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

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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
(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 in 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 deaths (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 (Renaud, 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 SARSCoV-2 (Guang 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 (Guang 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 cytototoxic 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-ferritinemia; 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. CD4þ and CD8þ 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 þ T cells enhance the synthesis of viral-specific antibodies by activating T cell-dependent B cells. While CD8þ 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 CD8þ T cells. They perform important functions in scavenging and coronaviruses in infected cells (Maloiy et al., 2018). Furthermore, T helper cells produce proinflammatory cytokines through the NF-κB signaling pathway (Mannit 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 (SARS-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
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 it by 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 Ca²⁺ ion channel that is related to SARS-CoV-2 gene 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-1β 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, Ca²⁺ influx, mitochondrial damage, and caspases activation converts pro-IL-1β to IL-1β 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 chemo-attractant 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 many other differences (Huang et al., 2020).

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...
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 cytoprotective 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.
are being used extensively in traditional medicine as malaria therapy. Table 1 below show the comprehensive list of indigenous medicinal plants used 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-Acetylsiwentienolide, 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-hydroxyoctadeca-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 *Boerhavia 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 boerainovine, Punarnarine, punarnavoside, hypoxanthine 9-L-arabino-furanoside, liiordanendrin 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 candidate 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 the enhancement 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 μg/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 α, and IFN α, j3. Furthermore, they are at least partially responsible for the antiviral activity of *Echinacea 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 aseous extract showed strong antiviral 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 phytocompounds contributed to the antiviral activities of the plant include rutin, gallic acid, caffeicquinic acid, geraniin, corilagen, galloylglyceropyranose, digalloylglyceropyranose, trigalloylglyceropyranose, 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 trans- fected 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-diethylthiazol-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 androg- rapholid 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 infec- tion, reduced the MDA content and increased the SOD activity. At the same time, the innate immunity was affected by regulating the expres- sion of TLR3, Tak1, TBK1, IRF3, and IFN-β in the TLR3-mediated sig- nalling pathway, thus exerting its antiviral effect in vitro (Li et al., 2019).

