Heliyon 6 (2020) e04897

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Review article

A systematic review on COVID-19 pandemic with special emphasis on curative potentials of Nigeria based medicinal plants

Johnson O. Oladele [a,*], Ebenezer I. Ajayi [b,c], Oyedotun M. Oyeleke [a], Oluwaseun T. Oladele [d], Boyede D. Olowookere [a], Boluwaji M. Adeniyi [e], Olu I. Oyewole [d], Adenike T. Oladiji [f]

[a] Biochemistry Unit, Department of Chemical Sciences, Kings University, Ode-Omu, Osun State, Nigeria
[b] Membrane Biophysics and Nanotechnology Laboratories, Mercedes and Martin Ferreyra Institute of Medicine, IMMF-INIMEC-CONICET-UNC, Cordoba, Argentina
[c] Diabesity Complications & Other Neglected Infectious Diseases Group, Department of Biochemistry, Osun State University, Osogbo, Nigeria
[d] Phytomedicine and Molecular Toxicology Research Laboratories, Department of Biochemistry, Osun State University, Osogbo, Nigeria
[e] Centre of Excellence for Food Technology and Research -Benue State University, Nigerian Stored Products Research Institute, Ibadan, Nigeria
[f] Department of Biochemistry, University of Ilorin, Ilorin, Nigeria

ARTICLE INFO

Keywords:
SARS-CoV-2
Antivirals
COVID-19
Phytochemicals
Coronavirus
Medicinal plants
Biochemistry
Epidemiology
Food science
Health sciences
Pathophysiology
Toxicology
Phytochemistry
Evidence based medicine

ABSTRACT

Despite the frightening mortality rate associated with COVID-19, there is no known approved drug to effectively combat the pandemic. COVID-19 clinical manifestations include fever, fatigue, cough, shortness of breath, and other complications. At present, there is no known effective treatment or vaccine that can mitigate/inhibit SARS-CoV-2. Available clinical intervention for COVID-19 is only palliative and limited to support. Thus, there is an exigent need for effective and non-invasive treatment. This article evaluates the possible mechanism of actions of SARS-CoV-2 and present Nigeria based medicinal plants which have pharmacological and biological activities that can mitigate the hallmarks of the pathogenesis of COVID-19. SARS-CoV-2 mode of actions includes hyper-inflammation characterized by a severe and fatal hyper-cytokinaemia with multi-organ failure; immunosuppression; reduction of angiotensin-converting enzyme 2 (ACE2) to enhance pulmonary vascular permeability causing damage to the alveoli; and further activated by open reading frame (ORF)3a, ORF3b, and ORF7a via c-Jun N- terminal kinase (JNK) pathway which induces lung damage. These mechanisms of action of SARS-CoV-2 can be mitigated by a combination therapy of medicinal herbs based on their pharmacological activities. Since the clinical manifestations of COVID-19 are multifactorial with co-morbidities, we strongly recommend the use of combined therapy such that two or more herbs with specific therapeutic actions are administered to combat the mediators of the disease.

1. Introduction

COVID-19, a global pandemic declared by WHO, is a highly infectious and severe acute respiratory disorder caused by a pathogenic virus called SARS-CoV-2 which is transmitted to humans via contact and/or feeding on infected animals. The COVID-19 clinical manifestations are very similar to viral pneumonia such as fever, fatigue, cough, shortness of breath, and other complications. According to reports obtained on WHO and NCDC websites as of 12th July 2020, the coronavirus breakout in Wuhan, a city in Hubei Province of China in November 2019 as spread to more than 200 countries in the world. This global pandemic has forced many nations to lock down their social activities which in turn have adverse effects on the economy. Globally, more than 13,000,000 people have been confirmed infected with over 500,000 deaths. Nigeria, being one of the countries seriously affected by the virus have over 33,000 cases and more than 500 mortalities (WHO, 2020; NCDC, 2020). Thus, there is an exigent need for effective and non-invasive treatment.

Coronaviruses (SARS-CoV) are non-segmented positive-sense single-stranded RNA viruses with a large viral RNA genome of diameter 80–120 nm (Figure 1). They belong to the family of Coronaviridae, in the subfamily Orthocoronaviridae which consists of four genera namely: Alpha, Beta, Gamma, and Delta coronavirus (Chan et al., 2013). Some of the proposed modes of actions of SARS-CoV-2 include hyper-inflammation characterized by a sudden and fatal hyper-cytokinaemia with multi-organ failure (Huang et al., 2020); immunosuppression; reduction of Angiotensin-Converting Enzyme 2

* Corresponding author.
E-mail addresses: oladelejohn2007@gmail.com, jo.oladele@kingsuniversity.edu.ng (J.O. Oladele).

https://doi.org/10.1016/j.heliyon.2020.e04897
Received 8 June 2020; Received in revised form 16 July 2020; Accepted 7 September 2020

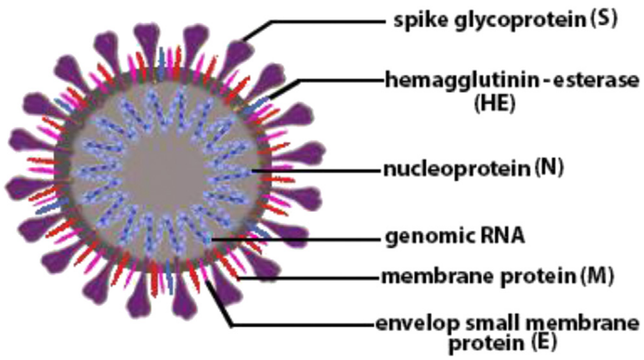

Figure 1. Structure of SARS-CoV-2.

(ACE2) to enhance pulmonary vascular permeability and damage the alveoli (Li and Clercq, 2020); and activated by ORF3a, ORF3b, and ORF7a via JNK pathway which induces lung damage (Liu et al., 2014).

Currently, there is no known effective treatment or vaccine that can mitigate/inhibit SARS-CoV-2. Available clinical interventions for COVID-19 are only palliative and limited to support. This article critically assesses the possible mechanism of actions of SARS-CoV-2 and pathogenesis of COVID-19 based on published clinical reports. We also present medicinal plants with pharmacological and biological activities that can mitigate the hallmarks of the pathogenesis of COVID-19.

2. Methods

The literature search for this article was done on PubMed Central, Google Scholar, and Medline using keywords: Coronavirus pandemic, SARS-CoV-2, COVID-19 pathogenesis, clinical features of COVID 19, antiviral plants, and medicinal plants. Articles search was conducted between April and May, 2020 and obtained articles were screened. Clinical reports, cohort studies, reviews, case series, and editorials were critical assessed. Articles that met the aim of this review were further screened and examined.

3. Prevalence

COVID-19 is stratified among the ninth deadliest world pandemic ever experienced in the globe and was first reported in late 2019 at a Chinese city called Wuhan. Since its first outbreak, the disease has spread to every continent of the world affecting many nations. This highly infectious and severe acute respiratory disease is transmitted to humans and animals by a pathogenic virus called SARS-CoV-2. Reports from epidemiological findings documented that the disease is comparatively less life-threatening and not common in children (Lu et al., 2020; Wu and McGoogan, 2020). Reports by WHO On 16th May 2020 showed that COVID-19 poses a major threat to global public health. The data revealed that more than 3,500,000 confirmed cases of SARS-CoV-2 infection and over 250,000 deaths globally since the first case was reported in late 2019. In Nigeria, a country located in the western region of Africa, over 6000 cases had been confirmed and 190 mortalities (WHO, 2020; NCDC, 2020).

COVID-19 spread rapidly from Wuhan in China to all the continents of the world within four weeks. This confirms that COVID-19 has a very high prevalence and the global population is generally susceptible to SARS-CoV-2. Using the IDEAL model, Majumder et al. documented that the basic reproduction number (R0) of SARS-CoV-2 is 2.0–3.3 (Majumder and Kenneth, 2020), while Wu et al. (2020c) reported that the R0 is between 2.47 and 2.86 using the SEIR model (Majumder and Kenneth, 2020). R0 is a parameter for measuring the transmission potential of contagious diseases. It indicates the average number of secondary infections that may occur in an entirely susceptible population (Remais, 2010). The values of R0 may vary between research groups due to many factors such as duration of infectiousness, probability of infection being transmitted during contact, and rate of contacts in the host population. The calculated R0 values of other beta coronaviruses are 2.2–3.6 (Lipsitch et al., 2003). This revealed that SARS-CoV-2 has relatively high communicability. The median age of cases reported in China was 47 years, 3% of the cases were aged people (≥80 years), 87% of the cases were people between the age of 30 and 79 years. Forty-two percent of the cases were female, suggesting that males may be more susceptible to SARS-CoV-2 (Guan et al., 2020; Wu and McGoogan, 2020).

4. Pathogenesis of COVID-19

COVID-19, a severe acute respiratory viral infection in humans caused by SARS-CoV-2 have an average incubation period of 3 days (Guan et al., 2020). The most common clinical features of COVID-19 are very similar to other viral pneumonia which include fever, fatigue, cough, shortness of breath, and other complications; organ failure and death were recorded in severe and critical cases (Figure 2) (WHO, 2020). These symptoms are markedly expressed in adults probably due to chronic underlying diseases such as heart diseases, neurodegenerative disorders, diabetes, or hypertension (Chen et al., 2020). Transmission of the virus among humans occurs when there is a penetration of infected aerosols from respiratory droplets, cough, or sneeze into the lungs via inhalation through the nose or mouth.

COVID-19 has been reported to have a higher mortality rate of about 3.7% when compared with influenza with >1% mortality rate (WHO, 2020). Some scientific evidence showed that some sets of severe COVID-19 cases might have a cytokine storm syndrome and respiratory failure due to acute respiratory distress syndrome (ARDS) which is the major cause of death (Ruan et al., 2020). Viral infections are the major factor that initiates secondary haemophagocytic lymphohistiocytosis (sHLH) (Ramos-Casals et al., 2014). sHLH also is known as Macrophage Activation Syndrome (MAS) is a life-threatening medical condition which comprises a heterogeneous group of hyper-inflammatory syndrome occurred when there is an infraction in the interplay of genetic predisposition and activators such as infections. It is characterized by a sudden and severe hyper-cytokinaemia due to inappropriate survival of histiocytes and cytotoxic T-lymphocytes and ultimately leads to haemophagocytosis, multi-organ failure, and high mortality (Henter et al., 2002). Fundamental characteristics of sHLH are cytopenias, persistent fever, and hyper-ferritinaemia; pulmonary involvement occurs in approximately 50% of patients (Seguin et al., 2016).

Although, the immunosuppression pathway depicting how SARS-CoV-2 affects the immune system has not been fully elucidated. However, MERS and SARS have been reported to evade immune detection and weaken immune responses. During viral infection, host factors produce an immune response against viruses. CD4+ and CD8+ are important T cells which perform a pivotal role in mitigating against the virus and decrease the chance of acquiring autoimmunity/inflammation (Cecere et al., 2012). The CD4 + T cells enhance the synthesize of viral-specific antibodies by activating T cell-dependent B cells. While CD8+T cells are cytotoxic and wipe out virus-infected cells. Approximately 80% of total inflammatory cells in the pulmonary interstitial in SARS-CoV infected patients are CD8+T cells. They perform important functions in scavenging and coronaviruses in infected cells (Maloir et al., 2018). Furthermore, T helper cells produce proinflammatory cytokines through the NF-kB signaling pathway (Manni et al., 2014).

5. Modes of action of SARS-CoV-2

The analysis of SARS-CoV-2 genetic sequences using sequencing technology showed that the complete genome sequence recognition rates of SARS-CoV and bat SARS coronavirus (SARSr-CoV-RaTG13) were 79.5% and 96.2%, respectively (Chen et al., 2020). Like other coronaviruses, SARS-CoV-2 has specific genes in ORF1 regions that stimulate proteins for viral replication, spikes formation, and nucleocapsid (van

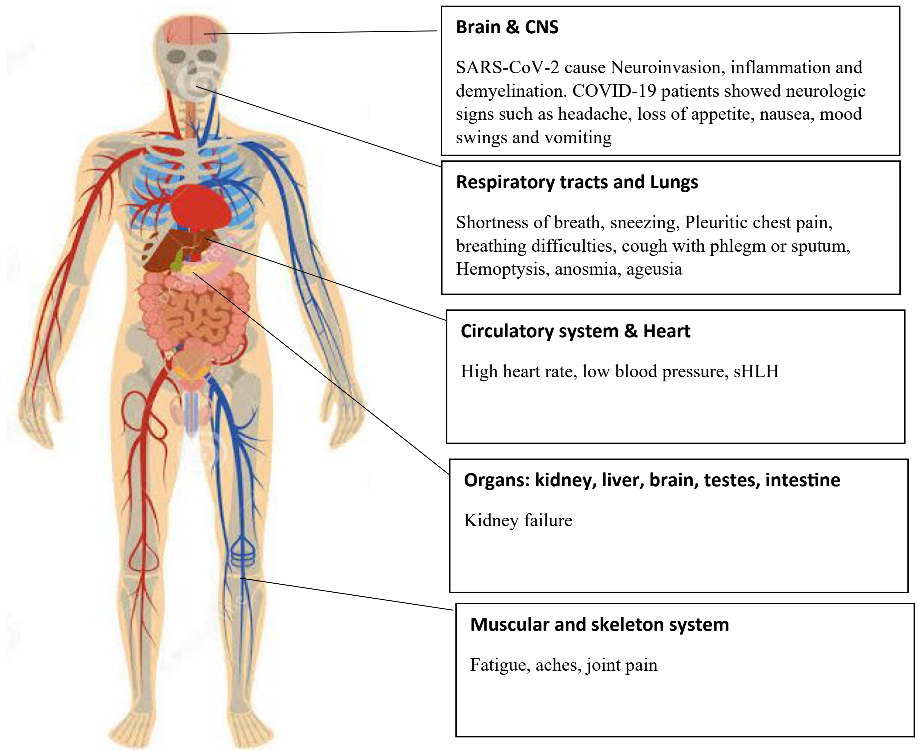

Figure 2. Pathological manifestations of SARS-CoV-2 infection (COVID-19).

Boheemen et al., 2012). The SARS-CoV-2 enter into and affect the host cell by undergoing a few steps of modifications similar to other kinds of beta-coronaviruses. Thereafter, it binds to the ACE2 receptor in the alveoli of the lungs and respiratory epithelium (Liu et al., 2020a, b). Binding of SARS-CoV to the receptor results in the mobilization of cellular proteases to cleave the S protein into S1 and S2 domains. These cellular proteases include cathepsins, human airway trypsin-like protease (HAT), and transmembrane protease serine 2 (TMPRSS2) that split the spike protein and establish further penetration changes (Glowacka et al., 2011; Bertram et al., 2011). This cleavage enhances the activation of S2 via a conformational change thus allow the interpolation of the internal fusion protein (FP) into the membrane mediating the entrance of the virus into the cell.

There is a probability that SARS-CoV-2 employed a similar mechanism as SARS-CoV because its receptor-binding domain (RBD) binding motif consists of the nucleotides associated with ACE2. After SARS-CoV-2 gained entrance in its host cell, ACE2 is cleaved and ADAM metallopeptidase domain 17 (ADAM17) shed by it into the extra membrane space. This may lead to the conversion of angiotensin I to angiotensin II by ACE2, a negative regulator of the renin-angiotensin pathway thus, increasing pulmonary vascular permeability and damage the alveoli (Chan et al., 2020). After SARS-CoV-2 proteins are translated in the host cell, ORF3a protein which codes for a Ca^{2+} ion channel that is related to SARS-CoV-2 is synthesized. It interacts with TRAF3 and activates the transcription of Nuclear Factor kappa-light-chain-enhancer of activated B-cells (NF-kB) pathway, leading to the transcription of the pro-IL-1B gene (Siu et al., 2019), ORF3a along with TNF receptor-associated factor 3 (TRAF3) and ORF3a mediates the inflammasome complex which contains caspase 1, Apoptosis-associated speck-like protein containing a CARD (ASC), and Nod-like receptor protein 3 (NLRP3). Second signal like the ROS production, Ca^{2+} influx, mitochondrial damage, and caspases activation converts pro-IL-1B to IL-B and results in cytokine production. Another ORF8b protein also activates the inflammasome pathway through NLRP3. This protein is longer in SARS-CoV-2 (Siu et al., 2019). The E protein forming an ion channel is also involved in the overproduction of cytokines (a phenomenon known as cytokine storm syndromes which cause respiratory distress) through the NLRP3 inflammasome pathway (Figure 3) (Nieto-Torres et al., 2015).

JNK is another important pathogenic pathway of SARS-CoV. In this pathway, there is an overproduction of pro-inflammatory factors via activation of ORF3a, ORF3b, and ORF7a which may lead to increased production of proinflammatory factors, critical damage of the lung (Huang et al., 2020). A cytokine profile resembling secondary haemophagocytic lymphohistiocytosis (sHLH) with a hyperinflammatory syndrome characterized by a fulminant and severe hypercytokinaemia with multiorgan failure is associated with COVID-19 disease severity. This is characterized by increased tumor necrosis factor-α, interleukin (IL)-2, IL-7, interferon-γ inducible protein 10, granulocyte-colony stimulating factor, macrophage inflammatory protein 1-α, and monocyte chemoattractant protein 1 (Huang et al., 2020).

Furthermore, when compared with other kinds of respiratory syndrome coronaviruses: The Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV), SARS-CoV-2 showed higher infectivity and transmissibility but a low mortality rate. The observed increase in virulence of SARS-CoV-2 may be due to much higher strength at which SARS-CoV-2 binds to ACE2 and mutation noted in its genome sequence. The detected changes on the SARS-CoV-2 gene include differences in orf8 and orf10 proteins, alteration on Nsp 2 and 3 proteins, shorter 3b segments, absent 8a, and longer 8b (Wu et al., 2020a,b; Xu et al., 2020a,b).

