



Can antimalarial, antiviral and anti-respiratory infections Cameroonian medicinal plants be used as one of the potential ways to cure COVID-19? Pharmacological and ethnomedicinal proof

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ABSTRACT

COVID-19 is a severe acute respiratory syndrome-related corona-virus SARS-CoV-2, that constitutes a pandemic threat to global public health. Unfortunately, there are no specific available therapies. This research work presents the findings of an investigation on traditional Cameroonian remedies of respiratory tract infections, malaria and viral infections, and also recipes that could serve as a baseline for the prevention, alleviate symptoms, treatment and perhaps may help for the anti-COVID-19 drugs discovery. Data on the medicinal plants were collected from traditional healers, Cameroonian medicinal plants books, the internet, and in addition to our personal experience as researchers and herbalists. Details of 85 plant species used to manage these three mentioned diseases in Cameroon and their pharmacological properties are recorded. Due to their ethnomedicinal uses and pharmacological activities, twenty-eight (28) plant species and 13 recipes are suggested for COVID-19 prevention, alleviate symptoms, treatment and baseline for anti-COVID-19 drug discovery. Amongst the proposed plants we have the following, *Curcuma longa*, *Azadirachta indica*, *Zingiber officinale*, *Allium sativum* and *Ocimum gratissimum* which were reported to possess certain inhibition properties against COVID-19 protease. **Conclusion:** These plants can be used as precursors for the synthesis of useful drugs to fight against COVID-19; however, non-clinical and clinical assays still need.

KEYWORDS: COVID-19 disease, antimalarial, antiviral, anti-respiratory, Cameroonian medicinal, plants.

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INTRODUCTION

Since the prehistoric society, man has been in way to search the cures and relief from physical and mental illness by using

numerous plants and plant-derived products [1]. Traditional medicine is used globally and is rapidly growing in economic importance. In developing countries, traditional medicine is often the only accessible and affordable treatment available

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for the population. The World Health Organization (WHO) reports that traditional medicine is the primary health-care-system for important percentage (80%) of the population in developing countries [2]. Many drugs have plant origin, and several plants are currently undergoing investigation to ascertain their therapeutic efficacies. In numerous countries, several herbs of different plant species have been used against a lot of diseases, that is the cases with respiratory infections, malaria and viral infections. Respiratory diseases can involve the respiratory tract, lungs or blood vessels and generally a combination of these abnormalities can be seen in many respiratory diseases. In that vein, respiratory diseases can usually be classified into the following groups: obstructive pulmonary disease, restrictive lung disease, pulmonary vascular and other diseases [3]. Respiratory diseases symptoms such as flu are fever, chill, cough, nasal congestion runny nose, sore throat, hoarseness, earache, muscle pains, fatigue, headache, watering eyes, reddened eyes, (skin, mouth, throat & nose), vomiting, diarrhea and abdominal pain. Besides, malaria symptoms include high fever, headache, fatigue, muscle ache, nausea, abdominal discomfort, vomiting, diarrhea and profuse sweating. However, in extreme cases and cases of prolonged illness without treatment, brain tissue injury, pulmonary edema, kidney failure, severe anemia, yellow discoloration of the skin, and low blood sugar may be noted [4,5]. Concerning viral infections like acute HIV infection, within two to three weeks after infection, about two-thirds of people will have a flu-like illness (fever, chills, rash, night sweats, muscle aches, sore throat, fatigue, swollen lymph nodes, mouth ulcers). These symptoms can last anywhere from a few days to several weeks. However, some people do not have any symptoms at all during this early stage of HIV. Bringing these three diseases symptoms altogether with those of COVID-19, it is clear that there are important similarities (such as cough, fever, fatigue, myalgia and diarrhea).

Although the epicenter of the COVID-19 outbreak in December of 2019 was located in Wuhan, China [6,7], this disease has spread to more than 213 countries around the world with over 3,568,143 confirmed cases and over 248,346 confirmed deaths worldwide as of May,04,2020 [8]. Therefore, COVID-19 is a serious global health problem, which calls for agents of anti-COVID-19 therapies as more as possible. Unfortunately, specific antiviral drugs or vaccines currently have not been available for the treatment of COVID-19 [9]. Some researchers have proposed the use of remdesivir and chloroquine [10,11]; hydroxychloroquine [9,12]; hydroxychloroquine-darunavir-ritonavir [13] may be of strongly linkage of its symptoms as compared to those of malaria, flu and in some cases acute HIV or RNA virus. It may be for the same reason that, scientists and other governments allowed the use of Hydroxychloroquine or chloroquine in combination with lopinavir/ritonavir etc [11,14].

Medicinal plants have long been known for their protective effects against a broad range of microorganisms, such as viruses, protozoa, bacteria and parasites [15,16,17]. Using plant extracts, a number of studies have shown their protective action against viral diseases, such as HIV & 1,2; Herpes simplex virus, Hepatitis B & C virus etc. [18,19,20]. However, only few reports have

described the therapeutic effect of medicinal herbs against COVID-19. For instance, Luo *et al.* [21], Yang *et al.* [22] have mentioned some herbal formulation used in China to alleviate COVID-19. For example, a polyherbal product of traditional Chinese medicine Yin Qiao San and Yu Ping Feng San have been found to be effective in COVID-19 [22]. Therefore, both medicinal plants and conventional medicine might be used as solution for the treatment of patients with COVID-19, as it has been adopted in China [21,22].

Due to the fact that Cameroon is situated in a sub-Saharan tropical region where a large number of medicinal plants species have been growing naturally, and probably some of these plants can be used to fight against this pandemic disease (COVID-19). Furthermore, some ethnobotanical studies can provide valuable information to scientists, and this information paves the way for clinical research to produce new drugs. Many studies have been carried out to identify and introduce anti-COVID-19 drugs with inhibitory actions, but the effects of medicinal herbs have received few preoccupation [23]. Hence, the present study was conducted to propose to the scientific community, the evidence of some Cameroonian medicinal plants species that can serve as baseline for anti-COVID-19 drug discovery, prevention and alleviator of symptoms.

MATERIALS AND METHODS

The data on the medicinal plants were collected from Adjanohoun *et al.* [24] book, internet search such as www.google.com, www.scholar.google.com and www.pubmed.gov. Data were also obtained from traditional healers, in addition to our personal experience as researcher and herbalist. The search terms were ethnomedicinal, pharmacology, active constituents, mode of action, *in vivo* and *in vitro* activity. Data extraction and analysis followed Luo *et al.* [21] method (source of proof, author, target disease (COVID-19, malaria, viral and respiratory diseases), herbal formulation, effect, pharmacology action, toxicity, adverse reaction). The data was qualitatively and quantitatively described and presented. Moreover, this review was mainly based on the results of articles obtained from the sus-mentioned databases.

RESULTS

Conventional Treatment of COVID-19 Adopted by Some Countries

Due to the absence of a specific antiviral treatment and vaccine for COVID-19, each country has adopted his own fighting strategy against this pandemic disease. Thus, combination of broad-spectrum Oxygen therapy (extracorporeal membrane oxygenation, Nasal cannula, Non-invasive mechanical ventilation, Invasive mechanical ventilation); antibiotics (Amoxicillin, Azithromycin, Fluoroquinolones); antivirals (Lopinavir/ ritonavir, Ribavirin, Favipiravir, Remdesivir, Oseltamivir, Chloroquine, Interferon); corticosterols (Methylprednisolone); and convalescent plasma are being used in many countries (e.g. China [9,11,12], France, Burkina Faso,

Benin, Cameroon etc). Scientific evidence of this combination has been largely discussed by Yang *et al.* [22].

Plants used to Treat Malaria, Respiratory Tract Infections and Viral Diseases in Cameroonian Pharmacopoeia

Some plant extracts used in Cameroonian traditional system to cure the above-mentioned diseases could help to fight against COVID-19 due to their related symptoms, and also help to prevent this global health problem. In our findings, we recorded 85 plants species (42 plants for respiratory tract infections, 26 plants for malaria therapy and 17 plants for viral infections) belonging to 40 botanical families (Table 1, 2 and 3), of which 59 plants species have been investigated pharmacologically. The dominant botanical plant families are Asteraceae, Fabaceae, Euphorbiaceae, Rubiaceae, Poaceae, Zingiberaceae, Apocynaceae and Acanthaceae. Out of the 85 plant species, twenty-eight (28) plant species are suggested for recipe formulations (Appendix A), amongst which 13 recipes (eight polyherbal and four monoherbal) are proposed for COVID-19 prevention, alleviator of symptoms, treatment and baseline for anti-COVID-19 drugs discovery. Some of these plant families (Fabaceae, Asteraceae and Lamiaceae) have been reported in China to treat and alleviate COVID-19 disease [21,22].

Ethnomedical and Pharmacological Evidence

Many plants have been reported in Cameroonian pharmacopoeia as remedy of malaria, respiratory tract infections and viral

infections, amongst which a few prominent are listed here (Table 1, 2 & 3). These plants grow in many localities of Cameroon and are well recognized by healers and some common people for their effectiveness, that is primarily based on traditional directives. Some of these plants have been studied for their scientific validation. For instance, the leaves or leafy stems of *Alchornea cordifolia* are used to treat a variety of respiratory conditions in Nigeria such as sore throat, cough and bronchitis [23]. Fruit slurries are administered for asthma and coughs [24].

Odeku *et al.* [25] and Odugbemi *et al.* [26] reported the anti-malarial property of *Alstonia boonei*. Other studies conducted by Majekodunmi *et al.* [27] revealed that, recently, the stem bark extract, of *A. boonei* was formulated into tablets and made available as an antimalarial drug.

Artemisia annua tea infusion has been used for the treatment of malaria in African countries. Most common ethnobotanical practice involves the use of whole plant decoction for the treatment of malaria, cough and cold. Its dry leaf powder has been reported in the treatment of diarrhea. The whole flowering plant is known to be anthelmintic, antipyretic, antiseptic, antispasmodic, carminative, stimulant, tonic and stomachic. It contains artemisinin, which provides a structural chemical base for combinatorial treatment therapy for worldwide antimalarial programs. Research studies also reported that artemisinin is effective for killing human breast cancer cells.