*Boireira* are genera of *Rubiaeae* 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, anti-tumor, anti-ulcer, larvicidal, gastrointestinal, and hepatoprotective have been reported from various extracts *Boireira*. These biological activities have been attributed bioac- tive compounds from the plant such as terpenoids, flavonoids, with al- kaloids and iridoids as the major active principles (Conserva et al., 2012). Phychochemical screening has shown the presence of alkaloid called emetine (Moreira, 1964). And this emetine has been re- 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 concentra- tion (IC50) in vitro and potant activity in vivo. Two mechanisms of action for emetine was also identified which are inhibition of ZIKV NS5
| S/N | Name of plant          | Local/common Names | Active ingredient                                                                 | Reference                        |
|-----|------------------------|--------------------|-----------------------------------------------------------------------------------|----------------------------------|
| 1   | Acanthospermum hispidum | Egungun arugbo     | 1 (15-acetoxy-β-[2-(methylbutyryloxy)]-4-o xo-4,5-cis-acanthospermolide) and 2 (9α-acetoxy-15-hydroxy-β-[2-(methylbutyryloxy)]-4-o xo-4,5-trans-acanthospermolide). | Ganfon et al., 2012             |
| 2   | Allium sativum         | Ayuu               | Allicin, Ajoene                                                                    | Coppi et al., 2006               |
| 3   | Alstonia boonei        | Ahun               | DPs-Octyl phthalate; 3-Nitrophthalic acid, bis-(2, ethylhexyl-ester) and Bis-(3, 5, 5-trimethylhexyl) phthalate | Imam et al., 2017               |
| 4   | Anacardium occidentale | Kasu               | kasu anacardic acids, cardols, and 2-methylcardols derivatives                     |                                  |
| 5   | Ananas comosus         | Ope-Oyinbo         | Fatty acids (linoleic acid and palmitic acid)                                      | Uzor et al., 2020                |
| 6   | Azadirachta indica     | Dogonyaro          | Azadiractin and limonoids                                                          | Mull and Su, 1999, Dhar et al., 1996, Nathan et al., 2005 |
| 7   | Bridelia ferruginea    | Ido                |                                                                                  |                                  |
| 8   | Canass indica          |                    |                                                                                  |                                  |
| 9   | Capsicum frutescens    |                    |                                                                                  |                                  |
| 10  | Carica papaya          | Ibepe              | Papain, cystatin                                                                  | Seigler et al., 2002             |
| 11  | Ceiba pentandra        | Araba              | pentandrin and pentandrin glucoside and beta-sitosterol and 3-beta-D-glucopyranoside | Ngounou et al., 2000             |
| 12  | Chromolaena odorata    | Ewe Akintola       | 3, 5, 7, 3′ tetrahydroxy-4′-methoxyflavone                                        | Ezenyi et al., 2014              |
| 13  | Chrysophyllum albidum  | Aghalumo           | stigmastanol tetracosanoate                                                        | Idowu et al., 2016               |
| 14  | Cinus aurantifolia     | Osanweve           | apigenin                                                                          | Adeoye et al., 2019              |
| 15  | Cinus aurantium        | Orn ganingan       | D-limonene                                                                        | Sanel-Dekordi et al., 2016       |
| 16  | Cinus paradisi         | Osan gerepu        | 2-heptanone (24.18 %), 3(Z)-hexen-1-ol, (23.04 %), hibiscene (12.61 %), a-cadinol (6.51 %) | Ogunjinmi et al., 2017           |
| 17  | Curcuma longa          | Laali-pupa         | curcumin                                                                          | Zoraima et al., 2013             |
| 18  | Cymbopogon citratus    | Kooko-Oba          | geraniol, neral, myrcene and beta-pinene                                           | Tchombougoung et al., 2005       |
| 19  | Diospyros mespiliformis| Igidudu            | Lupeol                                                                            | Muhammad et al., 2017            |
| 20  | Enantia chlorantha     | Osopa              | palmatine and jatrophrizine, protoberberine alkaloids                              | Vennerstrom and Klayman, 1988    |
| 21  | Gossypium barbadense   | Owu                | gossypol                                                                          | Razakantoanina et al., 2000      |
| 22  | Gossypium hirsutum     | Ela-owu            | Kaempferol                                                                        | Somuak et al., 2018              |
| 23  | Harungana madagascariensis | Asunje, aroje     | Bazouanthrone, furuginin A, harunganin, harunganol-A, harunganol B, friedelanol-3-one and betulanic acid | Lenta et al., 2007               |
| 24  | Heliotropiumindicum    | Operi -akuko       | Pestalamide and Glycinamide,N-(1-oxooctadecyl)-glycinamide,L-histidyl               | Duttangupta and Dutta, 1977      |
| 25  | Hystis aucuoluens      |                    |                                                                                  |                                  |
| 26  | Khaya grandifoliola    | Oganwo             | oleic acid (33.83%), decylene 0.45, Methyl tridecanoate 0.32, Dodecanolic acid 1.00, Methyl tridecanoate 0.66, Palmitic acid 0.24, Tridecanoic acid, 6.42, Hexadecanoic acid 18, Linolesaidic acid, 5.4, Methyl-11-octadecenoate 0.52, Stearic acid 3.6, Stearic acid 9, 15-Tetraenoic acid 2.12, trans-13-Docosenoic acid 4.59, Methyl erucate 2.9, Methyl behenate 1.16 | Okpe et al., 2018 |
