Trichilia emetica Vahl	Pneumonia, Pain/aches, Blood.	None	Total phenolics, total tannins, total flavonoids, total flavonols and sterols/terpenes.[118]	Anti-inflammatory, antischistosomal, antiplasmodial, anticonvulsant, antitrypanosomal, antitussive, antimutagenic and hepatoprotective properties, anti-oxidant, antidiarrheal.[118,119]	None.
Xeroderris stuhlmannii (Taub.) Mendonca & Sousa	Continuous menstruation.	None.	None.	None.	None.
Zanha africana (Radlk.) Exell	Painkiller, headache.	None.	Anthocyanins, courmarins, saponins, steroids, triterpenoids, tannins and volatile oils.[120]	Anti-atherogenic, anti-oxidative, anti-inflammatory, anticancer properties, antibacterial, antifungal, antiviral, antidiabetic, insecticidal, antitrypanosomal.[120]	None.

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Table 5 Cont....

Zingiber officinale Roscoe	Immunity, Heart.	None.	[4]-gingerol, [6]-gingerol, [8]-gingerol, [10]-gingerol, [6]-paradol, [14]-shogaol, [6]-shogaol, 1-dehydro-[10]-gingerdione, [10]-gingerdione, hexahydrocurcumin, tetrahydrocurcumin, gingerenone A, 1,7-bis-(4′ hydroxyl-3′ methoxyphenyl)-5-methoxyhepthan-3-one, and methoxy-[10]-gingerol.[121-123]	Antioxidant, anti-inflammatory, antinausea, anticarcinogenic, cardiovascular, cardiovascular effects, antidiabetic, anti-asthmatic, antiviral.[121-123]	None.