Table 1: Cameroonian ingredients formula for preventing and treating malaria

Plants/Family	Common names	Parts used	Mode of preparation
<i>Alchornea cordifolia</i> / Euphorbiaceae	Mbienchie, aboue, enzezam, diboybonji, aboe, bambemi, kaka, saye, kibabar kewong	Leaves	Decoction
<i>Alstonia boonei</i> / Apocynaceae	Gouga, kodmot, ekuk, ekouk, lombo, mpoubieng leoup	Bark	Maceration, decoction
<i>Artemisia annua</i> / Asteraceae	Artemisia	Leaves	Decoction, infusion
<i>Aspilia africana</i> / Asteraceae	Kighavd, kigavir, kighair, pakbeng	Leaves	Decoction
<i>Azadirachta indica</i> / Meliaceae	Neem	Leaves	Decoction
<i>Bidens pilosa</i> /Asteraceae	Akwekwe asad, esomomo-comboh, yiere, fouwan, njim njim, pihanhua, lilip-nouk, atchiti, biakoua, guiepoura, liètemik	Leaves	Decoction
<i>Buchholzia coriacea</i> / Capparaceae	Ngale	Seeds	Powder
<i>Carica papaya</i> / Caricaceae	Tjai di popo, ekes fofo, fofo'o, fufuo, doukonje, jongarme, mborugwenda, papaye	Leaves	Decoction
<i>Chenopodium ambrosioides</i> / Chenopodiaceae	Ait, kedamtou, obu-helo'oh, konki, kedantou, mbolminson	Leaves	Decoction
<i>Cinchona officinalis</i> / Rubiaceae	Quinquina	Barks	Decoction, maceration
<i>Citrus aurantiifolia</i> / Rutaceae	Nkang sabe, lamasse	Roots	Decoction
<i>Coffea arabica</i> / Rutaceae	Cafi	Leaves	Decoction, infusion
<i>Conyza sumatrensis</i> / Asteraceae	Gueguaguem, kene, lamje, lamjeje, sqbakoube, shidji	Leaves	Decoction
<i>Cymbopogon citratus</i> / Poaceae	Disang, osanga, fipergrass	Whole plant	Decoction
<i>Guibourtia tessmannii</i> / Fabaceae	Lobp, nsim-gang, essingan, ynamoto ele,	Barks	Decoction
<i>Melinis minutiflora</i> / Poaceae	Mvirg li, njure-ji	Leaves	Decoction
<i>Microglossa pyrifolia</i> / Asteraceae	Folanvue	Leaves	Infusion, maceration
<i>Milletia sanagana</i> / Fabaceae	Djopo	Roots	Ash
<i>Picralima nitida</i> / Apocynaceae	Bamborutuk	Barks	Decoction
<i>Psorospermum senegalense</i> / Hypericaceae	Sawaika shrub	Leaves	Decoction
<i>Rauvolfia vomitoria</i> / Apocynaceae	Lele, Ikwadongdonui, menzanga menzanga, sebal, batakarack, nchokorock, fouti	Barks	Decoction
<i>Rumex abyssinica</i> / Polygonaceae	Sessotcha	Tubers	Powder
<i>Senna alata</i> / Fabaceae	Ekon-chuwe, seu-nansa, hu-makanju, nkokokora, ngom	Leaves	Decoction, infusion
<i>Senna hirsuta</i> / Fabaceae	Olou, fafe, ibilissi,	Leaves	Decoction, infusion
<i>Senna occidentalis</i> / Fabaceae	Kon bokugu, katchikatchouga mamatasba, raedaore	Leaves	Decoction, infusion
<i>Spathodea campanulata</i> / Bignoniaceae	Vivet, kilulone, evovone, fowara, bolabola, fukfuk	Leaves, barks	Decoction

Table 2: Cameroonian ingredients formula for treating respiratory tract infections

Plants/Family	Common names	Parts used	Mode of preparation
<i>Aframomum melegueta</i> /Zingiberaceae	<i>Didi, koge, Mbong, itoko, dok bayong, indokamokwe, sock kwa, lombongo, nbongo, ndong, ndon, mfonlo, mvonlo</i>	Fruits	Grind
<i>Allium sativum</i> /Amaryllidaceae	<i>Ail, garlic</i>	Bulb	Decoction, infusion
<i>Aloe buettneri</i> /Asphodelaceae	<i>Lagapegue, tokeshékurt, kagbayi, lah-ndih, gassa, adjan nkom</i>	Leaves	Decoction
<i>Asystasia buettneri</i> /Acanthaceae	<i>Nshare, loloni, awaimbe</i>	Leaves	Grind
<i>Bidens pilosa</i> /Asteraceae	<i>Akwekwe asad, esomomo-comboh, yiere, fouwan, njim njim, pihanhua, lilip-nouk, atchiti, biakoua, guiepoura</i>	Leaves	Decoction
<i>Boerhavia coccinea</i> /Nyctaginaceae	<i>obooti</i>	Leaves	Warm, grind
<i>Brachystephanus longiflorus</i> /Acanthaceae	<i>Keshimpon</i>	Fruits	Grind
<i>Bryophyllum pinnata</i> /Crassulaceae	<i>Nezouck</i>	Whole plant	Decoction, infusion
<i>Canarium schweinfurthii</i> /Burseraceae	<i>Bete, giin, brère</i>	Resin	Grind
<i>Chlorophytum macrophyllum</i> /Liliaceae	<i>Keng, mbalah</i>	Leaves	
<i>Cissus quadrangularis</i> /Vitaceae	<i>Coeur, ndieh gap, tohr-ngehkue, nkohsat, sango-di, njel, nyo, nnezu, alvarahala, chabal, chebal, chimbaral chembale, gadal, ndii, ndig, epripi. Chu, nwan</i>	Stem	
<i>Costus afer</i> /Costaceae		Stem, leaves	Decoction
<i>Croton oligandrum</i> /Euphorbiaceae	<i>Ebin</i>	Barks	Decoction
<i>Curcuma longa</i> /Zingiberaceae	<i>Kou kassa</i>	Rhizomes	Decoction, infusion
<i>Cyperus tenuiculmis</i> /Cyperaceae	<i>Gowe</i>	Nodules	Decoction
<i>Desmodium adscendens</i> /Fabaceae	<i>Pepeur, ton-ton, owondo bekone</i>	Whole plant	Trituration
<i>Dissotis rotundifolia</i> /Melastomataceae		Leaves	Grind
<i>Eremomastax speciosa</i> /Acanthaceae	<i>Kechukeba, banguimoh, ekunte, mejama njombe, maijai ,a njombe, pang ndjeniti, ndon agiri, banjim, ntamir, alio, tankebi, noni, basifim, essan dja, penkuzem</i>	Leaves	Decoction
<i>Eucalyptus globulus</i> /Myrtaceae	<i>Eucalyptus</i>	Leaves	Decoction
<i>Euphorbia hirta</i> /Euphorbiaceae	<i>Ndo, pengmey, mpemeu, tenkwuvue, ewuda manyongo, okoulbiles, endemhi, nepimou</i>	Whole plant	Concoction
<i>Ficus exasperata</i> /Moraceae	<i>Ekwoc, ghu ghu, cokguème</i>	Leaves	Grind
<i>Gossypium herbaceum</i> /Malvaceae	<i>Cotton</i>	Leaves	Decoction
<i>Gouania longipetala</i> /Rhamnaceae	<i>Badjoue, sobomissile, konteh</i>	Whole plant	Trituration
<i>Kalanchoe crenata</i> /Crassulaceae	<i>Ejome, elualuoc, ma'a-tout, tankeyai, zeimfeum, ebin, nezu, edandi, edibedibe, napkibali, kalmissi, keturkenjii, tukeji, you, yun, nezouck.</i>	Whole plant	Infusion
<i>Khaya grandifoliola</i> /Meliaceae	<i>Faturtu, fatiti</i>	Roots	Decoction
<i>Laportea ovalifolia</i> /Urticaceae	<i>Anelembu, talambo dop, kilikion, sogo.</i>	Leaves	Warm
<i>Mangifera indica</i> /Anacardiaceae	<i>Mangourè, kouap mangoro, endo'o</i>	Leaves, barks	Decoction
<i>Momordica cissoides</i> /Cucurbitaceae	<i>Ntomsapkel</i>	Leaves	Trituration
<i>Momordica foetida</i> /Cucurbitaceae	<i>Nyako, engokom, oyale zom</i>	Leaves	Trituration
<i>Pennisetum purpureum</i> /Poaceae	<i>Nto obwet, sisung, lekop, kikhiai, mjee, sussong, elephant grass</i>	Shoots	Decoction
<i>Polyscias fulva</i> /Araliaceae	<i>Npougge, biangzui, kikiokdiorè</i>	Roots	Decoction
<i>Portulaca oleracea</i> /Portulacaceae	<i>Kepingoup, koupugoup, derdegue, nyukutu nyukutu</i>	Leaves	Trituration/crushed
<i>Ocimum gratissimum</i> /Lamiaceae	<i>Ose-mo-se, lisepe, ndoli, masepo, nkuwri, masebi, messep, massep, mahepo, keyang, berem, foulomoh</i>	Leaves	Decoction
<i>Solanum aculeastrum</i> /Solanaceae	<i>Sircerka, kijah, kilum, kilun, kira</i>	Roots	Decoction
<i>Solanum torvum</i> /Solanaceae	<i>Elam-tam, ngaleni sumembre, ngunmbia, tchièè</i>	Fruits	Grind
<i>Spilanthes filicaulis</i> /Asteraceae	<i>Tuteombege, ehe ngui, kupe, panto'o, misomakosso, misso makuso, seke, gnigup, mbakouan, neh-ngup, leuk ngueb, ondududusi, ondodosi, ekukura, ekukure, odondongong-si, odongdong-si, andong meleti, sichoucheshif, shishur sheshir, menek megue</i>	Whole plant	Grind
<i>Synedrella nodiflora</i> /Asteraceae	<i>Dewangi, okpate black, borou</i>	Whole plant	Pound
<i>Torenia thouarsii</i> /Scrophulariaceae	<i>Iakngeb</i>	Flowers	Grind
<i>Urera trinervis</i> /Urticaceae	<i>Yangoue ajoumgan</i>	Leaves	Trituration
<i>Urginea altissima</i> /Liliaceae	<i>Eyang, mpoum pou, tombou, bougoulou, ninyang, foubà</i>	Barks	Decoction
<i>Vernonia ampla</i> /Asteraceae	<i>Mako, merke, shiji</i>	Leaves	Decoction
<i>Zingiber officinale</i> /Zingiberaceae	<i>Njindja, ginger</i>	Rhizomes	Decoction, infusion

Several ethnobotanical uses in Africa claimed that the *A. annua* tea is also effective against human immunodeficiency virus (HIV) [20,28]. De Donno *et al.* [29] showed that a tea infusion

constituted of 5 g dried leaves of *Artemisia annua* in one liter was effective against both Chloroquine resistant and Chloroquine sensitive strains of *Plasmodium falciparum* with IC50 values

Table 3: Cameroonian ingredients formula for treating viral infections

Plants/Family	Common names	Parts used	Mode of preparation
<i>Chrysanthellum indicum</i> /Asteraceae	Gueguametetet, jabia, guetegor-tegelhe, guitebani		Infusion
<i>Cucurma longa</i> /C. domestica	Cucurma, kou kassa	Rhizome	Decoction, infusion
<i>Euphorbia lateriflora</i> /Euphorbiaceae	Nepimou	Stem	Decoction
<i>Ficus thonningii</i> /Moraceae	Kidzem, guème	Barks	Decoction, infusion
<i>Gardenia ternifolia</i> /Rubiaceae	Metouc bouor, metobouo	Leaves, barks	Decoction
<i>Glyphae brevis</i> /Tiliaceae	Mon akak, anaga	Leaves	Infusion
<i>Gossypium herbaceum</i> /Malvaceae	Cotton	Leaves	Infusion
<i>Hallea stipulate</i> /Rubiaceae	Ajobo jam	Barks	Decoction
<i>Jatropha curcas</i> /Euphorbiaceae	Jatropha, ele meveng, chini da zoughou	Leaves	Trituration
<i>Leucas martinicensis</i> /Lamiaceae	Hore gaudjo	Leaves	Infusion
<i>Phyllanthus amarus</i> /Euphorbiaceae	Income, kojaleyi, akoua, nsanyuy, bome anegate	Whole plant	Decoction
<i>Sarcocephalus latifolius</i> /Rubiaceae	Bakouedje, bokoriyi, gamoyi, zadeyi, edindingue		
<i>Smilax kraussiana</i> /Smilacaceae	Bounk, bii	Leaves	Decoction
<i>Senna alata</i> /Fabaceae	Ekon-chuwe, enange ijo, seu nansa, humakanju, nkot okara, ngom, plasko, to'o, foupang	Leaves	Decoction, infusion
<i>Stereospermum accuminatissimum</i> /Bignoniaceae	Wate-fè, ware-fè, siton	Barks	Decoction
<i>Terminalia glaucescens</i> /Combretaceae	Sa'ah,	Barks	Decoction
<i>Rauvolfia vomitoria</i> /Apocynaceae	Lele, ikwadongdongii, batat ndkwesoc, medzanga medzanga, sebal, batarack nchokorock, fouti	Barks	Decoction

of 5.60 nmol/L et 7.08 nmol/L. Artemisinin and its derivatives have been established in various combination therapies as effective anti-malarial treatments against multidrug-resistant *P. falciparum* [30,31]. Moreover, Marchand *et al.* [32], Lubbe *et al.* [33] have demonstrated its anti-HIV activity. Thus, oral consumption of the dried leaves of this plant will not only treat malaria, but will also enhance the well-being of HIV/AIDS patients. In addition, Warghurst [34] retrieved that, artemisinin has a higher chemotherapeutic index than chloroquine and is effective in chloroquine-resistant strains of human malaria.

