

Experiences and challenges of African traditional medicine: lessons from COVID-19 pandemic

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To cite: Mutombo PN, Kasilo OMJ, James PB, *et al*. Experiences and challenges of African traditional medicine: lessons from COVID-19 pandemic. *BMJ Glob Health* 2023;**8**:e010813. doi:10.1136/bmjgh-2022-010813

Handling editor Seye Abimbola

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjgh-2022-010813>).

Received 29 September 2022
Accepted 24 April 2023



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ABSTRACT

Management of COVID-19 in Africa is challenging due to limited resources, including the high cost of vaccines, diagnostics, medical devices and routine pharmaceuticals. These challenges, in addition to wide acceptability, have resulted in increased use of herbal medicines based on African traditional medicines (ATMs) by patients in Africa. This is in spite of the often-significant gaps in evidence regarding these traditional medicines as to their efficacy and safety for COVID-19. African scientists, with some support from their governments, and guidance from WHO and other bodies, are addressing this evidence gap, developing and testing herbal medicines based on ATMs to manage mild-to-moderate cases of COVID-19. Such efforts need further support to meet public health needs.

BACKGROUND

Since the emergence of COVID-19 in China in 2019, the health, social and economic impacts of the disease have been felt across the globe. While there has been rapid and unprecedented progress in development of vaccines and new therapies, access to these products in sub-Saharan Africa is constrained. Global therapeutics and vaccine inequities and the emergence of new variants have created challenges in controlling COVID-19 across the African continent.¹⁻⁵

Thus, in considering Africa's pandemic preparedness, it is important to understand and learn from, the current experiences from COVID-19. At the onset of COVID-19, there was general concern about how Africa would manage the pandemic given its limited resources, and poorly developed and fragile healthcare systems.⁶⁻⁷ The balance between protecting livelihoods while managing the pandemic with non-pharmacological measures such as lockdowns and social distancing; was also of concern, and debate

SUMMARY BOX

- ⇒ African traditional medicines (ATMs) or therapies are widely used on the continent to meet healthcare needs because of ease of access, low cost and cultural acceptance. However, there is a paucity of clinical evidence on their safety, efficacy and quality to support their use in general. As a result of the COVID-19 pandemic, there was increased use of ATMs as people tried to protect themselves and their families.
- ⇒ The WHO issued position statements acknowledging the importance of traditional medicine, established a Regional Expert Advisory Committee on Traditional Medicine for COVID-19 Response, strengthened the capacity of experts and researchers through a series of regional consultations on the contribution of traditional medicine to COVID-19 and is providing technical support and guidance for clinical testing of ATMs.
- ⇒ This paper highlights some of the ATM-based interventions that were used and identifies the obstacles to the integration/mainstreaming of traditional medicines proposed for COVID-19 as the absence or paucity of clinical data on the safety, efficacy and quality as well as the lack of resources (human and financial) for robust clinical trials.
- ⇒ There is a need for resources to be invested in mainstreaming ATMs as part of pandemic preparedness and response in Africa given the low access to, and high cost of, vaccines and conventional medicines. Such resources would include building and strengthening the capacity of researchers and clinicians to conduct research into plant-based remedies, capacitating national regulatory authorities, increased funding of clinical research to validate medicinal claims.
- ⇒ There is a need to create collaboration between conventional and traditional healthcare workers so that there is complementarity to the benefit of African patients.
- ⇒ This paper aims to draw attention how ATMs can be mainstreamed by conducting appropriate clinical testing and providing adequate regulation to ensure that good quality, safe and efficacious remedies are promoted. Additionally, this will build and maintain trust in traditional health workers.

still rages on the effectiveness of the latter and long-term impact of the former.⁸ COVID-19 disease management was largely limited to supportive treatment for symptomatic cases, with severe cases more likely to have higher mortality due to the lack of specialised care and access to basic treatments such as corticosteroids, antibiotics, oxygen and ventilators.⁹

With limited access to conventional health products and amid a deadly global pandemic, some Africans turned to the use of traditional therapies such as herbal medicines, one of the few therapies to which they had easy access. This is not unprecedented, as the use of traditional medicines in Africa has been reported recently for patients with AIDS symptoms in Malawi, South Africa, Uganda and Zimbabwe and as the main source of healthcare for mental illnesses in Uganda.¹⁰ Due to the high proportion of patients using herbal medicines (as high as 70% in Ghana for example), some health facilities have initiated the use of herbal medicines as a component of healthcare delivery.^{10 11} More recently, in the context of infectious diseases with some similarity to COVID-19, Ebola survivors in West Africa appeared to turn to herbal medicines not only for treatment but also to fill the gaps in conventional healthcare services.¹²

The practice of traditional medicine has always been popular in Africa though it remains largely sidelined from the formal healthcare system for various reasons, chief among them being the paucity of data on the safety, efficacy and quality of most medicinal plants; stigmatisation due to poor perceptions and attitudes; inadequate efforts to conserve medicinal plants and Indigenous knowledge; modernisation; exploitation of communities that own the knowledge; the history of colonialism and secrecy in traditional medicine practices with few reports or documentations of adverse reactions.¹⁰ However, the future of African traditional medicines (ATMs) is bright if viewed in the context of service provision, an increase of healthcare coverage, economic potential and poverty reduction. Formal recognition and integration of traditional medicine into conventional medicine will ensure a promising future.

Due to the increased health needs and largely unknown nature of COVID-19, the WHO and its partners called on African scientists to urgently accelerate research and development (R&D) of traditional medicines for COVID-19.^{13 14}

ATM-BASED THERAPIES IN THE MANAGEMENT OF COVID-19 IN AFRICA

ATMs can complement healthcare systems if they are proven to be safe, effective and of high quality through R&D, a process that has been completed for malaria, HIV/AIDS, diabetes, hypertension and sickle-cell disease.^{15 16} Such advancement in R&D has resulted in more than 40 herbal medicines being included in national essential medicines lists across the WHO-AFRO region.¹⁷ In the absence of curative conventional

medicines for COVID-19, most African communities in Eastern,¹⁸ Southern and West Africa, reported wide use and perceived high efficacy of traditional medicines to prevent and treat suspected symptoms of COVID-19.¹⁹ These were generally obtained from preparations that were indicated in traditional African medicine systems for 'respiratory diseases' with antiviral, anti-inflammatory, antioxidant, antipyretic, immunomodulatory and cytoprotective properties. Early research appeared to support the potential of African medicinal plants. For example, investigators in Nigeria reported at least a hundred indigenous medicinal plants with potential therapeutic value in the treatment of COVID-19 based on their antiviral, anti-inflammatory, antioxidant, antipyretic, immunomodulatory and cytoprotective properties.^{20 21} The herbal medicines were used alone or combined with public health recommendations, and were relatively easy to use. The oral route was the most common means of administration, with the most commonly used plants being spices such as cinnamon, clove, garlic, ginger, lemon and leaves of plants such as eucalyptus, guava, lemon, lemongrass, local mint plant and neem. The most commonly reported parts used for herbal medicine were seeds, followed by leaves.

