



Review

African Herbal Medicines: Adverse Effects and Cytotoxic Potentials with Different Therapeutic Applications

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Abstract: The African continent is naturally endowed with various plant species with nutritional and medicinal benefits. About 80% of the people in developing countries rely on folk medicines to treat different diseases because of indigenous knowledge, availability, and cost-effectiveness. Extensive research studies have been conducted on the medicinal uses of African plants, however, the therapeutic potentials of some of these plants has remained unexploited. Over the years, several studies have revealed that some of these African floras are promising candidates for the development of novel drugs. Despite the plethora of studies on medicinal plant research in Africa, there is still little scientific data supporting the folkloric claims of these plants. Besides, safety in the use of folk medicines has been a major public health concern over the year. Therefore, it has become mandatory that relevant authority should take measures in safeguarding the populace on the use of herbal mixtures. Thus, the present review extracted relevant information from different scientific databases and highlighted some problems associated with folk medicines, adverse effects on reproductive systems, issue about safety due to the toxicity of some plants and their toxicity effects with potential therapeutic benefits are discussed.

Keywords: African herbal medicines; adverse effects; toxicity; therapeutic values



Citation: Okaiyeto, K.; Oguntibeju, O.O. African Herbal Medicines: Adverse Effects and Cytotoxic Potentials with Different Therapeutic Applications. *Int. J. Environ. Res. Public Health* **2021**, *18*, 5988. <https://doi.org/10.3390/ijerph18115988>

Academic Editor: Oliver Grundmann

Received: 7 May 2021

Accepted: 25 May 2021

Published: 2 June 2021

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1. Introduction

The African continent is magnificently endowed with different plant diversity, mainly due of the prevailing climatic conditions and this advantage has supported the richness of secondary metabolites in the plants for surviving under harsh environmental conditions [1,2]. Besides, the ultraviolet rays in this region are stronger than those observed in other parts of the world, and this also enables the plants to accumulate some important bioactive substances of economic importance [1]. These reasons justify the exploitation of these plants for their therapeutic values that have been in continual use in this region for the past several decades [3,4].

According to a report by the WHO [5], about 80% of the people in developing countries rely on traditional herbal mixtures to treat different diseases. Most villages in Africa still depend solely on traditional herbal mixtures as a source of health treatments because of their beliefs and culturally acceptable indigenous knowledge, accessibility, and affordability. Many herbal mixtures are indubitably expedient for maintaining good health or treating diverse diseases [6,7]. Besides, numerous African rural dwellers believe that since their ancestors used herbal mixtures/concoctions for their wellbeing in the past and with no side effect, they habitually assume that because the herbal mixtures are natural, therefore their safety is guaranteed. Unfortunately, this assumption has led to several instances of organ damage and death of the users [8,9]. In addition, traditional healers are very secretive about their indigenous practices handed down from their ancestors to the new generation and this makes their treatment prescriptions vague, often resulting in overdoses of the mixtures by their patients since no regulatory body controls the usage of herbal medicines. Perhaps

nothing indicates to the patients that “too much of a good thing” could be dangerous. Sadly, some people ignorantly combine herbal mixtures with orthodox medicines without a doctor’s prescription and perhaps, not considering their adverse interactions. It is important to note that uncontrolled consumption of herbal mixtures could lead to liver damage, kidney failure and stomach upsets, diarrhoea, etc. [10]. Herbal mixtures contain some bioactive compounds that are potentially toxic. The reports documented in the literature have shown that despite the crucial role of herbal medicine for man, some plant species are reported to cytotoxic at high dosage. This simply means that a very safe compound can be toxic at a high dose and vice versa. The toxicity-related issues about herbal medicines such as carcinogenicity, hepatotoxicity, mutagenicity, genotoxicity have been highlighted by Fanell et al. [11]. Therefore, safety relating to herbal mixtures or products cannot be disregarded, as knowledge is key in preventing overdoses or abuse. On the other hand, deforestation of the natural habitat due to anthropogenic activities has mounted pressure on the African ecosystem [1]. Nevertheless, it is worth noting that Africa represents about 25% of the world trade in biodiversity and it is still surprising that despite the contribution, only a few drugs from African plants have been commercialized compared to other continents.

2. Factors Influencing the Use of Herbal Medicines

According to the WHO [5], traditional medicine is the total of knowledge, skills, and experiences based on the theories, beliefs, and practices indigenous to different cultures, whether explicable, that are used to maintain health, and to prevent, diagnose, improve, or treat physical and mental illnesses. Hence, these practices have been explored by people since time immemorial to treat various diseases before the arrival of orthodox medicines. These herbal medicines may include herbs, herbal materials, herbal concoctions and finished herbal products [3]. Over the years, the patronage of people towards herbal medicine has been increasing tremendously because of several reasons that include but are not limited to the following:

- (a) The belief of rural dwellers and their indigenous cultures: Numerous rural dwellers have strong convictions that their beliefs and cultural practices for treating diseases are far better than modern medicine. Some even have a strong phobia towards orthodox medicines. As a result, nothing can make them opt for orthodox medicine even if the government is willing to pay their medical bills. They prefer consulting their gods and searching for a practical solution by sacrificing animals to please their gods. Different African traditional healers have their unique ways of consulting their oracles and communicating their findings to clients on their health-related issues and the possible solutions. In addition, these patients are more comfortable in expressing their health problems to the traditional healers in their local dialects than to a professional medical doctor [12].
- (b) A perception that herbal medicines are natural and safe: Most herbal medicine users believe that herbal medicines are safe because they are products of plant naturally found in the environment and thus, they assume that being natural implies safety with no adverse effect compared to those reported from the use of orthodox medicine [13].
- (c) Accessibility and cost-effectiveness: Herbal medicines have been the only option source of treatment in some African communities because they are cheap and the raw materials for preparing the mixtures are easily available. Besides, their cost-effectiveness cannot be compared with orthodox medicines, as most people living in these areas are poor and unable to afford the cost of modern treatments. These salient reasons have mitigated the rural dwellers towards the use of herbal medicines [14].
- (d) Superior efficacy of herbal medicines: Many people believe that herbal medicines are more potent than orthodox medicines and the failure of orthodox medicines to treat some complicated health problems has diverted people’s attention in seeking herbal mixtures as an alternative source. Herbal mixtures contain several bioactive