| 27  | Mangifera indica       | Mangoro            | Quercetin and mangiferin                                                          | Awe et al., 1998, Bidla et al., 2004, Zirhi et al., 2005 |
| 28  | Melicocoxelas          | Iroko               | berberine                                                                        | Dkhiil et al., 2015              |
| 29  | Mondia whita           | Isirigun           | 2-Hydroxy-4-methoxybentaldehyde                                                   | Kokwaro, 1993                   |
| 30  | Morinda lucida         | Oruwo              | asperuloside, asperulosidic acid, stigmasterol, β-sitosterol, cycloartenol, campesterol and 5,15-O-dimethylmorinol | Chithambo et al., 2017           |
| 31  | Nauclealatifolia        | Egberesi           | strictosamide, naucleamide A, naucleamide B, quinovic acid-3-O-β-rhamnosylpyranoside, and quinovic acid 3-O-β-fucosylpyranoside | Ata et al., 2009 |
| 32  | Ocimum gratissimum     | Efinrin-nla         | 3-allyl-6-methoxypheno1, 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        |
| 33  | Parquequina nigrescens | Ogbo               | cardenolides                                                                     | Nafiu et al., 2014              |
| S/N | Name of plant                     | Local/common Names          | Active ingredient                                                                                                                                                                                                 | Reference                                      |
|-----|----------------------------------|-----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|
| 37  | Pergularia daemia                  | Atusa, Isirgun              |                                                                                                                          | (Ss et al., 2011).                            |
| 38  | Physalis angulata                  | koropo                      | Physalins F and D                                                                                                      |                                               |
| 39  | Psidium guajava                    | guava                       | Eugenol                                                                                                               | Raja et al., 2015                              |
| 40  | Pycnanthus angolensis              | Akomu                       | Pycnantonol, lignans (\text{-})-dihydroguaiaetic acid, heliobuphalmin, talamudin, hinokinin, the labdanetype diterpenes oic acid, and the steroids stigmat-\text{-}4-en-\text{-}6\text{-}ol-3\text{-}one, \text{-}\text{-}sittosterol and stigmastoterol | Abrantes et al., 2008                         |
| 41  | Rauvolfia vomitoria                 | zofeyeje                    | raucacafficine                                                                                                        | Tlapi et al., 2019                             |
| 42  | Senna podocarpa                    | 1,2-benzeneedicarboxylic acid, mono (2-ethylhexyl) ester phthalate (26.6%) and \text{-}\text{-}elemene (27.9%). These were significant amounts of caryophyllene oxide (7.3%), urs-12-en-24-oic acid, 3-oxo-methyl ester (5.5%), \text{-}\text{-}caryophyllene (3.1%), \gamma\text{-}murolone (3.0%) and (3\text{-}\text{-}lup-20 (29)-en-3-ol, acetate (3.0%). | Adebayo et al., 2014                         |
| 43  | Senna siamea                       | Kania                       | caxsinar A                                                                                                            | Ekasari et al., 2009                           |
| 44  | Solanum nigrum                     | Odu                         | 1, 2-benzeneedicarboxylic acid, dibutyl phthalate, phytol, Lauric acid, 3,7,11,15-Tetramethyl-2 hexadec, 7-Hexadecenal | Rawani et al., 2017                            |
| 45  | Sphenocentrum zollinum             | Akererejpon                  | \alpha\text{-}xylanego, guaia-6,9-diene-4s-ol, globolol, guaniene-11-o, \alpha\text{-}eudesmol, isocaryophyllene, aromadendrene, selina-4 (15),6-dien E \beta\text{-}isocaryophyllene, \gamma\text{-}terpinene, humidulene, epiz zonearenre, 6-amorphone, 1,8-cineol, camphene, B pinene, p-cymene, d3-carene | Olorunnisola and Afolayan, 2013               |
| 46  | Tithonia diversifolia              | Jogbo Aghale                | Taginin C                                                                                                             | Goffin et al., 2002,                          |
| 47  | Trema orientalis                   | Afefe                       | dihydrophenanathrene and phenyl-dihydrosoxocumin                                                                   | Djoux-Franca et al. (2001)                     |
| 48  | Vernonia amygdalina                | Ewuro                       | vernolide, vermodalin, hydroxyvermolide and vernolodol, vernoniosides B1-B2 and vernoniosides A1-A4                     | Kraft et al. (2003), Challand and Willcox (2009) |
| 49  | Xylopa aethiopica                  | Erinje Euru                 |                                                                                                                          |                                               |
| 50  | Zingiber officinale                | Ajo, Ata-ile                | \alpha\text{-}zingiberene, ar-carcumene, \beta\text{-}bisabolene and \beta\text{-}sesquiphellandrene, gingerol             | Sharifi-Rad et al. (2017)                      |

