ETHNOPHARMACOLOGICAL PROPERTIES OF VERNONIA AMYGDALINA PLANT-A REVIEW

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ABSTRACT

Ethnopharmacology, studies natural medicines derived from plants and other substances that have been traditionally used by diverse ethnic groups to treat various types of human diseases. Generally, the term can be used to refer to the studies correlating ethnic groups, their health, and how it relates to their physical habits and methodology in the preparation and use of medicines. This review aims to collate and emphasize various attempts by different groups of researchers to investigate Vernonia amygdalina, commonly known as bitter leaf, with respect to the method of collection, extraction, preparation and its ethnopharmacologic properties that are widely exploited as nutritional green vegetable or herb, to treat malaria and diabetes in some diverse cultures, including, Nigeria. These properties of V.amygdalina were originally observed by Scientists studying chimpanzees’ feeding on this shrub that resulted in self-parasitization. Since that discovery, subsequent studies had revealed more bioactives present in extracts of this medicinal plant such as antidiabetic, antibacterial,antifungal, antioxidant, antimalarial, etc which are beneficial to human health. Toxicological studies on this plant also show that V. amygdalina (bitter leaf) has no
significant toxicity, thereby supporting its safe use for the benefits of human health and consequently, requiring or recommending further investigations.

KEYWORDS: Ethnopharmacology, *V. amygdalina*, Phytomedicine, Diabetes, Culture.

INTRODUCTION
Plants have been used for alleviating human suffering from the very beginning of human civilization and records of the use of plants are available since about 5000 years ago. The active principles isolated have provided leads in the development of several life saving drugs, which are in use today. Different civilizations developed their own indigenous system of medicines. Historically, about two centuries ago, our medicinal practices were largely dominated by plant-based medicines. However, the medicinal use of herbs went into decline in the West when more predictable synthetic drugs were made commonly available. However, many developing nations continued to benefit from the rich knowledge of medical herbalism. For example Ayurvedie medicine in India, Kampo medicine in Japan, Traditional Chinese Medicine and Unani Medicine in the Middle East and South Asia are still used by a large majority of people.

All around the world there is talk about “health for all” but it has been realized that modern pharmaceuticals are and will remain out of reach of a large proportion of the human population for the foreseeable future. This necessitates the use of other sources of human knowledge to provide common health benefits. Thus, herbal medicine is now regarded as important but underutilized tool against diseases. The World Health Organization (WHO) recognized this fact in the early 1970s and later in the 2000’s and encouraged governments to effectively utilize local knowledge of herbal medicines for disease prevention and health promotion.

There is now a popular belief that allopathic drugs have serious side effects on human body. As against the same, herbal medicines work better and provide long lasting healing effect and are without any serious side effects when used cautiously. As such there is now a growing demand of herbal medicines and herbal therapeutic applications. The primary health care of 70–80 percent of the world’s population is based on the use of medicinal plants derived from traditional systems of medicine and local health practices. During the past few decades, public interest in traditional, complementary and alternative medicine (TCAM) and use of herbal medicines has increased dramatically in industrialized countries.
The knowledge of medicinal plants has continued to be useful in the production of drugs, food, spices, perfumes and preparation of surgical dressings. With modern technology, medicine has moved from a purely traditional phase to high technological production of synthetic chemicals and the extraction of chemicals from plants to produce drugs. Several of these drugs are derived from plants that form the basis of traditional medicine.

Therefore, medicinal plants are plants that contain medicinal products as their active ingredients. They are used commercially in modern medicine and pharmacology. The standardization of Nigerian medicinal has long been on-going in Nigeria in the attempt to set appropriate pharmacopoeia standards and obtain the quality of plants in our natural environment.