In addition, inhalation of vapour produced by boiling a combination of plant parts or spices while covered up with cloth was also used as a means of administration of herbal medicines for COVID-19 in several countries such as Tanzania, Zambia and Uganda.^{18 22}

In some countries, shea butter was applied on the nose of children to relieve congestion.²² Other herbal medicines used include onion (Ghana), honey mixed with plants (Algeria) and lemon leaves (Mali).^{22 23}

This flexibility, accessibility and relative ease of administrative options resulted in high utilisation of ATMs. A study conducted in Ethiopia, for example, indicated that almost half (46.2%) of the participants used traditional medicines to prevent and treat COVID-19 cases.²⁴ This finding mirrored results globally—in Hong Kong, for example, 44% of the surveyed participants were found to have practised traditional medicines to prevent and treat COVID-19.²⁵

With fewer resources to contain the spread of COVID-19 in Africa, the potential for new variants and endemicity, and underlying support for integration, there is a strong case for enhanced R&D of ATMs-derived herbal medicines for the prophylactic and therapeutic management of the disease, particularly as a complementary treatment measure.^{13 14} The results of early scientific examination suggest, for example, that traditional medicines from ATMs and other traditions can be effective as adjuvant symptomatic treatment for some clinical manifestations of COVID-19.²⁶ Reverse pharmacology approach to investigate medicinal plants used in ATMs with putative anti-viral properties could serve to identify new preventive and therapeutic agents for inhibition of SARS-CoV-2 and the treatment of COVID-19. Ethnopharmacological evidence highlights the extensive use of specific

medicinal plants for COVID-19-like symptoms by certain ethnic groups in Africa, which may assist with identifying candidate medicinal plants or plant recipes for further R&D.²⁷ Results may have regional or even global significance, as there is anecdotal evidence suggesting that some traditional medicines are effective across various diseases and sociocultural contexts.^{28 29} The shared flora between Africa and other continents with similar cross-cultural therapeutic uses may further help refine potential resources for examination.²⁹ For example, *Zingiber officinale* (ginger), which is found in Africa is used in the traditional medicine systems of Bangladesh³⁰ and Thailand³¹ for the symptomatic treatment of COVID-19.

Several ATMs-based therapies are undergoing evaluation for their role in the treatment/management of COVID-19, including clinical trials by scientists.³² Clinical trials of herbal medicines as adjuncts in the treatment of COVID-19 are either completed or ongoing in Burkina Faso, the Democratic Republic of Congo (DRC), Ghana, Guinea, Madagascar, Nigeria (which has the only privately funded study), South Africa, United Republic of Tanzania and Uganda, while clinical observational studies were conducted in Benin, Burkina Faso, Congo and DRC.³³ In South Africa and Tanzania, multicentre clinical trials of herbal medicines are ongoing. In some countries such as DRC, Guinea, Madagascar and Uganda, some of these products have received marketing authorisation.

BENEFITS AND CHALLENGES ASSOCIATED WITH THE USE OF ATMS

The easy access to ATMs by most Africans, regardless of demographic and socioeconomic status,^{10 34 35} is largely due to its affordability and roots in the culture of the people. Such attributes make it a potentially valuable component of the healthcare system, especially in responding to health emergencies, as with the COVID-19 pandemic. Studies have also shown that traditional health practitioners (THPs) are more accessible to the populace with a significantly higher proportion of THPs (1:500 persons) than conventional medical practitioners (1:40 000 persons).³⁵ Further, Africa has high biodiversity, which enriches the *materia medica* of the continent with over 5000 of the 40 000–45 000 000 known plant species found on the African continent, believed to have medicinal properties.³⁶ Studies have indicated that some of these plant species might have a role in managing COVID-19 (online supplemental table 1) due to their antiviral activities and its associated symptoms (online supplemental table 2). In some African countries, the use of these herbal medicines is reported to have been useful in the early management of the pandemic before the introduction of standard treatment guidelines.

Despite the abundant natural resources and the anecdotal value of traditional medicine, ATMs remains under-represented and underused in conventional health settings in Africa,²⁶ as demonstrated during the pandemic. While there are several reasons for this,^{11 37}

in the course of the COVID-19 pandemic, the challenges observed include widely publicised unsubstantiated claims of therapeutic activity, insufficient preclinical data, lack of clinical data to validate ethnobotanical claims and insufficient regulatory oversight.³⁸ Therefore, research needs to be directed at addressing these issues, especially the generation of clinical data to validate the use, while regulatory capacity should be strengthened. In addition, ethical and regulatory requirements for approval of national clinical trial protocols across Africa should be harmonised by the WHO.

The absence of a two-way referral system and linkage between ATMs and conventional health systems in most African nations creates mistrust between the two systems to the detriment of patients. As a result, most patients may not disclose ATMs use, thus increasing the potential for adverse reactions and the possibility of delayed diagnosis, among other risks.^{39 40} The unregulated status of many THPs and their medicines also creates accountability gaps increasing the potential for sub-standard and counterfeit products, professional malpractice and unethical conduct.

While there are ongoing efforts at undertaking the necessary research to validate the claims of efficacy of ATMs derived herbal medicines for COVID-19, they are hampered by the fact that many of the governments in these countries cannot afford to invest adequate financial resources to conduct phase III clinical trials. Second, the substantial reduction in the number of COVID-19 patients has made it difficult to obtain the sample size adequate to obtain robust data on the safety and efficacy of required to validate therapeutic claims according to universally accepted standards. Multicentre and multi-country clinical trials can be a way of addressing this challenge. The WHO, Africa CDC, the African Union Commission and the international community should jointly support countries fast track R&D and mobilise financial resources so that the products confirmed to be safe, efficacious and quality-assured (category 3 herbal medicines) can be locally manufactured and commercialised regionally and internationally.