Investigation on traditional uses of *Aspilia Africana*, revealed that, crushed leaves have been used for patients suffering from rheumatic pains and to clean surfaces of sores by absorption of exudates, wound healing [35,36,37]. Infusion of the leaves of this plant is usually taken by pregnant women at child birth and used as cough remedy for children. The anti-malaria activity has been reported in mice [38,39]. Decoction of leaves of *Aspilia Africana* are used in Ivory Coast [40], tribes of the Amazon to treat Malaria [41]. Besides, Juice from the root and the whole plant is used for the treatment of malaria in many Africa countries and localities in China [42,43].

Azadiracta indica (neem) is one of the most used plants in the treatment of malaria in many parts of Africa and Asia where malaria is endemic. Findings revealed that, this plant is widely effective in the treatment of malaria caused by various strains of Plasmodium, even those resistant to conventional antimalarial drugs [44,45,46,47]. The antimalarial effect was also reported by Udeinya *et al.* [48,49,50]. Neem extracts have been proved to be antihelminthic, antimicrobial, contraceptive and sedative ingredient [51,52]. Mahommad [53] reported that the therapeutic effects of neem are due to the richness source of antioxidant and other valuable active constituents such as nimbolin, azadirachtin, nimbin, nimbidin, nimbidol, salannin

and quercetin. The same authors also indicated that the leaves of neem exhibit hepatoprotective, wound healing, anti-diabetic, antimicrobial, anti-nephrotoxicity, neuroprotective and immunomodulatory effects. Furthermore, other studies revealed that *A.indica* extracts notably inhibited the polio, HIV, coxsackie B group, and dengue viruses at early step of viral genome replication [54,55,56,57,58,59,60,61]. Moreover, neem extract act as a viricidal agent against coxsackie virus B-4 as suggested by virus inactivation and yield reduction assay besides interfering at an early event of its replication cycle [58]. Similarly, the virus inhibition and RT-PCR assays confirmed inhibitory potential of neem extract at virus replication step for Dengue virus type-2 [60,61] (Parida *et al.*,2002; Tiwari *et al.*,2010).

Bidens pilosa is known as Picao preto in Brazil, and is widely used as a medicinal plant for treating inflammation, arterial hypertension, ulcers, diabetes and all types of infections [62]. In India, *B. pilosa* is frequently used in traditional medicine as a remedy to treat glandular sclerosis, wounds, colds and flu, acute or chronic hepatitis, and urinary tract infections [63]. The methanolic extract of the whole plant of *B. pilosa* exhibited a comparable anti-pyretic activity *in vivo* to paracetamol in the rabbit pyrogen test [63]. In some *in vitro* and *in vivo* studies, aqueous extracts obtained by hot maceration of dried leaves of *B. pilosa* displayed higher oxytocic/uterotonic and estrogenic/utero trophic effects than other organic extracts [64]. These results explain why *B. pilosa* leaves are used as a folk medicine to enhance labor in many countries. Due to their oxytocic effects, decoctions of *B. pilosa* should not be taken by pregnant women [65]. Nevertheless, some preliminary specific experimental studies provided no evidence of toxicity when a dosage of 1 g per kg of body weight was injected into mice [62]. It has also been reported to possess effective pharmacological properties like antibacterial activity, anti-

inflammatory and anti-allergic activity, T helper cell modulator, immunosuppressive, anti-hyperglycemic, anti-hypertensive, anti-ulcerogenic, hepatoprotective, antileukemic, anticancer, antipyretic, antiviral, anti-angiogenic, antirheumatic and antibiotic activity [66]. About 201 compounds comprising 70 aliphatic, 60 flavonoids, 25 terpenoids, 19 phenylpropanoids, 13 aromatics, 8 porphyrins, and 6 other compounds, have been identified from this plant [67]. Chloroquine or mefloquine-resistant *Plasmodium falciparum* strains are susceptible to *B. pilosa* (IC₅₀ = 10.4-49.8 µg/mL) *in vitro* [19]. Many studies have reported that *B. pilosa* has strong antimicrobial activities, including anti-viral activities against type I and II herpes simplex viruses (HSV) [19].

Burkill [68] reported the medical uses of *Buchholzia coriacea*, e.g. in the treatment of malaria and other fevers. The grained seeds when mixed with palm oil are taken orally as treatment for malaria [24]. *Buchholzia coriacea* is widely used in Nigeria by traditional medical practitioners for the treatment of various disorders including cough, urinary tract infections, bronchitis, fever, diabetes, inflammation and malaria [69,70]. The antiparasmodial activity of the seeds of the plant has been demonstrated [71]. Previous studies also demonstrated the hypoglycemic activity [72], antibacterial and antifungal activities [73], as well as anti-inflammatory activity of the seed extract. Fruit scrapings are administered to treat asthma and cough. Seed preparations are taken to treat fever, diabetes, hypertension, cough, psychiatric disorders and impotence [74].

The leaves extract of *Carica papaya* were reported to have anti-proliferative against prostate cancer, antifungal activity, antibacterial, antidengue, anti-inflammatory and antimalaria [75]. *Carica papaya* is widely grown in the tropics for its edible fruit and also used as a weak decoction of its leaves against malaria [76]. The flowers are used for jaundice, fevers, and the strengthening of the lungs, while its fruits are used to aid digestion, as a diuretic, tonic, and for ringworm. The roots are used as abortifacient, diuretic, anti-fungal, and for piles and sores, while the stem bark is used for jaundice and venereal diseases. The seeds have carminative effects and are also used for ringworm and as an abortifacient. The leaves are used for malaria [77,78,79,80]. Several studies have investigated the antimalarial properties of *C. papaya* extracts but only two papers have reported the isolation of active compounds. The ethanol extract of *C. papaya* leaves obtained from Soxhlet extraction inhibited growth of chloroquine-sensitive and chloroquine-resistant *P. falciparum* [81]. Other findings, showed that *C. papaya* extracts (leaf & seed) possess an ability to modulate inflammatory markers in various cell types exposed to a variety of stressors [82].

Chenopodium ambrosioides is used to treat respiratory problems, painful processes and bronchitis. Pollack *et al.* [83] reported that the ascaridole isolated from the essential oil of *Chenopodium ambrosioides* effectively inhibited the growth of malaria parasites *in vitro*. Moreover, the anti-inflammatory and analgesic effect of *C. ambrosioides* [84]; Trivellato-Grassi *et al.*, [85] corroborate the potential use of this plant species as an antimalarial agent. Wright (2005), discussing about the development of

plant-derived antimalarial drugs, highlighted that they can also be important in reducing the characteristic symptoms of malarial infection, including pain and fever. Dalila *et al.* [86] revealed that the hydroalcoholic crude extract of *Chenopodium ambrosioides* leaves had a significant antiparasmodial potential in different *in vitro* and *in vivo* experimental models.

The first report regarding the effect of quinine extracted to *Cinchona* species on influenza virus infections in mice was published in 1946 [87]. Afterwards, *in vitro* evaluation of quinine sulfate has been conducted with other viruses, such as herpes simplex virus-1 and influenza A virus. Lately, quinine sulfate was tested *in vitro* against emerging dengue virus strains in different cell lines, showing a reduction in dengue virus-2 virion production up to 80% compared to that of the untreated control and a concentration-dependent reduction in DENV RNA and viral proteins. The inhibition of replication was then confirmed for all four different serotypes of dengue virus [88]. Other studies retrieved that, combination of artesunate (100 mg/kg) and *C. officinalis* completely clear the blood stage infection of *Plasmodium berghei*.

The chemical composition of the *Citrus* plant is characterized by the used to treat several health problems such as gastrointestinal disturbances, respiratory disorders (cough), insomnia, stress disorders, epilepsy, and anxiety. *C. sinensis* is a rich source of vitamin C, a natural antioxidant that supports the immune system activity. *C. sinensis* has been used traditionally to treat ailments like constipation, cramps, colic, diarrhea, bronchitis, tuberculosis, cough, cold, obesity, menstrual disorder, angina, hypertension, anxiety, depression and stress [89].

The medicinal uses attributed to *Conyza* species include the treatment of malaria, wounds antibacterial, antioxidant, cytotoxic, anti-inflammatory, analgesic, antiviral, antiproliferative, anti-schistosomal, antiprotozoal and antidiarrheic activities [90].

Cymbopogon citratus is widely used in Asia. In India it is used as sedative, febrifuge and immunostimulant [91]. In Nigeria, it is used for stomach problem and typhoid [92]. The essential oils of *C. citratus* were found to produced 86.6% suppression in growth of *Plasmodium berghei* when compared to a standard drug chloroquine [93]. Other studies revealed *C. citratus* as remedy of coughs, flu, headache, gingivitis, leprosy, ophthalmia, vascular disorders, elephantiasis and pneumonia [94]. Minami *et al.* [95] reported its antiviral, antibacterial and antifungal activities. A number of researches retrieved its anti-inflammatory, antipyretic, antiprotozoal and antimalarial properties [76]. This plant has been classified as safe herb for human consumption [96,96].

Guibourtia tessmannii bark, leaves and fruits are used in Cameroon to treat malaria, anaemia, typhoid, haemorrhoids, lumbago, cancer, sexual transmitted infections and hepatitis [98].

The leaves decoction of *Microglossa pyrifolia* is used to treat malaria in Kenya [99]. These leaves are also used to treat jaundice in Ethiopia [100].

The investigation carried out by Adjanohoun *et al.*, [24] reported that the stem bark of *Picralima nitida* is used to prepare remedies to cure malaria and sexual impotence, while the fruits are used for dysmenorrhea and gastrointestinal disorders [24]. The various parts of the plant have been reported to be effective antipyretic, antihypertensive, hypoglycemic and antitussive in Central and West Africa [101,102]. Similar results were obtained by Nwakile *et al.* [103] in Southeastern Nigeria. The seed, fruit rind and stem bark extracts showed remarkable inhibition activity against drug resistant clone of *Plasmodium falciparum*. Ethanolic and methanolic of its seed and bark extracts demonstrated significant activity against the chloroquine-resistant *P. falciparum* [104]. Mabeku *et al.* [105] reported the acute toxicology profile of the methanol fruit rind extract of *P. nitida* in rats on the liver, kidneys and the lungs after prolonged exposure at high doses (1.5-6 g/kg) with LD50 values of 14.5 and 12.5 g/kg for male and female rats respectively. Other studies reported analgesic, antipyrexia and anti-inflammatory of *P. nitida* fruit on rabbits [106]. Other studies revealed that the seeds are rich in alkaloids (e.g. akuammine, akuammicine, akuammidine, picratidine, akuammigine, pseudoakuammigine, picraline and picralicine) [107,108]. The plant has also been reported to have anti-inflammatory antioxidant and analgesic properties [109]. Moreover, Erharuyi *et al.* [110] reported that chronic administration could reduce the chances of fertility in females and develop low sperm count in males what will make them infertile. It's worthwhile to mentioning Dapaah *et al.* [111] works reported antitussive activity of its seed.

In Ghana and Nigeria *Rauwolfia vomitoria* is used traditionally against snake bites, malaria, fever and nervous disorders as well as emetic and purgative [112]. *R. vomitoria* are also used in the treatment of cerebral cramps, jaundice and gastrointestinal disorders in children [113]. In Mali, the roots of *Rauwolfia* have been used in the treatment of hemorrhoids and hepatomegaly [114]. Omoya & Falusi [115], showed its anti-plasmodial activity. Phytochemical analysis revealed high concentration of reserpine and ajmaline. These compounds are known to have pharmacological properties including antimalarial, anti-tumor and antidiabetes efficacies [116,117].