6. Medicinal plants with pharmacological and biological action capable of mitigating SARS-CoV-2

Various therapeutic approaches are being used since time immemorial for many health ailments apart from the pharmacological treatment. Approximately eighty percent of the World population still depends upon the use of herbal remedies for their health care. Nigeria and many other countries in West Africa are blessed with several

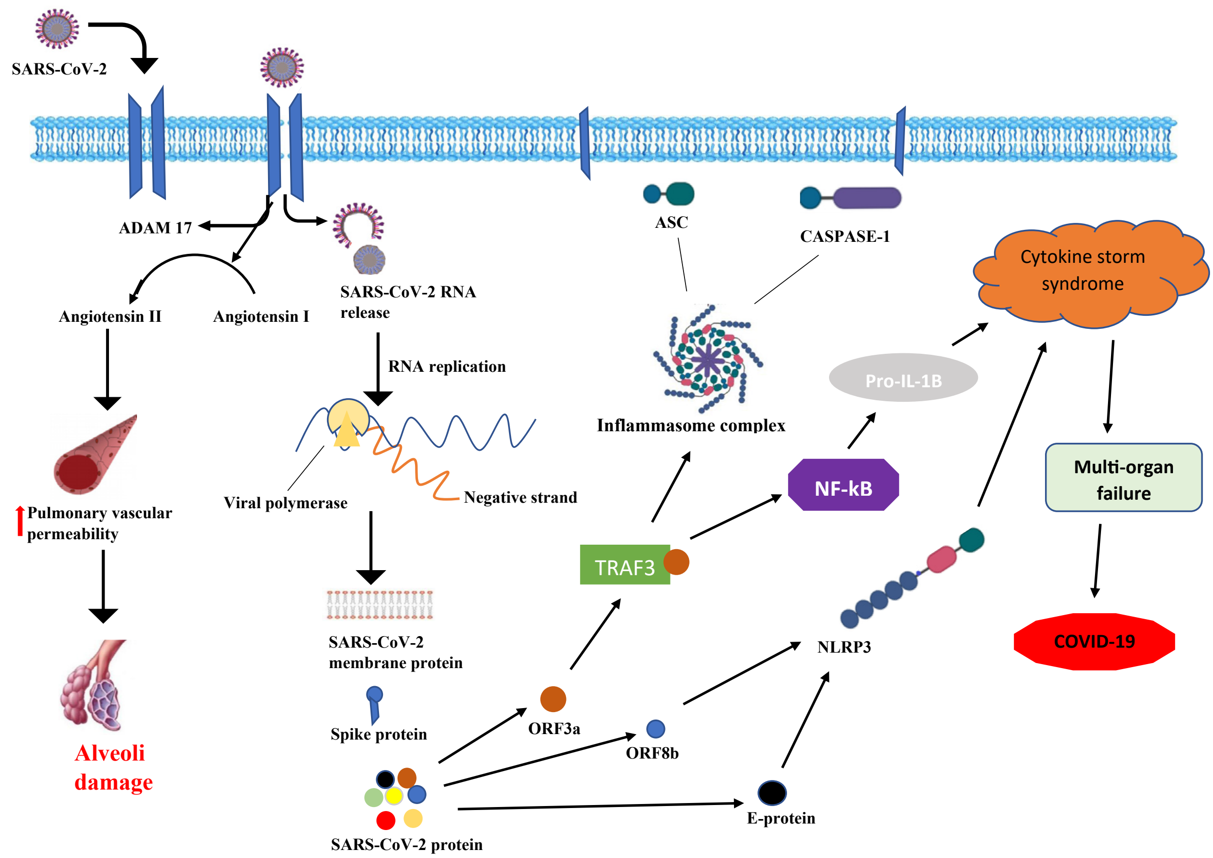

Figure 3. Possible mechanism of action of SARS-CoV-2.

varieties of medicinal plants which are of used for various purposes. This traditional method of treating ailment is transferred from one generation to the other all over the world. Dependence on plants usage has been attributed to their affordability, effectiveness, safety, cultural preferences, and ample accessibility at all times and when it is needed. Globally, traditional healers are using various medicinal plants for the treatment of COVID-19. We therefore present some of the Nigeria indigenous medicinal plants with therapeutic abilities which may serve as effective treatment for COVID-19 due to their antiviral, anti-inflammatory, antioxidant, antipyretic, immunomodulatory and cyto-protective properties (Figure 4).

6.1. Medicinal plants with antimalarial and antipyretic properties

High fever and malaria have been reported as clinical manifestations or symptoms of COVID-19. Malaria is a global health burden caused by infection with a parasite of genus plasmodium. Scientific studies have tried to investigate the link between malaria and other diseases such as cancers especially lymphoma, Burkitt lymphoma (caused by gamma herpes Viruses, Epstein-Barr virus), Kaposi sarcoma (caused by Kaposi sarcoma-associated herpesvirus), nasopharyngeal carcinoma and liver cancer. Nigerian indigenous medicinal plants such as *Enantiachlorantha, Khaya grandifoliola, Alstoniaboonei, Morinda lucida,* and *Azadirachta indica*

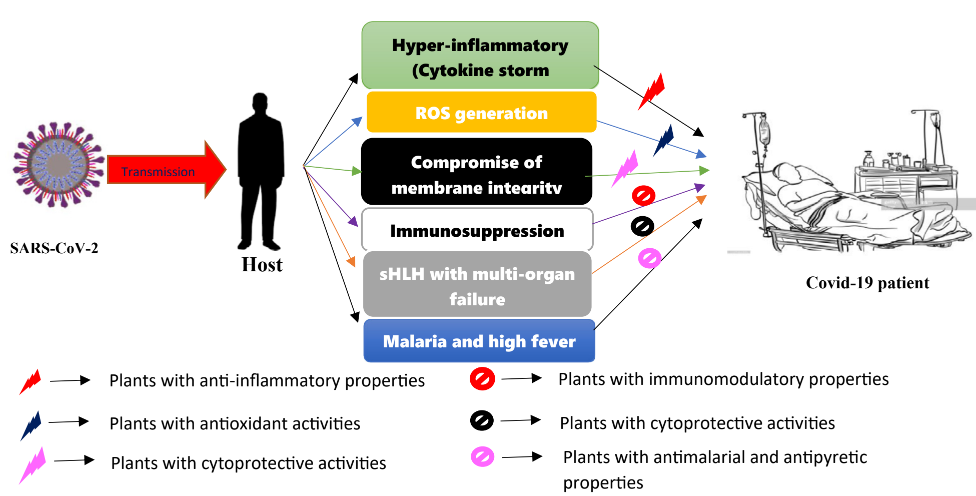

Figure 4. Pathological features of Covid-19 and possible clinical interventions by medicinal plants.

are being used extensively in traditional medicine as malaria therapy. Table 1 below show the comprehensive list of indigenous medicinal plants use for malaria therapy. The leaves, barks, roots, or whole plants are used for the treatment. We suggest that any of these plants administered alone or in combinations may offer beneficial effects in alleviating malaria in COVID-19 patients. Recently, an *in silico* screening of african medicinal plants revealed that 6-Acetylswietenolide, a terpenoid from *Khaya grandifoliola* showed significant inhibition against coronavirus 3-chymotrypsin-like protease (Gyebi et al., 2020).

6.2. Medicinal plants with antiviral properties

Nigerian plants have shown to house a number of novel compounds with antiviral activities (Figure 2). A number of scientific research have elucidated the curative mechanisms by which these plants provide their therapeutic actions while clinical research has presented the ability of some medicinal plants in treating many viral infections and diseases. For instance, *Sida cordifolia* has been reported to be a natural anti-human immunodeficiency virus (HIV) agent (Tamura et al., 2010). One of the active compound isolated from the plant is (10E, 12Z)-9-hydroxyocta-deca-10,12-dienoic acid, a hydroxyl unsaturated fatty acid was found to be an exceptional NES (nuclear export signal) non-antagonistic inhibitor for nuclear export of Rev. Replication of HIV-1 is essentially dependent on the regulatory protein Rev or the Rev protein. Rev protein is involved in the nucleus-cytoplasm export of mRNA, which is very essential for the synthesis of the viral proteins necessary for viral replication. *Sida cordifolia* has also been proven act as an immune booster serving as immune stimulants to strengthen and harmonize degenerative body systems and assists the immune system in its fight against invading antigens (bacteria and viruses) (Odukoya and Inya-Agha, 2007).

Another plant with potent antiviral activities is *Boerhavia diffusa*. Active compound isolated from *Boerhaavia diffusa* extract is a glycoprotein with a molecular weight between 16,000 and 20,000. The protein and carbohydrates component of the glycoprotein are about 8 to 13 % and 70–80% its composition respectively (Verma and Awatshi, 1979; Awasthi and Menzel, 1986). Other compounds whose biological activity with antiviral properties have been discovered from the plant include: boeravinone, Punarnavine, punarnavoside, hypoxanthine 9-L-arabino-furanoside, liirodendrin and ursolic acid (Lami et al., 1992). Recipes from this plant alone or in combination with other medicinal plant shows appreciable antiviral effects against many viruses which cause infections of the respiratory tract, liver and heart diseases. Obviously, there is no uniform principle of action against RNA viruses. Experimental findings on inhibition showed intense and broad antiphytoviral activity which suggested the mode of action of the glycoprotein inhibitor in medicinal plants. This causes a significantly effective antiviral drug candidtate to be synthesized in the plant cells, which then offers protection against viral infections (Verma and Awatshi, 1979).

scientific literatures on *Echinacea* species have shown its health benefits with special focus often on immunological effects based on in vitro and in vivo studies. *Echinacea* and its preparations exert immune stimulant activity through three mechanisms: activation of phagocytosis, stimulation of fibroblasts, and the enhancement of respiratory activity that results in augmentation of leukocyte mobility. The production of cytokines (interleukin-1 (IL-1), IL-10) and tumour necrosis factor-α (TNF-α) is stimulated by *Echinacea purpurea* (Burger et al., 1997). Some in vitro studies have proved the antiviral activity of various different preparations of Echinacea. Direct antiviral activity of *Echinacea purpurea* radix was analysed by means of a plaque-reduction- assay. The assay showed that the extract caused a 100% plaque-reduction down to concentrations of 200 ug/ml. The glycoprotein-containing fractions exhibited antiviral activity and decreased plaques numbers by up to 80%. It was concluded that the glycoprotein-containing fractions of *Echinacea purpurea* root extracts are able to induce the secretion of Il-1, TNF a, and IFN a, j3. Futhermore, they are at least partially responsible for the antiviral activity of Fchinacea purpurea radix (Bodinet and Beusher, 1991).

Assessment of antiviral activities of *Phyllanthus* species have shown its extract were most effective when administered either simultaneously with the initiation of virus infection or post infection but not when given pre-infection, and this suggested that the extract may act at the early stage of infection such as during viral attachment and entry as well as viral replication. The evidence from aueous extract showed strong activity against viruses like HSV1 and HSV2 in vero cells by a process called quantitative polymerase chain reaction (Tan et al., 2013). Western blot and 2D-gel electrophoresis were used to examined protein expressions of treated and untreated infected vero cells. *Phyllanthus amarus* and *Phyllanthus urinaria* showed the strongest antiviral activity against both HSV1 and HSV2 viruses. Their therapeutic actions were proposed to be at the early stage of replication and infection (Tan et al., 2013). The phytochemicals contributed to the antiviral activities of the plant include rutin, gallic acid, caffeolquinic acid, geraniin, corilagen, galloylglucopyranose, digalloylglucopyranoside, trigalloylglucopyranoside, quercetin glucoside and quercetin rhamnoside (Tang et al., 2010; Lee et al., 2011).

The antiviral activity of *Andrographis paniculata* (Burm. f.) extract was determined using Real Time – Polymerase Chain Reaction (RT-PCR) analysis to examine its ability to inhibit virus load in A549 cells transfected with Simian Retro Virus (SRV). The immune-stimulant activity of extract was determined by its ability to enhance lymphocytes cell proliferation using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The result of this study revealed that ethanol extract of *A. paniculata* inhibited the SRV virus titer and it was not toxic to the cell line. Also, *A. paniculata* extract at low concentration enhanced lymphocyte cell proliferation (Churiyah et al., 2015). These results were also similar to that of Wiart et al. (2005) which demonstrated andrographolide viricidal activity against herpes simplex virus 1 (HSV-1) without significant cytotoxicity. Lin et al. (2008) also established that ethanol extract *A. paniculata* and andrographolide inhibited Epstein-Barr virus (EBV) lytic proteins during the viral lytic cycle in P3HR1 cells.

Astragalus membranaceus is the dry root of *Astragalus mongolicus* or *Membranous astragalus*. The active compounds isolated from *Astragalus membranaceus* are flavonoids, saponins, and polysaccharides (Agyemang et al., 2013). Previous studies showed that the *Astragalus membranaceus* injection showed obvious anti-influenza virus activity. It improved the survival rate of Raw264.7 cells which were infected with influenza virus, enhanced the blocking effect of influenza virus on cell cycle after infection, reduced the MDA content and increased the SOD activity. At the same time, the innate immunity was affected by regulating the expression of TLR3, TAK1, TBK1, IRF3, and IFN-β in the TLR3-mediated signalling pathway, thus exerting its antiviral effect in vitro (Liang et al., 2019).

Borreira are genera of *Rubiaceae* widespread in tropical and subtropical Africa. Some species of these genera perform crucial functions in herbal and traditional medicine in Europe, Africa South America, Asia. They are used in the treatment and management of diseases such as respiratory infections, inflammation of eye, malaria, skin diseases, fever, hemorrhage, urinary infections, diarrheal and other digestive problems, headache, and gums. Different biological activities such as antioxidant, antimicrobial, anti-inflammatory, antitumor, anti-ulcer, larvicidal, gastrointestinal, and hepatoprotective have been reported from various extracts *Borreira*. These biological activities have been attributed bioactive compounds from the plant such as terpenoids, flavonoids, with alkaloids and iridoids as the major active principles (Conserva et al., 2012). Phytochemical screening has shown the presence of alkaloid called emetine in *B. verticillata* (Moreira, 1964). And this emetine has been reported to have antiviral effect against SARS-CoV-2 virus in Vero E6 cells with the estimated 50% effective concentration at 0.46 μM when tested alongside with Remdesivir, lopinavir and homoharringtonine in their capacity to inhibit SARS-CoV-2 replication in vitro. Results have also shown that emetine, an anti-protozoal agent, potently inhibits ZIKV and EBOV infection with a low nanomolar half maximal inhibitory concentration (IC50) *in vitro* and potent activity in vivo. Two mechanisms of action for emetine was also identified which are inhibition of ZIKV NS5

Table 1. List of medicinal plants with antimalarial properties.