Lessons learnt from the pandemic

The recourse to the use of ATMs in the early days of the pandemic in Africa demonstrated its continued acceptance by the general public. The poor documentation and validation of the claimed therapeutic value of the ATMs-derived herbal medicines limited their value in the fight against the pandemic. There is an urgent need to encourage and provide the resources needed for continuous research into ATMs-based herbal medicines with a view to provide necessary safety and efficacy data. This is particularly important for infectious disease outbreaks, where traditional medicines are often embraced enthusiastically by the public, and research demonstrates a potential role only after the acute phase.⁴¹ Strategies should therefore be implemented to maintain the enthusiasm that resulted in the provision of resources by most

African governments for the study of herbal medicines for COVID-19 during the pandemic.

The pace of R&D of herbal medicines will be enhanced by the establishment of consortia of researchers, the private sector and state institutions. In addition, regional collaborations will provide better access to resources and clinical trial participants to achieve the needed statistical power for studies.

There is a need to urgently strengthen the capacity of the National Regulatory Authorities and Ethics review committees to effectively and efficiently regulate the development and use of herbal medicines.

CONTRIBUTION OF WHO TO THE DEVELOPMENT OF ATMS FOR COVID-19

The WHO, in acknowledgement of the potential value of ATMs, is collaborating with partners to encourage and guide the development of ATMs for COVID-19 while alerting of the dangers of using non-approved herbal remedies without clinical evidence of their safety, efficacy and quality.⁴²

In collaboration with Africa Centers for Disease Control and Prevention (Africa CDC) and the African Union Commission (AUC) for Social Affairs, WHO set up a Regional Expert Advisory Committee on traditional medicine for COVID-19 Response (REACT) as a coordinating mechanism to elevate the standards of R&D through the pooling of expertise across the African continent for multicentre studies. Membership of the Committee which comprises country experts in various disciplines related to clinical trials on traditional medicines-based therapies includes the Africa Academy of Sciences and African scientists within the EDCTP (European & Developing Countries Clinical Trials Partnership).

As a demonstration of its support for the use of scientifically proven ATMs in the management of COVID-19, WHO, in collaboration with Africa CDC and the European and Developing Countries Clinical Trial Partnership (EDCTP), developed the standard protocols for the randomised, double-blind placebo-controlled phase III multicentre clinical trials to evaluate the safety and efficacy of herbal medicine compared with the standard of care for the treatment of hospitalised patients with mild-to-moderate cases of COVID-19; as well as a protocol for Clinical Observational Studies for preliminary assessment of the safety and efficacy of herbal medicines for the treatment of mild to moderate cases of COVID-19. The committee endorsed the protocols and charter for establishing the data and safety monitoring board, which the WHO Ethics Review Committee and the other relevant Ethics Committees and National Regulatory Authorities subsequently approved at regional and national levels.

A series of regional consultations organised by the WHO during 2020–2022 have encouraged experience sharing by countries in areas such as: Preclinical safety and efficacy studies of ATMs; Ethical and regulatory requirements for approvals and conditional registration

of herbal medicines for clinical trials of COVID-19; Clinical trials of ATMs for COVID-19; and Requirements of local manufacturing and good manufacturing practices.

WHO, Africa CDC and African Union continued to work together to harmonise the process for joint support to countries for conducting the clinical trials. Joint field missions composed of WHO, REACT, Africa CDC/AUC and EDCTP to monitor clinical trials of ATMs for COVID-19 were conducted.

Several informal and formal meetings of REACT held between 2020 and 2022, which culminated in the meeting on fast-tracking R&D of ATMs for COVID-19 and local manufacturing of herbal medicines convened by WHO in July 2022, resulted in the development of the criteria for selecting proposed COVID-19 traditional medicines that could be fast-tracked for R&D and local manufacturing. The REACT developed terms of reference for the selection of centres of excellence and hubs for the R&D and local manufacturing of herbal medicines in Africa as well as strategies to mobilise resources for fast-tracking R&D and local manufacturing of herbal medicines.

CONCLUSION

The devastating nature of COVID-19 forced countries to reconsider the resilience, capacity and available infrastructure of their health systems. Some countries employed innovative and unconventional interventions agents. In Africa and some parts of Asia, this has led to a repurposing of herbal medicines since traditional medical practice is already widely accepted and trusted in those regions. For instance, in Bangladesh and Thailand similar medicinal plants have been repurposed to combat COVID-19. An example is *Andrographis paniulata*, known locally in Thailand as ‘Fah Talai Jone’ has been used to treat COVID-19 in both Thailand and Indian traditional medicine systems.⁴³ Also, *Z. officinale* is used in folk medicine of Bangladesh and Thailand for symptomatic treatment of COVID-19.^{30 31} These examples strongly suggest traditional systems of medicine of other regions need to be considered and harnessed to facilitate drug discovery and development to tread COVID-19.

There was also widespread political support for such practices by African governments in the face of their populations’ low access to vaccines and conventional pharmaceuticals. However, few governments could mobilise resources for the relevant laboratory infrastructure to enable testing of the remedies people were using. Thus, while the potential contribution of ATMs to the COVID-19 response cannot be ignored, its credibility hinges on research to validate its use and establish the efficacy and safety of the products which are touted as being useful. To do this requires a strategy that provides resources to researchers, creates mutually beneficial collaborations between THPs and researchers and the active involvement of regulators in directing what needs to be done.

It is evident that African scientists collaborating with WHO and other bodies are addressing this evidence gap,

developing and testing herbal medicines to manage mild to moderate cases of COVID-19, though such efforts need further support to meet public health needs. Some early reports from preclinical safety and efficacy studies on ATMs have been encouraging. However, more funding for larger clinical trials is required to complete the evaluation that would provide evidence to inform clinical use. Collaborations between biomedical scientists, THPs and the private sector are critical to achieving this goal. Several research challenges in this field have been identified by African researchers, including limited funding for phase III clinical research, lack of involvement of knowledge holders (healers) and lack of implementation of enabling policies around mainstreaming ATMs and intellectual property and Indigenous knowledge protection and governance. Other challenges unrelated to resources include laborious administrative processes required by national ethics committees and national regulatory authorities to process clinical trial research protocols for ATMs can delay the research results of ATMs.