Mukungu *et al.* [99] reported the use of pound leaves of *Rumex abyssinica* as treatment of cold, wounds, liver diseases, malaria, gonorrhea. Similar founding was reported by Ramadhani *et al.* [118] in Tanzania. Derksen *et al.* [119] showed the inhibition effect of *R. acetosa* extracts on herpes simplex type-1 and influenza A virus. Moreso, they observed that the efficacy of this plant extract in patient with acute respiratory distress (flu) was similar to those treated with oseltamir.

The leaf extracts from *Cassia alata* or *Senna alata* have been retrieved in many studies as anti-microbial, anti-fungal, anti-inflammatory, analgesic and anti-hyperglycemic ingredient [120,121]. In Indian medicine, its leaves are used as purgative, expectorant, astringent, vermicide and to cure all skin infections [122]. The leave decoctions are used in Nigeria to treat infectious diseases [123]. Sarkar reported *S. alata* as potential source of natural antioxidant agent. Moreover, Woradulayapinij *et al.* [124] showed slight inhibition action

of ethanolic extracts on HIV type 1. Studies carried out by Da *et al.* [125] revealed no significant changes in weight, tissues morphology, biochemical and hematological at doses above or equal to 2779.5 mg/kg body weight. Quinones and terpenes extract from *Cassia alata* significantly displayed *in vitro* antiparasmodial activity against *Plasmodium falciparum* [126].

In Ghana, leaves, fruits, root barks and stem barks decoction of *Spathodea campanulata* were reported to treat some types of wounds, skin rashes, haemorrhoids, malaria, dyspepsia, arthritis, fracture, toothache and stomach ulcer [127,128,129]. Decoction of stem bark is used to treat malaria in many countries [130,131]. Makinde *et al.* [132] reported the antimalarial activity of *S. campanulata* stem bark on *P. berghei* in mice. Other findings, revealed the decrease of parasitemia charge in mice, when *S. campanulata* is combined with *Conyza sumatrensis* [133]. Niyonzima *et al.* [134] showed anti-HIV, anti-complement effects of stem bark fraction of *S. campanulata*. Other studies described *in vitro* anti-inflammatory and antioxidant activity of aqueous and methanol extracts of leaves, stem bark and flowers [135,136]. Boniface [137] reported that extract of *S. campanulata* is safe up to 5000 mg/kg when taken orally at a single dose.

Aloe vera possesses a vast array of healing benefits. It's a rich source of over 200 naturally occurring nutrients which contain water soluble and fat-soluble vitamins, minerals, enzymes, polysaccharides, phenolic compounds and organic acids [138]. Its secondary constituents have various properties such as anti-inflammatory, antibacterial, antioxidant, immune boosting, anticancer, antiageing and antidiabetic potentials [139,140]. *Aloe* juice mixed with water and honey is used as an effective antimalarial and antipyretic treatment in Yemen [141]. Other studies also reported anti-malarial property [142]. Leaf decoction is drunk to cure cough [143]. A decoction of the chopped whole plant is taken to treat venereal diseases [144]. A leaf decoction is also applied to the treatment of cancer and rheumatism.

In Brazil, root infusion of *Boerhavia coccinea* is taken for liver complaints associated with malaria [145].

Medicinal uses assigned to *Bryophyllum pinnatum* include antimicrobial [146], anti-malarial [147] and virucide [148] activity. Other findings revealed relaxation of smooth muscles properties [149], hepatoprotective [150], anti-inflammatory and immunomodulatory activity [151]. Sofowora [152] reported that leaves and stems are soaked overnight in cold water and then drink for heartburn, urethritis, fevers, all sorts of respiratory disorders, acute inflammations, kidney stones, gastric ulcers, edema of the legs and gastric ulcers. Herbalists in Nigeria use an aqueous leaf extract for the treatment of cough and in the prophylaxis of asthma [153]. Fürer *et al.* [154] reported that *B. pinnatum* is well tolerated in patients.

Ethnobotanically, *Canarium schweinitzii* is used in African system to treat dysentery, gonorrhea, coughs, chest pains, pulmonary affections, stomach complaints, food poisoning, purgative, emetic, roundworm infections, intestinal parasites,

emollient, stimulant, diuretic, skin infections, eczema, leprosy, ulcers, diabetes, mellitus, colic, pains after child birth, gale, fever, constipation, malaria, sexually transmitted infection and rheumatism [155]. Its essential oils revealed anti-lipoxygenase activity with an IC₅₀ of 62.6 µg/ml [156], and interesting antioxidant and radical scavenging activities and the inhibition of lipid peroxidation [157]. Ramadhani *et al.* [118] reported antiparasitic activity of *C. schweinfurthii* against chloroquine-resistant *Plasmodium falciparum*. Other studies retrieved protective actions of aqueous and methanol extracts of its stem bark on kidney, when acetaminophen is used to induce renal injury in rats [158].

Hasani-Ranjbar *et al.* [159] reported promoting role of *Cissus quadrangularis* as a weight loss agent. In addition to weight reduction, *Cissus quadrangularis* also reduced blood glucose levels and serum lipids [160]. It also alleviated insulin resistance and scavenged free radicals [161]. Antioxidant and antimicrobial activity are also reported with *C. quadrangularis* consumption [162]. *C. quadrangularis* shows gastroprotective [163] and hepatoprotective properties [164]. Other studies reported anti-inflammatory and analgesic properties [165], anti-tumor activity of *C. quadrangularis* [166]. Attawish *et al.* [167], reported safe effect of *C. quadrangularis* extract (1mg/Kg daily for 10 days) in mice, rats and guinea pigs even at higher dose for a prolonged duration of treatment formulation and preparations.

Costus afer is used to treat various diseases such as malaria, measles, diabetes mellitus, arthritis, and stomach disorders. In West Africa, the succulent stem is chewed to quench thirst and also to treat cough and its accompanying sore throat [168]. Various solvent extracts of the plant leaves, stem, rhizomes, and roots have been studied and reported to contain chemical compounds that could be useful in the alleviation of oxidative stress-related conditions [169,170]. Findings conducted by Ezejirofor *et al.* [171] showed that *C. afer* leaf and stem extracts are able to reverse histopathological damage of pancreatic β-cells in alloxan-induced diabetes mellitus. Other findings have demonstrated the *in vitro* and *in vivo* antioxidant abilities of *C. afer*. Ijioma *et al.* [172] described its anti-inflammatory propriety. Furthermore, Ezejirofor *et al.* [173] and Anysor *et al.* [174] indicated that *C. afer* leaf extract is safe even at a dosage of 2000 mg/kg. *Costus afer* has been reported to have antimalarial properties [175].

Curcuma longa plays a role in many traditional systems. It is used in China and India to treat dermatologic infections, liver complaints and depression. Most studies analyzed curcumin's anti-cancer effect and it has been shown to inhibit tumor cell proliferation, invasion and metastatic dissemination [176]. Besides this, curcumin has been documented to act as anti-inflammatory and anti-infective Hatcher *et al.*, [177], and due to its wide spectrum of biological and pharmacological properties it is often called "cure-cumin. Other works reported a modest inhibition of the HIV-1 and HIV-2 proteases by curcumin. The authors found that the molecule binds to multiple sites of the enzyme, with micro molar concentrations leading to a suppression of enzymatic activity. It has been

shown that curcumin is a potent HIV integrase inhibitor, as it is able to bind acidic residues in the integrases catalytic core domain, preventing it from binding its substrates [178,179]. Kim *et al.* [180] reported the inhibition effect of aqueous extract of *C. longa* on hepatitis B virus (HBV). Further study reported that indeed curcumin inhibits HBV gene expression and replication by down-regulating PGC-1α, a protein co-activating HBV transcription [181]. Similar work described that curcumin inhibits the entry of all hepatitis C virus genotypes into hepatoma cells and primary human hepatocytes. Han *et al.* [182], showed that curcumin inhibits replication of influenza A virus. Similar studies reported that curcumin and artemisinin act through similar mechanisms [182].

Traditionally, *Desmodium adscendens* has been used to treat asthma, bronchitis and central nervous system disorders [183]; vaginal infections [184]; promote lactation in women; treat wounds and sores, malaria and diarrhea [185]; ovarian and uterine problems [186]. In the Amazon rainforest of Peru, South America and in Africa, aqueous extracts are used to treat pains, fever, epilepsy, asthma, gonorrhea, diarrheas, body aches, excessive urination and ovarian inflammations [24,187]. In France it used as food health supplement for its hepatoprotective action since it was demonstrated that *D. adscendens* has a positive action against hepatic infection *in vivo* [188]. *In vitro* study carries out by François *et al.* [189], revealed that 1 to 10 mg/kg of *D. adscendens* protected liver and kidney against glucose-induced oxidative stress.

Dietrich [190] & Ansah *et al.* [191] reported low toxicity of *Dissotis rotundifolia*. In Nigeria this plant is used to cure rheumatism, painful swellings; leaves decoction is used to relieve stomach ache, diarrhea, dysentery, cough, stop abortion, conjunctivitis, circulation problems and venereal diseases [192]. The leaves are used for dysentery in Cameroon [193].

Eremomastax speciosa is used in Cameroonian traditional medicine to treat stomach complaints, malaria, kidney pains, diabetes, nerves pain, male infertility, irregular menstruation, menstrual pains, gonorrhea, appendicitis and diarrhea [194,195,196,197]. Ekokon *et al.* [197] demonstrated anti-anaemic, anti-microbial activities. Siwe *et al.* [198] reported that daily administration of *E. speciosa* extract to mice for one week decreased the stomach colonization by *Helicobacter pylori* in a dose-dependent manner.

Titanji *et al.* [199] reported an anti-malarial activity of *Eucalyptus globulus*. In traditional therapy, essential oil is used to treat respiratory tract infections, pharyngitis, bronchitis and sinusitis. Other studies revealed antibacterial and antiviral activity against *Streptococcus pyogenes*, *pneumoniae*, *agalactiae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Parafluenzae* and *Stenotrophomonas maltophilia* [200,201,202]. Nagata *et al.* [203] demonstrated antimicrobial activity of *E. globulus* against oral bacteria, such as *Porphyromonas gingivalis*. It has been reported as a therapeutic plant in airway inflammatory diseases. Jori & Briatica [204] have shown that cineole compound extract for *E. globulus* can not cross the blood-milk barrier, but it is able to penetrate the placenta tissue. Kristiansen & Madsen [205]

found that the treatment of Wistar rats with 1,8-cineole in feed at doses of 500 and 1000 mg/kg body weight for 28 days can cause renal lesions.

Antimalarial activity of *Euphorbia hirta* extracts has been reported by [206]. In addition, Oyewale *et al.*, [207] retrieved antimicrobial; Wang & Huang [208] reported anti-*Helicobacter pylori* of *E. hirta* extract. On the other hand, Lanher *et al.* [209] described its analgesic and antipyretic activities. Abu *et al.* [210] reported antioxidant activity of *Euphorbia hirta*. Bronchodilator effect of alcoholic extract of *Euphorbia hirta* has been reported by Karpagam *et al.* [211]. Anti-HIV-1 and anti-HIV-2 of the its extract was reported by Agnes *et al.* [212].