S/N	Name of plant	Local/common Names	Active ingredient	Reference
1	*Acanthospermum hispidum*	Egungun arugbo	1 (15-acetoxy-8β-[(2-methylbutyryloxy)]-14-oxo-4,5-cis-acanthospermolide) and 2 (9α-acetoxy-15-hydroxy-8β-(2-methylbutyryloxy)-14-oxo-4,5-trans-acanthospermolide).	Ganfon et al., 2012
2	*Allium sativum*	Ayuu	Allicin, Ajoene	Coppi et al., 2006
3	*Alstonia boonei*	Ahun	Din -Octyl phthalate; 3-Nitrophthalic acid, bis-(2, ethylhexyl-ester) and Bis-(3, 5, 5-trimethylhexyl) phthalate	Imam et al., 2017
4	*Anacardium occidentale*	Kasu	anacardic acids, cardols, and 2-methylcardols derivatives	Gimenez et al.,. 2019
5	*Ananas comosus*	Ope-Oyinbo Ehin-ahun Ekunkun	Fatty acids (linoleic acid and palmitic acid)	Uzor et al., 2020
6	*Azadirachta indica*	Dogonyaro	Azadirachtinand limonoids	Mulla and Su 1999, Dhar et al., 1996, Nathan et al., 2005
7	*Bridelia ferruginea*	Ira odan		
8	*Canna indica*	Ido		
9	*Capsicum frutescens*	Ata-Ijosi		
10	*Carica papaya*	Ibepe	Papain, cystatin	Seigler et al., 2002
11	*Ceiba pentandra*	Araba	pentandrin and pentandrin glucoside and beta-sistosterol and 3-beta-D-glucopyranoside	Ngounou et al., 2000.
12	*Chromolaena odorata*	Ewe Akintola Ewe Awolowo	3, 5, 7, 3' tetrahydroxy-4'-methoxyflavone	Ezenyi et al., 2014
13	*Chrysophyllum albidum*	Agbalumo	stigmasterol tetracosanoate	Idowu et al., 2016
14	*Citrus aurantifolia*	Osanwewe	apigenin	Adeoye et al., 2019
15	*Citrus aurantium*	Osan ganinganin	Dl-limonene,	Sanei-Dehkordi et al., 2016
16	*Citrus paradisi*	Osan gerepu	2-heptanone (24.18 %), 3(*Z*)-hexen-1-ol, (23.04 %), hibaene (12.61 %), α-cadinol (6.51 %)	Ogunjinmi et al., 2017
17	*Curcuma longa*	Laali-pupa	cucurmin	Zoraima et al., 2013
18	*Cymbopogon citratus*	Kooko-Oba	geranial, neral, myrcene and beta-pinene	Tchoumbougnang et al. 2005
19.	*Diospyros mespiliformis*	Igidudu	Lupeol	Muhammad et al., 2017
20	*Enantia chlorantia*	Osopa Awopa Dokitaigbo	palmatine and jatrorrhizine, protoberberine alkaloids	Vennerstrom and Klayman, 1988
22	*Gossypium barbadense*	owu	gossypol	Razakantoanina et al., 2000
23	*Gossypium hirsutum*	Ela-owu	Kaempferol	Somsak et al. 2018
24	*Harungana madagascariensis*	Asunje, aroje	Bazouanthrone, feruginin A, harunganin, harunganol-A, harunganol B, friedelan-3-one and betulinic acid	Lenta et al., 2007
25.	*Heliotropiumindicum*	Operi -akuko	Pestalamide and Glycinamide,N-(1-oxooctadecyl) glycyl-L-alanylglycyl-L-histidyl	Duttagupta and Dutta 1977
26	*Hyptis suaveolens*			
27	*Khaya grandifoliola*	Oganwo	oleic acid (33.83%), decylene 0.45, Methyl tridecanoate 0.32, Dodecanoic acid 1.00, Methyl tridecanoate 0.66, Palmitic acid 0.24, Tridecanoic acid, 6.42, Hexadecanoic acid 18, Linolelaidic acid, 5.4, Methyl-11-octadecenoate8.52, Stearic acid 3.6, Stearic acid 9, 15-Tetracosenoic acid 2.12, trans-13-Docosenoic acid 4.59, Methyl erucate 2.9, Methyl behenate 1.16	Okpe et al., 2018
29	*Mangifera indica*	Mangoro	Quercetin and mangiferin	Awe et al. 1998, Bidla et al. 2004, Zirihi et al. 2005
30	*Meliciaexcelsa*	Iroko	berberine	Dkhil et al.,. 2015
31	*Mondia whitei*	Isirigun	*2-Hydroxy-4-methoxybenzaldehyde*	Kokwaro, 1993
32	*Morinda lucida*	Oruwo	asperuloside, asperulosidic acid, stigmasterol, β-sitosterol, cycloartenol, campesterol and 5,15-O-dimethylmorindol	Chithambo et al., 2017
34	*Nauclealatifolia*	Egberesi Gberesi	strictosamide, naucleamide A, naucleamide F, quinovic acid-3-*O*-®-rhamnosylpyranoside, and quinovic acid 3-*O*-®-fucosylpyranoside	Ata et al., 2009
35	*Ocimumgratissimum*	Efinrin-nla	3-allyl-6-methoxyphenol, 4-(5-ethenyl-1-azabicyclo (2, 2, 2) octan-2), 1-(2, 5-dimethoxyphenyl) -propanol and 1-(1-hydroxybutyl) -2, 5-dimethoxy-benzene in the concentration of 19.30 %, 16.82 %, 12.23 %, and 5.53 % respectively.	Sumitha and Thoppil, 2016
36	*Parquetina nigrescens*	Ogbo	cardenolides	Nafiu et al. 2014

(*continued on next page*)

Table 1 (*continued*)

S/N	Name of plant	Local/common Names	Active ingredient	Reference
37	*Pergularia daemia*	Atufa, isirigun		
38	*Physalis angulata*	koropo	Physalins F and D	(Sá et al.,2011).
39	*Psidium guajava*	guava	Eugenol	Raja et al., 2015
40	*Pycnanthus angolensis*	Akomu	Pycnantolol, lignans (–)-dihydroguaiaretic acid, heliobuphthalmin, talaumidin, hinokinin, the labdanetype diterpene ozic acid, and the steroids stigmast-4-en-6β-ol-3-one, β-sitosterol and stigmasterol	Abrantes et al., 2008
41.	*Rauvolfia vomitoria*	asofeyeje	raucaffricine	Tlhapi et al., 2019
42.	*Senna podocarpa*		1,2-benzenedicarboxylic acid, mono (2-ethylhexyl) ester phthalate (26.6%) and β-elemene (27.9%). There were significant amounts of caryophyllene oxide (7.3%), urs-12-en-24-oic acid, 3-oxo-methyl ester (5.5%), β-caryophyllene (3.1%), γ-muurolene (3.0%) and (3β)-lup-20 (29)-en-3-ol, acetate (3.0%).	Adebayo et al., 2014
43.	*Senna siamea*	Kasia	cassiarin A	Ekasari et al., 2009
44.	*Solanum nigrum*	Odu	1, 2-Benzenedicarboxylic acid, dibutyl phthalate, phytol, Lauric acid, 3,7,11,15-Tetramethyl-2 hexadec, 7-Hexadecenal	Rawani et al., 2017
45.	*Sphenocentrum jollyanum*	Akerejupon	α-ylangene, guaia-6,9-diene-4α-ol, globulol, guaiene-11-ol, α-eudesmol, isocaryophyllene, aromadendrene, selina-4 (15),6-dien *E*-β-isocaryophyllene, γ-terpinene, γ-humulene, epi-zonarene, δ-amorphene, 1,8-cineol,camphene, B-pinene, p-cymene, d3-carene	Olorunnisola and Afolayan, 2013
46	*Tithonia diversifolia*	Jogbo Agbale	Taginin C	Goffin et al., 2002),
47	*Trema orientalis*	Afefe	dihydrophenanthrene and phenyl-dihydroisocoumarin	Dijoux-Franca et al. (2001)
48	*Vernonia amygdalina*	Ewuro	vernolide, vernodalin, hydroxyvernolide and vernodalol, vernonioside B_1-B_3 and vernoniosides A_1-A_4	Kraft et al. (2003), Challand and Willcox (2009)
49	*Xylopia aethiopica*	Erinje Eeru		
50	*Zingiber officinale*	Ajo, Ata-ile	α-zingiberene, ar-curcumene, β-bisabolene and β-sesquiphellandrene, gingerol	Sharifi-Rad et al. (2017)

polymerase activity and disruption of lysosomal function. Emetine also inhibits EBOV entry (Yang et al., 2018).

It was reported that the Licorice root has been used for ages in ancient Egyptian medicine and also in Indian Ayurvedic medicine and also in traditional Chinese medicine. The antiviral properties of licorice root has been established but scientists observed that certain groups of people drinking concoctions of traditional Chinese medicine which contained licorice root were not infected during the SARS outbreak (Watch-arachaijunta, 2020). The licorice root contains different kinds of natural products such as flavonoids like Glabridin, Liquiritigenin, and Glycyrrhizin that also had antiviral activity against the SARS coronavirus. Triterpenoids such as glycyrrhizic acid and glycyrrhetinic acid has been identified in licorice root and they have been reported to be very potent against the SARS coronavirus (Gerold et al., 2005).

Glycyrrhizin affects cellular signaling pathways such as protein kinase C; casein kinase II; and transcription factors such as activator protein 1 and nuclear factor κB. Furthermore, glycyrrhizin and its aglycone metabolite 18β glycyrrhetinic acid upregulate expression of inducible nitrous oxide synthase and production of nitrous oxide in macrophages (Jeong and Kim, 2002). Preliminary results showed that glycyrrhizin induces nitrous oxide synthase in Vero cells to suppressed virus replication (Cinat et al., 2003).

Glycyrrhizin reduced concentrations of P24 antigen and upregulation of chemokines in patients with HIV-1 and chronic hepatitis C virus. However, infrequent side-effects such as increase in blood pressure and hypokalaemia were documented in some patients after many months of glycyrrhizin treatment (Booth et al., 2003).

6.3. Medicinal plants with anti-inflammatory properties

Inflammation has been implicated in the pathogenesis of COVID-19. It is a physiological/defense response of the host to harmful stimuli such as pathogenic infections, allergens, chemical toxicity or injury to the tissues. If left uncontrolled, inflammatory response can results into deleterious effects such as cancer, cardiovascular dysfunctions, autoimmune diseases and metabolic syndrome (Bagad et al., 2013). Modern medicines like non-steroid anti-inflammatory drugs, steroids, and immunosuppressant have been used to control and suppress inflammatory diseases but with associated unwanted side effects. Thus, the need for natural anti-inflammatory agents with increased pharmacological response and no or lowest degree of adverse effects (Bagad et al., 2013; Oladele et al., 2017) which is obtainable in medicinal plants. *Curcuma longa* (Turmeric) is one of such medicinal plant, the most essential metabolite of turmeric is curcumin and its responsible for its anti-inflammatory properties (Jurenka, 2009; Oladele et al., 2020a). Many clinical studies have been carried out to prove the anti-inflammatory effect of curcumin in diseases such as rheumatoid arthritis and reduced its clinical manifestation such as joint swelling and morning stiffness when compare with standard drug, phenylbutazone (Deodhar et al., 1980). Curcumin also offers beneficial effects in treatment of ulcerative colitis (Hanai et al., 2006), irritable bowel syndrome (IBS) (Bundy et al., 2004), psoriasis (by the selective prohibition of phosphorylase kinase) (Heng et al., 2000) and act as a reducing agent to delayed graft rejection (DGR) after kidney transplant surgery (Shoskes et al., 2005).

Table 2. List of medicinal plants with antiviral properties.

S/N	Name of plant	Local/common Names	Active ingredient	Reference
1	*Sida cordifolia*	Isankotu in Yoruba	(10E, 12Z)-9-hydroxyoctadeca-10 and 12-dienoic acid	Tamura et al. (2010)
2	*Echinacea Purpurea*	Dagumo/asofeyeje in Yoruba, Kashinyaro in Hausa, Yawo in Fulani	cichoric acid, polyacetylenes and alkamides	Binns et al. (2002a); Hudson and Towers (1999)
3	*Boerhaviadiffusa*	Etiponla, olowojeja in Yoruba	Boeravinone.	Awasthi and Verma (2006)
4	*Phyllanthus amarus*	Oyomokeisoamankedem" in Efik, "IyinOlobe" in Yoruba and "Ebebenizo" in Bini	gallotannin, ellagitannins geraniin and corilagin	Patela et al. (2011)
5	*Andrographis paniculata*	Ewe-epa in yoruba	andrographolide	Churiyah et al. (2015)
6	*Astragalus membranaceus*	Shekanbera" in Hausa and "aluki	Astragaloside.	Juan et al. (2007)
7	*Borreria verticillata*	Hausa: damfark'ami, Yoruba: irawo-ile	borreverine	Balde et al. (2015)
8	Licorice (*Glycyrrhiza glabra*)	Ewe omisinmisin in Yoruba,asukimaizaki in Hausa and Telugu in Igbo	glycyrrhizin (GL), 18β-glycyrrhetinic acid (GA)	Wang et al. (2015)
9	Sage plants (*Salvia officinalis* L.)	Egbogi in Yoruba	safficinolide and sageone,	Tada et al. (1994)

Similarly, *Zingiber officinale* (ginger) has been shown to have potent anti-inflammatory effects. Ginger powder has had ameliorative effect in musculoskeletal and rheumatism patients through inhibiting cyclooxygenase and lipoxygenase pathway in synovial fluid (Srivastava and Mustafa, 1992). Shimoda et al. (2010) reported the anti-inflammatory potential of *Zingiber officinale* in acute and chronic inflammation models. The result showed that ginger possess an effective inhibitory effects on acute and chronic inflammation, and suppressed activation of macrophage via anti-inflammatory pathway. *Zingiber officinale* have been reported to decrease serum level of TNF-α and high-sensitivity C-reactive protein (hs-CRP) in type 2 diabetic patients (Mahluji et al., 2013). Other medicinal plants with anti-inflammatory properties that could offer protection against coronavirus-induced inflammation include *Combretum mucronatum, Ficus iteophylla, Moringa oliefera (Moringaceae), Schwenkia americana, Alafia barteri, Dichrostachys cinerea, Capparis thoningii Schum, Cassia occidentalis (Caesalpiniaceae), Asparagus africanus,* and *Indigofera pulchra.*

Table 3. List of medicinal plants with antioxidant properties.

S/N	Name of plant	Local/common Names	Antioxidant component	Reference
1	*Zingiber officinale,*	Ata-ile in Yoruba	Gingerols, shogaols, paradols	Teschke and Xuan (2018); Stoner (2013)
2	*Cucurma longa*	Gangamau (Hausa) or Atale pupa (Yoruba) or Boboch (Igbo)	Curcumin, eugenol	Shreejayan and Rao (1994)
3	*Allium sativum*	Aayu in Yoruba Ayo-ishi in Igbo and Tafarunua in Hausa	Allicin	Nencini et al. (2011)
4	*Cannabis sativa L*	Igbo in Yoruba	9-tetrahydrocannabinol	Khajuria et al. (2020)
5	*Ageratum conyzoides*	Imi esu in Yoruba	Squalene, hexadecanoic acid	Kelly (1999); Cowan (1999)
6	*Ficus exasperata*	Epin in Yoruba	alkaloids, flavonoids, tannins and saponins	Ijeh and Ukwemi (2007); Woode et al. (2009)
7	*Telifarria occidentalis*	Ugwu in Igbo	anthocyanin, ascorbic acid, β-carotene, flavonoids, folic acid, polyphenol and alkaloid	Scalbert et al. (2005)
8	*Vernonia amygdalina*	ewuro	Vernodalin, Vernomygdin, Epivernodalol, Vernodalol	Kupchan et al. (1969); Owoeye (2010); Erasto et al. (2006)
9	*Garcinia kola*	Orogbo in Yoruba, Adu/aku-inu and Namiji goro in Hausa	apigenin-5,7,4'-trimethyl ether, apigenin-4'-methylether, fisetin, amento-flavone, kolaflavanone and GB1	Iwu (1982)
10	*Ocimum basillicum*	Efirin in Yoruba Nchanwu in Igbo and Dadoya in Hausa	Eugenol, methyl eugenol and methyl chavicol	Bunrathep et al. (2007)
11	*Psidium guajava*	gurofa	Saponin, oleanolic acid, lyxopyranoside, arabopyranoside, guaijavarin, quercetin and flavonoids	Das (2011), Arima and Danno (2002)
12	*xylopia aethiopica*	Eeru/Erunje in Yoruba, Uda in Igbo and Kimba in Hausa	β-pinene (16,016%), α-pinene (10,39%) and β - eudesmol (12,66%), α – eudesmol (3.7 %), α- cubebene (4.05%), aryophyllene oxid (3.21%)	Karioti and Hadjipavlou-Litina (2004)
13	*Parkia bigglobossa*	Iru in Yoruba, ogiri in Igbo and dadawa in Hausa	Ascorbic acid, rutin, butylated hydro-anisole (BHA) and alpha-tocoherol	Adaramola et al. (2012)
14	*Spondia mombi*	Iyeye in Yoruba,	Geraniin and galloyl geraniin	Corthout et al. (1991)
15	*Musa paradisiaca*)	Ogede Agbagbain Yoruba, Abrika in Igbo and ayaba in Hausa	Ferulic acid	Kumar and Pruthi (2014)
16	*Azadirachta indica*	Dongoyaro in Yoruba, *Atu yabasi*/ogwu akom in Igbo and Maina in Hausa	(2,3-(S)-hexahydroxydiphenoyl-(α/β)-D-glucopyranose, Avicularin and Castalagin)	Abdelhady et al. (2015)

6.4. Medicinal plants with immune-boosting properties

Survival of homo sapiens against traumas from foreign pathogenic microorganisms depend on the status of their immune defense mechanisms. It is well established that the immune system safeguards the host against attacks from infective microorganism such as virus, allergic or toxic molecules (Chaplin, 2010). Once a defect occurs within the immune system, it results in response impairment against infectious agents. The cause of impairment (immunosuppression) can be either intrinsic (inherited) or extrinsic and referred to as primary or secondary immunodeficiency respectively (Abbas et al., 2016; Chinen and Shearer, 2010).

Immunomodulatory agents are non-specific compounds that work without antigenic specificity similar to the adjuvants that are associated with some vaccines (Gupta et al., 2010; Liu et al., 2016). Medicinal plants and natural products with immunomodulatory activities have been employed in traditional medicine and phytomedicine. They improve the humoral and cell-mediated immunity and mediate the initiation of "non-specific" immune responses which include the induction of macrophages, natural killer cells, granulocytes, and the complement system. These processes trigger the synthesize and release of diverse molecules such as cytokines which participate in the improvement and modulation of the immune responses (Gummet et al., 1999; Vigila and Baskaran, 2008). Put together, the entire series of reactions serves as substitutes for the present chemotherapy for immunodeficiency offering protection against infections caused by various pathogenic agents (Sultana et al., 2011).

Plants that are copious carotenoids, vitamin C or flavonoids can act as an immune-stimulant. Medicinal plants that are rich in flavonoids may also possess anti-inflammatory action. They induce interferon production, enhance the activity of lymphocytes and increase phagocytosis. Examples of these immunomodulatory plants include garlic which remarkably enhance immune system activities. Garlic as an immune system booster has been found to exert an immune-potentiating effect by stimulating natural killer cell activity. Some studies strongly present garlic as a promising candidate as an immune modifier, which preserves the homeostasis of immune functions (Kyo et al., 2001) because it has a higher concentration of sulfur combinations which are responsible for its therapeutic effects (see Tables 1 and 2).

Other medicinal plants used by traditional healers as immune-boosters are garlic (*Allium sativum*), guava leave (*Psidium guajava*), lemongrass (*Cymbopogon citratus*), cinnamon (*Cinnamomum zeylanicum*).