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 result in 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 immunosuppressants have been used to control and suppress inflammatory diseases but with associated unwanted side effects. Thus, the need for natural anti-inflammatory agents has 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 compared 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 inhibition 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).
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. The result showed that ginger possess an 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 (Mahalji et al., 2013). Other medicinal plants with anti-inflammatory properties that could offer protection against coronavirus-induced inflammation include *Combretum mucronatum*, *Ficus isolepida*, *Moringa oleifera* (*Moringaceae*), *Schwenkia americana*, *Alafia barteri*, *Dichrostachys cinerea*, *Capparis thornyii Schum*, *Cassia occidentalis* (*Caesalpiniaeae*), *Asparagus africanus*, and *Indigofera pulchra*.

### 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/asoyeye in Yoruba, Kashinyaro in Hausa, Yawo in Fulani | chicoric acid, polyacetylenes and alkamides | Binns et al. (2002a); Hudson and Towers (1999) |
| 3   | *Boerhavia diffusa* | Etiponla, olowoje in Yoruba | Boeravonine. | Awasthi and Verma (2006) |
| 4   | *Phyllanthus amarus* | Oyomokeisomankewed in Efik, ‘IyinOlobe’ in Yoruba and ‘Ebebenizo’ in Bini | gallotannin, ellagittannins geraniin and corilagin | Patela et al. (2011) |
| 5   | *Andrographis paniculata* | Ewe-ega in yoruba | andrographolide | Churiyah et al. (2015) |
| 6   | *Astroglossus membranaceus* | Shakanbera in Hausa and ‘alalaki | Astragaloside. | Juam et al. (2007) |
| 7   | *Borretia verticillata* | Hausa: damfurkami, Yoruba: irawo-ile | boorereverine | Balde et al. (2015) |
| 8   | *Licorice (Glycyrrhiza glabra)* | Ewe ominsimisim in Yoruba, asukimateazi 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 | saffinicolide and sageone, | Tada et al. (1994) |

### 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   | *Curcuma longa* | (Igbo) | 9-tetrahydrocannabinol | Khajuria et al. (2020) |
| 3   | *Allium sativum* | (Igbo) | Allicin | Nencini et al. (2011) |
| 4   | *Cannabis sativa L.* | Igbo in Yoruba | 9-tetrahydrocannabinoil | 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   | *Telifaria occidentalis* | Ugwu in Igbo | anthocyacin, ascorbic acid, β-carotene, flavonoids, folic acid, polyphenol and alkaloid | Scalbert et al. (2005) |
| 8   | *Vernonia amygdalina* | evuro | Vernodalin, Vernomyglin, Epivernodal, Vernodalol | Kupchan et al. (1969); Owoeye (2010); Ezro et al. (2006) |
| 9   | *Garcinia kola* | Orue-ewuro in Yoruba, Adu/aku-imu and Namiji goro in Hausa | apigenin-5,7,4’-trimethyl ether, apigenin-4’-methylether, fisetin, amento-flavone, kolaflavonane and GB1 | Iwu (1982) |
| 10  | *Ocimum basilicum* | Efirin in Yoruba Nchauwu in Igbo and Dadoya in Hausa | Eugenol, methyl eugenol and methyl charvicol | Bunrathep et al. (2007) |
| 11  | *Psidium guajava* | gurola | Saponin, oleasolic acid, lypoxygenaste, aromoypuranoids, geuajavarin, quereretin and flavonoids | Das (2011), Arima and Dann (2002) |
| 12  | *xyllopia aethiopica* | Eru/Erunje in Yoruba, Udu in Igbo and Kimba in Hausa | β-pinene (16,016%), α-pinene (10,39%), and β-eudesmol (12,66%), α – eudesmol (3.7 %), α- cubeene (4.05%), aryozyllene ox (3.21%) | Karioti and Hadjipavlou-Litina (2004) |
| 13  | *Parkia biglobossa* | 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 mombii* | Iyeye in Yoruba, | Geraniin and galloyl geraniin | Cortiout et al. (1991) |
| 15  | *Mus communis* | Ogede Aghbaghai Yoruba, Ahrak in Igbo and ayaha in Hausa | Ferulic acid | Kumar and Pruthi (2014) |
| 16  | *Asparagus officinalis* | Dongoyaro in Yoruba, Atu yabanogwu akon in Igbo and Maina in Hausa | (2,3-S)-hexahydroxylphenyl-(α/β)-D-glucopyranose, Aviculain and Castalingin | 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 synthesis and release of diverse molecules such as cytokines which participate in the improvement and modulation of the immune responses (Gumnet et al., 1999; Vigila and Baskaran, 2009). 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-booster 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 naphroprotective 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 viscosa, Barlieranacti- flora, Anacardium occidentale, Dutta fustusos, Caesalpinia pendunculata 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 peroxide (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 de-rivatives 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 been 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 ‘Dongyaro in Yoruba, Atuyabasi/ogwuakom in Igbo and Maina in Hausa word. Seeds, oil, 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, antiplasmodial, 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 purposes. Ginger belongs to the Zingiberaceae family which has been reported to contain over 2500 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 anti-inflammatory, 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 Subba, 2018). All main active constituents of Zingiber officinale Roscoe, such as zingerone, gingerdil, zingibrene, gingerols and shogaols, has been proven to have anti-oxidative activities (Chrubask et al., 2005) and this antioxidant activity in ginger is due to the existence of polyphenol compounds like (g-terpineol and its derivatives. The main active constituents of ginger are Volatile oil (zingiberene, curcumene, farnesene, zingiberal, 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 ‘konys’ is the Greek name of Inula heliomen 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-terpinenone, 1% of it contains sabine, 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, 1.6% contains α-pinene, and 1.8% methyleugenol (Rao and Nigam, 1973). The major sesquiterpenes are beta-caryophyllene, δ-cadinene (Rao and Nigam, 1973), Sesquiphellandrene and Caryophylleneoxide (Ekundayo et al., 1988). The plant has been examined on the basis of the 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 ascorbic acid and polyphenols. The polyphenols are major antioxidants which are very important both for proper functioning of life and help to mitigate free radicals activities. Guava 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). Allcic 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 allin, 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, calcium, alkaloids, flavonoid, polybetalin and glycoside (Pathari et al., 2011). Alpinetin and fisetin have also been documented as potential inhibitors of coronavirus-2 in an in silico investigation (Oladele et al., 2020e). Concerted efforts have already been made to synthesise new compounds and find new uses for the drug. The present report is an attempt to revive the interest in the drug and assessing the current situation with the present findings.