Ficus exasperata have many uses. For instance, its leaves are used for treatment of hemostatic ophthalmia, coughs, hemorrhoids anxiety disorders, epilepsy, high blood pressure, rheumatism, arthritis, cancer, intestinal pains, colics, bleeding and wounds [213,214]. In Nigeria, Republic of Congo and Central African Republic the leaves are used as an antipyretic [215,216,217]. The leaves are particularly valued in the treatment of malaria in Cameroonian folk system [199]. In some parts of Cameroon, leaves are used in the treatment of hemorrhoids [218], and the water extract of the leaves is administered orally for diarrhea [193]. Infusion of dried leaves are used to treat ulcers and stomachache [219]. In Ivory Coast, the leaves mixed with palm oil used for the management of cardiac arrhythmias [220]. Leaves combined with lemon juice are used for the treatment of the respiratory tract infections such as asthma, bronchitis, tuberculosis and emphysema. Fresh leaves are used as hemostatic externally [221], and a polyherbal remedy containing the leaves are used for insomnia. In Sierra Leone, dried leaf powder is used to treat vaginal rash and the infusion is taken orally as an abortifacient [222]. Water extract of the dried leaves is taken orally and also rubbed on the abdomen to stimulate contractions during child birth [223]. In Gambia, the leaves are boiled in water and the steam is inhaled in cases of chest pain [223]. In Ghana, the sap is used to stop bleeding. Irene and Iheanacho [224], reported the traditional use of the plant in hastening the expulsion of placenta in cows after calf delivery and its use by traditional birth attendants in hastening childbirth. The roots are also used to manage asthma, dyspnea and venereal diseases [224]. In Tanzania, a decoction made from dried root bark is given orally to treat asthma; fresh leaf is rubbed for the inflammation of throat and tonsillitis, and also used to treat common eye problems. Fresh leaves are also used as anthelmintic. Dried flowers are eaten to relieve throat pain and also valued as ascaricide. *F. exasperata* root paste alone and the bark crushed with the root of *Croton roxburghii* in coconut milk are applied externally to treat eczema [225]. Other studies reported antioxidant and antimalarial dose-dependant effects of *Ficus exasperata* extracts [226,227]. Similarly, Adebayo *et al.* [228] revealed antimicrobial effects of the hydroalcoholic extracts of its leaves. Woode *et al.* [230] (2009) reported anti-inflammatory, antipyretic and antinociceptive activities of *F. exasperata*.

The Seeds, leaves and other parts of *Gossypium herbaceum* are used to cure various infections in different part of the

world. For example, the seeds are used to treat pain, headache, migraine, epilepsy, antidote to snake poison and fever. The decoction of the seed and juice of the seed are used to cure dysentery [231,232,233]. The leaves, root and seeds of *Gossypium herbaceum* are reported to facilitate labour, retention of placenta and as emmenagogues. In Senegal a root maceration is given to new-born babies and sickly or rachitic children, to strengthen them. In Somalia a root decoction is used as an abortifacient and the juice of the heated unripe fruit was dropped into the ear against earache. In Ethiopia the root is used to treat snake bite and fruit powder is applied on the head for the treatment of fungal infections. In Namibia the root bark powder is used as a haemostatic ingredient. In Botswana root preparations is used for the treatment of heart palpitations. In Mozambique root decoctions are used as a tonic and to control vomiting, and the infusion of the root against lack of appetite [234]. Bommannavar & Patil [235] reported histopathology protective effects of *G. herbaceum*.

The decoction stems of *Gouania longipetala* is used as treatment of stomach ache, gastro-intestinal infections, malaria, skin diseases, gynecological complaints and pregnancy problems. The leaves are used for the treatment of swellings, edema venomous stings, gout, febrifuges. It is also used as genital stimulants, laxatives and for venereal diseases. The leaf sap is used for eye treatments, as pain killers and for treating heart diseases [236]. Ekuadzi *et al.* [237] reported antibacterial and anti-inflammatory activities of *Gouania longipetala*.

The leaves of *Kalanchoe crenata* have been reported as the treatment of earache, burns, abscesses, insect bites, whitlow, diarrhea and cithiasis [238], diabetes, dissolving kidney stones, respiratory tract infections, boils and insect bites [239]. Some authors reported hepatoprotective, immunomodulatory properties, antithrombotic sway and implemented for cardiovascular treatment [150,240,241]. Other researchers retrieved antimicrobial activity of its leaves [242]. Moreover, Amaral *et al.* [243]; Kamboj & Saluja, [244] have shown that *B. pinnatum* leaves extract is used to treat sever ulcers, cough, bronchitis, various bacterial, viral and fungal infections, respiratory infections, some tumors, hypertension and fever. Some findings have shown the potential activity of *B. pinnatum* against hematological parasites such as *Leishmania*, *Plasmodium* and *Trypanosoma*.

The aqueous decoction of *Kaya grandifoliola* is commonly used to treat malaria [245]. evaluated its anti-malarial activity. Agbedahunsi *et al.* [246] also reported the anti-inflammatory and toxic effects of this plant.

The bark and leaves of *Mangifera indica* have astringent properties and are used as lotion to relieve toothache, sore gums, sore throat or as an infusion in malaria, diarrhea and dysentery [247,248]. Other studies reported antioxidant, anti-inflammatory, analgesic and immunomodulator of its stem bark [249]. Furthermore, different parts of this plant have been extensively used to prevent disease progress or improve the patient's quality of life in diseases like HIV/AIDS, cancer, asthma, gastric and dermatological infections [247]. Arrey

Tarkang *et al.* [250] reported *in vivo* anti-malarial activities against *Plasmodium berghei* and *P. chabaudi* in rodent model. In the study conducted by Zheng & Lu [251], Zhu *et al.* [252] and Shah *et al.* [253] on mangiferin isolated from *M. indica*, they retrieved that mangiferin has high ability to achieve inhibition of HSV-1 virus duplication within cells and to antagonize the cytopathic effects of HIV. Similarly, Rawi *et al.* [254] reported antiviral activity of *M. indica* against influenza virus. Nithitanakool *et al.* [255] described hepatoprotective properties in mango seed kernels. Gbeassor *et al.* [256] studied the effect of *M. indica* stem bark aqueous extract (mangiferin) on rat trachea contracted by acetylcholine and histamine. These experiments suggested that the aqueous extract of *M. indica* (mangiferin) could block both the histaminic and muscarinic receptors on rat trachea and thus suggesting its potential use in the treatment of asthma. Amien *et al.* [257] reported significant prophylactic effect against kidney injury by the enhancement of the kidney function *via* the decreasing serum creatinine, urea and uric acid.

Momordica foetida and *M. charantia* are used in traditional medicine to treat hypertension, diabetes mellitus, fever and especially symptoms of malaria [258]. Akanji *et al.* [259] reported the antimalarial activity of *M. charantia*. Inderdeep *et al.* [260] revealed that balsamin isolated for *Momordica balsamina* inhibits HIV-1 replication not only in T cell but also in human primary CD4+. The same authors also demonstrated that balsamin activity is broad since it also impedes influenza virus replication.

Polyscias fulva is used to treat malaria, fever, mental illness [261], venereal infections and obesity [218,262] and cancer [263]. Other findings, reported that its traditional use against venereal infections and dermatoses [264,265].

Portulaca oleracea endowed many pharmacological compounds with various properties; such as skeletal muscle relaxant [266], analgesic and anti-inflammatory [267,268], antifungal [269], antifertility [270], antidiabetic [271], and wound healing activities [272]. Moreover, *Portulaca oleracea* have been reported to exhibit protective effect against oxidative stress caused by vitamin A deficiency [273]. Malek *et al.* [274] revealed that the administration of 0.25 ml/kg of boiled extract to asthmatic patients increased pulmonary function, similar to theophylline.

Ocimum gratissimum an important tropical plant has been used in traditional medicine since ancient times. A study conducted by many researchers demonstrated its antimicrobial, insect repellent, antimalarial, insecticides and pesticide effects. For instance, Ayisi *et al.* [275] reported that the leaf extract exhibits potent inhibition of HIV-1 & HIV-2 replication with antiviral value 110. It equally expresses cytotoxic inhibition reverse transcriptase and proviral DNA copying of HIV-1, thus, justifying the antiviral potential of the plant. Arrey Tarkang *et al.* [250] reported an excellent effect of its leaves against multi-drug resistant *Plasmodium falciparum* along with *in vivo* suppression of *P. berghei* and *P. chabaudi* malaria parasites. Less side effects of this plant were also reported [276]. Essential oils from the plant have been reported to possess antinociceptive properties. It's used as an excellent gargle for sore throat and

tonsillitis. It is equally used as an expectorant and cough suppressant [277].

The decoction of the fruits and leaves of *Solanum aculeastrum* are taken orally to treat cancer, indigestion and stomach disorders. The fresh and boiled berries are used to cure gonorrhea and acne [278]. Koduru *et al.* [279] (2006) reported antimicrobial activity of *Solanum aculeastrum*.

Solanum torvum is a sedative and diuretic and the leaves are used as a haemostatic. The ripened fruits are used in the preparation of tonic and haemopoietic agents and also for the treatment of pain. It has antioxidant properties. It is intensively used worldwide in the traditional medicine as poison anti-dote and for the treatment of fever, wounds, tooth decay, reproductive problems and arterial hypertension. *S. torvum* also possesses antimicrobial, antiviral, immuno-secretory, antioxidant, analgesic and anti-inflammatory, anti-ulcerogenic activities, cardiovascular, nephroprotective, antidiabetic, angiotensin and serotonin receptor blocking activities [280]. On the other hand, Cushnie [281] reported its anti-viral, anti-bacterial, anti-fungal, anti-helminthic and anti-inflammatory properties. Rajathi *et al.* [282] retrieved antimicrobial action of *S. torvum* against respiratory tract pathogens. Yuanyuan *et al.* [283] indicated that *S. torvum* is used in the treatment of coughs and colds. Extract of the fruits and leaves are said to be useful in case of liver and spleen enlargement and in the treatment of cough. Paste of root is used to cure cracks in feet. The fume of burning seeds is inhaled for toothache [284].

Spilanthes filicaulis/Acmella caulirhiza is used to treat toothache, for pain relief, swelling, gum infections, periodontosis and in mouthwashes. Peiris *et al.* [285] revealed that the aqueous extract of fresh flowers of *S. filicaulis* has significant analgesic activity at doses of 111,335 and 671 mg/kg when administered to the male rats. The analgesic effects were studied using different extracts and animal models [286]. Barman *et al.* [287] reported that *Spilanthes* spp. are important source of anti-inflammatory compounds. Hepatoprotective effect has been reported for its ethanolic extract [288]. Savadi *et al.* [289] equally reported immunomodulatory activity and they attributed to the presence of alkaloids and polysaccharides in its compound extracts.

The leaves of *Synedrella nodiflora* are used to prevent spontaneous abortion, as treatment of hiccup, as a laxative [290]. The hydro-ethanolic extract of the whole plant has demonstrated anticonvulsant [291], sedative [292] and *in vitro* antioxidant activities [293].

The seed oil of *Jatropha curcas* is used in the treatment and management of various conditions like arthritis, gout, eczema, skin diseases, rheumatic pain, jaundice, burns, inflammation, gonorrhoea, and as an abortifacient. The leaf infusion or decoction of *Jatropha curcas* is administered for the treatment of vaginal bleeding conditions in many communities and is also used both internally and externally to treat fever and jaundice. Rheumatic conditions are treated and managed by the external application of the leaf decoction or by massaging the affected joint-part using the juice/sap extract from the fresh leaves. The

leaf decoction is also taken to treat malaria, mouth infections, guinea worm sores, as well as the treatment of dysentery and colic conditions [294]. Igbinosa *et al.* [295] reported *in vitro* the anti-RT enzyme activity and anti-HIV activity of branches of *Jatropha curcas*. Another study that looked at traditional medicines in the management of HIV/AIDS in Tanzania found that *Jatropha curcas* leaves were being used for treatment in HIV related conditions such as skin rash and oral candidiasis [296]. Furthermore, Dahake *et al.* [297] showed anti-viral activity of the leaves against potentially drug-resistant HIV.

The literature indicated that plants of the genus *Garcinia* have been reported to display both anti-HIV and cytotoxicity activity [298]. Other findings, have been reported by Gustafson *et al.* [299] on the isolation of guttiferones, benzophenone compounds with anti-HIV activities from species of the same genus. Ethnomedicinally, different organs of *Garcinia* plants have been retrieved to exhibit many pharmacological effects. For instance, fruit of *G. kola* have been claimed to be effective at stopping *Ebola* virus replication.