6.5. Medicinal plants with antioxidant properties

Numerous plants that grow in Nigeria are well-known to have countless therapeutic potentials that could be due to their antioxidant properties (Oladele et al., 2020b,c). Plants are known to be the main source of natural antioxidants in the form of phenolic compounds (phenolic acids, flavonoids and polyphenols) (Table 3). Most of the anti-inflammatory, digestive, neuroprotective, hepatoprotective and nephroprotective drugs derived from natural origin have been reported to have antioxidant/radical scavenging mechanism as part of their activity (Oladele et al., 2020b,c; Oyewole et al., 2017). The ingestion of natural antioxidants has been associated with the reduced risk of cancer, cardiovascular disease, diabetes and other diseases associated with ageing (Ajayi et al., 2017). Hence, interest has been increased for finding antioxidants of plant source, which are safe and suitable for use in food and/or medicine. In that regard, due to the increasing numbers of diseases ravaging the continent of Africa and of course the World at large there are has been an increase interest in for finding antioxidants from plant source, which are safe and suitable for use in food and/or medicine. For that reason, many indigenous plants were selected for their significant antioxidant activities.

The use of artificial and natural food antioxidants regularly in medicine and foods particularly those having fats and oils to shield the food from oxidation. Butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) are some of those artificial natural food antioxidants which have been used expansively in food, cosmetic, and in many healing products industries. Nevertheless, due to the effect of high temperatures which brings instability in them, high volatility, synthetic antioxidant's carcinogenic behaviour, users dispositions steered to shift in respect to the producers or manufacturers from man-made to natural antioxidants (Papas, 1999).

Considering the increasing numbers of risk issues of humans to various harmful diseases, this brought about the need for the use of natural constituents present in dietary and medicinal plants as curative and helpful antioxidants. A vast number of indigenous plants in Nigeria have been reported to reveal antioxidant activity, including *Allium sativum, Zingiber officinale, Crocus sativus, Dodonaea viscose, Barlerianoctiflora, Anacardium occidentale, Datura fastuosa, Caesalpiniabonducella* and many more as in Table 3. Several of these antioxidants from plants has been shown to be an active oxygen scavengers or free radicals, with have no any harmful effect on human body (Oyewole et al., 2017; Oladele et al., 2020b,c; Farombi et al., 2019). For detrimental effects of reactive oxygen species to be stopped, plants have shown a powerfully in-built enzymatic and non-enzymatic scavenging capacity. These Enzymes included dehydroascorbate reductase (DHAR), catalase (CAT), glutathione S-transferase (GST), superoxide dismutase (SOD), glutathione peroxidase (GPX), ascorbate peroxidase (APX), glutathione reductase (GR), monodehydroascorbate reductase (MDHAR) and peroxidases (POX) while, non-enzymatic compounds include tocopherols, ascorbate (AsA), glutathione (GSH), and carotenoids. In plants, any form of rise in the levels of antioxidants has been established to exhibit a better resistance to different types of environmental stresses (Hasanuzzaman et al., 2011).

Consistent eating of dietary foods like fruits and vegetables is well documented to have potentials in the management of various chronic ailments affecting human in Africa. These supplements of antioxidant are directly being obtained from fresh fruits and vegetables, which contain a vast quantity of alkaloids, flavonoids and antioxidant complements which can take part in the defense mechanisms against different cardiovascular ailments including different types of cancers and many health problems (Oladele et al., 2020a,b; Ajayi et al., 2017).

Documented reports have revealed that a diet with rich antioxidants has an great impact on health in many ways such that vast variety of plants and plant parts have been established to contain a large amount of antioxidants such as strawberries, Blueberries, grapes, spinach, plums, broccoli flowers, alfalfa sprouts and many more, that have antiviral properties. Citrus fruits like lemons, oranges etc. also contain a high quantity of natural antioxidants, most significantly vitamin C (Al-snafi, 2015; Oladele et al., 2020d).

However, there are some new and unique antioxidants like derivatives of flavonoids and p-coumaric acid that have been found in spinach. NAO- a spinach-derived natural antioxidant that contains derivatives of flavonoids and p-coumaric acid plays a significant role in the prevention of prostate cancer as the case may be. Just of recent it has also be established that fruits like araticudomato, pindo palm and jackfruit are good sources of vitamin C, vitamin A and other phenolic compounds, analysis on these fruits is being carried out to create the genetic, chemical or biological variations so as to enhance the antioxidant potential of the same (Shebis et al., 2013; Oladele et al., 2020d).

Neem (*Azadirachta indica*) as it is fondly called is a tree inside the family of *Meliaceae*. Neem is also known as 'Dongoyaro in Yoruba, Atuyabasi/ogwuakom in Igbo and Maina in Hausa word. Seeds, oil, roots, roots, bark, leaves and seeds as part of the tree is somehow bitter and contain compounds with a proven potential as an anti-inflammatory, anti-ulcer and antifungal, antiviral, antiplasmiodal, cytotoxic, antipyretic anti-microbial and antiseptic in nature (Emran et al., 2015). The incorporated chemical constituents with many biologically energetic compounds that can be extracted from neem which include flavonoids, alkaloids, carotenoids, triterpenoids, phenolic compounds, steroids and ketones. Azadirachtin is validly an incorporation of seven isomeric compounds which was labelled as azadirachtin A-G and azadirachtin E is more efficient (Verkerk and Wright, 1993).

Ginger (*Zingiber officinale* Roscoe) is an important tropical valued medicinal herb that is found globally as a spice and used for healing and therapeutic proposes. Ginger belongs to the *Zingiberaceae* family which has been reported to contain over 1250 species in fifty genera, together with 4 other families which is positioned in the order Zingiberales and class Monocotyledones (Berg, 1997). They have been reported to have many vital pharmacological actions to treat various types of diseases by the actions of antiemetic, antioxidant, anti-cancer, anticoagulant property, anti-inflammatory, and soon. clinical studies have documented its efficacy in treatment of post-operative vomiting and vomiting of pregnancy.

The pungency characteristics of the ginger is said to be due to gingerols and shogaols found in them. it has been established that the main components of ginger are the aromatic essential oils, the antioxidants and the pungent oleo-resin also. Pungent compound has been identified as the phenylalkylketones, known as gingerols, shogaols, and zingerone (Rajesh and Subha, 2018). All main active constituents of *Zingiber officinale* Roscoe, such as zingerone, gingerdiol, zingibrene, gingerols and shogaols, has been proven to have anti-oxidant activities (Chrubasik et al., 2005) and this antioxidant activity in ginger is due to the existence of polyphenol compounds like (6-gingerol and its derivatives. The main active constituents of ginger are Volatile oil (zingiberene, curcumene, farnesene, zingiberol, D-camphor), Shogaols, Diarylheptanoids, Gingerols, Paradol, Zerumbone, 1-Dehydro-(10) gingerdione, Terpenoids and Ginger flavonoids (Baliga et al., 2012) these compounds give ginger its characteristic hot sensation.

Ageratum conyzoides Linn commonly known as Billy goat weeds, belongs to Asteraceae family, an annual herb with a broad history of traditional medicinal use in the tropical and sub-tropical region of the world. *Ageratum* is derived from the Greek words *'ageras'* meaning non-aging which refers to long life-time of plant and the species epithet *'konyz'* is the Greek name of *Inula helenium* which resembles the plant. The stems and leaves of the plant are fully covered with fine white hairs (Adewole, 2002).

The analysis of the Ageratum oil sample from Nigeria revealed about 51 constituents which makes it the highest including 20 monoterpenes (6.6%) of which 0.5% contains α-terpineol, 1% of it contains sabinene, 1.6% contains β-phellandrene and β-pinene, 0.6% contains terpenen-4-ol, and 2.9% contains 1.8-cineole and limonene, and further found 20 sesquiterpenes (5.1%). Indian Ageratum oil from goat weed is found to contain 5.3% ocimene which was found in traces from Nigerian plant, 4.4% eugenol, 6.6% α-pinene, and 1.8% methyleugenol (Rao and Nigam, 1973). The major sesquiterpenes are beta-caryophyllene, δ- cadinene (Rao and Nigam, 1973), Sesquiphellandrene and caryophylleneepoxide (Ekundayo et al., 1988). The plant has been examined on the basis of the scientific *in vitro*, *in vivo* or clinical evaluations to have possessed the major pharmacological activities that includes analgesic activity, antimicrobial activity, anti-inflammatory activity, spasmolytic effects, gamma radiation effects, anti-cancer and radical scavenging activity, antimalarial activity and others activities based on the listed bioactive earlier discussed (Singh et al., 2013).

Guava has been reported to have high number of antioxidants and anti-providing nutrients which are very important both for proper functioning of life and help to mitigate free radicals activities. Guava contained different kinds of phytochemicals which are useful for human health like high blood pressure, obesity and diabetes. Extracts of guava in aqueous and organic solvents have a large quantity of antioxidants which can stop oxidation reactions. Pink guava also has a high antioxidant activity (Musa et al., 2011). In fruits, the most abundant oxidants are ascorbic acid and polyphenols. The polyphenols are major flavonoids which are mainly present in glycoside and ester forms. The free elagic acid and glycosides of quercetin-3-O-glucopyranoside, apigenin, quercetin, myricetin, and morinare found to be present in guava and the presence of all these bioactive make it a potent antioxidant (Nantitanon and Okonogi, 2012).

Garlic is well acceptable spice around the Africa continent in which Nigeria is not left out and it has been proven to act as an herbal remedy for the prevention and treatment of several diseases. It has also been reported to have an anti-bacterial, anti-viral, anti-protozoal, anti-cancer, anti-fungal, immunomodulatory, anti-inflammatory, hypoglycemic and hypocholesterolemic potentials (Rehman and Munir, 2015). Allicin being the principal compound in aqueous garlic extract or raw garlic homogenate which is responsible for the cholesterol-lowering effect in humans and animals. When garlic bulb is crushed, the enzyme allinase activates alliin, a non-protein amino acid present in the intact garlic, to produce Allicin (Chowdhury et al., 2002). The phytochemical screening of garlic has also been reported to have chemical compounds such as saponin, tannin, carbohydrates, cardio glycoside, alkaloids, flavonoid, phlobatannin and glycoside (Pavni et al., 2011). Apigenin and fisetin have also been documented as potential inhibitors of coronavirus-2 in an *in silico* investigation (Oladele et al., 2020e).

6.6. Medicinal plants that enhance membrane integrity

The antiviral mechanisms of different extracts preparations of many vegetal products have been by the disturbance of cell membrane integrity thereby increasing the membrane permeability, and invariably causing the leakage of the RNA or DNA of the virus (Bouyahya et al., 2019), whereas fortifying or strengthening the cell membrane with nutraceuticals that offer protection to the integrity promises to be a functional approach to preventing invasion by known viruses and by extension the novel SARS-COV-2. Among the protective vegetal natural products reported to preserve or enhance cell membrane integrity are the following, some of which also have antiviral activities against respiratory viruses causing flu (gripe), while a few others have been studied against the earlier members of the coronavirus family such as the MERS and SARS. Many bioactive compounds from the vegetal sources have been shown to interact with the surface of cell membranes to prevent viral entry, specifically binding to membrane carrier proteins, regulating ion channels, modulating enzymes, influencing the order of the membrane lipid bilateral to elicit their medicinal activities. While there exists a plethora of membrane-modulating bioactive vegetal components, nutraceuticals, and phytochemicals, a variety of peptides are also secreted by plants with lipophilic properties that enhance their ability to pass across cell membranes (Tsuchiya, 2015). Many of these structural compounds have been studied to decipher their mechanistic transportation across cellular, intracellular, and artificial membranes, as well as their effects on gene expression within the nucleus following possible participation in signalling pathways. The structure-activity relationships often some of them have been described by several authors vis-a-vis how they affect the fluidity, micro-viscosity, order, elasticity, and permeability of both biological and artificial membranes.

Among these are *Allium cepa* of the Amaryllidaceae family, rich in quercetin, which inhibits the SARS main proteases, 3CLpro and PLpro, and the Middle Eastern Respiratory Syndrome virus (MERS) 3CLpro protease, *in vitro* (Mani et al., 2020). It has also been proposed that the modulation of cellular unfolded protein response (UPR) and autophagy signalling being important to coronaviruses to complete different stages of the viral life cycle during infection, if perturbed by quercetin and resveratrol through the mitochondrial permeability transition pores (MPTP) and NLRP-3 inflammasome pathways may have anti-coronavirus effects (Nabirotchkin et al., 2020). *Artemisia annua* (qinghao) is a plant of the Asteraceae family from which artemisinin is extracted. Together with its derivative, dihydroartemisinin, they have shown promise against parasites and viruses, including the human cytomegalovirus, *in vitro* (Flobinus et al., 2014). The plant has also shown potent anti-HIV (Lubbe et al., 2012), and anti–SARS-CoV effects (Li et al., 2005). The leaf and bark of *Azadirachta indica* L belonging to the family *Meliaceae* showed antiviral activity against herpes simplex virus type-1 infection as a potent entry inhibitor (Tiwari et al., 2010). Some of its bioactive compounds also boost the immune system by upregulating polymorphonuclear

(PMN) leukocytes, macrophage activity, and lymphocyte proliferation response (SaiRam et al., 1997). The aqueous extract of the branches was found to be effective against the Newcastle disease virus in embryonated SPF chicken eggs and SPF chickens. The plant is known to be rich in salanin, nimbin, azadirone, and azadirachtins (Ong et al., 2014) and show potent antiviral activities (Sarah et al., 2019).

Camellia sinensis of the family Theaceae is rich in catechins and flavonoids [epigallocatechingallate] (EGCG), epicatechin (EC), epigallocatechin (EGC) and epicatechin gallate (ECG)] (Baibado et al., 2011), and alkaloids (caffeine, theobromine, theophylline. They are known as anti-inflammatory and antioxidant compounds (Mahmood et al., 2016) that efficiently relieve chronic obstructive lung disease (COPD), while at the same time reducing the risk of lung cancer and type 2 diabetes, which can constitute serious underlying conditions that predispose to grave clinical outcomes for the SARS-COV-2. *Chamaemelum nobile* contains apigenin, a dietary flavonoid indicated for inflammation, cold, and asthma (Kim et al., 2014) based on its antioxidant, anti-inflammatory, and properties (Cardenas et al., 2016). The bark of *Cinchona officinalis* (quina-quina), *Rubiaceae* is rich in quinine ((8S, 9R)-6′-methoxycinchonana-9-ol; (αR)-α-(6-methoxy-4-quinoyl)-α-[(2S, 4S, 5R)-(5-vinylquinuclidin-20yl)] methanol), which has been in use for the treatment of malaria as far back as 1632 (Baird et al., 1996). It was shown to have therapeutic effects against influenza virus infections in animal studies (Seeler et al., 1946). *Cinnamon verum,* of the genus Cinnamomum (Family Lauraceae), contains proanthocyanidin and (epi) catechins. It is known to have antiviral, antibacterial, antioxidant, anti-inflammatory, and immunomodulatory properties (Kumar et al., 2019; Polansky and Lori, 2020). Its extract has anti-RNA viral effects and inhibited the wild type SARS infection, *in vitro* possibly blocking cell entry via endocytosis (Zhuanga et al., 2009). *Citrus aurantium/Sinensis* (Rutaceae) peel, containing hesperidin and vitamin C, has antioxidant and antiviral activities (M'hiri et al., 2017). The flower extract of *Citrus aurantium* protected cardiomyocyte cell membrane in Isoproterenol pre-treated male rats (Keshtkar et al., 2017). *Curcuma longa* (turmeric) contains curcumin which like pterostilbene interacts with the C-terminal of S1 domain with significant binding energies (Jitendra et al., 2020). *Cymbopogon citratus* Stapf of the Poaceae family possesses anti-allergic property indicated for the treatment of asthma by limiting the infiltration of inflammatory cells into the lungs (Santos et al., 2015).

Euphorbia hirta Linn. is a common plant used to treat asthma and other respiratory diseases including chronic flu, including asthma and bronchitis due to its anti-inflammatory and antiasthmatic activities (Kumar et al., 2010). *Piper nigrum* is another plant whose seeds have been indicated for the treatment of pharyngitis arising from flu and viral infection (DeFilipps and Krupnick, 2018). The antiviral action has been attributed to the ability to fracture, disrupt, and completely collapse the plasma membrane of pathogens, thereby increasing cell permeabilization and disrupting membrane integrity (Zou et al., 2015).

Fragaria ananassa of the rose family (Rosaceae) contains fisetin (3,3′,4′,7-tetrahydroxyflavone), a pigment flavonol also abundant in grapes, apples, onions, and cucumbers. It is also a senolytic agent, as it selectively induces death of senescent cells to alleviate age-related diseases (Yousefzadeh et al., 2018). Fisetin, quercetin, isorhamnetin, genistein, luteolin, resveratrol, and apigenin have been reported to interact with both S 1 and S2 domains of the spike protein of SARS-COV-2 with appreciable binding energies thus disrupting viral attachment and internalization into the host (Jitendra et al., 2020).

Garcinia kola Heckel (Clusiaceae), known to contain the biflavonoid kolaviron, is popular for the treatment of malaria, hepatitis, neurodegenerative disease, male sexual dysfunction, and immune-destructive diseases (Farombi et al., 2019; Uko et al., 2001). It also protects against the oxidation of lipoprotein (Farombi et al., 2008). *Garcinia kola* is also used to relieve cold and cure laryngitis (Manourova et al., 2019). Computational study have revealed that kolaviron may be a potential inhibitor of the main protease of coronavirus-2 thus, inhibiting its transmission into the host (Oladele et al., 2020e) *Phyllanthus emblica L. (Euphorbiaceae),* contains appreciably small molecular weight tetra-O--galloyl-β-d-glucose, an anti-HBV bioactive compound (Xiang et al., 2010), while *Eclipta prostrata* L. (Asteraceae) as well as peanut shells, green leafy vegetables such as spinach contain the anti-inflammatory and antioxidant luteolin (Arunachalam et al., 2009). These two bioactive compounds were reported to be able to bind strongly to the S-protein of SARS-CoV. By this mechanism, they were able to delay or prevent viral entry into host cells via the membrane receptors (Yi et al., 2004).