The research of plants’ bioactive substances has continued immensely for the betterment of mankind through the provision of value added economic returns. Natural products as the term imply are naturally occurring compounds that are the end products of secondary metabolism and they are unique compounds for particular organism or classes of organisms. Until the 1950’s, the structures of natural products were determined by degradative techniques, and structure was not proven until the compound has been synthesized in an unambiguous manner. Now, structures have been elucidated primarily by spectroscopic techniques, and the stereochemistry is an important feature of the structure. The botanical overview of *Vernonia amygdalina* (VA), belongs to the family Asteraceae that has a rough bark with dense black straits, and elliptic leaves and it is drought resistant, though it grows best in a humid environment. It thrives on a range of ecological zones and is used as a hedge plant in some communities. Previous studies on phytochemical investigation of the leaves and stem bark of *Vernonia amygdalina* revealed the presence of secondary metabolites such as Terpinoids. A wide array of phytochemical including anti-nutritional factors, has been shown to be present in *V. amygdalina*. Many authors have described the medicinal and biological activity of *Vernonia amygdalina* (VA). The leaves of VA are crushed to make a paste to be rubbed on the body of livestock for destroying ectoparasites. It is one of the traditionally used antifertility plants in Ethiopia. Preliminary study also confirmed that the plant has antifertility effect. Earlier investigations on VA showed that purified chloroform fractions identified as vernodaline, vernolide and vernomygdine elicited cytotoxic effects on human carcinoma narcopharynx cells.
The plant is well known for its antidiabetic and antihypertensive properties. The common and documented medicinal uses include the treatment of schistosomiasis, amoebic dysentery, and gastrointestinal problems. It is also used in the treatment of headache, fever, malaria, venereal diseases, wounds, hepatitis, and diabetes. In Ethiopia the plant is used in cleaning the container used for fermentation purpose. The leaves are used for human consumption and washed before eating to get rid of the bitter taste. They are used as vegetable and stimulate the digestive system.

HERBAL DRUG INDUSTRY

According to the World Health Organization, “a medicinal plant is any plant which, one or more of its organs, contains substances that can be used for therapeutic purposes, or which are precursors for chemopharmaceutical semi synthesis”. This definition distinguishes between the already known medicinal plants whose therapeutic properties or characters are precursors of certain molecules which have been established scientifically, with that of other plants used in traditional medicine which are regarded as medicinal, but have not yet been subjected to a thorough scientific study. Medicinal plants have been used for the treatment of diseases since antiquity. According to Alves and Rosa (2007), 20,000 plant species are used for medicinal purposes, India and China have been on the forefront when one refers to the history of herbal drugs. The traditional systems of medicines viz: Ayurveda, Siddha, Unani, Western Herbal Medicine, Traditional Chinese Medicine and Homeopathy have roots in medicinal herbs. Herbal medicines have been produced by a number of renowned researchers and due to its accessibility to traditions it is still practiced even by lay practitioners. Ayurveda, the ancient healing system flourished in India in the Vedic era. The classical texts of Ayurveda, Charaka Samhita and SushrutaSamhita were written around 1000 BC. The Ayurvedic Materia Medica includes 600 medicinal plants along with therapeutics. herbs like turmeric, fenugreek, ginger, garlic and holy basil are integral parts of Ayurvedic formulations. The formulations incorporate a single herb or more than two herbs (polyherbal formulations).

The history of traditional Chinese medicine is renowned and the herbal system is very well preserved. It originated about 3000 years ago and is a popular science in western countries. Some of the medicinal herbs mentioned in Chinese medicine are common to Ayurveda. Traditional Chinese medicine favors the use of medicinal herbs in their natural form rather than by extraction. Herbal drugs have a different history in Europe and America and have
produced healers like Culpeper. The use of tinctures in homeopathy is based on medicinal herbs.