- compounds that are believed to work together in synergy and thus enhancing their potency over orthodox medicines [15,16].
- (e) Confidentiality of health problem information: Most people are not comfortable when information regarding their health problem is revealed to many people other than their doctor [13]. All patients have files containing their health information and the medical record clerks are responsible for handling these files. However, local people who use herbal medicines feel safer and prefer to discuss their health problem with the traditional healers to a modern health system where their files will be handle by different people on duty.
 - (f) Self-medication: This habit is common among the people living in the rural and semi-urban communities in African countries since the plant materials are easily accessible coupled with the little knowledge they acquired from generation about herbal concoctions, they tend to prescribe herbs preparations for people around them with similar kind of illnesses. The assumption is that since the concoctions have worked for other people, they would also serve the same purpose for any sick person with related symptoms [6].
 - (g) Fear of erroneous diagnosis: Most people prefer to opt for traditional medicines because of the fear of the wrong diagnosis from the modern health system. There are several reasons why a patient can be wrongly diagnosed in the hospital and such factors include unskilled medical operators (lack of advanced training of medical operators on the usage of new medical equipment), failure of old medical equipment, over the labour of medical staff, underpayment of medical staff, the inexperience of medical staff, mismanagement of patient's file, inconsistency/changing of the medical doctor in charge of a patient [13].
 - (h) Long waiting period and queue involved to see a medical doctor: The queue involved, and time spent in seeing a medical doctor at the hospital is unbearable for most people in Africa, most especially, people without medical aid that patronize the government hospitals. Most hospitals in Africa are understaffed, so the population of patients overwhelms the capacity of these hospitals, and consequently, patients often seek an immediate alternative to solve their health problems. In some cases, sick people in the village might need urgent attention, with no ambulance available in the villages to convey them to the modern hospital in the town or city. In addition, a bad road network in the villages has been a huge challenge for the rural dwellers to get proper medical treatment. Besides, even the so-called mobile clinics are always frustrated or unwilling to go to the villages to attend to the poor people because of the poor road network, consequently, the villagers tend to opt for the most available alternative treatment [17].
 - (i) Advertisement of herbal products: Over the years, the market strategies of herbal mixtures or products in different ways have captured people's attention in testing the efficacy of these products. Some traditional healers go on the street advertising their products by sharing handbills, pasting their posters everywhere in the town, or even employing marketing agents that will help them display their products on the television, different social media platforms. Marketing promotes business because of the awareness it creates for people and the visibility of a product is usually enhanced with an advertisement [18].

3. WHO Views on African Herbal Medicine

WHO has a substantial contribution to the acknowledgement and acceptance of traditional herbal medicine in African countries. Between 2002–2005, WHO provided a framework to promote traditional medicine to reduce the high death rate occurring in developing countries. WHO inspires African member states to endorse and incorporate folk medicine in their health system [19]. Therefore, four strategic objectives to incorporate folk medicine into the national healthcare systems include [20,21]:

- i. To ensure that traditional medicines are easily accessible, available, and affordable for the poor populace.
- ii. To ensure that traditional medicines are of high quality and effective without compromising on their safety for the populace.
- iii. To promote the therapeutic use of traditional medicines for consumers.
- iv. To ensure that traditional healers/specialists get the appropriate training and education required to improve on the preparation and prescription of their herbal products.

4. Justifications for Research on African Medicinal Plants

A plethora of supporting documents in the literature have validated the efficacy of African medicinal plants for the treatment of different human illnesses, however, there are still several gaps that are needed to be addressed, especially concerning the safety of these herbal mixtures or products to public health on the African continent. Thus far, the extensive research on African plants is geared towards drug discovery and development; there is a dire need to compile a list of promising African flora with significant therapeutic values, as most of these plants are not well documented. Likewise, there is a need to introduce African traditional healers to modern scientific practices. For the acceptance of folk medicines, the issue relating to active principles in the plant extracts, identification of secondary metabolites, mechanism of actions, and their toxicology need to be addressed. For that reason, WHO instigates further rigorous research on traditional medicines to substantiate their potency and establish safety for their usage [19].

Acceptance of Traditional Medicines by Developed Countries

Folkloric medicine has been embraced by other people beyond their original indigenous culture, and this is referred to as complementary or alternative medicine [11,19]. The utilization of traditional medicines has been accepted in several advanced nations of the world, and complementary or alternative medicine has gained huge popularity in Europe, North America, and Australia [22,23]. The people living in these regions use medicinal herbal products to promote healthier living, as a blood cleanser, diet supplements, or for reducing body size. This therapeutic option drastically reduces the amount of money spent to purchase expensive drugs at the pharmacy and justifies the growth in the marketability of herbal products in these regions [6,24].