Zanthoxylum zanthoxyloides Lam. (Rutaceae), contains tortozanthoxylamide (N-(isobutyl) 3, 4-methylenedioxy cinnamoyl amide) (Dofuor et al., 2019) which has anti-inflammatory, antitrypanosomal and antispasmodic properties (Guendehou et al., 2018). *Zingiber officinale* Roscoe, of the Zingiberaceae family, contains gingerols which showed antiviral properties against the human respiratory syncytial virus on HEp2 and A549 cell line (Chang et al., 2013). The anti-inflammatory and antioxidant properties have also been described in dopaminergic neurons in Parkinson's disease models (Park et al., 2013), and other cell types. Oleoresin, gingerol, shogaol, and zingerone from ginger increased the percentage of CD3+CD4+ thus improving cellular and humoral immune response in HIV patients (Tejasari, 2007). Ginger also alleviated bronchopulmonary dysplasia and inflammation induced by hyperoxia and intrauterine LPS in a chorioamnionitis rat model (Cifci et al., 2018).

Many of these vegetal products promote bronchodilation, thus relieving fluid in the lungs, preventing lung fibrosis or plague formation, naso-/trachea-pharyngeal clogging, alleviating (dry) cough, chest pain, and difficulty in breathing. Overall, these novel chemical entities can be explored as formulations or cocktail containing promising druggable agents against the novel SARS-CoV-2 for blocking receptor binding and/or viral phagocytotic internalization of the SARS-CoV-2 following the binding of the S- (spike) protein to the angiotensin-converting enzyme 2 (ACE-2) receptors, and its associated proteases such as the transmembrane protease serine 2 (TMPRSS2), Cathepsin L (CTSL) and Cathepsin B (CTSB), which are ubiquitously present in almost all of the human cells; the existence of which does not indicate that the virus can always infect the cells that express them.

6.7. Medicinal plants used in the treatment of respiratory infections, cough, and flu

Phytochemical-based treatments for respiratory infections and related syndromes have been in use in many nations in Africa for many decades. Respiratory infections particularly pneumonia, asthma, tuberculosis, sinusitis, and rhinitis represent the main factors of morbidity and mortality in both developed and developing nations of the world (Ait-Khaled et al., 2007).

Anogeissus leiocarpa belonging to the family of *Combretaceae* is also called "Idi Ayin" among the Yoruba people of Nigeria. It is a deciduous plant indigenous to the savannas of tropical Africa. It is also referred to as African birch. *A. leiocarpa's* root and bark are used traditionally in the treatment of cough, gonorrhea, asthma, tuberculosis.

Allium sativim belonging to the Amaryllidaceae family, known as Aayu among the Yoruba people is also popularly called garlic among the three tribes of Nigeria. It is being used as a food supplement and in folklore medicine for several centuries, is the most researched medicinal plant (Milner, 1996). Garlic has been used useful to the treatment of a wide range of diseases such as coronary heart disease, high blood pressure, heart attack, high cholesterol, and hardening of the arteries due to its biologically active component allicin and its derivative (Mikaili et al., 2013). It has also been reported that these bioactive constituents are responsible for the antiviral, antibacterial, anti-fungal, and anti-protozoa activities of *A. sativum.* According to Amagase (2006), garlic has also been used to prevent different kinds of cancer including breast cancer, bladder cancer, colon cancer, stomach cancer, prostate cancer, rectal cancer, and lung cancer, and that it could be useful in the treatment of Cardiovascular disease including Antilipemic, antihypertensive, anti-atherosclerotic, an enlarged prostate, diabetes, osteoarthritis, cold and flu, and so on. It is also effective for building the immune system, preventing tick bites, preventing and treating bacterial and fungal infections.

Azadirachta indica is a member of the Meliaceae family of mahogany usually called neem or Indian lilac (USDA, 2020). It is typically grown in tropical and semi-tropical regions. The Siddha and Ayurvedic practitioners believed that Neem plant has anthelmintic, antifungal, antidiabetic, antibacterial, contraceptive, and sedative properties (Agrawal, 2013). The plant is believed to be the main constituent of Unani, Ayurvedic, and Siddha medicine in the treatment of skin diseases (Tamilnadu, 2012). short-term use of neem is safe in adult but long-term use may harm the kidneys or liver in small children. Neem oil has been documented to enhance healthy hair, detoxify the blood, ameliorate liver function, and balance blood sugar levels (Tamilnadu, 2012).

Tetrapleura tetraptera belonging to Fabaceae family is also called Aidan in Yoruba, Uhio in the Igbo language of Nigeria is a specie of flowering plant in the pea family which is native to Western Africa (Margaret, 1988) is also called Prekese or Soup Perfume in the Twi language of Ghana (Osie-Tutu et al., 2010). In Tropical African traditional medicine, its fruit is frequently used for the treatment and management of some of human diseases such as hypertension, diabetes mellitus, hypertension, epilepsy, arthritis, and other inflammatory conditions, schistosomiasis, asthma, postpartum (after delivery) recovery, as immune system booster (Ojewole and Adewumi, 2004). The pod has been reported to contain polyphenol, flavonoid, tannins, and alkaloids which are antioxidants that protect the body from free radicals and oxidative damages responsible for aging.

Khaya grandifoliola belonging to the Meliaceae family is popularly called Oganwo in Yoruba native of Nigeria, and also called Benin Mahogany, African mahogany, Senegal mahogany is a tall woody tree is a medicinal plant endemic to Nigeria (Hutchinson and Dalziel, 1978). It is also found in Benin, the Democratic Republic of the Congo, Ivory Coast, Ghana, Guinea, Sudan, Togo, and Uganda. It is threatened by habitat loss. Traditionally, it has been reported to have used in the form of concoction for the treatment of convulsion, cough, stomach ache, fever, threatened abortion, rheumatism, dermatomycosis, and malaria fever in Nigeria (Odugbemi et al., 2007).

Heliotropium indicum known in English as Indian heliotrope is also called Agogo Igun in Yoruba native of Nigeria is an annual plant considered as a weed by farmers, but as a valuable medicinal plant by traditional medicine practitioners. The plant is native to Asia. In Natore district, Bangladesh, a folk medicinal practitioner used the root for blood purification and to treat infection (Akhter et al., 2016). The sap is applied to gumboil, to clean ulcers, and to cure eye infections in Nigeria and Ghana. it is also used to treat warts, inflames, and tumors. Throughout tropical Africa, it is used as an analgesic to ease rheumatic pain, as a diuretic and to treat numerous skin problems including yaws, urticaria, scabies, ulcers, eczema, impetigo. A decoction of the whole plant is used to treat thrush, diarrhea, diabetes, venereal diseases, and frequent excretion of urine (Burkill, 1935).

Opuntia dillenii belonging to the Cactaceae family of the genus Opuntia grows in dry and desert environments to a height of about 1–1.8 m. It is a great medicinal herb and a shrub. The plant has been suggested that the fruit may be useful as a medication for gonorrhea, whooping cough, and constipation, as well as controlling the bile secretion, spasmodic cough, and expectoration, while the leaves of the plant have been reported to have used as a medication for wound and inflammation as well as a treatment for ophthalmic disorders (Raj, 2015; Kirtikar, 2006). Among the reported diverse pharmacological activities of this plant; anti-oxidant, anti-inflammatory, anti-tumor, neuroprotective, hepatoprotective, hypotensive, and immuno-modulation is the basis of the application of this plant in the preservation and treatment of some chronic diseases. Scientific studies on *Opuntia dillenii* can help better understanding its pharmacological mechanism of action to elucidate its traditional uses and to identify its potential new therapeutic applications.

Capsicum frutescens is a member of the Solanaceae family with five domesticated species: *C. annuum, C. baccatum, C. chinense, C. frutescens*, and *C. pubescen* (Moscone et al., 2007). They are normally very small and pungent. The Fruit usually grows a pale yellow and matures to a bright red, but can also be other colors. This plant has been reported to have used in traditional medicine for the treatment of rheumatoid arthritis, osteoarthritis, digestion problems, and conditions of the heart and blood vessels. Pepper is one of the most important plants that have been used as medicine for a long time in different countries and civilizations. In old civilizations it was used by the Mayas for treating asthma, coughs, and sore and by the Aztecs to relieve toothaches (Bosland, 1996). Dietary antioxidants have protective role against many diseases such as cancer, diabetics, cardiovascular, and anemia. Vitamins E, C, and β-carotene are important as protective antioxidants, and peppers are rich in vitamin C and E as well as carotenoids and xanthophylls (Perucka and Materska, 2007; Mateos et al., 2013).

Turmeric is a medicinal plant of *Curcuma longa* which belongs to the *Zingiberaceae* family. It is popularly referred to as Atale or Ajo among the Yoruba speaking parts of Nigeria (Priyadarini, 2014; Oladele et al., 2020a). Turmeric is a perennial plant. It is grouped among the rhizomatous and herbaceous plants. The rhizomes of *Curcuma longa* plants are gathered each year either for propagation in the next season or for consumption. The rhizome of *C. longa*, Linn has been reported to have many therapeutic activities such as anti-inflammatory, anti-diabetic, hepatoprotective, hypolipidemic, anti-diarrhoeal, anti-asthmatic, and anti-cancerous drug (Sastry, 2005; Sharma, 2006; Chunekar, 2010; Pandey, 2002; Oladele et al., 2020a).

Honey is a sweet, viscous food substance made by honey bees and some related insects (Crane, 1990). Bees produce honey from the sugary secretions of plants (floral nectar) or secretions of other insects (such as honeydew), by regurgitation, enzymatic activity, and water evaporation. Bees store honey in wax structures called honeycombs (Crane, 1990). The variety of honey produced by honey bees (the genus Apis) is the best-known, due to its worldwide commercial production and human consumption (Al-kafaween et al., 2020). Honey is collected from wild bee colonies, or hives of domesticated bees, a practice known as beekeeping or apiculture. Honey gets its sweetness from the monosaccharides: fructose and glucose, and has about the same relative sweetness as sucrose (table sugar) (NHB, 2012). The antimicrobial activity of honey against microorganisms such as bacteria, viruses, fungi, and protozoa has been reported in many scientific literatures (Carter et al., 2016).

7. Conclusion

COVID-19 is a highly infectious and severe acute respiratory disorder caused by a pathogenic virus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Its clinical manifestations include fever, fatigue, cough, shortness of breath, and other complications. The mode of actions of SARS-CoV-2 includes hyper-inflammation characterized by a fulminant and fatal hyper-cytokinaemia with multi-organ failure; immunosuppression; reduction of ACE2 to enhance pulmonary vascular permeability and damage the alveoli; and activated by ORF3a, ORF3b, and ORF7a via JNK pathway which induces lung damage. These mechanisms of action of the virus can be mitigated by combine therapy of the medicinal herbs based on their pharmacological activities. Furthermore, plant materials and natural products have been very effective in the treatment of symptoms related to COVID-19. Experimental research is needed to prove the efficacy of these medicinal plants and their product against COVID-19. As a recommendation, since COVID-19 is a multifactorial clinical disorder with co-morbidities, we strongly recommend the use of combined therapy such that two or more herbs with specific therapeutic actions are administered to combat the key players in the pathogenesis of the disease.

Declarations

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

Abbas, A.K., Lichtman, A.H.H., Pillai, Shiv, 2016. Basic Immunology: Functions and disorders of the immune system, fifth ed., 2. Saunders Elsevier Science, Philadelphia, PA, pp. 239–243. 3.

Abdelhady, S.I.M., Bader, A., Usama Shaheen, U., El-Malah, Y., Abourehab, M.A.S., BarghashF, M., 2015. Azadirachta indica as a source for antioxidant and cytotoxic polyphenolic compounds. Biosci. Biotechnol. Res. Asia 12 (2), 1209–1222.

Abrantes, M., Mil-Homens, T., Duarte, N., Lopes, D., Cravo, P., Madureira, M., Ferreira, M.-J., 2008. Antiplasmodial activity of Lignans and extracts fromPycnanthus angolensis. Planta Med. 74 (11), 1408–1412.

Adaramola, T.F., Ariwaodo, J.O., Adeniji, K.A., 2012. Distribution, phytochemistry and antioxidant properties of the genus Parkia R.br. (Mimosaceae) in Nigeria. Int. J. Pharmacogn. Phytochem. Res. 4 (4), 172–178.

Adebayo, A.M., Lawal, A.O., SikiruA, A., OgunwandeI, A., AvosehO, N., 2014. Chemical constituents and antimicrobial activity of essential oil of Senna podocarpa (Guill. Et Perr.) lock. Am. J. Plant Sci. 5, 2448–2453.

Adeoye, O.A., Olanlokun, J.O., Tijani, H., Lawal, O.C., Babarinde, O.C., Akinwole, M.T., Bewaji, C.O., 2019. Molecular docking analysis of apigenin and quercetin from ethylacetate fraction of Adansonia digitata with malaria-associated calcium transport protein: an in silico approach. Heliyon 5 (9), e02248.

Adewole, L.O., 2002. Ageratum conyzoides L. (Asteraceae). Fitoter 73, 1–16.

Agrawal, D.P., 2013. Medicinal Properties of Neem: New Findings. "Neem".

Agyemang, Kojo, Han, L., Liu, E., Zhang, Yi, Wang, T., Gao, X., 2013. Recent advances in Astragalus membranaceus anti-diabetic research: pharmacological effects of its phytochemical constituents. Evid. base Compl. Alternative Med. 2013, 9. Article ID 654643.

Ait-Khaled, N., Odhiambo, J., Pearce, N., 2007. Prevalence of symptoms of asthma, rhinitis and eczema in 13-14-year-old children in Africa: the international study of asthma and allergies in childhood phase III. Allergy 62 (3), 247–258.

Ajayi, E.I.O., Adeleke, M.A., Adewumi, T.Y., Adeyemi, A.A., 2017. Antiplasmodial activities of ethanol extracts of Euphorbia hirta whole plant and Vernonia amygdalina leaves in Plasmodium berghei-infected mice. J. Taibah Univ. Sci. 11, 831–835.

Akhter, J., Khatun, R., Akter, S., Munni, T.T., Malek, I., Rahmatullah, M., 2016. Ethnomedicinal practices in Natore district, Bangladesh. Wotld J. Pharm. Pharmaceut. Sci 5 (8), 212–222.

Al-kafaween, M.A., Hilmi, A.B.M., Jaffar, N., Al-Jamal, A.M.N., Zahri, M.K., Jibril, F.I., 2020. Antibacterial and antibiofilm activities of Malaysian *Trigona* honey against *Pseudomonas aeruginosa* ATCC 10145 and *Streptococcus pyogenes* ATCC 19615. Jordan J. Biol. Sci. 13 (1), 69–76.

Al-Snafi, A.E., 2015. Therapeutic properties of medicinal plants: a review of their antiviral activity (part 1). Int. J. Pharmacol. Screen. Methods 5 (2), 72–79.

Amagase, H., 2006. Clarifying the real bioactive constituents of garlic. J. Nutr. 136, 716S–725S.

Arima, H., Danno, G., 2002. Isolation of antimicrobial compounds from guava (Psidium guajava L .) and their structural elucidation. Biosci. Biotechnol. Biochem. 66, 1727–1730.

Arunachalam, G., Subramanian, N., Pazhani, G.P., Ravichandran, V., 2009. Anti-inflammatory activity of methanolic extract of Eclipta prostrata L. (Astearaceae). Afr. J. Pharmac Pharmacol. 3 (3), 97–100.

Ata, A., Udenigwe, C.C., Matochko, W., Holloway, P., Eze, M.O., Uzoegwu, P.N., 2009. Chemical constituents of Nauclea latifolia and their anti-GST and anti-fungal activities. Nat. Prod. Commun. 4 (9), 1185–1188.

Awasthi, L.P., Menzel, G., 1986. Effect of root extract from Boerhaavia diffusa containing an antiviral principle upon plaque formation of RNA bacteriophages. Zentralbl. Bakteriol. 141, 415–419.

Awasthi, L.P., Verma, H.N., 2006. Boerhaavia diffusa-a wild herb with potent biological and antimicrobial properties. Asian Agri. Hist. 10, 55–68.

Awe, S.O., Olajide, O.A., Oladiran, O.O., Makinde, J.M., 1998. Antiplasmodial and antipyretic screening of Mangifera indica extract. Phytother Res. 12 (6), 437–438.

Bagad, A.S., Joseph, J.A., Bhaskaran, N., Agarwal, A., 2013. Comparative evaluation of anti-inflammatory activity of curcuminoids, turmerones, and aqueous extract of *Curcuma longa*. Adv. Pharmacol. Sci. 2013, 7. Article ID 805756.

Baibado, T.J., Mei, Y., Xiaofang, P., Hon-Yeung, C., 2011. Biological activities and functions of *Camellia sinensis* (tea). Hong Kong Pharmaceut. J. 18, 31–39.

Baird, J.K., Caneta-Miguel, E., Masba, S., Bustos, D.G., Abrenica, J.A., Layawen, A.V., Calulut, J.M., Leksana, B., Wignall, F.S., 1996. Survey of resistance to chloroquine of *falciparum* and *vivax* malaria in Palawan, the Philippines. Trans. Roy. Soc. Trop. Med. Hyg. 90 (4), 413–414.

Balde, A.M., Pieters, L.A., Traore, M.S., Camara, A., Balde, M.A., Oulare, K., Barry, M.S., 2015. Chemotherapeutical evaluation of Borreria verticillata extracts. J. Plant Sci. 3 (1-2), 28–31.