Zingiber plants possess various pharmacological and physiological properties and are common ingredients in traditional medicines. The rhizomes have been shown to be effective in the treatment of several diseases such as stomach problems, nausea, vomiting, epilepsy, sore throat, cough, common cold, bruises, wounds, liver complaints, rheumatism, muscular pains, atherosclerosis, migraine headaches, high cholesterol, ulcers, and stomach discomfort [300]. Furthermore, phenolic compounds, especially the gingerols, in ginger root have been shown to have chemopreventive properties that have been associated with their antioxidant and anti-inflammatory activities [300]. Sabulal *et al.* [301], Ghosh *et al.* [302] and Shukla & Singh [303] demonstrated the antimicrobial potential of *Zingiber* plant extracts against broad spectrum Gram-negative and Gram-positive bacteria. On the other hand, Mozaffari-Khosravi *et al.* [304] reported antioxidant of the *Zingiber officinale* extract. This antioxidant effect was attributed to ginger single constituents, namely 6-gingerol, 8-gingerol, 10-gingerol, and 6-shogaol [305] as well as geranial and neral-zingiberene, camphene, farnesene, sesquiphellandrene [306] and zingerone [307]; 6-shogaol in particular, showed the most potent antioxidant and anti-inflammatory activities. Antimicrobial activity of *Z. officinale* were also reported [308]. Besides, *Z. officinale* has been reported to be effective on various viruses [309,310]. Sharma *et al.* [114] revealed antiviral activity against dengue virus. Chang *et al.* [311] also reported anti-viral effects against human respiratory syncytial virus.

Chrysanthemum indicum is used to combat diseases which cause inflammation and elevated blood pressure as well as those that target the respiratory apparatus of the human body [312,313]. Several studies have concluded that *C. indicum* possesses particularly potent effects on bacteria and viruses as well as having antioxidant, anti-inflammatory, and immunomodulatory properties [314,315].

Sonibare & Gbile [316] reported the use of *Euphorbia laterifolia* in South Western Nigeria as good ingredient of asthma treatment.

The leaves of *Ficus thonningii* are used in Nigeria to treat toothache, as analgesic and anti-irritant ingredient [317]. Macerations of fresh *F. thonningii* leaves, taken orally, have been used by traditional healers for treating diarrhoea, gonorrhoea and diabetes mellitus in Uganda [318,319]. In Angola decoctions of *F. thonningii* leaves are used for treating wounds. The wounds are washed with the leaf extract whilst bleeding gums are rubbed with leaves in cases of gingivitis. Leaf extracts are also used for treating bronchitis and urinary tract infections [214,319]. A decoction of the leaves is used in Mali for treating urinary schistosomiasis [320]. The leaves can also be used for treating liver disorders and disease conditions associated with jaundice [319,321]. The stem bark is pounded and the infusion used for treating influenza, sore throat, colds, arthritis, rheumatism and to relieve inflammation [322]. The roots are used for the treatment of malaria, fever, hepatitis and dental pains [323]. In Zimbabwe roots have been reportedly used for preventing miscarriages and for stopping nose-bleeding [319,324]. Additionally, the roots are also used for relieving stomach pains, diarrhea, pneumonia and chest pains [318,319,325]. Otimenyin [326] demonstrated that methanolic extracts of *F. thonningii* have analgesic effects as compared to aspirin. Other studies reported antioxidant activity [327]. Coker *et al.* [328] demonstrated the anti-inflammatory properties of *F. thonningii*. The cardioprotective, vasoprotective and renoprotective effects of this plant were reported by Baur & Sinclair [329] and Ramawat *et al.* [330]. Minikawa *et al.* [331] showed that stilbene resveratrol a chemical compound of *F. thonningii* exhibit hypoglycemic activities by enhancing glucose uptake by muscle cells and by activating hepatic AMPK. Falade *et al.* [332] demonstrated that this plant content antimalarial activity. Similar results were obtained by Koukouikila-Koussounda *et al.* [333].

Gardenia ternifolia has been reported to treat malaria, hypertension, diabetes, cough, asthma, rheumatism, diarrhea, tooth decay, leprosy, hernia, hemorrhoids and cancer. Toxicological study revealed safe effects of fruits and roots of the plant. Antimalarial, antioxidant, anticancer and antimicrobial activity were recorded effects [334].

Glyphae brevis has been reported as a source of phenolic antioxidant properties [335]. Several studies reported the anti-inflammatory activity of *G. brevis* in both acute and chronic inflammatory models [335,336].

Few studies have been conducted on *Leucas martinicensis*. Its antimicrobial activity was demonstrated by Vlietinck *et al.* [337] and Anisa [338]. Clarkson *et al.* [339] reported *in vitro* antiplasmodial effects of the whole plant extract.

The antimalarial activity of *Phyllanthus amarus* has been reported. On the other hand, *P. amarus* has been shown to preserve renal function and hepatoprotective [340]. The same authors also reported that *P. amarus* enhanced antioxidant defense capacity. *Phyllanthus* family and many species members such as the *P. amarus*, *P. niruri*, *P. urinaria* and *P. orbicularis* have reported to demonstrate potential inhibitory effect against broad spectrum of viruses, such as the hepatitis B virus (HBV),

hepatitis C virus (HCV), human immunodeficiency virus (HIV) and herpes simplex virus (HSV) [18,341,342,343].

Past findings have revealed that *Sarcocephalus latifolius*/*Nauclea latifolia* possesses antiplasmodial properties [344,345]. Donalisio *et al.* [346] demonstrated anti-herpes simplex virus type 2. This plant is commonly employed for the treatment of malaria, hypertension, diarrhea, tuberculosis, dysentery and also as a laxative [345]. Fakae *et al.* [347] reported antibacterial and antidiabetic effects of *Nauclea latifolia*.

The leaves of *Smilax krausiana* are largely employed in Africa for the treatment of infertility, inflammation diseases, haemorrhoids and stomach pains. Roots are employed as antidote and treat fever and malaria [348,349].

Plant species of the genus *Terminalia* are extensively used in traditional medicine in several countries in the world for curing numerous diseases including, diarrhea, dysentery, fever, gastric ulcers, headaches, heart diseases, hookworm, hypertension, jaundice, leprosy, abdominal disorders, bacterial infections, colds, sore throats, conjunctivitis, nosebleed, edema, pneumonia and skin diseases [350]. Most *Terminalia* species were reported to possess antioxidant, hepatoprotective, cardioprotective, gastroprotective and antimicrobial properties [351]. For instance, *Terminalia glaucescens* is traditionally used to treat several diseases. Such as dysentery, other microbial infections and asthma. Leaves are retrieved to be useful in the last phase of AIDS [352]. Okpekon *et al.* [353] have reported its activities against *Plasmodium falciparum*. Leaf and root extracts of *T. glaucescens* have been found to be greatly active against both *Candida* species and dermatophytes such as *Trichophyton* spp [354]. Mustofa *et al.* [355] have demonstrated antiplasmodial potentiality of its ethnolic extract. *T. glaucescens* is one of the plants used in the preparation of the “wonder cure” concoction used in the treatment of tuberculosis in Nigeria. The activity of the plant extracts on *Mycobacterium tuberculosis* was reported by Adeleye *et al.* [356].

Rauvolfia vomitoria is extensively used to manage HIV/AIDS in Tanzania traditional medicine [296]. Various parts of this plant are used to treat coughs, malaria skin infections and as antipsychotic. Eteng *et al.* [357] revealed the toxicity of roots and leaves of *R. vomitoria* [358,359].

Possible Ingredients of Herbal Formulation for Prevention, Alleviate Symptoms or Treating COVID-19

Due to their pharmacological properties and their ethnomedicinal uses, we suggest the usage of *Artemisia annua*, *Cinchona officinalis*, *Aspilia africana*, *Bidens Pilosa*, *Conyza sumatrensis*, *Eucalyptus globulus*, *Ocimum gratissimum*, *Bryophyllum pinnatum*, *Picralima nitida*, *Senna alata* or *Cassia alata*, *Spathodea campanulata*, *Aloe buettneri*, *Citrus aurantiifolia*, *Canarium schweinfurthii*, *Cucurma domestica*/*Cucurma longa*, *Mangifera indica*, *Terminalia glaucescens*, *Zingiber officinale*, *Phyllanthus amarus*, *Gossypium herbaceum*, red *Jatropha curcas*, *Ficus thonningii*, *Rauvolfia vomitoria*, *Garcinia kola*,

Carica papaya, *Azadirachta indica*, *Solanum torvum* and *Ficus exasperata* in recipes formulation. These plant species could destroy the COVID-19 cell membrane, DNA gyrase, also harm the COVID-19 glycoprotein, inhibit his activity and thus replication. On the other hand, may reinforce the immune system. For instance, Khan *et al.* [18,341,342,343] reported that, *Phyllanthus amarus* exhibits potential activity against broad spectrum of viruses, such as the hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and herpes simplex virus (HSV). Coker *et al.* [328] demonstrated the anti-inflammatory properties of *Ficus thonningii*. Phenolic compounds, especially the gingerols, in ginger (*Zingiber officinale*) root have been shown to have chemopreventive, antioxidant and anti-inflammatory activities [300]. *Garcinia* genus have been reported to display both anti-HIV [298]. Gustafson *et al.* [299] reported that guttiferones, benzophenone compounds extracted from the genus *Garcinia* have anti-HIV activities. The fruit of *G. kola* have been claimed to be effective at stopping *Ebola* virus replication.

Proposition of Recipe Formulations Against COVID-19

The proposed recipes can be taken for prevention, alleviate symptoms or for treatment, and even during the phase of patient observation and isolation.

Polyherbal Recipes

Recipe 1: Boil in 4 litres of water 300 g of leaves of *Eucalyptus globulus*, 250 g of whole plant of *Bryophyllum pinnatum*, 250 g of leaves of *Ocimum gratissimum*, 200 g of leaves of *Ficus thonningii*, 200 g of leaves of *Gossypium herbaceum*, 200g of whole plant or leaves of *Conyza sumatrensis*, 300 g of leaves or whole plant of *Artemisia annua*, 200 g of leaves of *Aspilia Africana* and 200 g of leaves or whole plant of *Bidens pilosa* for about 15 minutes. Posology for adults: drink one glass of 150 ml twice a day for “prevention”. For children: 100 ml twice daily. In case of disease: steam up the vapor and drink 200 ml (adult) or 150 ml (children) thrice daily. Dose can be increased depending on the disease severity.

Recipe 2: Soak in 5 liters of water for one hour, 300g of fruits of *Picralima nitida*, 500 g of stem barks of *Cinchona officinalis*, 250 g of leaves of *Cassia alata*, 250 g of leaves of *Bryophyllum pinnatum*, 200 g of bulbs of *Allium sativum*, 250 g of leaves or bark of *Spathodea campanulata*, 200 g of leaves of *Eucalyptus globulus* and 200 g of leaves of *Bidens pilosa*, and boiled for about 25 minutes. Posology for adults: drink one glass of 120 ml twice a day for “prevention” For children: 100 ml twice daily. In case of disease: steam up the vapor and drink 150 ml (adult) or 100 ml (children) thrice daily. Dose can be increased depending on the disease severity.

Recipe 3: Prepare a decoction of 250 g of leaves of *Eucalyptus globulus*, 250 g of leaves of *Ocimum gratissimum*, 250 g of leaves or whole plant of *Bryophyllum pinnatum*, 100 g of leaves of *Senna alata*, 400 g of barks or leaves of *Spathodea campanulata*, 300 g of barks of *Mangifera indica*, 400 g of barks of *Terminalia*

glaucescens, 300 g of leaves or whole plant of *Phyllanthus amarus* and 250 g of yellow leaves of *Carica papaya* in 5 liters of water for about 25 minutes. Posology for adults: drink one glass of 150 ml twice a day for “prevention”. For children: 100 ml twice daily. In case of disease: steam up the vapor and drink 200 ml (adult) or 150 ml (children) thrice daily. Dose can be increased depending on the disease severity.