5. Safety of Traditional Herbal Medicines

Despite the numerous advantages associated with folkloric medicines, the big question is always about their safety to public health. The primitive techniques used by traditional healers are not modern or either scientific, hence, there are high chances of microbes and heavy metals contamination in the herbal products that could affect the health of the populace [16]. Therefore, the relevant authority needs to give a directive on how to protect the public from the negative effects (including death) that could result from the use or abuse of herbal products [25–27]. Microbial contamination is often common in herbal medicines, and it is always difficult for traditional healers to prevent or control this contamination. Thus, there is a need to recommend some quality control guidelines in their practices and perhaps awareness regarding the potential health risks associated with the use or abuse of herbal mixtures [25,27].

5.1. Adverse Effects of African Medicinal Plants and Role in Humans' Reproductive System

In African communities, the introduction of herbal mixtures to the market is a norm even without scientific evaluation to ascertain their safety. There is also a belief that herbal products are safe. Besides, traditional healers lack regulatory control to guide their products, all these factors have worked together to misinform millions of people, resulting in the death of people [16]. Apart from microbial contamination, heavy metals have been reported to be contributors to the toxicity of herbal products that have led to life-threatening situations or death [6]. Several plants contain toxic bioactive compounds that can disturb

normal physiological activities by chelating with cellular macromolecules such as DNA and proteins, leading to cellular toxicity and mutation [28]. The problem of herbal toxicity could result from production factors such as incorrect use of plants, species or plant parts, the quality of herbal products, high level of impurities, contaminants, and adulterants. Other possible factors could be resulting from the patient, such as co-morbidity, co-medication, and self-medication [29]. Several studies in the literature have highlighted the adverse effect of medicinal plants on the liver [30,31]. Liver enzymes are key biomarkers that indicate the level of liver damage and their presence in the blood is used to monitor liver disease in patients in the developing countries of the world [32]. In addition, the clinical symptoms of liver damage include asymptomatic mild biochemical irregularities to severe hepatitis with jaundice [33]. In agriculture, organophosphate pesticides are usually used to control pest in developing countries [33]. For instance, dichlorvos acts by irreversibly inhibiting acetylcholinesterase enzyme (AChE) at the cholinergic junctions of the nervous system and produces hepatotoxicity in rats [34]. Furthermore, aflatoxin, a potent hepatocarcinogen and hepatotoxin, is another potential microbial contaminant that has been identified in herbal products [35].

There is a general notion that traditional healing is dominated by men, as the percentage of male traditional healers is far greater than that of females. Notwithstanding this, the rich knowledge of indigenous women about folk medicines cannot be underrated [36]. Besides, female patients are always comfortable discussing women's problems with the female traditional healers. Medicinal plant intake has contributed substantially to treating women-related health problems such as irregular menstruation, birth control, fertility, abdominal pain, pregnancy, waist pain, vomiting during pregnancy, child delivery, and postpartum care, lactation, infant care, etc. [37–39]. Examples of the medicinal plants commonly used by pregnant women includes *Zingiber officinale*, *Allium sativum*, *Ocimuml antiifolium*, *Eucalyptus* and *Rutachalepensis*, etc. [40]. For example, the usage of *Clivia miniata* has been reported to be associated with some side effects such as salivation and diarrhoea while *Callilepis laureola* causes confusion, convulsion, hepatic, and renal failures. Also, *Scadoxus puniceus* has been reported to be associated with visual disturbances and dizziness [41].

Medicinal plants have been folklorically used for the treatment of different types of reproductive diseases. However, contaminants such as heavy metals and persistent organic pollutants picked up by medicinal plants from the environment, especially when their concentrations are above the permissible limits, disrupt the normal physiological function of the human reproductive system [42,43]. Contaminant toxicity in plant extracts has been reported to be associated with a decrease in sex organs, sex performance, implantation rate, fertility, chromosome aberration, and mitotic inhibition in some in vivo studies [44–46]. These contaminants in plant extracts could trigger the production of free radicals and higher accumulation may lead to oxidative damage of the organ or tissues and macromolecules followed by oxidative stress thereby resulting in impaired reproductive systems [47–49]. For example, the report of a study conducted in Nigeria by Nwangwa [50] on ethanolic extract of *Xylopi aethiopica* showed a decrease in sperm viability, motility, and counts in rats. Another study by Akbarsha et al. [51] with *Andrograpis paniculata* in rats caused a decrease in spermatogenesis and degenerative changes in seminiferous tubules.

It is quite unfortunate that folk medicines are the only source of treatment for pregnant women in some Africa countries [52,53]. Normally, conventional antimalarial drugs are encouraged for pregnant women [4], however, the cost implication of these drugs in the developing countries by low-income earners has impelled this category of people to seek folk medicines, without considering the side effects on their foetus [54]. In addition, the use of medicinal plants for child delivery is a normal practice in some rural areas in African countries [55].

5.2. Hurdles to Safeguarding the Quality/Safety of Herbal Products

With the drastic upsurge in the number of people interested in herbal products, adverse effects associated with the use of these herbal products have posed a serious threat to public health. Hence, there is a dire need to monitor the production of these products, enlighten the populace about their toxicity and give adequate advice on their consumption and use [56,57]. Several challenges affect the quality of herbal products, which could result from the following:

- i. Insufficient knowledge or information about the plant species: Most people that practice traditional medicine in Africa do not have good knowledge about the plants used in the treatment of different ailments since they strongly believe in the information passed to them from one generation to another. They do not know the scientific information about the toxicity of one plant to another when used in combination. Besides, the collection or harvest time for medicinal plants is one of the significant factors that affect the potency of the plant for their therapeutic usages and when the traditional healers lack the basic information about the plant, there is a high possibility of misidentification or the use wrong plant species that could result in the toxicity of the herbal mixtures or products [13].
- ii. Lack of quality control on the herbal products: The preparation of most herbal products in the market or those used by the people in the villages are devoid of quality control assessment and the chances of their toxicity or adverse effect on human are very high, though some have been proven to be promising. There is no regulatory or standard set aside for the preparation of herbal products in the villages in Africa, hence, microbial contamination from the harvesting stage, production, and packaging is common in these products. Hence, the quality of materials used for the preparation of the herbal products determines the level of their safety [58].
- iii. Lack of standard preparation methods: Different communities in Africa have their ways of preparing herbal mixtures and the method used in the preparation influences the extraction of the bioactive compounds in these plants, which are significant to their therapeutic values. Lack of standard methods may indirectly affect the difference in the efficacy of plants from various communities [59].
- iv. Complex nature of the plant extracts: Several researchers have reported that the plant extracts contain many bioactive compounds and the complex nature of the method used in isolating and purifying individual bioactive compounds is critical and such analysis might not be possible in a local setting [60].
- v. Overdose prescription: The prescription of herbal mixtures/products by traditional healers in the African communities is one of the factors that have resulted in many deaths in this region [61]. Most herbal mixtures contain several bioactive ingredients and adequate knowledge about the pharmacokinetics and the mechanism of actions of these products is lacking, hence, the prescription about the dosage used by the patients is not evidenced-based, which consequently leads to liver or kidney damage [8].
- vi. Lack of scientific proof: Most herbal products in African countries lack any scientific validation [62].

6. Cytotoxic Effects of African Medicinal Preparations with Different Therapeutic Uses

From ancient times, the plant kingdom has been a reliable source of therapeutic agents for the treatment of different human illnesses because of the secondary plant metabolites [63]. Usually, plants produce numerous secondary metabolites as a defense mechanism against an array of pathogens [64]. The abundance and concentration of these secondary metabolites differ from plant to plant, geographical locations as well as abiotic factors that trigger their production [65]. A report by Samuelsson [66] has revealed that about 25–28% of orthodox drugs originated from plants. As a result, it has been predicted that the plant-based drug market could grow up to US\$ 39.2 billion in 2022 [67]. Thus, continual screening of African biodiversity to search for cost-effective,

novel, and effective plant secondary metabolites could play an important role in the biopharmaceutical industries [68–70]. However, it is worth noting that from a biological perspective, the cytotoxicity of a plant does not only mean adverse effects, as this also has some therapeutic uses, and these have been well documented in the literature [71]. Unlike some protective roles such as antioxidant, antidiabetic, hepatoprotective, neuroprotective activities demonstrated by African plants, their cytotoxic effects have been reported to be beneficial to humans [72,73].

6.1. Antibacterial Activity

Bacterial infections represent a high percentage of the global causes of ill health and mortality because of the high prevalence of multidrug-resistant bacteria leading to antibiotic treatment failure thereby exposing the public to risk therefore, immediate intervention is highly imperative [74–76]. On the other hand, plants represent a significant source of novel antimicrobial agents. Plants are always exposed to different stresses from abiotic and microorganisms' assault, and this prompts them to produce some defensive substances with antimicrobial activity [77]. Remarkably, these secondary metabolites produced by various plants have been recognized to have some therapeutic uses, including antibacterial activity [78,79]. A perusal of the literature indicated that several antibacterial studies on African plants have been documented [63,80,81]. However, poor toxicological documentation of plants used in folk medicines is the major limitation facing Africa traditional medicine, and this research gap has been the subject of active research lately [82]. Table 1 presents some African plants that have been reported to have antibacterial activity.

Table 1. Antibacterial activity of some African flora.