Baliga, M.S., Haniadka, R., Pereira, M.M., Thilakchand, K.R., Rao, S., Arora, R., 2012. Radioprotective effects of *Zingiber officinale* roscoe (ginger): Past, present and future. Food Funct. 3 (7), 714–723.

Berg, L.R., 1997. Introductory Botany: Plants, People and the Environment. Saunders College Publication, Ft. Worth, p. 466.

Bertram, S., Glowacka, I., Müller, M.A., Lavender, H., Gnirss, K., Nehlmeier, I., et al., 2011. Cleavage and activation of the severe acute respiratory syndrome coronavirus spike protein by human airway trypsin-like protease. J. Virol. 85 (24), 13363–13372.

Bidla, G., Titanji, V.P.K., Joko, B., El-Ghazali, G., Bolad, A., Berzins, K., 2004. Antiplasmodial activity of seven plants used in African folk medicine. Indian J. Pharmacol. 36 (4), 245–246.

Binns, S.E., Hudson, J., Merali, S., Arnason, J.T., 2002. Antiviral activity of characterized extracts from Echinacea. spp. (Heliantheae: Asteraceae) against herpes simplex virus (HSV-1). Planta Med. 68, 780–783.

Bodinet, C., Beuscher, N., 1991. Antiviral and immunological activity of glycoproteins from Echinacea purpurea radix. Planta Med. 57 (2), A33–A34.

Booth, C.M., Matukas, L.M., Tomlinson, G.A., 2003. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. JAMA 289, 1–9.

Bosland, P.W., 1996. Capsicums: innovative uses of an ancient crop. In: Janick, J. (Ed.), Progress in New Crops. ASHS Press USA, pp. 479–487.

Bouyahya, A., Abrini, J., Dakka, N., Bakri, Y., 2019. Essential oils of *Origanum compactum* increase membrane permeability, disturb cell membrane integrity, and suppress quorum-sensing phenotype in bacteria. J. Pharm. Anal. 9 (5), 301–311.

Bundy, A.F., Walker, R.W., Middleton, Booth, J., 2004. Turmeric extract may improve irritable bowel syndrome symptomology in otherwise healthy adults: a pilot study. J. Alternative Compl. Med. 10 (6), 1015–1018.

Bunrathep, S., et al., 2007. Chemical composition and antioxidantive activities of essential oils from four ocimum spiecies endemic to Thailand. J. Health Res. 21, 210–213.

Burger, A., Torres, A.R., Warren, R.P., Caldwell, V.D., Hughes, B.G., 1997. Echinacea-induced cytokine production by human macrophages. Int. J. Immunopharm. 19, 371–379.

Burkill, I.H., 1935. Some changes in plant-names. Bulletin of Miscellaneous Information (Royal Botanic Gardens, Kew). JSTOR 1, 316–319.

Cardenas, H., Arango, D., Nicholas, C., 2016. Dietary apigenin exerts immune-regulatory activity in vivo by reducing NF-kappaB activity, halting leukocyte infiltration and restoring normal metabolic function. Int. J. Mol. Sci. 17 (3), 323.

Carter, D.A., Blair, S.E., Cokcetin, N.N., Bouzo, D., Brooks, P., Schothauer, R., et al., 2016. Therapeutic manuka honey: No longer so alternative. Front. Microbiol. 7 (569), 1–11.

Cecere, T.E., Todd, S.M., LeRoith, T., 2012. Regulatory T cells in arterivirus and coronavirus infections: do they protect against disease or enhance it? Viruses 4, 833–846.

Challand, S., Willcox, M., 2009. A clinical trial of the traditional medicine Vernonia amygdalina in the treatment of uncomplicated malaria. J. Alternative Compl. Med. 15, 1231–1237.

Chan, J.F., To, K.K., Tse, H., Jin, D.Y., Yuen, K.Y., 2013. Interspecies transmission and emergence of novel viruses: lessons from bats and birds. Trends Microbiol. 21 (10), 544–555.

Chang, J.S., Wang, K.C., Yeh, C.F., Shieh, D.E., Chiang, L.C., 2013. Fresh ginger (Zingiber officinale) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. J. Ethnopharmacol. 145 (1), 146–151.

Chaplin, D.D., 2010. Overview of the immune response. J. Allergy Clin. Immunol. 125 (2), S3–23.

Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., et al., 2020. Epidemiological and clini-cal characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395, 507–513.

Chinen, J., Shearer, W.T., 2010. Secondary immunodeficiencies, including HIV infection. J. Allergy Clin. Immunol. 125 (2), S195–203.

Chithambo, B., Noundou, X.S., Krause, R.W., 2017. Anti-malarial synergy of secondary metabolites from Morinda lucida Benth. J. Ethnopharmacol. 199, 91–96.

Chowdhury, R.S., Chowdhury, D.S., Smith, K.T., 2002. Effects of dietary garlic on cholesterol metabolism in laying hens. Poultry Sci. 81 (12), 1856–1862.

Chrubasik, S., Pittler, M.H., Roufogalis, B.D., 2005. Zingiberis rhizoma: a comprehensive review on the ginger effect and efficacy profiles. Phytomedicine 12, 684–701.

Chunekar, K.C., 2010. Bhavpraakash Nighantu of BhavaMisra, 2. Chaukhambha Bharti Academy publisher Varanasi India, pp. 110–112.

Churiyah, Pongtuluran, Olivia Bunga, Rofaani, Elrade, Tarwadi, 2015. Antiviral and immunostimulant activities of andrographis paniculata. Hayati J. Biosci. 22 (2), 67–72.

Çifci, A., Tayman, C., Yakut, H.I., Halil, H., Çakir, E., Çakir, U., Aydemir, S., 2018. Ginger (Zingiber officinale) prevents severe damage to the lungs due to hyperoxia and inflammation. Turk. J. Med. Sci. 48, 892–900.

Cinat, J., Morgenstern, B., Bauer, G., Chandra, P., Rabenau, H., Doerr, H.W., 2003. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. Lancet 361, P2045–2046.

Conserva, Lucia Maria, Ferreira Jr., Jesu Costa, 2012. Borreria and Spermacoce species (Rubiaceae): a review of their ethnomedicinal properties, chemical constituents, and biological activities. Pharmacogn. Rev. 6 (11), 46–55.

Coppi, A., Cabinian, M., Mirelman, D., Sinnis, P., 2006. Antimalarial activity of allicin, a biologically active compound from garlic cloves. Antimicrob. Agents Chemother. 50 (5), 1731–1737.

Corthout, J., Pieters, L.A., Claeys, M., Vanden Berghe, D.A., Vlietinck, A.J., 1991. Antiviral ellagitannins from Spondias mombin. Phytochemistry 30 (4), 1129–1130.
Cowan, M., 1999. Plant products as antimicrobial agents. Clin. Microbiol. Rev. 12, 564–582.
Crane, E., 1990. Honey from honeybees and other insects. Ethol. Ecol. Evol. 3 (1), 100–105.
Das, A.J., 2011. Review on nutritional, medicinal and pharmacological properties of Centella asiatica (Indian pennywort). J. Biol. Act. Prod. Nat. 1 (4), 216–228.
DeFilipps, R.A., Krupnick, G.A., 2018. The medicinal plants of Myanmar. PhytoKeys (102), 1-341.
Deodhar, S.D., Sethi, R., Srimal, R.C., 1980. Preliminary study on antirheumatic activity of curcumin (diferuloyl methane). Indian J. Med. Res. 71 (4), 632–634.
Dhar, R., Dawar, H., Garg, S., Basir, S.F., Talwar, G.P., 1996. Effect of volatiles from neem and other natural products on gonotrophic cycle and oviposition of *Anopheles stephensi* and *An. culicifacies* (Diptera: Culicidae). J. Med. Entomol. 33 (2), 195–201.
Dijoux-Franca, M.G., Noungoué Tchamo, D., Cherel, B., Cussac, M., Tsamo, E., Mariotte, A.M., 2001. New dihydrophenanthrene and phenyl-dihydroisocoumarin constituents of *Trema orientalis*. J. Nat. Prod. 64 (6), 832–835.
Dkhil, A.M., Al-Quraishy, S., Al-Shamrany, A., Ahmed, S., Alazzouni, S.A., Lubbad, Y.M., Al-Shaebi, M.E., Taiba, T.N., 2015. Protective effect of berberine chloride on Plasmodium chabaudi-induced hepatic tissue injury in mice. Saudi J. Biol. Sci. 22 (5), 551–555.
Dofuor, A.K., Kwain, S., Osei, E., Mawuli Tetevi, G., Okine, L.K., Ohashi, M., Gwira, T.M., Kyeremeh, K., 2019. N-(Isobutyl)-3,4-methylenedioxy cinnamoyl amide. Molbank 2019 (3), M1070.
Duttagupta, S., Dutta, P.C., 1977. Pharmacognostic study of the leaf of Heliotropium indicum. J. Crude Drug Res. 15, 141–151.
Ekasari, W., Widyawaruyanti, W., Zaini, N.C., Syafruddin, Honda, T., Morita, H., 2009. Antimalarial activity of cassiarin a from the leaves of Cassia siamea. Heterocycles 78 (7), 1831–1836.
Ekundayo, O., Laasko, I., Hiltunen, R., 1988. Essential oil of Ageratum conyzoides. Planta Med. 519, 55–57.
Emran, T.B., Nasir Uddin, M.M., Rahman, A., Uddin, Z., Islam, M., 2015. Phytochemical, antimicrobial, cytotoxic, analgesic and anti-inflammatory properties of Azadirachta indica: a therapeutic study. J. Bioanal. Biomed. 1 (s12).
Erasto, G., Grierson, D.S., Afolayan, A.J., 2006. Bioactive sesquiterpene from leaves of Vernonia amygdalina. J. Ethnopharmacol. 106, 117–129.
Ezenyi, I.C., Salawu, O.A., Kulkarni, R., Emeje, M., 2014. Antiplasmodial activity-aided isolation and identification of quercetin-4'-methyl ether in Chromolaena odorata leaf fraction with high activity against chloroquine-resistant Plasmodium falciparum. Parasitol. Res. 113 (12), 4415–4422.
Farombi, E.O., Akanni, O.O., Emerole, G.O., 2008. Antioxidant and scavenging activities of flavonoid extract (Kolaviron) of *Garcinia kola* seeds. Pharmaceut. Biol. 40 (2), 107–116.
Farombi, E.O., Awogbindin, I.O., Farombi, T.H., Oladele, J.O., Izomoh, E.R., Aladelokun, O.B., Ezekiel, I.O., Adebambo, O.I., Abah, V.O., 2019. Neuroprotective role of kolaviron in striatal redo-inflammation associated with rotenone model of Parkinson's disease. Neurotoxicology 73, 132–141.
Flobinus, A., Taudon, N., Desbordes, M., Labrosse, B., Simon, F., Mazeron, M.C., Schnepf, N., 2014. Stability and antiviral activity against human cytomegalovirus of *artemisinin* derivatives. J. Antimicrob. Chemother. 69 (1), 34–40.
Ganfon, H., Bero, J., Tchinda, A.T., et al., 2012. Antiparasitic activities of two sesquiterpenic lactones isolated from Acanthospermum hispidum D.C. J. Ethnopharmacol. 141 (1), 411–417.
Gerold, Hr, Lidia, B., Martin, M., Rimma, O., Lia, B., Tolstikov, Genrich A., Doerr, Hans W., Jindrich Jr., C., 2005. Antiviral activity of glycyrrhizic acid derivatives against SARS-coronavirus. J. Med. Chem. 48, 1256–1259.
Gimenez, M.M., Alvarenga, A.T., Groppo, M., et al., 2019. Antiplasmodial evaluation of *Anacardium occidentale* and alkyl-phenols. Revista Brasileira de Farmacognosia 29 (1), 36–39.
Glowacka, I., Bertram, S., Müller, M.A., Allen, P., Soilleux, E., Pfefferle, S., et al., 2011. Evidence that TMPRSS2 activates the severe acute respiratory syndrome coronavirus spike protein for membrane fusion and reduces viral control by the humoral immune response. J. Virol. 85 (9), 4122–4134.
Goffin, E., Ziemons, E., De Mol, P., 2000. In-vitro: antiplasmodial activity of Tithonia diversifolia and identification of its main active constituent: tagitinin C. Planta Med. 68 (6), 543–545.
Guan, W.-J., Ni, Z.-Y., Hu, Y., Liang, W.-H., Ou, C.-Q., He, J.-X., et al., 2020. Clinical characteristics of 2019 novel coronavirus infection in China. N. Engl. J. Med. 382, 1708–1720.
Guendéhou, F., Djossa, B.A., Kènou, C., Assogbadjo, C.A.E., 2018. Review of studies on *Zanthoxylum zanthoxylo*ids (Lam): availability and ethnomedical, phytochemical, pharmacological uses. Schol. J. Res. Agric. Biol. 3 (3), 244–254.
Gummert, J.F., Ikonen, T., Morris, R.E., 1999. Newer immunosuppressive drugs: a review. J. Am. Soc. Nephrol. 10 (6), 1366–1380.
Gupta, A., Gautam, M.K., Singh, R.K., Kumar, M.V., Rao, C.H.V., Goel, R.K., et al., 2010. Immunomodulatory effect of Moringa oleifera Lam. extract on cyclophosphamide induced toxicity in mice. Indian J. Exp. Biol. 48 (11), 1157–1160.
Gyebi, G.A., Ogunro, O.B., Adegunloye, A.P., Ogunyemi, O.B., Afolabi, S.O., 2020. Potential inhibitors of coronavirus 3-chymotrypsin-like protease (3CLpro): an *in-silico* screening of alkaloids and terpenoids from African medicinal plants. J. Biomol. Struct. Dyn.
Hanai, H., Iida, T., Takeuchi, K., et al., 2006. Curcumin maintenance therapy for ulcerative colitis: randomized, multicenter, doubleblind, placebo-controlled trial. Clin. Gastroenterol. Hepatol. 4 (12), 1502–1506.
Hasanuzzaman, M., Hossain, M.A., da Silva, J.A.T., Fujita, M., 2011. Plant response and tolerance to abiotic oxidative stress: antioxidant defense is a key factor. In: Venteswarlu, B., Shanker, A., Maheswari, M. (Eds.), Crop Stress and its Management: Perspectives and Strategies. Springer Publisher Netherland.
Heng, M.C.Y., Song, M.K., Harker, J., Heng, M.K., 2000. Drug induced suppression of phosphorylase kinase activity correlates with resolution of psoriasis as assessed by clinical, histological and immunohistochemical parameters. Br. J. Dermatol. 143 (5), 937–949.
Henter, J.I., Samuelsson-Harne, A., Arico, M., Egeler, R.M., Elinder, G., Filipovich, A.H., et al., 2002. Treatment of haemophagocytic lymphohistiocytosis with HLH-94 immunochemotherapy and bone marrow transplantation. Blood 100, 2367–2373.
Huang, C., Wang, Y., Li, X., et al., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395 (10223), 497–506.
Hudson, J.B., Towers, G.H.N., 1999. Phytomedicines as antivirals. Drugs Future 24, 295–320.
Hutchinson, J., Dalziel, J.M., 1978. Flora of West Tropical Africa, Part 1, second ed. Crown Agents for Overseas Government and Administration, Millbank, London SWI, pp. 345–520.
Idowu, T.O., Ogundaini, A.O., Adesanya, S.A., et al., 2016. Isolation and characterization of chemical constituents from *chrysophyllum albidum* g. don-holl. stem-bark extracts and their antioxidant and antibacterial properties. Afr. J. Tradit., Complementary Altern. Med. 13 (5), 182–189.
Ijeh, I.I., Ukwemi, A.I., 2007. Acute effect of administration of ethanol extracts of Ficus exasperata vahl on kidney function in albino rats. J. Med. Plants Res. 1, 27–29.
Imam, A.A., Ezema, M.D., Muhammad, I.U., Atiku, M.K., Alhassan, A.J., Idi, A., Abdullahi, H., Mohammed, A., 2017. In vivo antimalarial activity of solvents extracts of Alstonia boonei stem bark and partial characterization of most active extract(s). Ann. Res. Rev. Biol. 17 (5), 1–11.
Iwu, M.M., 1982. Traditional Igbo Medicine. Institute of African studies, University of Nigeria, Nsukka, Nigeria, pp. 104–110.
Jeong, H.G., Kim, J.Y., 2002. Induction of inducible nitric oxide synthase expression by 18β-glycyrrhetinic acid in macrophages. FEBS Lett. 513, 208–212.
Jitendra, S.R., Aroni, C., Abhijeet, K., Shashikant, R., 2020. Targeting SARS-CoV-2 spike protein of COVID-19 with naturally occurring phytochemicals: an in silico study for drug development. ChemRxiv. Preprint.
Juan, Z., Jian-Zong, C., Jin-Ping, Z., Xin, J., Wei-Feng, J., 2007. Inhibitory effect of astragaloside IV on human hepatitis B virus replication in vitro. J. Fourth Mil. Med. Univ. 24.
Jurenka, J.S., 2009. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. Alternative Med. Rev. 14 (2), 141–153.
Karioti, A., Hadjipavlou-Litina, D., 2004. Composition and antioxidant activity off the essential oils of Xylopia aethioca (Dun.) A. Rich (Annonaceae) leaves, stem bark, and fresh and dried fruits, growing in Ghana. J. Agric. Food Chem. 52 (26), 8094–8095.
Kelly, G.S., 1999. Squalene and its potential clinical uses. Alternative Med. Rev. 4, 29–36.
Keshtkar, S., Komeili, G., Keshavarzi, F., Jahantigh, M., 2017. Cardioprotective effects of hydroalcholic *Citrus aurantium* extract on myocardial infarction induced by isoproterenol in male rats. J. Cardiol. Curr. Res. 10 (2), 00359.
Khajuria, Rahul P.V., Vya, D., 2020. Photochemical efficiency is negatively correlated with the 9-tetrahydrocannabinol content in cannabis sativa L. Plant Physiol. Biochem. 151, 589.
Kim, A.R., Jin, Q., Jin, H.G., 2014. Phenolic compounds with IL-6 inhibitory activity from *Aster yomena*. Arch Pharm. Res. (Seoul) 37, 845–851.
Kirtikar, K.R., 2006. Indian Medicinal Plants, 2. International Book Distributors.
Kokwaro, J.O., 1993. Medicinal Plants of East Africa, East African Lit. Bureau, Nairobi.
Kraft, C., Jenett-Siems, K., Siems, K., Jakupovic, J., Mavi, S., Bienzle, U., Eich, E., 2003. In vitro antiplasmodial evaluation of medicinal plants from Zimbabwe. Phytother Res. 17, 123–128.
Kumar, N., Pruthi, V., 2014. Potential applications of ferulic acid from natural sources. Biotechnol. Rep. (Amsterdam, Netherlands) 4, 86–93.
Kumar, S., Malhotra, R., Kumar, D., 2010. *Euphorbia hirta*: its chemistry, traditional and medicinal uses, and pharmacological activities. Pharmacogn. Rev. 4 (7), 58–61.
Kumar, S., Kumari, R., Mishra, S., 2019. Pharmacological properties and their medicinal uses of Cinnamomum: a review. J. Pharm. Pharmacol. 71, 1735–1761.
Kupchan, S.M., Hemmnigway, R.J., Karim, A., Werner, D., 1969. Tumor inhibitors. XLVII Vernodalin and Vernomygdin. Two new cytotoxic sesquiterpene lactones from Vernonia amygdalina. Del. J. Org. Chem. 34, 3908–3911.
Kyo, E., Uda, N., Kasuga, S., Itakura, Y., 2001. Immuno modulatory effects of aged garlic extract. J. Nutr. 131 (3s), 1075S–1079S.
Lami, N., Kadota, S., Kikuchi, T., 1992. Constituents of the roots of *Boerhaavia diffusa* Linn. IV. Isolation and structure determination of boeravinones D, E and F. Chem. Pharm. Bull. 39 (7), 1863–1865.
Lee, S.H., Jaganath, I.B., Wang, S.M., Sekaran, S.D., 2011. Antimetastatic effects of phyllanthus on human ling (A549) and breast (MCF-7) Cancer Cell. PloS One 6 (6), e20994.
Lenta, B.N., Ngouela, S., Fekam Boyom, F., et al., 2007. Anti-plasmodial activity of some constituents of the root bark of Harungana madagascariensis LAM. (Hypericaceae). Chem. Pharm. Bull. (Tokyo) 55 (3), 464–467.
Li, G., Clercq, E., 2020. Therapeutic options for the 2019 novel coronavirus (2019-nCoV). Nat. Rev. Drug Discov. 19, 1449–14150.
Li, S.Y., Chen, C., Zhang, H.Q., Guo, H.Y., Wang, H., Wang, L., 2005. Identification of natural compounds with antiviral activities against SARS-associated coronavirus. Antivir. Res. 67 (1), 18–23.
Liang, Yuxi, Zhang, Qiuyan, Zhang, Linjing, Wang, Rufeng, Xu, Xiaoying, Hu, Xiuhua, 2019. Astragalus membranaceus treatment protects Raw264.7 cells from influenza