Before the availability of synthetic drugs, man was completely dependent on medicinal herbs for prevention and treatment of diseases. The use of the medicinal herbs for curing diseases has been documented in the history of all civilizations. The drugs were used in crude forms like expressed juice, powder, decoction or infusion. Although the formulations mentioned in ancient texts are difficult to understand in terms of scientific parameters, some of them are reputed for their curative values. The Napralert database at the University of Illinois\cite{20}, establishes ethnomedicinal uses for about 9200 of the 33,000 species of monocotyledons, dicotyledons, gymnosperms, lichens, pteridophytes and bryophytes. Ancient healers, who developed formulations based on medicinal herbs, were probably not aware of the chemical composition of the herbs. However the advances they made despite the non-availability of scientific procedures were astonishing\cite{21} Initially, the term Materia Medica was coined for the study of natural products. Malaria Medica is defined as the knowledge of natural history, physical characteristics, and chemical properties of drugs. It includes the study of herbs, minerals and drugs from the animal kingdom. The Ayurvedic equivalent for Malaria Medica is Dravyaguna, which is the study of medicinal herbs in Ayurvedic terms. The term ‘Malaria Medica’ is now known as pharmacognosy.

Phytomedicines and Herbal Extracts
A medicinal herb is considered to be a chemical factory as it contains a multitude of chemical compounds like alkaloids, glycosides, saponins, resins, cleoresins, sesquiterpene lactones and oil (essential and fixed). The active constituents are usually secondary metabolites, derived from biosynthetic pathways present within the plant tissue. In 1985 it was recorded that 74% of the 119 plant derived drugs were discovered as a result of chemical studies to isolate the active substances responsible for their traditional use. Plants are used in different forms varying from powders to extracts. Powder represents the drug in the ground form and these types of preparations are considered to be crude. The Pharmacopoeia mentions standardized vegetable powder for therapeutic application. Herbal systems of medicine have become increasingly popular in recent years\cite{22} In light of the growing demand of herbal drugs, quality control and assurance is primarily important. The standardized herbal extracts are considered to be more scientific than crude drugs.
The commonly employed technique for removal of the active substance from the crude drug is called extraction. Selection of the solvent is very critical in preparing the extracts, because the active constituent of the plants have an affinity for solvents.

a. Water and petroleum ether are used for extraction of fixed and essential oils and steroids.
b. Chloroform and ether are used for extraction of alkaloids.
c. Water and alcohol are used for extraction of glycosides.
d. Tannins and phenols are extracted with alcohol and ethyl acetate.

Extracts are prepared by separating the soluble matter from vegetable tissues by application of a suitable solvent like alcohol, water or ether. The resultant liquid is concentrated by evaporation to obtain a liquid extract or concentrated almost to dryness to obtain the solid extract. Depending on the solvents used the extracts are classified as alcohol, ethereal or aqueous.

The standardized herbal extract is a preparation which contains a certain fixed proportion of the active constituent. Although the most obvious aspect of standardization is the guaranteed content of one or more active constituents or marker compounds, standardization involves much more than guaranteed levels of constituents. For example, a standardized extract of Papver somniferum contain not less than 9.5% of morphine. Standardization helps adjusting the herbal drug formulation to a definite content of a constituent or constituents with therapeutic activity.\textsuperscript{[22]} The biological source of a drug has great impact on finished products in herbal drug preparation. Proper identification of the drug is significant for phytochemical screening, which further exerts importance on therapeutic activity of the medicinal herb. Thus presence of the identification standard is necessary in finished products of an herbal drug preparation. A constituent of a medicinal herb, which is used for quality control and assurance of the herbal product is known as marker compound. A marker compound may or may not have therapeutic activity.

**Advantages of standardized extracts**

Standardized extracts retain the chemical complexity typical of the natural plant, but offer the added advantage of guaranteed levels of certain key constituents. An increasing number of botanical medicines have had their clinical efficacy confirmed in clinical trials. The vast majority of clinical trials involving botanical medicines have used standardized extracts. The reason is simple: standardized extracts offer constituent and reproducible therapeutic effects and the highest degree of safety.
Why standardization?
As botanical extracts are made directly from crude plant material, they can show very substantial variation in composition, quality, and therapeutic effects. The variation and diversity of life is enormous, even within a species. In other words, two medicinal plants of the same species may look similar, yet be substantially different in the levels of active constituents that they contain. Botanical medicines made from plants that differ markedly in their chemical constituents cannot produce the same therapeutic effects. Since the practitioner or consumer will not be able to assess the difference, they cannot compensate for it. The consequence will be inconsistent clinical results.[19,23]

Standardized extracts are
a. High quality extracts containing consistent levels of specified compounds.
b. Broad spectrum extracts containing recognized active constituents as well as a variety of other plant constituents (some of which may contribute to the overall therapeutic quality of the extract).
c. Extracts subjected to rigorous quality control during all phases of the growing, harvesting and manufacturing processes.