Family	Genus	Part Used	Solvent	Tested Bacterial Strains	Country	Reference
Anacardiaceae	<i>Mangifera indica</i> Linn	Stem	Methanol	<i>Pseudomonas aeruginosa</i> (isolate); <i>Escherichia coli</i> (ATCC 8739); <i>Staphylococcus aureus</i> (ATCC 25922); <i>Proteus mirabilis</i> (isolate); <i>Enterococcus faecalis</i> (ATCC 10541)	Cameroon	[83]
Cactaceae	<i>Opuntia streptacantha</i>	Fruit skin	Ethanol and water	<i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>Micrococcus luteus</i> , <i>Salmonella enteritidis</i> , <i>Bacillus cereus</i> , <i>Klebsiella pneumoniae</i>	Tunisia	[84]
Celastraceae	<i>Lauridia tetragona</i>	Leaves	Acetone and methanol	<i>Enterococcus faecalis</i> (ATCC 29212), <i>Staphylococcus aureus</i> (OK), <i>Bacillus subtilis</i> KZN, <i>Bacillus cereus</i> , and <i>Streptococcus pyogenes</i> , <i>Vibrio cholerae</i> , <i>Klebsiella pneumoniae</i> (ATCC 4352), <i>Pseudomonas aeruginosa</i> (ATCC 19582), <i>Salmonella typhi</i> (OK), and <i>Escherichia coli</i> (ATCC 8739)	South Africa	[85]
Fabales	<i>Elephantorrhiza elephantina</i>	Rhizome	Methanol	<i>Bacillus cereus</i> , <i>Shigella flexneri</i>	South Africa	[86]
Zingiberaceae	<i>Zingiber officinale</i>	Rhizome	Methanol	<i>Pseudomonas aeruginosa</i> , <i>Salmonella typhi</i> , <i>Klebsiella pneumoniae</i> , <i>Staphylococcus aureus</i> and <i>Escherichia coli</i>	Nigeria	[70]
Vitaceae	<i>Cissus quadrangularis</i>	Aerial	Methanol	<i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i>	Ethiopia	[87]
Araceae	<i>Colocasia esculenta</i>	Whole plant	Methanol	<i>Pseudomonas aeruginosa</i> , <i>Klebsiella pneumoniae</i> , <i>Enterobacter aerogenes</i> , <i>Escherichia coli</i> and <i>Providencia stuartii</i>	Cameroon	[88]
Asphodelaceae	<i>Bulbine frutescens</i>	Whole plant	Methanol	<i>Escherichia coli</i>	Kenya	[89]
Salvadoraceae	<i>Salvadora persica</i> L.	Bark	Aqueous and methanol	<i>Staphylococcus aureus</i> ATCC33862 and <i>Escherichia coli</i> ATCC25922	Zimbabwe	[69]
Hypericaceae	<i>Hypericum roeperianum</i>	Leaves	Acetone	<i>Staphylococcus aureus</i> , <i>Enterococcus faecalis</i> and <i>Bacillus cereus</i> , <i>Escherichia coli</i> , <i>Salmonella typhimurium</i> and <i>Pseudomonas aeruginosa</i>	Nigeria	[68]
Phyllanthaceae	<i>Bridelia ferruginea</i>	Root	Ethanol	<i>Escherichia coli</i> and <i>Staphylococcus aureus</i>	Nigeria	[90]
Verbenaceae	<i>Lippia javanica</i>	Leaves	Dichloromethane:methanol (1:1)	<i>Clostridium perfringens</i>	South Africa	[91]
Agavaceae	<i>Agave americana</i>	Leaves	Dichloromethane and methanol (1:1)	<i>Neisseria gonorrhoeae</i>	South Africa	[92]
Myrtaceae	<i>Myrtus nivellei</i>	Aerial	Butanol	<i>Bacillus cereus</i> , <i>Escherichia coli</i> , <i>Listeria monocytogenes</i>	Algeria	[93]

* ATCC—American Type Culture Collection.

6.2. Antiplasmodial Activity

Malaria remains one of the most prevalent public health issues in the African countries of the world [94,95]. The high resistance of malaria parasites to the existing antimalarial drugs poses a serious threat to public health globally [96]. Hence, there is a pressing need to strategize on how to identify effective, inexpensive, and innocuous novel antimalarial agents. As part of this perpetual quest, African researchers and foreign collaborators have explored African biodiversity in the exploration of secondary metabolites from extracts of African plants for new antimalarial agents [94]. Traditionally, herbs have been the major treatment of malaria in most developing countries, especially in African countries [97]. These plants have been reported to be promising and could serve as a good alternative source for the isolation of lead compounds that could be used in the development of new antimalarial agents from this continent, and this could solve the problem of resistance of the malarial parasites [98]. Nevertheless, further studies on their toxicities such as carcinogenicity, teratogenicity, mutagenicity, toxicity should be the subject of active research to ensure their safety. Table 2 summarizes a few African floras with proven antiplasmodial activity.

Table 2. Antiplasmodial activity of selected African flora.

Family	Species	Part Used	Solvent	Assay Type	Tested Organisms	Country	Reference
Phyllanthaceae	<i>Phyllanthus amarus</i>	Whole plant	Aqueous and Ethanol	In vivo	<i>Plasmodium yoelii</i>	Nigeria	[99]
Asclepiadaceae	<i>Periploca linearifolia</i>	Stem bark	Hexane, chloroform, ethyl acetate and methanol	In vitro	D-6 <i>Plasmodium falciparum</i>	Kenya	[100]
Anacardiaceae	<i>Haematostaphis barteri</i>	Stem bark	Dichloromethane/methanol	In vivo	<i>Plasmodium berghei</i>	Ghana	[101]
Solanaceae	<i>Withania frutescens</i>	Leaves and roots	n-hexane	In vitro	<i>Plasmodium falciparum</i>	Morocco	[102]
	<i>Neobegua mahafaliensis</i>	Leaves	Methanol	In vitro	<i>Plasmodium falciparum</i> FcM29-Cameroon	Congo	[103]
Ebenaceae	<i>Diospyros</i> species	stem bark	Methanol	In vitro	<i>Plasmodium falciparum</i> 3D7	Tanzania	[104]
Euphorbiaceae	<i>Sebastiania chamaelea</i>	Whole plant	Methanol	In vitro	<i>Plasmodium falciparum</i> FcM29, FcB1, F32 and W2	Niger	[105]
Fabaceae	<i>Baphia pubescens</i>	Stem	Hydroethanolic	In vivo	<i>Plasmodium berghei</i>	Nigeria	[106]
Burseraceae	<i>Commiphora africana</i>	Stem	Dichloromethane and methanol in a 1:1 ratio (v/v)	In vitro and in vivo	<i>Plasmodium falciparum</i> (D6 and Dd2)	Tanzania	[107]
Zingiberaceae	<i>Aframomum giganteum</i>	Stem bark	Dichloromethane and methanol	In vitro	<i>Plasmodium falciparum</i> (FCB and W2)	Gabon	[108]
Combretaceae	<i>Terminalia avicennioides</i>	leaves	CH ₂ Cl ₂ , MeOH and MeOH/H ₂ O (1/1)	In vitro	<i>Plasmodium falciparum</i> strain K1	Burkina Faso	[109]
Meliaceae	<i>Melia azedarach</i>	leaves	Cyclohexane, ethyl acetate, dichloromethane, and methanol	In vitro	<i>Plasmodium falciparum</i> (3D7 and W2)	Senegal	[110]
Asteraceae	<i>Bidens pilosa</i>	leaves	Methanolic and Ethyl Acetate	In vitro	<i>Plasmodium falciparum</i> (Pf3D7 and PfINDO)	Cameroon	[111]
Labiatae	<i>Ajuga remota</i>	leaves	Hydroethanolic	In vivo	<i>Plasmodium berghei</i> (ANKA strain)	Ethiopia	[112]
Euphorbiaceae	<i>Alchornea laxiflora</i>	leaves	Ethanol	In vivo	<i>Plasmodium falciparum</i> (Pf 3D7) and (Pf INDO)	Nigeria	[113]

Table 2. Cont.