virus by regulating G1 phase and the TLR3-mediated signaling pathway. Hindawi Evid.-Based Compl. Altern. Med. 10. Article ID 2971604.
Lin, T.P., Chen, S.Y., Duh, P.D., Chang, L.K., Liu, Y.N., 2008. Inhibition of the Epstein-barr virus lytic cycle by andrographolide. Biol. Pharm. Bull. 31 (11), 2018–2023.
Lipsitch, M., Cohen, T., Cooper, B., Robins, J.M., Ma, S., James, L., et al., 2003. Transmission dynamics and control of severe acute respiratory syndrome. Science (New York, NY) 30, 1966–1970.
Liu, D.X., Fung, T.S., Chong, K.K.L., Shukla, A., Hilgenfeld, R., 2014. Accessory proteins of SARS-CoV and other coronaviruses. Antivir. Res. 109, 97–109.
Liu, Z., Luo, L., Zheng, S., Niu, Y., Bo, R., Huang, Y., et al., 2016. Cubosome nanoparticles potentiate immune properties of immunostimulants. Int. J. Nanomed. 2016 (11), 3571–3583.
Liu, Y.T., Chen, H.W., Lii, C.K., Jhuang, J.H., Huang, C.S., Li, M.L., Yao, H.T., 2020a. A diterpenoid, 14-deoxy-11, 12-didehydroandrographolide, in Andrographis paniculata reduces steatohepatitis and liver injury in mice fed a high-fat and high cholesterol diet. Nutrients 12, 523.
Liu, Z., Xiao, X., Wei, X., Li, J., Yang, J., Tan, H., Zhu, J., Zhang, Q., Wu, J., Liu, L., 2020b. Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS-CoV-2. J. Med. Virol. 92 (6), 595–601.
Lu, X., Zhang, L., Du, H., Zhang, J., Li, Y.Y., Qu, J., Zhang, W., Wang, Y., Bao, S., Li, Y., Wu, C., Liu, H., Liu, D., Shao, J., Peng, X., Yang, Y., Liu, Z., Xiang, Y., Zhang, F., Silva, F.M., Pinkerton, K.E., Shen, K., Xiao, K., Xu, S., Wong, G.W.K., 2020. SARS-CoV-2 infection in children. N. Engl. J. Med. 382 (17), 1663–1665.
Lubbe, A., Seibert, I., Klimkait, T., van der Kooy, F., 2012. Ethnopharmacology in overdrive: the remarkable anti-HIV activity of *Artemisia annua*. J. Ethnopharmacol. 141 (3), 854–859.
Mahluji, S., Ostadrahimi, A., Mobasseri, M., Attari, V.E., Payahoo, L., 2013. Anti-inflammatory effects of *Zingiber officinale* in type 2 diabetic patients. Adv. Pharmaceut. Bull. 3 (2), 273–276.
Mahmood, M.S., Martinez, J., Aslam, A., et al., 2016. Antiviral effects of green tea (*Camellia sinensis*) against pathogenic viruses in human and animals (a mini-review). Afr. J. Tradit., Complementary Altern. Med. 13 (2), 176.
Majumder, M.A.M., Kenneth, D., 2020. Early transmissibility assessment of a novel coronavirus in Wuhan, China, 55 (6), 105948.
Maloir, Q., Ghysen, K., Louis, R., Guiot, J., 2018. Acute respiratory distress revealing antisynthetase syndrome. Rev. Med. Liege 73, 370–375.
Mani, J.S., Johnson, J.B., Steel, J.C., et al., 2020. Natural product-derived phytochemicals as potential agents against coronaviruses: a review. Virus Res. 284, 197989.
Manni, M.L., Robinson, K.M., Alcorn, J.F., 2014. A tale of two cytokines: IL-17 and IL-22 in asthma and infection. Expet Rev. Respir. Med. 8, 25–42.
Manourová, A., Leuner, O., Tchoundjeu, Z., Van Damme, P., Verner, V., Pribyl, O., Lojka, B., 2019. Medicinal potential, utilization and domestication status of bitter kola (*Garcinia kola* Heckel) in West and Central Africa. Forests 10 (124), 1–18.
Margaret, S., 1988. Flowering Plants in West Africa. Tetrapleura tetraptera fruits are similarly useful, the seeds being rich in oil, 6th ed. Cambridge University Press, pp. 550–551. 54(6):550–551.
Mateos, N., et al., 2013. Antioxidant systems from pepper (capsicum annuum L.): involvement in the response to temperature changes in ripe fruits. Int. J. Mol. Sci. 14, 9556–9580.
Mikaili, P., Maadirad, S., Moloudizargari, M., Aghajanshakeri, Sh, Sarahroodi, S., 2013. Therapeutic uses and pharmacological properties of garlic, shallot, and their biologically active compounds. Iran J. Basic Med. Sci. 16, 1031–1048.
Milner, J.A., 1996. Garlic: its anticarcinogenic and antitumor properties. Nutr. Rev. 54, S82–86.
Moreira, E.A., 1964. Identification of emetine in some Borreria species (paper chromatography). Trib. Farm. (Curitiba) 32, 9–30.
Moscone, E., Scaldaferro, M.A., Grabiele, M., et al., 2007. The evolution of chili peppers (Capsicum-Solanaceae): a cytogenetic perspective. Acta Hortic. 745, 137–170.
Muhammad, N.A., Adoum, O.A., Yusuf, A., Hassan, Y., 2017. Anti-plasmodial effect of lupeol isolated from the stem bark of *diospyros mespiliformis* (hostch*)*. Eur. J. Biomed. Pharmaceut. Sci. 4 (8), 878–882.
Mulla, M.S., Su, T., 1999. Activity and biological effects of neem products against arthropods of medical and veterinary importance. J. Am. Mosq. Contr. Assoc. 15 (2), 133–152.
Musa, K.H., Abdullah, A., Jusoh, K., Subramaniam, V., 2011. Antioxidant activity of pinkflesh guava (Psidium guajava l.): effect of extraction techniques and solvents. Food Anal. Methods 4 (1), 100–107.
M'hiri, N., Ioannou, I., Ghoul, M., Boudhrioua, N.M., 2017. Phytochemical characteristics of citrus peel and effect of conventional and nonconventional processing on phenolic compounds: a review. Food Rev. Int. 33 (6), 587–619.
Nabirotchkin, S., Peluffo, A.E., Bouaziz, J., Cohen, D., 2020. Focusing on the Unfolded Protein Response and Autophagy Related Pathways to Reposition Common Approved Drugs against COVID-19. Preprints, 2020030302.
Nafiu, O.M., Akanji, A.M., Raji, A.Z., Abdulsalam, A.T., 2014. Phytochemical analysis and in vivo anti-malarial activities of aqueous extracts of Tithonia diversifolia and Parquetina nigrescens leaves in mice. Int. J. Nigerian Soc. Exp. Biol. 26 (2), 63–68.
Nantitanon, W., Okonogi, S., 2012. Comparison of antioxidant activity of compounds isolated from guava leaves and a stability study of the most active compound. Drug Discov. Ther. 6 (1), 38–43.
Nathan, S.S., Kalaivani, K., Murugan, K., 2005. Effects of neem limonoids on the malaria vector *Anopheles stephensi* Liston (Diptera: Culicidae). Acta Trop. 96 (1), 47–55.
National Honey Board, 2012. Carbohydrates and the Sweetness of Honey" Archived 1 July 2011 at the Wayback Machine. (Accessed 1 June 2012).
NCDC. Coronavirus COVID-19. https://covid19.ncdc.gov.ng. (Accessed 19 May 2020).
Nencini, C., Menchiari, A., Franchi, G.G., Micheli, L., 2011. In vitro antioxidant activity of aged extracts of some Italian Allium species. Plant Foods Hum. Nutr. 66, 11–16.
Ngounou, E.N., Meli, A.L., Lontsi, D., Sondengam, B.L., Atta-Ur, R., Choudhary, M.I., Akhtar, F., 2000. New isoflavone from *Ceiba pentandra*. Phytochemistry 54, 107–110.
Nieto-Torres, J.L., Verdiá-Báguena, C., Jimenez-Guardeño, J.M., Regla-Nava, J.A., Castaño-Rodriguez, C., Fernandez-Delgado, R., Torres, J., Aguilella, V.M., Enjuanes, L., 2015. Severe acute respiratory syndrome coronavirus E protein transports calcium ions and activates the NLRP3 inflammasome. Virology 485, 330–339.
Odugbemi, T.O., Odunayo, R., Akinlusire, E.A., Peter, O.F., 2007. Medicinal plants useful for malaria therapy in Okeigbo, Ondo state ans Southwestern Nigeria. Afr. J. Trad. Compl. Altern. Med. 4 (2), 191–198.
Odukoya, O.A., Inya-Agha, S.I., Ilori, O.O., 2007. Immune boosting herbs: lipid Peroxidation in liver homogenate as index of activity. J. Pharmacol. Toxicol. 2, 190–195.
Ogunjinmi, O.E., Olawore, N.O., Aliyu, A.A., 2017. Comparative studies of chemical constituents and antimalarial activity of essential oils extracted from the stem, root and fruit peel of *Citrus paradisi* grown in Nigeria. IOSR J. Appl. Chem. 10 (12), 1–11.
Ojewole, John AO., O Adewumi, Clement, 2004. Anti-inflammatory and hypoglycaemic effects of tetrapleura tetraptera (taub) [Fabaceae] fruit aqueous extract in rats. J. Ethnopharmacol. 95, 177–182.
Okpe, O., Ndidi, U.S., Ojowu, J., Maifada, S.R., Etim, E.E., Awen, D.A., Ovur, C.E., 2018. GC–MS profiling and antimalarial activity of Khaya grandifoliola on Plasmodium berghei–infected mice. J. Herbs, Spices, Med. Plants 1–12.
Oladele, J.O., Oyewole, O.I., Bello, O.K., Oladele, O.T., 2017. Hepatoprotective effect of aqueous extract of *Telfairia occidentalis* on cadmium chloride-induced oxidative stress and hepatotoxicity in rats. J. Drug Design Med. Chem. 3 (3), 32–36.
Oladele, J.O., Oyeleke, O.M., Awosanya, O.O., Oladele, T.O., 2020a. Effect of *Curcuma longa* (turmeric) against Potassium bromate-induced cardiac oxidative damage, hematological and lipid profile Alterations in rats. Singapore J. Sci. Res. 10, 8–15.
Oladele, J.O., Oladele, O.T., Ademiluyi, A.O., Oyeleke, O.M., Awosanya, O.O., Oyewole, O.I., 2020b. Chaya (Jatropha tanjorensis) leafs protect against sodium benzoate mediated renal dysfunction and hepatic damage in rats. Clin. Phytosci. 6, 13.
Oladele, J.O., Oyeleke, O.M., Oladele, O.T., Babatope, O.D., Awosanya, O.O., 2020c. Nitrobenzene-induced hormonal disruption, alteration of steroidogenic pathway, and oxidative damage in rat: protective effects of Vernonia amygdalina. Clin. Phytosci. 6, 15.
Oladele, J.O., Adewale, O.O., Oyewole, O.I., Oyeleke, O.M., Ilori, O.T., Olayinka, O.E., 2020d. Modulatory effects of vitamin C and E on cypermethrin-induced cardiac and hepatic damage in female wistar rats. Adv. Clin. Toxicol. 5 (1), 1–7.
Oladele, J.O., Oyeleke, O.M., Oladele, O.T., Olowookere, B.D., Oso, B.J., Oladiji, A.T., 2020e. Kolaviron (Kolaflavanone), apigenin, fisetin as potential Coronavirus inhibitors: *In silico* investigation. Preprint.
Olorunnisola, O.S., Afolayan, A.J., 2013. In Vivo antioxidant and biochemical evaluation of Sphenocentrum jollyanum leaf extract in P. berghei infected mice. Pak. J. Pharm. Sci. 26, 445–450.
Ong, G.H., Syamsiah, A.S., Hasrul, A.H., Zunaida, B., Maizatul, Z., Jihan, R., Redzwan, S., Leow, B.L., Faizul, F.M.Y., Chandrawathani, P., Ramlan, M., 2014. Antiviral effect of aqueous neem extract from branches of neem tree on Newcastle disease virus. Malays. J. Vet. Res. 5 (2), 5–9.
Osei-Tutu, P., Kwabena, N., Boateng, K., Owusu-Ansah, M., Faniyan, J., 2010. Hidden Forestry Revealed: Characteristics, Constraints and Opportunities for Small and Medium forest Enterprises in Ghana. IIED publisher London.
Owoeye, O., 2010. Anticancer Activity of Vernonia Amygdalina Del. Leaf Extract, its Antioxidant and Radioprotective Properties in the Brain of Rats. Ph. D Thesis. Department of Veterinary Medicine, University of Ibadan, Ibadan, Nigeria.
Oyewole, O.I., Oladele, J.O., Oladele, O.T., 2017. Methanolic leaf extract of *Ficus Exasperata* Leaf attenuates Arsenate-Mediated hepatic and renal oxidative stress in rats. Res. J. Health Sci. 5 (2), 115–123.
Pandey, G.S., 2002. Dravyaguna Vijnana, second ed., 1. Krishnadas Academy publisher Varanasi, India, pp. 737–746.
Papas, A.M., 1999. Diet and antioxidant status. Food Chem. Toxicol. 37 (9), 999–1007.
Park, G., Kim, H.G., Ju, M.S., Ha, S.K., Park, Y., Kim, S.Y., Oh, M.S., 2013. 6-Shogaol, an active compound of ginger, protects dopaminergic neurons in Parkinson's disease models via anti-neuroinflammation. Acta Pharmacol. Sin. 34 (9), 1131–1139.
Patela, R.J., Tripathib, P., Sharmaa, V., Nagendra Singh Chauhana, S.N., DixitaK, V., 2011. *Phyllanthus amarus:* ethnomedicinal uses, phytochemistry and pharmacology: a review. J. Ethnopharmacol. 138, 286–313.
Pavni, K., Esha, B., Neha, J., Tushar, A., 2011. Phytochemical screening of developing garlic and effect of its aqueous extracts on viability of cardiac cell line. J. Pharm. Res. 4 (3), 902–904.
Perucka, I., Materska, M., 2007. Antioxidant vitamin contents of Capsicum annum fruit extract as affected by processing and varietal effects. Acta Sci. Pol. Technol. Aliment. 6 (4), 67–74.
Polansky, H., Lori, G., 2020. Coronavirus disease 2019 (COVID-19): first indication of efficacy of Gene-Eden-VIR/Novirin in SARS-CoV-2 infection. Int. J. Antimicrob. Agents 55 (6), 105971.
Priyadarsini, K.I., 2014. The chemistry of curcumin: from extraction to therapeutic agent. Molecules 19 (12), 20091–20112.
Raj, V., 2015. Plant Opuntia dillenii: a review on its traditional uses, phytochemical and pharmacological properties. EC Pharmaceut. Sci. 1, 29–43.
Raja, C.R.M., Srinivasan, V., Selvaraj, S., Mahapatra, K.S., 2015. Versatile and synergistic potential of eugenol: a review. Pharm. Anal. Acta 6, 5.
Rajesh, W., Subha, G., 2018. Phytochemistry and pharmacological properties of ginger (Zingiber officinale). In: Book: Molecular Biology and Pharmacognosy and Beneficial Plants.
Ramos-Casals, M., Brito-Zeron, P., Lopez-Guillermo, A., Khamashta, M.A., Bosch, X., 2014. Adult haemophagocytic syndrome. Lancet 383, 1503–1516.