Mistrust between THPs, conventional medical practitioners and scientists remains a barrier to mainstreaming, product development and testing ATMs. Furthermore, the lack of specific training in ATMs in many academic and health institutions may reduce the potential for the inclusion of ATMs in scientific and research agendas.

To fully develop and exploit the potential of ATMs in the fight against COVID-19 and other priority diseases, African governments must take ownership of the development process and facilitate the building of a robust industry and attract private investment. This can be achieved by prioritising strengthening of research capacity in the national budgets of African countries. ATMs should also be explicitly included in national research strategies with aggressive fund mobilisation. It is only when ATMs products can be commercialised regionally, and internationally that they can gain global acceptance.

The COVID-19 pandemic has resulted in increased appreciation and use of ATMs and demonstrates the wide acceptability and confidence in its usefulness. In preparing for the next pandemic, given its wide acceptance and popularity, it is important to position ATMs to better serve as part of the response mechanism.

It is obvious that the infrastructure and attention set up in response to the challenges brought by the COVID-19 pandemic, would be equally suitable to other African health priority areas, where lack of adequate research capacity into ATMs derived herbal medicines has hampered development.

We conclude that traditional medicines can complement conventional pharmaceuticals in a time of crisis if they are proven to be safe and efficacious. The integration of such therapies is explicitly promoted in the Alma Ata declaration in 1978 and reaffirmed—and further expanded on—by the Astana Declaration of Primary Health Care in 2018. This will, however, require the generation of robust scientific data from well-designed studies. There is a need for the development

of new protocols, modification of existing ones, or the endorsement of appropriate existing protocols to ensure integration is done in a way that maximises the potential benefits of ATMs while minimising the risks of inappropriate promotion and misuse. The protocols developed by the WHO Regional Office for Africa specifically for testing ATMs for clinical efficacy in COVID-19 are a useful tool in this regard.

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Acknowledgements Special thanks to Maria de Lourdes PEREIRA from the CICECO-Aveiro Institute of Materials & Department of Medical Sciences, University of Aveiro, Aveiro, Portugal; Arletha W. LIVINGSTON from the Innovation Learning Laboratory for Population Health, Morehouse School of Medicine; Rianasoambolanoro RAKOTOSAONA from the Ecole Supérieure Polytechnique d'Antananarivo and Centre National d'Application de Recherches Pharmaceutiques CNARP, Antananarivo, Madagascar; and Polrat WILAIRATANA from the Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand)

Contributors All coauthors made substantial contribution to the conceptualisation, literature search, writing—original draft, editing and review.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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Supplement material

Table 1: Medicinal plants from African Traditional Medicine used against viral respiratory pathogens, with potential in the management of COVID-19

Medicinal Plant	Family	Parts used	Formulations	Antiviral/other activity reported	Results	References
<i>Acokanthera schimperi</i> (A.DC.) Schweinf.	Apocynaceae	Leaves	Multiple solvent extracts were tested	Antiviral activity	Inhibited 50% parainfluenza at a 1 in 10 dilution	1
<i>Aframomum melegueta</i> K. Schum.	Zingiberaceae	Seed.	Ethanol extract	Extract inhibited measles and yellow fever virus	Inhibited measles and yellow fever viruses at MICs of 125 and 250 µg/mL respectively	2
<i>Alepidia amatymbica</i> Eckl. & Zeyh	Apiaceae	Rhizomes and roots.	Aqueous extract	Isolated compound has moderate anti-HIV activity.	The extract contains rosmarinic acid with promising anti-HIV activity	3
<i>Allium sativum</i> L.	Amaryllidaceae	Bulb	Hexane extract	HIV-1 reverse transcriptase inhibitory effect of hexane extract	Inhibited HIV-1 reverse transcriptase activity. IC ₅₀ = 64.08 µg/mL	1
<i>Artemisia afra</i> Jacq. ex Wild	Asteraceae	Leaf	Tea infusions	Anti-HIV activity	Infusions showed anti-HIV activity	1,4
<i>Artemisia annua</i> L.	Asteraceae	Leaf	Tea infusions	Anti-HIV activity	Infusions showed anti-HIV activity. IC ₅₀ = 2.0 µg/mL	4
<i>Aspalathus linearis</i> (Burm.f.) R. Dahlgren	Fabaceae	Herbal tea made from dried leaves	Fermented and unfermented aqueous, Methanol and Ethanol extracts, infusions	Anti-HIV activity	Consumption of herbal tea can suppress human immunodeficiency virus (HIV) infections	5
<i>Aspalathus linearis</i> (Burm.f.) R. Dahlgren	Fabaceae	Leaves	Leaf infusions	Antiviral activity	The extract inhibited influenza virus A and B production by 50% at 0.2% of the extract	6
<i>Aspilia pluriseta</i> Schweinf	Asteraceae	Leaf	Ethanol extract	Anti-HIV activity	The extract showed a complete cell protection against HIV-induced cytopathic effect	7
<i>Bambusa vulgaris</i> Schrad. ex J.C. Wendl	Poaceae	Leaf	Ethanol extract	Antiviral activity	Inhibition of measles virus at an MIC of 62.5 µg/mL	8
<i>Barleria prionitis</i> L. subsp. <i>delagoensis</i> (Oberm.) Brummitt & J.R.I. Wood	Acanthaceae	Whole plant	Compound isolated from the Dichloromethane extract (6- <i>O</i> -trans- <i>p</i> -coumaroyl-8- <i>O</i> -acetylshanzhiside methyl ester and its <i>cis</i> isomer)	Antiviral activity	The compound inhibited syncytial virus (RSV) production (EC ₅₀ ¼ 2.5 µg/mL).	9
<i>Burkea africana</i> Hook.	Fabaceae	Bark	Purified saponins from Bark extract	Antiviral activity	Bark extracts and eight individual saponins purified from the bark produced potent inhibition of H3N2 influenza Hong Kong strain, with IC ₅₀ values 0.05–0.27 µM.	10