Clinical advantages
a. High quality extracts with consistent activity.
b. Consistent activity allows for more accurate prescribing.
c. Consistent activity allows for consistent clinical results.
d. Extensive quality control ensures the quality and safety of standardized extracts.

Quality control ensures:
a. That the correct botanical species is used.
b. That only high quality raw materials are used
c. That no other plants material has been used
d. That the plant materials is not contaminated with pesticides, heavy metals, or other noxious agents, that the final extract complies with international limits for microbial content and that the final product is of a consistent high standard preparation.[24,25]

Ethnopharmacology
With the isolation of quinine from Cinchona in 1820, an ancient herbal cure was transformed into a chemical drug. This was the inspiration for a new scientific discipline—ethnopharmacology—as Western scientists began to reinvent traditional herbal cures by
extracting their active principles to make new and profitable drugs.\textsuperscript{[21]} Traditional medicine is a term applied to pre-scientific medical systems that possess bodies of medical knowledge, including pharmacopoeia, that are passed through generations from healer to healer.

**Differentiation between ethno-pharmacology and pharmacognosy**

According to Wardwell, ethno-pharmacology and pharmacognosy overlap considerably, but can be differentiated by several distinct features as explained below:

1. Pharmacognosy considers a broad range of natural products used as therapeutic agents, for medical purposes (such as cotton), as pharmaceutical aids, and poisons; ethnopharmacology is restricted to natural products used in a traditional manner.

2. Pharmacognosy is concerned with the history, economics, and commercial processing of natural substances that affect human health; ethno pharmacology seeks to provide a comprehensive view of the human use of crudely processed drugs that includes ethnographic information.

3. Pharmacognosy has tended to move toward specialized fields such as biosynthesis and fermentation microbiology; ethnopharmacology aims to support interdisciplinary collaboration.

**Ethnopharmacology and Traditional Medicine**

Numerous drugs have entered the international pharmacopoeia in the study of ethnopharmacology and traditional medicine. For traditional medicines, newer guidelines of standardization, manufacture and quality control and scientific research for traditional treatments will be required. This can offer a more holistic approach to drug design and myriad possible targets for scientific analysis. Powerful new technologies such as automated separation techniques, high-throughput screening and combinatorial chemistry are revolutionizing drug discovery. Traditional knowledge can serve as a powerful search engine, which will greatly facilitate and rediscover intentional, focused and safe natural produce drug discovery. By looking at the historical trends in drug and medical developments, it is possible to understand how current drug development will benefit from this partnership.

Ayrvedic and traditional Chinese systems are great living traditions. These traditions have relatively organized databases, and more exhaustive descriptions of botanical material that are available and can be tested using modern scientific methods. Both systems of medicine thus have an important role in bio-prospecting of new medicines. Good botanical practices which can improve the quality control procedures of monitoring impurities, heavy metals and
other toxins in the raw material can make ethno-pharmacology research more meaningful.[26,27,28]

**VERNONIA AMYGDALINA**

**Plant description / Botanical classification**

*Vernonia amygdalina* is an edible plant of the Asteraceae family. It is a small shrub that grows in the tropical Africa to a height of about 2–5 meters with pefiolate leaf of about 6mm diameter and are elliptical and up to 20cm long. The leaves are green with a characteristic odour and a bitter taste.[29,30] The leaves are domesticated in many parts of West Africa. African common names include grawa (Amharic), ewuro (Yoruba), etido (Ibibio), onugbu (Igbo), ityuna (Tiv), oriwo (Edo), chusar-doki (Hausa), labwori (Acholi), olusia (Luo) and ndole (Cameroon).[31] The plant is scientifically classified as belonging to the kingdom plantae. It is an angiosperm, of the order Asterales, of the family Asteraceae, genus Vernonia, and species Vernonia amygdalina. The full binomial name is Vernonia amygdaline Del.[32]