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 (Bounaya 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 vegetative 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 bilayer 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 lipophelic 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., 2019). 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 I. 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 salicin, nimbain, 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)) (Bisbado 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), _Rubiaeaceae_ is rich in quinine (8S, 9R)-6-methoxychinconchelana-9-ol; (8R)-α-(6-methoxy-4-quinoryl)-α-(25, 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). _Cinnamomum verum_, of the genus Cinnamonum (Family Lauraceae), contains proanthocyandin (epi) catechins. It has been shown to have antiviral, antibacterial, antioxidant, anti-inflammatory, and immunomodulatory properties (Kumar et al., 2019; Polansky and Lori, 2020). Its extract has anti-IRNA 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 (Mhiri et al., 2017). The flower extract of _Citrus aurantium_ protected cardiomyocyte cell membrane in Isoproteon pre-treated male rats (Keshhtar 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-inflammatory 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 (DeFilips and Kupnich, 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, which selectively induces death of senescent cells to alleviate age-related diseases (Yousefzadeh et al., 2018). Fisetin, quercetin, isorhamnetin, genistein, 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 (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.

_Alilium sativum_ belonging to the Amaryllidaceae family, known as Anyu 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 folkloric 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 (Mikail 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

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).

_A. leiocarpa’s_ root and bark are used traditionally in the treatment of cough, gonorrhea, asthma, tuberculosis.
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, antidia- betic, 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).

*Heliotropium indicum* known in English as Indian heliotrope is also called Agogo Igun in Yoruba native of Nigeria is an annual plant belonging to the Cactaceae family of the genus *Heliotropium* endemic to Nigeria (Hutchinson and Dalziel, 1978). It is popularly called Oganwo in Yoruba native of Nigeria, and also called Benin Ma-

*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 rheuma, malaria fever in Nigeria and also used to treat warts, in 

*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 rhizo-

**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; immuno-

**Declarations**

**Author contribution statement**

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