Family	Species	Part Used	Solvent	Assay Type	Tested Organisms	Country	Reference
Compositae	<i>Vernonia adoensis</i>	Leaves	Aqueous, methanol and chloroform	In vivo	<i>Plasmodium berghei</i>	Ethiopia	[114]
Lamiaceae	<i>Clerodendrum rotundifolium</i>	Leaves	ethyl acetate	In vitro	<i>Plasmodium falciparum</i> (NF54 and FCR3)	Uganda	[115]
Apocynaceae	<i>Tabernaemontana elegans</i>	Stem bark	Dichloromethane: 50% methanol (1:1)	In vitro	<i>Plasmodium falciparum</i> (NF54)	South Africa	[96]
Zygophyllaceae	<i>Balanites aegyptiaca</i>	aerial	Methanol	In vitro	<i>Plasmodium falciparum</i>	Togo	[116]
Caesalpiniaceae	<i>Cassia occidentalis</i>	Leaves	Ethanol	In vitro	<i>Plasmodium falciparum</i>	Congo	[117]
Fabaceae	<i>Pericopsis laxiflora</i>	Bark	Ethanol	In vitro	<i>Plasmodium falciparum</i> (NF54 and K1)	Côte d'Ivoire	[118]
Canellaceae	<i>Warburgia salutaris</i>	stem bark	Dichloromethane	In vitro and in vivo	NF54 <i>Plasmodium falciparum</i>	South Africa	[119]
Asterales	<i>Oedera genistifolia</i>	leaves	Chloroform, ethyl acetate, and ethanol	In vitro	<i>Plasmodium falciparum</i> strain 3D	South Africa	[120]

6.3. Antifungal Activity

Fungal infections have been recognized as one of the deadly diseases that are difficult to treat in humans, animals, and plants because of the multidrug-resistant of the fungal pathogens to the existing antifungal agents. Besides, the current antifungal drugs have adverse effects both on the patients and the environment [121,122]. Thus, the need to search for alternative cost-effective and effective alternatives is indispensable. On the other hand, rural dwellers are highly knowledgeable about the culture and traditional practices used by their ancestors for treating fungal infections [123,124]. Herbs have been the only source for the treatment of fungal diseases and as a result, the antifungal activity of these plants has been validated by some African researchers to establish the therapeutic claims of these plants. Hence, continual ethnobotanical survey and screening of African plants in search of novel bioactive compounds that could be used in the development of effective antifungal drugs have been the focus of research in this field [125,126]. Table 3 summarises a few African floras with proven antifungal activity.

Table 3. Antifungal activity of some African flora.

Family	Genus	Part Used	Solvent	Tested Organisms	Country	Reference
Asteraceae	<i>Scolymus hispanicus</i>	Leaves and stem	Ethanol and dichloromethane	<i>Candida neoformans</i> and <i>Candida albicans</i>	Morocco	[127]
Fabaceae	<i>Prosopis juliflora</i>	Whole plant	Methanol or water	<i>Colletotrichum musae</i>	Ethiopia	[128]
Asphodelaceae	<i>Aloe barbadensis</i>	leaves	Ethanol	<i>Candida albicans</i> and <i>Tessaracoccus flavus</i>	Ghana	[129]
Lythraceae	<i>Punica granatum</i>	Fruits	Ethanol	<i>Fusarium oxysporum</i> , <i>Fusarium culmorum</i> , <i>Fusarium graminearum</i> , <i>Aspergillus niger</i> and <i>Alternaria alternata</i>	Tunisia	[130]
Celastraceae	<i>Mystroxyylon aethiopicum</i>	Leave, stems and roots	Dichloromethane and ethyl acetate	<i>Candida albicans</i> and <i>Candida neoformans</i>	Tanzania	[131]
Canellaceae	<i>Warburgia ugandensis</i>	Leaves	Water, acetone, ethanol, and hexane	<i>Candida albicans</i> SC5314, <i>Candida glabrata</i> BG2, <i>Candida glabrata</i> ATCC 2001	Kenya	[132]
Lamiaceae	<i>Gmelina arborea</i>	seeds	Water	<i>Athelia rolfsii</i> and <i>Sclerotium rolfsii</i>	Nigeria	[133]
Ranunculaceae	<i>Clematis flammula</i>	leaves and bark	Ethanol	<i>Candida albicans</i>	Algeria	[134]
Lamiaceae	<i>Marrubium vulgare</i>	aerial	Methanol and acetone	<i>Botrytis cinerea</i> , <i>Pythium ultimum</i>	Tunisia	[135]

Table 3. Cont.