Recipe 4: Boil together 100 g of leaves of *Azadirachta indica*, 300 g of leaves of *Cassia alata*, 300 g of leaves of *Ocimum gratissimum*, 300 g of leaves or whole plant of *Bryophyllum pinnatum*, 300 g of leaves or whole plant of *Bidens pilosa*, 100 g of leaves of *Aloe buettneri*/ *Aloe vera* and 10 fruits of *Citrus aurantiifolia* in 4 liters of water for about 15 minutes. Posology for adults: drink one glass of 80 ml twice a day for “prevention”. For children: 60 ml twice daily. In case of disease: steam up the vapor and drink 120 ml (adult) or 80 ml (children) thrice daily. Dose can be increased depending on the disease severity.

Recipe 5: Prepare a decoction of 250 g of rhizomes of *Cucurma domestica*, 200 g of leaves of *Gossypium herbaceum*, 200 g of leaves or whole plant of *Bidens pilosa*, 200 g of leaves of *Ocimum gratissimum*, 200 g of leaves or whole plant of *Bryophyllum pinnatum*, 10 fruits of *Citrus aurantiifolia*, 250 g of barks of leaves of *Canarium schweinfurthii* in 4 liters of water for about 20 minutes. Posology for adults: drink one glass of 150 ml twice a day for “prevention”. For children: 100 ml twice daily. In case of disease: steam up the vapor and drink 200 ml (adult) or 150 ml (children) thrice daily. Dose can be increased depending on the disease severity.

Recipe 6: boil together 10 fruits of *Citrus aurantiifolia*, 200 g of rhizomes of *Zingiber officinale*, 200 g of leaves of *Ficus exasperata*, 300 g of barks or leaves of *Spathodea campanulata*, 250 g of barks or leaves of *Canarium schweinfurthii*, 300 g of leaves or whole plant of *Bryophyllum pinnatum*, 300 g of leaves or whole plant of *Bidens Pilosa*, 200 g of leaves or fruits of *Solanum torvum* in 4 liters of water for about 20 minutes. Posology for adults: drink one glass of 150 ml twice a day for “prevention”. For children: 100 ml twice daily. In case of disease: steam up the vapor and drink 200 ml (adult) or 150 ml (children) thrice daily. Dose can be increased depending on the disease severity.

Recipe 7: 100 g of barks of *Rauvolfia vomitoria*, 300 g of leaves of *Aspilina africana*, 300 g of leaves or whole plant of *Bidens Pilosa*, 300 g of leaves of *Occimum gratissimum*, 400 g of leaves or whole plant of *Bryophyllum pinnatum*, 300 g of leaves of *Conyza sumatrensis*, 250 g of barks of *Spathodea campanulata*, 250 g of yellow leaves of *Carica papaya*, 150 g of leaves or fruits of *Solanum torvum*, boiled all together with water for about 20 minutes. Posology for adults: drink one glass of 100 ml twice a day for “prevention”. For children: 50 ml twice daily. In case of disease: steam up the vapor and drink 150 ml (adult) or 80 ml (children) thrice daily. Dose can be increased depending on the disease severity.

Recipe 8: Boil 200 g of leaves or entire plant of *Artemisia annua* with 100 g of yellow leaves of *Carica papaya*, 200 g of rhizomes of *Cucurma domestica*/*Cucurma longa*, 200 g of leaves or whole plant of *Bryophyllum pinnatum*, 100 g of leaves of

Ficus exasperata and 100 g of leaves or entire plant of *Aspilina africana* in 4 liters of water for about 15 minutes. Posology for adults: drink one glass of 150 ml twice a day for “prevention”. For children: 100 ml twice daily. In case of disease: steam up the vapor and drink 200 ml (adult) or 150 ml (children) thrice daily. Dose can be increased depending on the disease severity.

Baby recipe (age comprised between one to seven years): See recipe 1,3,5 and 8. Posology: four teaspoons twice daily for prevention. In case of disease 40 ml thrice daily.

Monoherbal Recipes

Recipe 9: In case of COVID-19 and HIV infections, take 100 ml of juice of crush leaves of red *Jatropha curcas* twice daily plus one of the above recipes.

Recipe 10: Eat eight to ten leaves of *Bryophyllum pinnatum* with 5 g of salt every day for prevention and treatment.

Recipe 11: Eat five leaves of *Conyza sumatrensis* with 5 g of salt every day for prevention and treatment.

Recipe 12: Eat one to two fruit of *Garcinia kola* with 5 g of salt every day for prevention and treatment

Recipe 13: Eat ten to twenty leaves of *Acmella caulirhiza*/*Spilanthes filicaulis* with 5 g of salt every day for prevention and treatment.

Advice

Medicinal plants are widely used and assumed to be safe, however, they can somehow be toxic. It is the case with synthetic drugs, drug interactions and contraindications must be considered on an individual basis. Alike with synthetic drugs, herb consumption usually needs to be discontinued if adverse reactions took place [360]. For instance, consumption of large amounts of *Aloe vera* can caused dehydration, diarrhea, redness, abdominal cramps, hepatitis. Its prolonged used may lead to low potassium levels and increase the risk of colorectal cancer. Due to its purgative and irritant qualities aloe vera should not be taken by pregnant women, it may lead to uterine contractions, leading to miscarriage and birth defects. Persons suffering from heart diseases must not use *Aloe vera* because consumption of *Aloe vera* juice can lead the body to produce excessive amounts of adrenaline and can cause irregular heartbeats [361]. Other findings reported that ginger consumption in high doses induces histological changes in the kidneys [362]. It has been suggested that patients with pile and those taking anticoagulants should use precaution when taking garlic (*Allium sativum*) because of its antithrombotic effects [363].

DISCUSSION

Due to the fact that, hydrochloroquine/chloroquine and anti-virus drugs combination are not efficient on every patients of COVID-19. Combination of therapy system could be expected

as one of the best solutions to treat COVID-19. A number of medicinal plants have been shown to have antiviral, antipyretic and anti-inflammatory and anti-expectorant activities. It is worth mentioning that, Boli Zhang a Traditional Chinese Medicine (TCM) expert, claims that several plants used in China to manage COVID-19 have been employed to alleviate cough, weakness, anxiety and digestive infections [364]. Furthermore, on 17, February, National Health Commission (NHC) of the People's Republic of China reported that 60,107 confirmed COVID-19 patients (85.20% of total confirmed cases) had been treated with Traditional Chinese Medicine [365]. The suggested twenty-eight (28) plant species, belonging to 22 botanical families and are used in many countries to treat coughs, cold, fever, flu, asthma, bronchitis etc. Some of these plants are known as antiviral, anti-inflammatory, anti-oxidant, anti-pyretic, immunostimulant, antitussive ingredients. For example, *Allium sativum*, *Eucalyptus globulus* and *Curcuma longa* are well known medicinal plants in Ayurveda medicine for curing asthma, bronchitis, flu, cold [366], *Zingiber officinale*, *Aloe vera*, *Cinchona officinalis*, *Allium sativum* and *Mangifera indica* were reported as remedy for respiratory tract infections in Iran and Peru [2,367]. In Pakistan, Alamgeer *et al.* [368] mentioned the use of *Allium sativum*, *Aloe vera*, *Eucalyptus globulus*, *Euphorbia*, *Mangifera indica* and *Zingiber officinalis* in the same purpose. *Allium sativum*, *Curcuma longa* and *Zingiber officinale* are known in Krishna District of Andhra Pradesh India as treatment for cough, cold and asthma [369]. The use of these plants in different localities for the same purpose can be taken to be credible. It has been suggested that the identical use of a medicinal plant by different people from different areas or localities is often considered to be a good and reliable indicator of the plant's curative properties [370]. Some of these plant species family members are used in China to treat COVID-19, reinforced immunity and alleviated COVID-19 patients' symptoms. For instance, Lu & Wang [371] and Yao *et al.* [12] reported that, after administration of recipe formula "Lian Hua Qing Wen Capsule" (*Forsythia suspensa*, *Ephedra sinica*, *Lonicera japonica*, *Isatis indigotica*, *Mentha haplocalyx*, *Dryopteris crassirhizoma*, *Rhodiola rosea*, *Gypsum Fibrosum*, *Pogostemon cablin*, *Rheum palmatum*, *Houttuynia cordata*, *Glycyrrhizae uralensis* & *Armeniaca sibirica*) for COVID-19 patients, there is recovering after treatment or disappearance of characteristic symptoms of COVID-19 such as cough and fever. Moreover, the presence of *Curcuma longa*, *Azadirachta indica*, *Zingiber officinale*, *Allium sativum* and *Ocimum gratissimum* in suggested list and recipes formulation is praiseworthy; because Ambrish *et al.* [372] revealed that, compounds extracted from these plants possess certain inhibition properties against COVID-19 protease, and their activities are more potent than those of chloroquine and slightly similar to hydroxychloroquine activity. The presence of species of Fabaceae family in the propose list and recipes is respectively supported by the findings of Yang *et al.* [22] and Xu *et al.* [373] who's found that, glycyrrhizin extracted from *Glycyrrhiza glabra* (Fabaceae) strongly inhibited the replication of clinical isolates severe acute respiratory syndrome virus (SARS), and *Astragalus membranaceus* one member of the same family upgrade COVID-19 patients defense potentiality. Furthermore, members of the family Fabaceae (*Saposhnikovia divaricate*, *Radix*

platycodonis, *Astragalus membranaceus*, *Glycyrrhizae uralensis*), Asteraceae (*Rhizoma Atractylodis*, *Atractylodis Rhizoma Macrocephalae*) and Lamiaceae (*Agastache rugosa*) have been cited by Yang *et al.* [22], as the most used plant species against COVID-19 in China. It has been repoted that plants for the same genus or the same family can have similar activities [374]. For instance, *Phyllanthus* family and many species members such as the *P. amarus*, *P. niruri*, *P. urinaria* and *P. orbicularis* have been reported to demonstrate potential inhibitory effect against broad spectrum of viruses, such as the hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV) and herpes simplex virus (HSV) [18,341,342,343]. The proposed anti-COVID-19 recipes formulations plant species is sustained by their ethnomedicinal use and biological properties of each of suggested. For example, *Artemisia annua* tea infusion has been used to treat malaria, coughs, cold and human immunodeficiency virus (HIV) [20,28]. Marchand *et al.* [32], Lubbe *et al.* [33] have demonstrated its anti-HIV activity. On the other hand, Warghurst [34] reported that, artemisinin extracted from *Artemisia annua* has higher chemotherapeutic index than chloroquine and is effective in chloroquine-resistant *Plasmodium* sp. De Donno *et al.* [29] showed that 5 g of dried leaves in one liter of *Artemisia annua* tea infusion was effective against both Chloroquine resistant and Chloroquine sensitive strains of *Plasmodium falciparum* with IC50 values of 5.60 nmol/L et 7.08 nmol/L. the leaves of *Aspilia africana* are used in traditional system to cure cough and malaria [35]. *Azadirachta indica* (neem) is widely employed to treat malaria caused by various strains of *Plasmodium*, even those resistant to conventional antimalarial drugs [41,45,46,47]. Mahommad [53] reported valuable antioxidant from neem extracts such as nimbolinin, azadirachtin, nimbin, nimbidin, nimbidol, salannin and quercetin. Further, Parida *et al.* [375] and Tiwari *et al.* [61] showed the inhibition effect of neem extract against replication of polio-virus, HIV, coxackie B group virus and dengue virus. *Bidens pilosa* is used as a medicinal plant for treating inflammation, wounds, colds and flu, acute or chronic hepatitis, and urinary tract infections [63]. The methanolic extract of the whole plant of *B. pilosa* has been reported to exhibit a comparable anti-pyretic activity *in vivo* to paracetamol in the rabbit pyrogen test [63]. *B. Pilosa* has also been reported to possess effective pharmacological properties like antibacterial activity, anti-inflammatory and anti-allergic activity, T helper cell modulator, immunosuppressive, anti-hyperglycemic, anti-hypertensive, anti-ulcerogenic, hepatoprotective, antileukemic, anticancer, antipyretic, antiviral, anti-angiogenic, antirheumatic and antibiotic activity [66]. Chloroquine or mefloquine-resistant *Plasmodium falciparum* strains are susceptible to *B. pilosa* (IC50 = 10.4-49.8 µg/mL) *in vitro* [19]. Leaf decoction of *Carica papaya* are used against malaria [76]. Kovendan *et al.* [81] showed that ethanol extract of *C. papaya* leaves inhibited growth of chloroquine-sensitive and chloroquine-resistant *P. falciparum*. Other studies revealed that *C. papaya* extracts (leaf & seed) possess an ability to modulate inflammatory markers in various cell types exposed to a variety of stressors [82]. Studies demonstrated the antiviral activities of quinine extract from *Cinchona* sp against several virus, such as influenza virus, herpes simplex virus-1 and dengue virus [88]. Furthermore,