<i>Carissa spinarum</i> L.	Apocynaceae	Leaves	Multiple solvent extracts	Antiviral activity	Inhibited 25% parainfluenza production at a 1 in 10 dilution.	11
<i>Clerodendrum glabrum</i> E. Mey. var. <i>glabrum</i>	Lamiaceae	Leaves	Methanol extract	Antiviral activity	EC ₅₀ value 110 µg/mL against both pre- and post-penetration phases of viral replication. Solvent extracts were substantially more potent than aqueous extracts. No direct interaction with viral hemagglutinin glycoprotein.	12
<i>Costus afer</i> Ker-Gawler	Costaceae	Stalk	Decoction	Antiviral activity	Chicken pox, measles, influenza and genital herpes treatment	13
<i>Crassula globularioides</i> subsp. <i>argyrophylla</i> (Diels ex Schönlund & Baker f.) Toelken	Crassulaceae	Aerial parts	Methanol and Dichloromethane extracts	Antiviral activity	Dichloromethane extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >6 µg/mL	14
<i>Cucumis metuliferus</i> E. Mey ex Naudin	Cucurbitaceae	Fruit	Fruit powder	Antiviral activity	The alkaloids of the plant inhibited the replication of Infectious bursal disease virus (IBDV)	15
<i>Cussonia spicata</i> Thunb.	Araliaceae	Leaves	Methanol extract	Antiviral activity	EC ₅₀ values of 5–15 µg/mL effective against both pre- and post-penetration phases of influenza virus A replication. Solvent extracts more potent than aqueous extracts. No direct interaction with viral hemagglutinin glycoprotein	12
<i>Ekebergia capenses</i> Sparm.	Meliaceae	Bark	Extracted with multiple solvents of varying polarity	Antiviral activity	Inhibited 75% parainfluenza production at a 1 in 10 dilution	16
<i>Enantia chlorantha</i> Oliv	Annonaceae	Stem	Decoction	Antiviral activity	Hepatitis A, B, C and D treatment	17
<i>Helichrysum armenium</i> DC	Asteraceae	Leaves	Aqueous and ethanolic extracts	Antiviral activity	Inhibited parainfluenza virus production. MIC= 4 µg/mL	18
<i>Helichrysum melanacme</i> DC.	Asteraceae	Leaves	Ethanol extract	Antiviral activity	Inhibited influenza virus A production. IC ₅₀ = 10 µg/mL	18
<i>Heteromorpha arborescens</i> (Spreng.) Cham. & Schtdl.	Apiaceae	Root bark	Methanol and Dichloromethane extracts	Antiviral activity	Dichloromethane extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >25 µg/mL	18
<i>Holarrhena pubescens</i> Wall. ex G. Don	Apocynaceae	Bark	Methanol and Dichloromethane extracts	Antiviral activity	Dichloromethane extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >10 µg/mL	18
<i>Jasminum fluminense</i> Vell.	Olacaceae	Stems	Methanol and Dichloromethane extracts	Antiviral activity	Dichloromethane extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >50 µg/mL	18
<i>Momordica charantia</i> L	Cucurbitaceae	Entire plant	Palm wine and water macerate of plant, decoction, plant juice	Antiviral activity	Chicken pox, measles, genital herpes, shingles treatment	19

<i>Pelargonium sidoides</i> DC.	Geraniaceae	Unspecified	A proprietary preparation named EPs 7630 was tested	Antiviral activity	EPs 7360 at 100 µg/mL inhibited the replication of H1N1 and H3N2 influenza virus, parainfluenza virus, HRSV and human coronavirus strain 229E, but did not affect H5N1 influenza strain, adenoviruses and rhinoviruses	18
<i>Pittosporum viridiflorum</i> Sm.	Pittosporaceae	Leaf	Aqueous, methanol, ethanol and acetone extracts	Antiviral activity	EC ₅₀ 3–82 µg/mL against both pre- and post-penetration phases of influenza virus A. replication. Solvent extracts were substantially more potent than aqueous extracts. No direct interaction with viral hemagglutinin glycoprotein.	12
<i>Polygala lancifolia</i> A. St. -Hil. & Moq.	Polygalaceae	Aerial parts	Methanol and Dichloromethane extracts	Antiviral activity	Dichloromethane extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >12 µg/mL.	14
<i>Pteleopsis hylodendron</i> Mildbr.	Combretaceae	Bark	Decoction	Antiviral activity	Chicken pox treatment	20
<i>Pterocarpus angolensis</i> DC.	Fabaceae	Bark	Methanol and Dichloromethane extracts	Antiviral activity	Dichloromethane extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >12 µg/mL	18
<i>Rapanea melanophloeos</i> (L.) Mez.	Primulaceae	Leaves and twigs	Aqueous, methanol, ethanol and acetone extracts	Antiviral activity	EC ₅₀ 113 µg/mL against both pre- and post-penetration phases of influenza virus A. replication. No direct interaction with viral hemagglutinin glycoprotein.	12
<i>Spathodea campanulata</i> P. Beauv.	Bignoniaceae	Bark	Decoction	Antiviral activity	Chicken pox, genital herpes treatment	21
<i>Steganotaenia araliacea</i> Hochest.	Apiaceae	Root	Methanol and Dichloromethane extracts	Antiviral activity	Dichloromethane extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >60 µg/mL	14
<i>Tabernaemontana ventricosa</i> Hochst. ex. A.DC.	Apocynaceae	Leaves	Extracted with multiple solvents of varying polarity	Antiviral activity	EC ₅₀ values of 0.05 µg/mL against both pre- and post-penetration phases of influenza virus A. replication. Solvent extracts were substantially more potent than aqueous extracts. No direct interaction with viral hemagglutinin glycoprotein	18
<i>Vernonia amygdalina</i> Del.	Asteraceae	Leaf, root	Aqueous methanol extract	Anti-HIV activity	Extract contains phenols (caffeoylquinic acids) with antiviral activity	1
<i>Xanthocercis zambesiaca</i> (Baker) Dumaz-le- Grand	Fabiaceae	Leaves	Methanol and Dichloromethane extracts	Antiviral activity	Dichloromethane extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >60 µg/mL	18

Table 2 Medicinal plants used in African Traditional Medicine for some common COVID-19 related symptoms