Family	Genus	Part Used	Solvent	Tested Organisms	Country	Reference
Asteraceae	<i>Artemisia herba alba</i>	aerial	Water	<i>Usarium graminearum</i> (ITEM-6477) and <i>Fusarium sporotrichioides</i> (ITEM-692)	Algeria	[136]
Euphorbiaceae	<i>Ricinus communis</i>	Leaves	Aqueous, methanol and ethanol	<i>Candida albicans</i>	Ghana	[137]
Lecythidaceae	<i>Barringtonia asiatica</i>	Leaves	Methanol	<i>Aspergillus niger</i> , <i>Aspergillus flavin</i> , <i>Candida tropicalis</i> and <i>Fusarium oxysporium</i>	Nigeria	[138]
Asparagaceae	<i>Agave sisalana</i>	Roots	Acetone, n-hexane, dichloromethane and methanol	<i>Candida albicans</i> , <i>Candida glabrata</i> , <i>Candida krusei</i> , <i>Candida parapsilosis</i> , <i>Candida tropicalis</i> and <i>Cryptococcus neoformans</i>	South Africa	[139]

6.4. Anticancer Activity

Cancer is one of the topmost killer diseases globally, and it is predicted to be a major cause of death in the future [140]. It is a global public health issue affecting both developed and developing countries of the world, despite the innovation in the different therapy treatments [141]. This disease is a distressing issue, especially when not detected at the early stage, and the treatment costs are too high for the poor to afford [142]. However, radiotherapy and surgery have been acknowledged to be some of the most successful treatments, but the side effects and high treatment cost cannot be neglected [143]. Thus, this necessitates the urgent need to search for alternatives. Over the years, the use of herbal products for the treatment of different human diseases such as cancer has gained wide attention [144,145]. This means that plants or herbs may provide the main active principles for the development of new anticancer agents [146,147]. As a result, extensive studies on the anticancer activity of African plants have been well reported in the literature [148–150]. It has been established that bioactive compounds produced for plants' defense have the potential to inhibit cancer cell growth. In addition, the report of Kawashima et al. [151] has highlighted that some of these bioactive compounds are toxic to humans. Regrettably, the toxicity of these plants has been documented in many cases to originate from various contaminants, such as pesticides, heavy metals, and other pollutants in the environment [29]. Evidence to validate the therapeutic values of these plants is still scarce, hence, there is a need for further research to confirm the traditional anticancer claims of these plants [152–154]. Several researchers have been investigating how the antioxidant potential of a plant can be related to its anticancer effects [155]. The bioactive compounds responsible for the antioxidant properties could however be different from those accounting for the antiproliferative effect. Nevertheless, the most important approach should be directed towards producing anticancer agents that could completely inhibit the growth of cancerous cells with no effect on normal cells. However, the findings of Lobo et al. [156] have highlighted that oxidative stress caused by the excessive reactive oxygen species such as superoxide anion ($O_2^{\bullet-}$), nitric oxide (NO), hydroxyl radical ($\bullet OH$) and peroxy radicals ($ROO\bullet$) are involved in the pathogenesis of several pathologies, including cancer. The reactive species tend to cause DNA mutations, which could play a significant role in cancer [140]. Therefore, using plant-based antioxidant agents such as flavonoids, alkaloids and polyphenols could reduce the uncontrollable cell division caused by oxidative stress imposed by free radicals [157]. Thus, the use of natural antioxidants could play a lead role in the development of effective anticancer agents [158,159]. It is also worth noting that natural compounds have multi-target cellular effects [72,160,161]. Hence, this significant attribute could be more effective in the treatment of cancer than drugs that are target specific in their mode of action [72]. In Table 4, we have highlighted a few African plants that have been shown to possess anticancer activity.

Table 4. Anticancer activity of some African flora.

Family	Genus	Part Used	Solvent	Tested Organisms	Country	Reference
Curtisiaceae	<i>Curtisia dentata</i>	Leaves	Acetone	MCF-7, colorectal carcinoma cells (Caco-2), A549 and HeLa	South Africa	[73]
Lamiaceae	<i>Origanum compactum</i>	leaves	n-hexane	L20B, RD and Vero	Morocco	[162]
Liliaceae	<i>Allium ascalonicum</i>	Tuber	Methanol	MCF-7, MDA-MB-231 and fibroblast cells	Nigeria	[163]
Asparagales	<i>Boophone disticha</i>	Bulb	Chloroform, acetone, and ethanol	HeLa	South Africa	[164]
Annonaceae	<i>Uvariadendron anisatum</i>	Root	Methanol and water	4T1 breast cancer cell line	Kenya	[165]
Lauraceae	<i>Beilschmiedia acuta Kosterm,</i>	roots, leaves, bark	Methanol	Leukemia CCRF-CEM	Cameroon	[72]
Aristolochiaceae	<i>Aristolochia ringens Vahl.</i>	Root	Ethanol and water	A549 (lung), HCT-116 (colon), PC3 (prostate), A431 (skin), HeLa (cervix), and THP-1 (leukemia)	Nigeria	[166]
Fabaceae	<i>Acacia nilotica (L.) Delile</i>	Fruit	Dichloromethane or hexane with chloroform or ethyl acetate or ethanol or methanol 80%	Human leukemic CCRF-CEM and the ABCB1 (P-gp)	Sudan	[167]
Euphorbiaceae	<i>Jatropha zeyheri</i>	roots	Ethyl acetate	Human dermal fibroblast (HDF), colon adenocarcinoma (Caco-2), lung cancer (A547) and breast cancer (MCF-7)	South Africa	[168]
Poaceae	<i>Cymbopogon schoenanthus L. Spreng</i>	Aerial	Ethanol	MCF-7	Tunisia	[169]
Malvaceae	<i>Hibiscus sabdariffa</i>	Whole plant	Methanol	PC3 (prostate cancer cell line)	Sudan	[170]
Anacardiaceae	<i>Rhus tripartita</i>	Aerial	Methanol 70% and acetone 70%	CaCo-2 (colon carcinoma) and K-562 (myelogenous leukemia)	Tunisia	[171]
Myrtales	<i>Syzygium jambos</i>	Leaves	Ethanol	HeLa, Vero and HEK-293	South Africa	[172]
Bignoniaceae	<i>Jacaranda copaia</i>	leaves, bark, flower, root,	Ethanol	MDA-MB231 (breast) and PANC-1 (pancreas)	Venezuela	[173]
Asteraceae	<i>Ageratum conyzoides</i>	whole plant and parts - stem, leaves and flower	50% hydroethanolic	Jurkat, LNCap, MCF7	Ghana	[174]
Clusiaceae	<i>Pentadesma butyracea</i>	Fruits	Methanol	Skin cancer: A431	Cameroon	[175]
Sapotaceae	<i>Sideroxylon oxyacanthum</i>	Leaves	80% methanol (MeOH) in H ₂ O	MT-1, MCF-7 and MCF-10A	Ethiopia	[176]
Chrysobalanaceae	<i>Parinari curatellifolia (Planch ex Benth)</i>	leaves, roots stem and bark	Methanol	Wil 2 and Jurkat T	Zimbabwe	[177]