Gonuguntla [375] showed that the combination of artesunate and *C. officinalis* fully clears the blood stage infection of *Plasmodium berghei*. *Citrus* plants are employed in traditional medicine to treat respiratory disorders as agent for cough, insomnia, stress disorders, cold and anxiety. *C. sinensis* is a rich source of natural antioxidant that supports the immune system activity [89]. The genus *Conyza* has been reported as anti-malaria, antibacterial, antioxidant, anti-inflammatory, analgesic, antiviral, antiproliferative and antidiarrheic ingredients [90]. Stem barks of *Picralima nitida* are used to treat malaria. Various parts of this plant have been revealed to be effective antipyretic and antitussive [101,102]. Anti-inflammatory, antioxidant and analgesic were also retrieved in *Picralima nitida* [109]. Antiplasmodial activity of *Rauwolfia vomitoria* were demonstrated [115]. Several activities are recognized in *Senna alata*, such as anti-microbial and anti-inflammatory [120,121], expectorant [122], anti-HIV-1 [124] and anti-malaria [126,376]. Leaves and barks of *Spathodea campanulata* were reported to exhibit antimalarial activity against *Plasmodium berghei* [132], anti-HIV [134], anti-inflammatory and antioxidant effects [135,136]. *Aloe vera* possesses a vast array of healing benefits essentially anti-inflammatory, antibacterial, antioxidant, immune boosting, anticancer, antiaging and antidiabetic potentials [139,140], antimalarial and antipyretic [141]. Medicinal usages elected to *Bryophyllum pinnatum* encompass antimalarial [147], virucide [148], hepatoprotective [150], anti-inflammatory and immunomodulatory [152] and antitussive activities [153]. *Canarium schweinturthii* is used in many African countries to treat coughs, pulmonary infections, malaria and fever [155]. Antiplasmodial effect of *C. schweinturthii* against chloroquine-resistant *Plasmodium falciparum* and were described [118]. Curcumin extracted to *Curcuma longa* has been documented to act as anti-inflammatory, anti-infective [77], and anti-HIV type 1 and type 2. Other researches described the inhibition effects of aqueous extract of *C. longa* against hepatitis B virus and hepatitis C virus and influenza A virus [180,181,182]. *Eremomastax speciosa* was reported as antimalarial and anti-microbial [194,197]. Titanji *et al.* [199] reported the use of *Eucalyptus globulus* as traditional remedy of respiratory tract infections, pharyngitis, bronchitis and sinusitis. Furthermore, the antiviral activity against *Haemophilus influenzae*, *Parafluenzae* and *Stenotrophomonas maltophilia* was demonstrated [200,201,202,377]. *Eucalyptus* species is also known as remedy of airway inflammatory infections. Leaves of *Ficus exasperata* combined with lemon juice are used against respiratory tract infections such as asthma, bronchitis, tuberculosis and emphysema [24]. Its antiplasmodial activity was reported by Titanji *et al.* (2008). In addition, antioxidant, antimicrobial, anti-inflammatory and antipyretic activity of *F. exasperata* were mentioned [227,229,230]. Infusion of leaves or roots of *Gossypium herbaceum* is used to stimulate appetite [234]. Other findings revealed histoprotective effect of *Gossypium herbaceum* [235]. In the study conducted by Zheng & Lu [251], Zhu *et al.* [253] and Shah *et al.* [253] on mangiferin isolated from *M. indica*, they reported ability of mangiferin to achieve inhibition of HSV-1 virus duplication within cells and to antagonize the cytopathic effects of HIV. Similarly, Rawi *et al.* [254] reported the antiviral activity of *M. indica* against influenza virus. Ayisi *et al.* [275] reported the

inhibition effects of *Ocimum gratissimum* extract versus of HIV-1 & HIV-2 replication with antiviral value 110. Other activities such as anti-malarial multi-drug resistant *Plasmodium falciparum*, antimicrobial and antitussive were also reported with *O. gratissimum* parts [250,276,277]. Rajathi *et al.* [282] retrieved antimicrobial action of *S. torvum* against respiratory tract pathogens. Similar studies revealed antimicrobial, antiviral, immuno-secretory, antioxidant, analgesic, anti-inflammatory, anti-ulcerogenic activities, cardiovascular, nephroprotective, antidiabetic, angiotensin and serotonin receptor blocking activities [280]. *Spilanthes filicaulis* was reported as plant with analgesic [286], anti-inflammatory [287], hepatoprotective [288] and immunomodulatory activities [289]. Dahake *et al.* [297], shown anti-viral activity of *Jatropha curcas* (red) leaves against potentially drug-resistant HIV. Studies indicated that plants of the genus *Garcinia* have been reported to display both anti-HIV and cytotoxicity activity [298]. Moreover, fruit of *Garcinia kola* have been claimed to be effective at stopping *Ebola* virus replication. Chang *et al.* [378] retrieved that, administration of 300 µg/ml of fresh *Zingiber officinale* stimulated the production of antiviral protein called beta interferon by the respiratory cells. Other properties such as antioxidant and anti-inflammatory activities [300], antimicrobial [301] effect was also described in ginger extracts. Leaves *Ficus thonningii* are known in traditional medicine as remedy of gingivitis, bronchitis, malaria, fever, influenza, hepatitis [319,322,323]. *F. thonningii* extract has analgesic effects as compared to aspirin [326]. The cardioprotective, vasoprotective and renoprotective effects *F. thonningii* were also described [329,330]. The genus *Terminalia* is traditionally used to treat pneumonia [350]. Leaves of *Terminalia glaucescens* were reported to be useful in the last phase of AIDS [352]. Okpekon *et al.* [353] have reported antimalarial activity against *Plasmodium falciparum*. Various parts of *Rauwolfia vomitoria* are used to treat coughs, malaria and manage HIV/AIDS in many countries (Kisangau *et al.*, 2007). Merhbod *et al.* [362] revealed that, *Allium sativum* prevents replication of influenza virus. Other studies showed that *A. sativum* strongly impacts HIV, 45 times more powerfully than the drug dextran-sulfate and also demonstrably inhibit *in vitro* human cytomegalovirus [379].

It's important to note that, the suggested plants species should be used not only for their anti-COVID-19 properties but because of other therapeutic health properties, essentially shortening fever, headache, inflammation, cough and even increasing immunostimulatory effects [380]. In fact, plant remedies have been reported to enhance the natural resistance of the body against the infection and immunomodulatory activities [381,382].

CONCLUSION

To conclude in order to fight against this pandemic disease, plants traditionally used against cold, fever, flu, bronchitis, asthma, pneumonia, malaria and viral infections should be screened. As well as those with antioxidant, anti-inflammatory and immunostimulant activities. The eighty-five (85) plants employed in Cameroonian traditional medicine against malaria, respiratory tract diseases and viral infections need to be tested

for COVID-19 virus in both cell cultures and animal models. Yet, these plants should be appraised in delicately designed clinical trials, either used alone or integrated with conventional medicine, to cover the prevention, treatment and recovery of patients from the COVID-19, as mentioned by Chang-Quan in February 2020. Otherwise, these plants can be used as precursors for the synthesis of useful drugs to fight against COVID-19.

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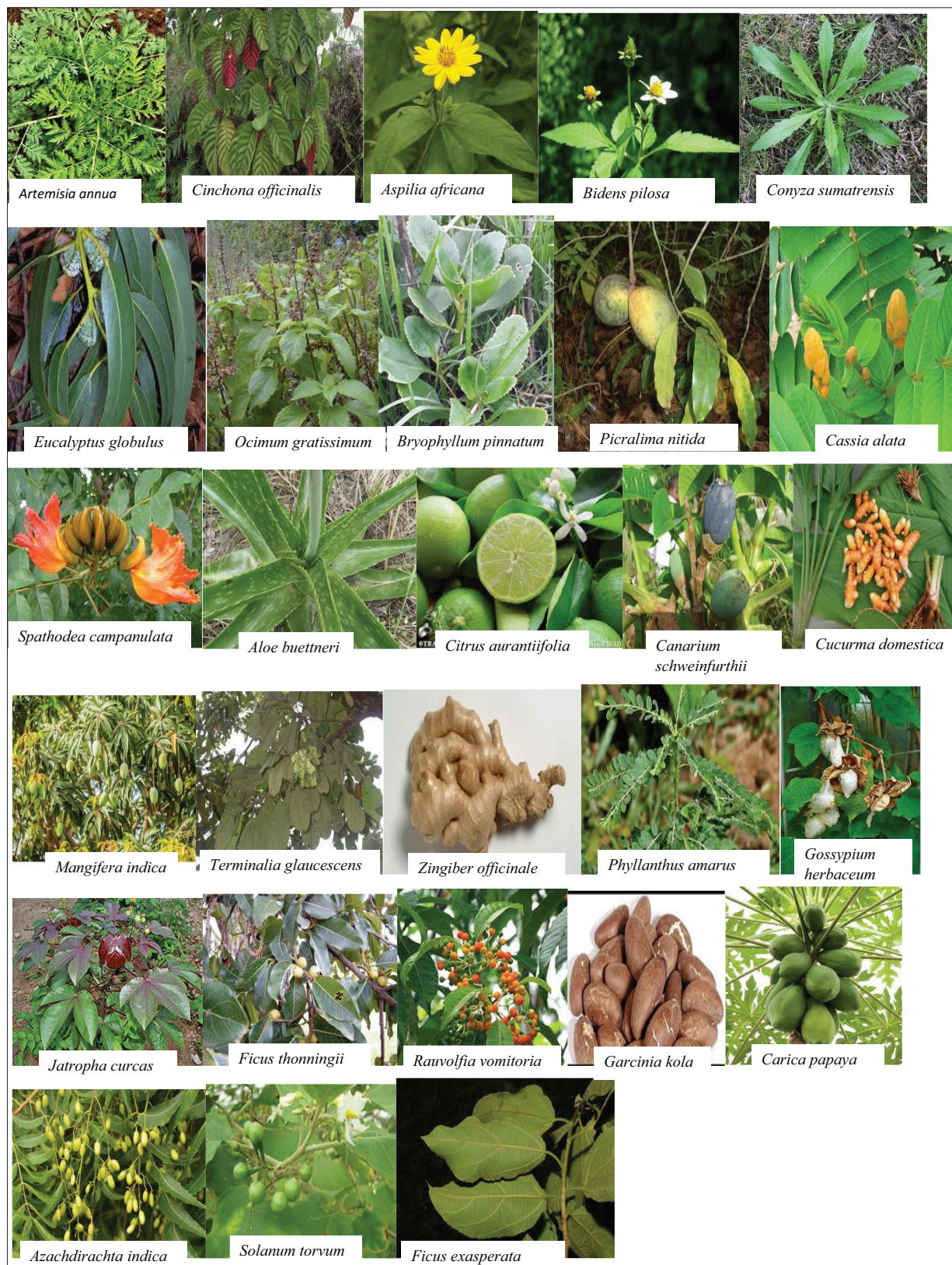
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Author Queries???

AQ1:Kindly cite refernces 97 and 229 in the text part

APPENDIX A



Appendix A: Possible ingredients of herbal formulation for prevention, alleviate symptoms or treating COVID-19 (end)