**Vernonia amygdalina**

**Scientific**

- Kingdom: Plantae
- (Unranked): Angiosperms
- (Unranked): Eudicots
- (Unranked): Asterids
- Order: Asterales
- Family: Asteraceae
- Genus: Vernonia
- Species: V. amygdalina

**Origin and geographical distribution**

*Vernonia amygdalina* plant occurs wild in most countries of tropical Africa, from Guinea east to Somalia and South to north-eastern South Africa, and in Yemen. It is commonly grown as a vegetable in Benin, Nigeria, Cameroon, Gabon and DR Congo, and to a lesser extent in their neighbouring countries. The Luhya people in western Kenya use *vernonia amygdalina* as a vegetable, but do not cultivate it. The genus was named in honour of an English botanist, Williams Vernom, traveler and plant collector in North America in the 17th century.
Figure1. 3 Photographs of *V. amygdalina*: (1a) *V. amygdalina* shrub. (1b & 1c) Flowers of *V. amygdalina*. (1d) Leaf of *V. amygdalina*.

Ecology / prospects

*Vernonia amygdalina* occurs naturally along rivers and lakes, in forest margins, woodland and grassland, up to 2000 metre altitude. It often occurs in disturbed localities such as abandoned farmland, and can be found growing spontaneously in secondary forest. It requires full sunlight in cultivation. Flowering is induced by short days. It prefers a humid environment although it is fairly drought tolerant. It can be found on all soil types, but performs best in humus-rich soils. Bitter leaf is an important vegetable in West and Central Africa, which once established, is easy to produce and rather resistant to drought, making it popular in home gardens. The laborious and time-consuming task of processing bitterleaf has encouraged the commercialization of processed leaves. This processing is fast becoming a source of income in urban areas. *Vernonia amygdalina* has multiple medicinal properties that deserve further research. Research on genetic variability and agronomy is also needed.\[29\]

Nutrientional Composition and Uses

An estimated 815 million people in developing countries are reported to suffer from malnutrition, and infants and children are the worst hit (FAO, 2004). Unfortunately, efforts at
improving food production and accessibility in these regions have been directed lopsidedly to roots/tubers, cereals, and animal production. The largely ignored dark green leafy vegetables can however augment the nutrients derivable from other sources, thereby reducing malnutrition tremendously. Leaves are easy to prepare, and contain appreciable quantities of nutrients. Unfortunately, the dietary use of the leaves of VA has remained limited only to the cultures that use it as vegetable (after maceration to remove the bitter principles) in soup and porridge preparation, suggesting an under-utilization of the plant’s leaves.

Table 1: Approximate nutrient composition of V. amygdalina Del.

| Moisture (79.7%) Ejoh et al., (2007) |
| Carbohydrates (68.4%) Ejoh et al., (2007) |
| Lipids (4.7%¶, #) ¶ Ejoh et al., (2007) and # Eleyinmi et al., (2008) |
| Ascorbic acid (mg/100g)(80-104*, 166.5¶) *Udensi et al., (2002) and ¶Ejoh et al., (2007) |
| Caroteinoid (mg/100g)(30) Ejoh et al. (2007) |
| Calcium (g/100g) (0.97¶, #) ¶Ejoh et al., (2007), # Eleyinmi et al. (2008) and Bonsi et al. (1995) |
| Iron (mg/100g) (7.5¶, #) ¶Ejoh et al. (2007) and # Bonsi et al. (1995). |
| Phosphorous (#) #Eleyinmi et al., (2008) and Bonsi et al. (1995) |
| Magnesium, Selenium: Atangwho et al., (2009) |

Note: # represents qualitative determination; *, + and ¶ identify the author(s) that reported the nutrient concentration bearing a corresponding sign.