Symptoms	Plant name	Family	Countries reported from	Parts used/ Formulations/anti-viral activities	Additional common uses
Fever	<i>Centella asiatica</i> (L.) Urb	Apiaceae	Nearly all African countries	Whole plant; a combination of <i>Centella asiatica</i> and <i>Mangifera indica</i> aqueous extracts showed anti-herpes simplex virus activities. ²²	Wounds, ulcers, leprosy, TB, lupus, skin disorders, eye illnesses, fever, asthma, inflammation, rheumatism, hypertension, syphilis, epilepsy, diarrhea, leprosy, and mental illness have all been treated with <i>C. asiatica</i> in the past. It's also used as a spice and eaten as a vegetable. ⁵
	<i>Crinum macowani</i> Baker	Amaryllidaceae	East, Central and Southern Africa	Bulb. Methanolic extract of bulbs showed activity against yellow fever virus and Japanese encephalitis virus. ²³	<i>Crinum macowani</i> 's bulbs, roots, and leaves are used to treat a variety of ailments throughout much of Africa, including back pain, as an emetic, and to increase lactation in both humans and animals, bodily swelling, urinary tract disorders, itchy rashes, acne, boils, diarrhoea, fever, tuberculosis, and sexually transmitted infections. The extracts of the plant show only moderate antifungal action, according to <i>in vitro</i> experiments. ²⁴
	<i>Vernonia amygdalina</i> Del.	Asteraceae	Cameroon, Uganda	Leaf, root. Traditionally used for HIV. Scientifically found to produce antioxidants in AIDS patients. ²⁵	Antiidiabetic, anthelmintic, antiplasmodial, antibacterial, cardiovascular, immunomodulatory, antiplasmodial, antioxidant, and antianaemic activities have been reported in <i>V. amygdalina</i> Del. ^{26,27}
Dry cough/coughs	<i>Acacia senegal</i> (L.) Willd	Leguminosae-Mimosoideae	Southern to Northern Nigeria, North Africa	Gum	Various components of the <i>A. senegal</i> plant have been used to cure infections such as bleeding, bronchitis, diarrhoea, gonorrhoea, leprosy, typhoid fever, and upper respiratory tract infections for millennia. ⁵
	<i>Tulbaghia violacea</i> Harv.	Amaryllidaceae	Southern Africa and Tanzania	Leaf. Used in traditional medicine for respiratory problems and also as an anti-viral, though specific viruses were not mentioned ²⁸	In African traditional medicine, <i>Tulbaghia violacea</i> Harv. (Alliaceae), a herbaceous plant also known as "wild garlic," "society garlic," and "sweet garlic," has been used to manage, regulate, and/or treat a range of human ailments, including hypertension and as an antifungal agent. ²⁹
	<i>Mangifera indica</i> L.	Anacardiaceae	Tanzania, Uganda	Bark, leaf. Dried fruit pulp extract inhibit influenza virus; ³⁰ mangiferin, obtained from fruit peels, exhibited inhibition of polio virus type 1 (PV-1); ³¹ aqueous extract of leaf showed inhibitory activity against Newcastle disease virus (NDV) and infectious bursal disease (IBD) virus. ³²	<i>M. indica</i> leaves are said to have anti-diabetic, antibacterial, antifungal, anthelmintic, antiparasitic, antitumor, anti-HIV, antispasmodic, antipyretic, antidiarrheal, antiallergic, immunomodulation, antimicrobial, and hepatoprotective properties, and have been used for centuries to treat malaria, throat infections, burns, and scalds. In the past, mango stem bark was used to cure menorrhagia, scabies, diarrhoea, syphilis, diabetes, skin problems, and anemia. ³³

<i>Cascabela thevetia</i> (L.) Lippold	Apocynaceae	Uganda	Root	An emetic made from a bark or leaf decoction is used to relax the bowels and is reported to be an excellent therapy for intermittent fevers. In Senegal, water with macerated leaves and bark is used to treat amenorrhea, while in Ghana, decoctions of the leaves are used to treat jaundice, fever, and as a purgative for intestinal worms. Latex is used in Mali to soften corns and calluses. The leaf sap is used as eye and nose drops in Benin and Côte d'Ivoire to treat strong headaches; it is also poured into the nostrils to revive patients who have fainted and to treat colds. To treat colds, the Luo people of Kenya drink water that has been crushed with leaves. Purgative properties are possible with the seeds. Because hazardous doses are just slightly greater than therapeutic doses, caution should be exercised in all medical applications, particularly those used internally.
<i>Acacia tortilis</i> (Forssk.) Schweinf.	Fabaceae	Djibouti	Plant is applied on burning charcoal and smoke inhaled nasally for dry coughs; same thing is done with roots for coughs with phlegm.	Diabetes mellitus is treated using polysaccharide extracted from gum exudates. For fungal illness, use stem bark. Diarrhoea is treated with Bark Tannins, Infectious Disease Stem Bark, Cough and Diphtheria with wood. Malaria treatment with root bark, hypercholesterolemia treatment with aqueous extract, and inflammation treatment with aqueous extract and methanol extract of <i>Acacia tortilis</i> for Leishmania and parasitic illness. ^{27,34}
<i>Guiera senegalensis</i> J.F. Gmel.	Combretaceae	Tropical Africa in dry areas from Senegal to Sudan	Decoction of leaves, roots and gall of the plant are used in the treatment of cough and tuberculosis ³⁵⁻³⁷ <i>Guiera senegalensis</i> J.F. Gmel is a broad-spectrum African folk-medicinal plant, having activities against fowlpox and herpes viruses and <i>G. senegalensis</i> leaves extract (GSLE) have potential for anti-hepatitis B virus (HBV). ³⁸	The extract from the leaves is used to treat jaundice, which accounts for more than 51.5 percent of the disorders treated; diabetes mellitus, hypertension, cough, arthritis, enteritis, diarrhoea, and malaria account for 48.5 percent of the other ailments treated. <i>Guiera senegalensis</i> root powder is used to heal wounds such as diabetic sores, skin inflammation, and injuries. ³⁹ Antitussive, bronchodilating, anti-infectious, analgesic, antipyretic, and anti-inflammatory qualities of the <i>Guiera senegalensis</i> could explain its use in the treatment of cough, bronchitis, tuberculosis, and colds. ⁴⁰
<i>Sterculia setigera</i> Del.	Sterculiaceae	East Africa, Ethiopia, Senegal, Sudan-Sahel, Sudan-Guinea, Nigeria and Togo	Décoction of stem barks of the plant ⁴¹ [Leaves, roots, bark of <i>S. setigera</i> have been found to possess anti-viral activity against three human and three animal viruses (Poliovirus (type 1), astrovirus, human herpes simplex virus (type 1), equine herpes simplex virus, bovine parvovirus and canine parvovirus have also been reported. ⁴²	Cough, stomachaches, gonorrhoea, acne, diarrhoea, rickets, wounds, and epilepsy are some of the conditions that <i>S. setigera</i> can help with. Stomachaches, heart palpitations, coughs, and rachitis are all treated with the bark. The stem bark decoction is used to treat asthma, bronchitis, wounds, fevers, toothaches, gingival sores, abscesses, and diarrhoea. To cure constipation, gum is utilized in the preparation of sauce. The gum is used to make couscous and sauces by Senegalese housewives. The herb is used to alleviate constipation in southwest Nigeria. Gum powder was used by Sudanese in the south-eastern part of the country to treat toothaches. ⁴³