Rao, J.T., Nigam, S.S.R., 1973. Ageratum conyzoides L. (Asteraceae). Aromen Koerperpfleg 23, 209–212.
Rawani, A., Ray, A.S., Ghosh, A., et al., 2017. Larvicidal activity of phytosteroid compounds from leaf extract of Solanum nigrum against Culex vishnui group and Anopheles subpictus. BMC Res. 10 (1), 135.
Razakantoanina, V., Phung, N., Jaureguiberry, G., 2000. Antimalarial activity of new gossypol derivatives. Parasitol. Res. 86, 665–668.
Rehman, Z., Munir, M.T., 2015. Effect of garlic on the health and performance of broilers. Open Access J. Vet. 3 (1), 32–39.
Remais, J., 2010. Modelling environmentally-mediated infectious diseases of humans: transmission dynamics of schistosomiasis in China. Adv. Exp. Med. Biol. 673, 79–98.
Ruan, Q., Yang, K., Wang, W., Jiang, L., Song, J., 2020. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 46 (5), 846–848.
Sá, M.S., Menezes, M.N., Krettli, A.U., Ribeiro, I.M., Tomassini, T.C.B., Santos, R.R., Azevedo, 2011. Antimalarial activity of physalins B, D, F, and G. J. Nat. Prod. 74 (10), 2269–2272.
SaiRam, M., Sharma, S.K., Ilavazhagan, G., Kumar, D., Selvamurthy, W., 1997. Immunomodulatory effects of NIM-76 a volatile fraction from neem oil. J. Ethnopharmacol. 55 (2), 133–139.
Sanei-Dehkordi, A., Sedaghat, M.M., Vatandoost, H., Abai, R.M., 2016. Chemical compositions of the peel essential oil of citrus aurantium and its natural larvicidal activity against the malaria vector Anopheles stephensi (Diptera: Culicidae) in comparison with citrus paradise. J. Arthropod-Borne Dis. 10 (4), 577–585.
Santos, Serafim, Machado, M., Ferreira Silva, H.B., Rios, R., et al., 2015. The anti-allergic activity of Cymbopogon citratus is mediated via inhibition of nuclear factor kappa B (Nf-Kb) activation. BMC Compl. Alternative Med. 6 (15), 168.
Sarah, R., Tabassum, B., Idrees, N., Hussain, M.K., 2019. Bio-active Compounds isolated from Neem tree and their applications. In: Akhtar, M., Swamy, M., Sinniah, U. (Eds.), Natural Bio-Active Compounds. Springer Nature Singapore, pp. 509–528.
Sastry, J.L.N., 2005. Illustrated Dravyaguna Vijnana, second ed. India publisher, Chaukhambha Orientalia, Varanasi, pp. 513–518.
Scalbert, A., Manach, C., Morand, C., Remesy, C., Jimenez, L., 2005. Dietary polyphenols and the prevention of diseases. Crit. Rev. Food Sci. Nutr. 45, 287–306.
Seeler, A.O., Graessle, O., Ott, W.H., 1946. Effect of quinine on influenza virus infections in mice. J. Infect. Dis. 79, 156–158.
Seguin, A., Galicier, L., Boutboul, D., Lemiale, V., Azoulay, E., 2016. Pulmonary involvement in patients with hemophagocytic lymphohistiocytosis. Chest 149, 1294–1301.
Seigler, D.S., Pauli, G.F., Nahrstedt, A., Leen, R., 2002. Cyanogenic allosides and glucosides from Passiflora edulis and Carica papaya. Phytochemistry 60, 873–882.
Sharifi-Rad, M., Varoni, E., Salehi, B., Sharifi-Rad, J., Matthews, K., Ayatollahi, S., Rigano, D., 2017. Plants of the genus Zingiber as a source of bioactive phytochemicals: from tradition to pharmacy. Molecules 22 (12), 2145.
Sharma, P.V., 2006. DravyaGuna Vijnana, Chaukhambha Bharti Academy. Varanasi India. IJCP 1, 162–166.
Shebis, Y., Iluz, D., Kinel-Tahan, Y., Dubinsky, Z., Yehoshua, Y., 2013. Natural antioxidants: function and sources. Food Nutr. Sci. 4 (6), 643–649.
Shimoda, H.S., Shan, J., Tanaka, et al., 2010. Anti-inflammatory properties of red ginger (Zingiber officinale var. Rubra) extract and suppression of nitric oxide production by its constituents. J. Med. Food 13 (1), 156–162.
Shoskes, D.C., Lapierre, M., Cruz-Corerra, et al., 2005. Beneficial effects of the bioflavonoids curcumin and quercetin on early function in cadaveric renal transplantation: a randomized placebo controlled trial. Transplantation 8 (11), 1556–1559.
Shreejayan, Rao, M.N.A., 1994. Curcuminoids as potent inhibitor of lipid peroxidase. J. Pharm. Pharmacol. 46, 1013–1016.
Singh, S.B., Devi, W.R., Marina, A., Indira Devi, W., Swapana, N., Singh, C.B., 2013. Ethnobotany, phytochemistry and pharmacology of *Ageratum conyzoides Linn (Asteraceae)*. J. Med. Plants Res. 7 (8), 371–385.
Siu, K.L., Yuen, K.S., Castaño-Rodriguez, C., Ye, Z.W., Yeung, M.L., Fung, S.Y., Yuan, S., Chan, C.P., Yuen, K.Y., Enjuanes, L., 2019. Severe acute respiratory syndrome coronavirus ORF3a protein activates the NLRP3 inflammasome by promoting TRAF3-dependent ubiquitination of ASC. Faseb. J. 33, 8865–8877.
Somsak, V., Damkaew, A., Onrak, P., 2018. Antimalarial activity of kaempferol and its combination with chloroquine in Plasmodium berghei infection in mice. J. Pathog. 2018, 7.
Srivastava, K.C., Mustafa, T., 1992. Ginger (*Zingiber officinale*) in rheumatism and musculoskeletal disorders. Med. Hypotheses 39 (4), 342–348.
Stoner, G.D., 2013. Ginger: is it ready for prime time? Canc. Prev. Res. 6, 257–262.
Sultana, S., Khanum, S., Devi, K., 2011. Immunomodulatory effect of methanol extract of Solanum xanthocarpum fruits. Int. J. Pharma Sci. Res. 2 (2), 93–97.
Sumitha, K.V., Thoppil, J.E., 2016. Larvicidal efficacy and chemical constituents of O. gratissimum L. (Lamiaceae) essential oil against Aedes albopictus Skuse (Diptera: Culicidae). Parasitol. Res. 115, 673–680.
Tada, M., Okuno, K., Chiba, K., Ohnishia, E., Yoshiia, T., 1994. Antiviral diterpenes from Salvia officinalis. Phytochemistry 35 (2), 539–541.
Tamura, S., Kaneko, M., Shiomi, A., Yang, G.-M., Yamaura, T., Murakami, N., 2010. Unprecedented NES non-antagonistic inhibitor for nuclear export of Rev from Sida cordifolia. Bioorg. Med. Chem. Lett 20, 1837–1839.
Tamilnadu.com. 6 December 2012. Archived from the original on 11 April 2013.
Tan, W., Jaganath, I., Manikam, I., 2013. Evaluation of antiviral activities of four local Malaysian Phyllanthus species against Herpes simplex viruses and possible antiviral target. Int. J. Med. Sci. 10 (13), 1817–1892.
Tang, T.Q., Jaganath, I.B., Sekaran, S.D., 2010. Phyllanthus spp. induces selective growth inhibition of PC-3 and MeWo human cancer cells through modulation of cell cycle and induction of Apoptosis. PloS One 5 (9), e12644.
Tchoumbougnang, F., Amvam Zollo, P.H., Ermias, D., Yalem, M., 2005. In vivo antimalarial activity of essential oils from cymbopogon citratus and ocimum gratissimum on mice infected with Plasmodium berghei. Planta Med. 71 (1), 20–23.
Tejasari, D., 2007. Evaluation of Ginger (*Zingiber officinale* Roscoe) bioactive compounds in increasing the ratio of T-cell surface molecules of CD3+CD4+:CD3+CD8+ *in vitro*. Malays J. Nutr. 13 (2), 161–170.
Teschke, R., Xuan, T.D., 2018. Viewpoint: a contributory role of shell ginger (Alpinia zerumbet) for human longevity in Okinawa, Japan? Nutrients 10, 166.
Tiwari, V., Darmani, N.A., Yue, B.Y., Shukla, D., 2010. *In vitro* antiviral activity of neem (*Azardirachta indica* L.) bark extract against herpes simplex virus type-1 infection. Phytother Res. 24 (8), 1132–1140.
Tlhapi, B.D., Ramaite, I.D.I., Ree, V.T., Anokwuru, P.C., Orazio, S., Hoppe, C.H., 2019. Isolation, chemical profile and antimalarial activities of bioactive compounds from rauvolfia caffra sond. Molecules 24 (1), 39.
Tsuchiya, H., 2015. Membrane Interactions of phytochemicals as their molecular mechanism applicable to the discovery of drug leads from plants. Molecules 20 (10), 18923–18966.
Uko, O.J., Usman, A., Ataja, A.M., 2001. Some biological activities of Garcinia kola in growing rats. Vet. Arh. 71 (5), 287–297.
USDA, Agricultural Research Service, National Plant Germplasm System, 2020. Germplasm Resources Information Network (GRIN-Taxonomy). National Germplasm Resources Laboratory, Beltsville, Maryland. https://npgsweb.ars-grin.gov/gringlobal/taxonomydetail.aspx?6161. (Accessed 27 June 2020).
Uzor, P.I., Ishiwu, B.U., Nwodo, N.J., 2020. In vivo antimalarial effect of *Ananas comosus (L) Merr* (*Bromeliaceae*) fruit peel, and gas chromatography-mass spectroscopy profiling: a possible role for polyunsaturated fatty acid. Trop. J. Pharmaceut. Res. 19 (1), 137–145.
van Boheemen, S., de Graaf, M., Lauber, C., Bestebroer, T.M., Raj, V.S., Zaki, A.M., et al., 2012. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. mBio 3 (6), e00473–e00512.
Vennerstrom, J.L., Klayman, D.L., 1988. Protoberberine alkaloids as antimalarials. J. Med. Chem. 31 (6), 1084–1087.
Verkerk, R.H.J., Wright, D.J., 1993. Biological activity of neem seed kernel extracts and synthetic azadirachtin against larvae of Plutella xylostella L. Pestic. Sci. 37, 83–91.
Verma, H.N., Awatshi, L.P., 1979. Prevention of virus infection and multiplication by leaf extract of Euphorbia hirta and the properties of the virus inhibitor. New Bot. 6, 49–59.
Vigila, A.G., Baskaran, X., 2008. Immunomodulatory effect of coconut protein on cyclophosphamide induced immune suppressed Swiss Albino mice. Ethnobot Leaflet 12, 1206–1212.
Wang, L., Yang, R., Yuan, B., Liu, Y., Liu, C., 2015. The antiviral and antimicrobial activities of licorice, a widely-used Chinese herb. Acta Pharm. Sin. B 5 (4), 310–315.
Watcharachaijunta, Jakkapong, 2020. Further Research into the Phytochemicals Contained in Licorice Root Might Yield A Treatment for the New Coronavirus Strain in China. Thailand Medical News. https://www.thailandmedical.news/news/further-research-into-the-phytochemicals-contained-in-licorice-root-might-yield-a-treatment-for-the-new-coronavirus-strain-in-china.com. (Accessed 26 January 2020).
WHO, 2020a. Coronavirus disease 2019 (COVID-19) situation report – 52. March 12, 2020. https://www.who.int/docs/default-source/coronaviruse/20200312-sitrep-52-covid-19.pdf?sfvrsn=e2bfc9c0_2. (Accessed 13 March 2020).
World Health Organization (WHO), 2020b. Q&A on Coronaviruses (COVID-19). Available from: https://www.who.int/news-room/q-a-detail/q-a-coronaviruses. (Accessed 6 March 2020).
Wiart, C., Kumar, K., Yusof, M.Y., Hamimah, H., Fauzi, Z.M., Sulaiman, M., 2005. Antiviral properties of ent-labdene diterpenes of Andrographis paniculata Nees, inhibitors of herpes simplex virus type I. Phytother Res. 19 (12), 1069–1070.
Woode, E., Poku, R., Ainooson, G., Boakye-Gyasi, E., Abotsi, W., Mensah, T., et al., 2009. An evaluation of the anti-inflammatory, antipyretic and antinociceptive effects of Ficus exasperata (Vahl) leaf extract. J. Pharmacol. Toxicol. 4, 138–151.
Wu, Z., McGoogan, J.M., 2020. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease Control and prevention. J. Am. Med. Assoc. 323 (13), 1239–1242.
Wu, A., Peng, Y., Huang, B., Ding, X., Wang, X., Niu, P., Meng, J., Zhu, Z., Zhang, Z., Wang, J., 2020a. Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. Cell Host Microbe 27, 325–328.
Wu, C., Liu, Y., Yang, Y., Zhang, P., Zhong, W., Wang, Y., Wang, Q., Xu, Y., Li, M., Li, X., 2020b. Analysis of therapeutic targets for SARS-CoV-2 and discovery of potential drugs by computational methods. Acta Pharm. Sin. B 10 (5), 766–788.
Wu, J.T., Leung, K., Leung, G.M., 2020c. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. Lancet 395 (10225), 689–697.
Xiang, Y., Ju, H., Li, S., 2010. Effects of 1,2,4,6-tetra-O-galloyl-β-D-glucose from *P. emblica* on HBsAg and HBeAg secretion in HepG2.2.15 cell culture. Virol. Sin. 25 (5), 375–380.
Xu, J., Zhao, S., Teng, T., Abdalla, A.E., Zhu, W., Xie, L., Wang, Y., Guo, X., 2020a. Systematic comparison of two animal-to-human transmitted human coronaviruses: SARS-CoV-2 and SARS-CoV. Viruses 12, 244.

Xu, X., Yu, C., Qu, J., Zhang, L., Jiang, S., Huang, D., Chen, B., Zhang, Z., Guan, W., Ling, Z., 2020b. Imaging and clinical features of patients with 2019 novel coronavirus SARSCoV-2. Eur. J. Nucl. Med. Mol. Imag. 47 (5), 1275–1280.

Yang, S., Xu, M., Lee, E.M., et al., 2018. Emetine inhibits Zika and Ebola virus infections through two molecular mechanisms: inhibiting viral replication and decreasing viral entry. Cell Discov. 4, 31.

Yi, L., Li, Z., Yuan, K., Qu, X., Chen, J., Wang, G., Zhang, H., Luo, H., Zhu, L., Jiang, P., Chen, L., Shen, Y., Luo, M., Zuo, G., Hu, J., Duan, D., Nie, Y., Shi, X., Wang, W., Han, Y., Li, T., Liu, Y., Ding, M., Deng, H., Xu, X., 2004. Small molecules blocking the entry of severe acute respiratory syndrome coronavirus into host cells. J. Virol. 78 (20), 11334–11339.

Yousefzadeh, M.J., Zhu, Y., McGowan, S.J., 2018. Fisetin is a senotherapeutic that extends health and lifespan. EBioMedicine 36, 18–28.

Zhuanga, M., Jiangc, H., Suzukia, Y., Lia, X., Xiaoa, P., Tanakad, T., Ling, H., Yange, B., Saitoha, H., Zhangc, L., Qinc, C., Sugamuraf, K., Hattori, T., 2009. Procyanidins and butanol extract of *Cinnamomi* cortex inhibit SARS-CoV infection. Antiviral Rev. 82 (1), 73–81.

Zirihi, G.N., Mambu, L., Guédé-Guina, F., Bodo, B., Grellier, P., 2005. In vitro antiplasmodial activity and cytotoxicity of 33 West African plants used for treatment of malaria. J. Ethnopharmacol. 98 (3), 281–285.

Zoraima, N., Marta, M., Lindeza, Ana, do Rosário, Virgílio, Gazarini, Marcos L., Dinora, L., 2013. Treatment of Plasmodium chabaudi parasites with curcumin in combination with antimalarial drugs: drug interactions and implications on the Ubiquitin/Proteasome system. Hindawi 2013, 11.

Zou, L., Hu, Y.Y., Chen, W.X., 2015. Antibacterial mechanism and activities of black pepper chloroform extract. J. Food Sci. Technol. 52 (12), 8196–8203.