6.5. Antiviral Activity

Apart from bacterial and fungal infections, the world, and Africa in particular, has to deal with the ruthless devastation of viral diseases, which in most cases are the most difficult to deal with [178]. Unlike bacterial and fungal cells, which exist as free-living entities, viruses are small infectious intracellular parasites, which contain little more than wads of genetic material in the form of either RNA or DNA, surrounded by a lipid-carbohydrate-containing envelope [179]. Viruses can infect all types of organisms, humans, animals, and plants alike. Several antiviral drugs are currently available [180], nonetheless, the high incidence of viral resistance to the existing antiviral drugs has called for an urgent need to search for effective alternative agents [181]. Hence, great attention has been shifted towards screening African plants for novel antiviral agents [182,183]. Antiviral chemotherapy is a standard practice in the management of viral infections in humans [184]. Further research to authenticate the safety of these plants, both in vivo studies and human

clinical trials, is necessary. Table 5 lists a few African plants that have been proven to demonstrate antiviral activity.

Table 5. Antiviral activity of some African flora.

Family	Genus	Part Used	Solvent	Tested Organisms	Country	Reference
Myrtaceae	<i>Syzygium jambos</i>	Leaves	Ethanol	HSV-1	South Africa	[172]
Euphorbiaceae	<i>Macaranga barteri</i>	Leaves	Methanol	Echoviruses (E7 and E19)	Nigeria	[185]
Meliaceae	<i>Trichilia dregeana</i>	Roots	Methanol	hepatitis C virus (HCV)	Cameroon	[186]
Celastraceae	<i>Cassine transvaalensis</i>	Bark	Methanol	HIV	South Africa	[187]
Fabaceae	<i>Caesalpinia decapetala</i>	Root	Water	HSV-1	Kenya	[188]
Apocynaceae	<i>Carissa edulis</i>	Root	Water	HSV-1 and HSV-2	Kenya	[189]
Fabaceae	<i>Cajanus cajan</i>	Leaves, stem, roots	Hot water	HSV-1	Nigeria	[190]
Poaceae	<i>Bambusa vulgaris</i>	Leaf	Ethanol	Measles and yellow fever virus	Nigeria	[191]
Combretaceae	<i>Combretum molle</i>	Roots	Methanol	HIV-1	South Africa	[192]
Amaryllidaceae	<i>Zephyranthes candida</i>	Stem bark and root bark	methanol	Poliovirus Type-PV1	Nigeria	[185]
Apocynaceae	<i>Tabernaemontana ventricosa</i>	Leaves	Methanol	influenza A virus (IAV)	South Africa	[183]
Amaryllidaceae	<i>Crinum macowani</i>	Leaves	Aqueous and ethanol	HIV	South Africa	[193]
Malvaceae	<i>Hibiscus sabdariffa</i>	Leaves	Ethanol	Measles Virus	Nigeria	[194]

7. Conclusions

Folk medicines are the oldest and most widely utilized out of the different therapeutic systems in African countries and other developing countries. In these countries, the native doctors prescribe easily available herbs to sick people in the rural and semi-urban communities to solve their immediate health problems, and as such, they have utilized several folkloric herbs for different therapeutic purposes. The big question about the safety of the folk medicines will continue to be a major public health issue as their preparation is not hygienic and scientific procedures are not followed. Despite the extensive efforts by researchers, there is still a paucity of information regarding the compilation of plants that can be used in the treatment of several human diseases and their adverse effects. The issues concerning the toxicity of herbal mixtures, appropriate doses to be used, identification of active ingredients, mode(s) of action, quality control measures in herbal preparation and labelling, integration of folkloric and orthodox medicines should be addressed by the relevant authorities to safeguard the life of the populace that explore folk medicines for therapeutic purposes. Awareness about the potential adverse effect, mode of action, and integration of herbal products with orthodox medicines should be encouraged.

Author Contributions: Conceptualization, K.O.; and O.O.O.; methodology, K.O.; investigation, K.O.; resources, O.O.O.; K.O.; writing—original draft preparation, K.O.; and O.O.O.; writing—review and editing, supervision, K.O.; funding acquisition, O.O.O. Both authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Cape Peninsula University of Technology, grant number CPUT-RJ23 and The APC was funded by Cape Peninsula University of Technology.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The authors duly acknowledge Cape Peninsula University of Technology for their financial support.

Conflicts of Interest: The authors declare no conflict of interest.

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