	<i>Bridelia ferruginea</i> Benth.	Euphorbiaceae	Benin, Nigeria, Burkina Faso and Ivory Coast	Infusion of roots of the plant. ⁴⁴	<i>Bridelia ferruginea</i> is often used to cure a range of conditions in both general African and West African traditional medicine, including bladder difficulties, diabetes, diarrhoea, arterial hypertension, and rheumatic pain. ⁴⁵
	<i>Terminalia avicennioides</i> Guill. & Perr.	Combretaceae	Nigeria, South Africa and Tanzania	Maceration of leaves of the plant. ⁴¹	Bronchitis and TB are treated with trunk bark and guis of <i>Terminalia avicennioides</i> . Extracts of <i>Terminalia avicennioides</i> have been shown to have antimicrobial effects in vitro against bacteria isolated from individuals with respiratory disease problems, as well as anti-Mycobacterium tuberculosis activity in extracts of triterpenoids obtained from root bark. Antimicrobial activity has also been discovered in flavonoids and saponosides extracted from root bark.
	<i>Euphorbia hirta</i> L.	Euphorbiaceae		Whole plant parts are used ⁴⁶ The aqueous and 50% MeOH extracts of <i>Euphorbia hirta</i> demonstrated a specific inhibition of three types of immunodeficiency viruses: SIVmac251, HIV-1 and HIV-2 replication in MT4 cells in vitro ⁴⁷	Intestinal parasites, diarrhoea, peptic ulcers, heartburn, vomiting, and amoebic dysentery are all treated with <i>Euphorbia hirta</i> decoction or infusion, as well as respiratory disorders like asthma, bronchitis, hay fever, laryngeal spasms, emphysema, coughs, and colds. The leaves are used to treat urogenital diseases (kidney stones, menstrual problems, sterility, and venereal diseases); skin and mucous membrane affections (including warts, scabies, tinea, thrush, aphthae, and fungal afflictions); and measles, Guinea-worm, and as an antiseptic to treat wounds, sores, and conjunctivitis. The herb is used as an analgesic, antipyretic, and anti-inflammatory to treat severe headaches, toothaches, rheumatism, colic, and pains during pregnancy. It's used to cure jaundice, hypertension, oedema, anemia, and malaria, as well as hart an aphrodisiac and to make childbirth easier. The plants are commonly used as a galactagogue in West Africa, and they are even sold as such in Nigeria. To induce labor during childbirth in Uganda, whole herbs are consumed. ⁴⁸
Tiredness	<i>Crassocephalum vitellinum</i> S. Moore	Asteraceae	Uganda, Burundi, Cameroon, Kenya, Rwanda, Tanzania, Zambia, Democratic Republic of Congo	Leaf. Mode of use not given for energy boosting effect.	Fever, diarrhoea, oral candidiasis, syphilis, energy boosting, tumors, uterine pains, and headaches are all symptoms of herpes zoster. Essential oil and fractions were also found to have potent antifungal activity against <i>C. neoformans</i> and <i>C. albicans</i> . On the yeasts, the fractions were more active than the pure oil. The study found that after further fractionation of <i>C. vitellinum</i> essential oils, the hexane soluble fractions had the maximum sensitivity to <i>C. neoformans</i> . The water and ethanol extracts, on the other hand, were ineffective against the bacterial strains tested. The 38 ethanolic extract has poor antibacterial action in <i>C. vitellinum</i> , according to similar observations. ⁴⁸

Aches and pains	<i>Aloe ferox</i> Mill.	Xanthorrhoeaceae	South Africa, Lesotho	Gel applied topically. Aqueous extract of plant active against herpes simplex virus type 1. ⁴⁹	It's best recognized for its laxative qualities and as a skin, eye, and mucous membranes topical treatment. Scientific investigations have backed up many of the traditional applications. The cosmetic industry's interest in <i>A. ferox</i> gel has recently increased. <i>A. ferox</i> gel, according to sources, has at least 130 medicinal compounds with anti-inflammatory, analgesic, calming, antiseptic, germicidal, antiviral, antiparasitic, antitumor, and anticancer activities, spanning all traditional uses and scientific studies on <i>A. ferox</i> and its constituents. ⁵
	<i>Artemisia herba-alba</i> Asso ⁵	Asteraceae	Tunisia	Herbal tea (tea made from boiling leaves in water).	It is used to treat arterial hypertension and diabetes in Moroccan herbal medicine, and diabetes, bronchitis, diarrhea, hypertension, and neuralgias in Tunisian traditional medicine. Herbal tea has been used in traditional medicine as an analgesic, antimicrobial, antispasmodic, and hemostatic agent. During an ethno-pharmacological survey among the Bedouins of the Negev desert, <i>A. herba-alba</i> was discovered to be used to treat stomach problems. ⁵
Sore throat	<i>Acacia senegal</i> (L.) Willd ⁵ .	Leguminosae-Mimosoideae	Northern Nigeria, North Africa	Gum	For millennia, the gum of <i>A. senegal</i> has been used to treat infections such as hemorrhage, bronchitis, diarrhoea, gonorrhoea, leprosy, typhoid fever, and infections of the upper respiratory tract. ⁵
Diarrhoea	<i>Acacia senegal</i> (L.) Willd ⁵⁵⁵⁵	Leguminosae-Mimosoideae	Northern Nigeria, West and	Gum	
	<i>Artemisia herba-alba</i> Asso	Asteraceae	Tunisia	Herbal tea (tea made from boiling leaves in water)	Cough, stomach and intestinal disturbance, the common cold, measles, diabetes, yellowed skin (jaundice), nervousness, irregular pulse, and muscle weakness are all treated with <i>Artemisia herba-alba</i> . Roundworms, pinworms, tapeworms, hookworms, and flukes are among the parasitic infections treated with it. ⁵
	<i>Mangifera indica</i> L.	Anacardiaceae	Tanzania, Uganda	Bark, leaf	The leaves of <i>Mangifera indica</i> are used to cure diabetes in Nigerian traditional medicine. According to studies, it contains anti-diabetic, antioxidant, antiviral, cardiogenic, hypotensive, and anti-inflammatory properties. Antibacterial, antifungal, anthelmintic, antiparasitic, antitumor, anti-HIV, antibone resorption, antispasmodic, antipyretic, antidiarrheal, antiallergic, immunomodulation, hypolipidemic, antimicrobial, hepatoprotective, and gastroprotective characteristics have all been looked at. ⁵⁰
	<i>Alepidia amatymbica</i> Eckl. & Zeyh.	Apiaceae	South Africa	Bark, root.	Also used for the treatment of digestive system disorders, which include indigestion, constipation, stomach aches, diarrhoea, and vomiting. Other uses include treatment of cold, coughs, influenza, and chest pain. Fresh roots and rhizomes may be chewed three times a day for common cold and cough. Dried roots are also boiled and ½ cup of the decoction is taken twice daily for constipation. ⁵¹
	<i>Tithonia diversifolia</i> (Hemsl.) A. Gray	Asteraceae	Rwanda	Leaf	

	<i>Vernonia amygdalina</i> Del.	Asteraceae	Tanzania, Uganda	Leaf, root	Flavonoids from VA have been shown to have strong antioxidant properties, while its saponins have been shown to have antitumoral properties in leukemia cells. VA peptides are known to be powerful inhibitors of mitogen-activated protein kinases (MAPKs), which are important for breast tumor growth and also serve as a critical regulatory point for the tumor. ^{52,53}
Conjunctivitis/Eye infections	<i>Aloe ferox</i> Mill.	Xanthorrhoeaceae	South Africa, Lesotho	Fresh bitter sap applied directly. ⁵	
	<i>Acacia etbaica</i> Schweinf.	Fabaceae	Djibouti	Leaves are grounded in water and the eye washed with the water. ^{27,54}	The extracts exhibited high cytotoxic, antibacterial, wound healing and antifungal activity. ⁵⁵
	<i>Aloe mcloughlinii</i> Christian	Aloaceae	Djibouti	Fresh leaves are soaked in water and the water used as eye drop. Exudate also used for eye infections in Ethiopia. ²⁷	
Headache	<i>Vernonia amygdalina</i> Del.	Asteraceae	Uganda	Leaf. Formulation not given. ⁵⁶	
Loss of taste or smell (ageusia, anosmia)j	No such plants as direct remedy for loss of taste or smell are known for African medicinal plants. African medicines treatments are holistic and treatment of colds which includes loss of smell associated with the condition. Again, the loss of taste can also be as a result of cold and flu. Ayurveda recommends garlic, lemon juice, mint or ginger to get relief from cold and so restore the sensory loss of taste or smell during cold. From that viewpoint, African plants against cold can be tried.				
A rash on skin, or discolouration of fingers or toes	<i>Vernonia amygdalina</i> Del.	Asteraceae	Tanzania, Uganda	Leaf, root ^{56,57}	Also used traditionally by AIDS patients for chronic diarrhoea, herpes zoster and herpes simplex in Bukoba rural district, Tanzania; also used by AIDS patients for treatment of fever, general rash, pain (headache, back), cough, and stomach ache in Kabarole district, Western Uganda. ⁵⁷
	<i>Elaeodendron transvaalense</i> (Burt Davy) R.H. Archer	Celastraceae	South Africa	Roots. Root extract	Also inhibits HIV Type 1 reverse transcriptase and integrase. ⁵⁸
Difficulty breathing or shortness of breath	<i>Acacia senegal</i> (L.) Willd.	Leguminosae-Mimosoideae	Northern Nigeria	Gum	
	<i>Aspalathus linearis</i> (Burm.f.) R. Dahlgren	Fabaceae	South Africa	Herbal tea made from dried leaves. <i>In vitro</i> data has shown that the daily intake of the alkaline extracts of the red rooibos tea could suppress HIV infections in the extract. ⁵	It has anti-inflammatory, immunomodulating, and chemopreventive properties. The plant is mineral-rich and tannin-free. There is mounting evidence that the flavonoids included in the plant have a significant role in the prevention of cardiovascular disease and other age-related diseases. Aspalathin has been demonstrated in recent research to have favorable effects on glucose levels, homeostasis in Type 2 diabetes by boosting glucose absorption in muscle tissues and insulin release from pancreatic beta-cells, according to evidence-based complementary and alternative medicine. <i>In vitro</i> and <i>in vivo</i> studies have shown that rooibos tea has bronchodilator, antispasmodic, and blood pressure-lowering properties. The antispasmodic effect through potassium ionchannel activation has been reported. ⁵

Chest pain or pressure	<i>Acacia mellifera</i> (Vahl) Benth ^{59,59,58,59}	Fabaceae	Djibouti	Fresh leaves are chewed ²⁷	In traditional Kenyan medicine, <i>Acacia mellifera</i> is a valuable medicinal shrub. Syphilis and pneumonia are treated using the plant's stem bark. The triterpenoids found in this plant have been isolated and found to be cytotoxic and antimalarial. ⁶⁰
Loss of speech (dysphasia/dysarthria) or movement (paresis)	<i>Diospyros sanza-minika</i> A. Chevalier	Ebenaceae	Sierra Leone, Ghana, Cameroon, Gabon and Congo	Leaf (for paresis). The possesses an anti-HBV activity and exerts its antiviral effects via inhibition of HBV transcription. ⁶¹	The antimalarial activity of the pure constituents of <i>Diospyros sanza-minika</i> and of the methanol extract from the stem bark of is reported for the first time. The results provide interesting baseline information for the potential use of the crude extract well as some of the isolated compounds in the search for novel antimalarial compounds. ⁶¹

Note: The claims in Tables 1 and 2 are based on data from preclinical studies and ethnobotanical surveys which have not been subjected to verification through randomized control clinical trials.

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