Table 2: Phytochemical constituents of V. amygdalina Del.

| Phytochemical / Author(s) |
| Stigmastane–type Saponins |
| Sesquiterpene lactones |
| Flavonoids |
| Terpenes, coumarins, Phnolic acids, lignans, Xanthones. |
Medicinal uses of *V. amygdalina*

*Vernonia amygdalina* is probably the most used medicinal plant in the genus Vernonia (Erasto et al., 2006). The observation that an apparently sick wild chimpanzee chewed *V. amygdalina Del.* and seemed to return to normal activity after a while, by Huffman and Seifu and Kriefs et al.\[^{36,37}\] elicited the attention of the phytomedicine community such that dozens of studies have been done since then to test the efficacy of different extracts of the plant in managing a wide array of medical ailments. Igile *et al.*, and other researchers reported that in traditional medicine, practitioners use the plant as an anti-helminth, anti-malarial and as a laxative.\[^{30,38,39}\] Others use it as a digestive tonic, appetizer, febrifuge and for the topical treatment of wounds. Dalziel (1937) was about the first to report that the root and twig of the plant are used for the treatment of stomach and gastrointestinal problems by the Hausas of Northern Nigeria, while the decoction from the leaves is used in treating malaria fever in Guinea and cough in Ghana.\[^{40}\] In some parts of Nigeria, the stems are used as chew sticks for oral hygiene, and for the management of some dental problems. In Malawi and Uganda, VA is used by traditional birth attendants to aid the expulsion of the placenta, after birth, aid post-partum uterine contraction, induce lactation and control post-partum hemorrhage. Many of these traditional uses of the plant have been scrutinized scientifically.\[^{30,41}\]

Hypoglycemic/anti-diabetic property of *V. amygdalina Del.*

Diabetes mellitus, a metabolic disorder that has arguably achieved epidemic proportions, is said to affect more than 200 million persons globally, and is projected to affect 366 million people by the year 2030.\[^{42}\] Phytotherapy for some decades has played an important role in the management of the disease especially in resource-poor countries. Clearly, the identification of plant materials that can manage diabetes and its complications would save millions of people, especially in developing countries, from untimely death. The blood sugar lowering effect of the aqueous extract of the leaves of *V. amygdalina* was reported by Akah and Okafor.\[^{43}\] This was strengthened by the observation that the aqueous extract produced significant reductions in the blood glucose concentrations of normal and diabetic rats, comparable to the effect of the standard drug chlorpropamide.\[^{44}\] Reports from Nwanjo and Nwokoro and Obarisiagbon *et al.*\[^{45,46}\] on the effects of the aqueous and ethanol extracts of the plant corroborate these claims. The ethanol and methanol extracts of the plant have also been shown to have blood sugar lowering effect in rats,\[^{47,48}\] suggesting that the active blood sugar lowering principles may be extracted by both polar and non-polar solvents. Okolie *et al.*, administered the leaves of *V. amygdalina* by ‘squeeze-wash-drink’ and ‘chew-raw’
options to normoglycemic humans, and found that *V. amygdalina* (irrespective of mode of administration) had significant blood sugar reduction effects post-priandially at 30 min intervals for 2 hours. Whether the same effect could be reproduced in diabetics is yet to be studied.

**Antibiotic/Antimicrobial/Antimalaria properties of *V. amygdalina Del.***

The sap of the leaves of VA was found to show inhibitory capacities against *Staphylococcus epidermidis, Staphylococcus aureus, Escherichia coli,* and *Pseudomonas aeroginosa.* A 60% methanol extract of the leaves gave antimicrobial activity against *Bacillus subtilis, Klebsiella pneumonia,* *P. aeruginosa,* *Proteus vulgar,* *Shigella dysenteriae* and *S. aureus.* Both vernolide and vernodalol isolated from VA showed activity against the Gram positive *Bacillus cereus,* *S. epidermidis,* *S. aureus,* *Micrococcus krisinae* and *Streptococcus pyogenes* and the Gram negative *Slamonella pooni,* but neither of the two had any activity against the Gram negative *E. coli,* *serrata marcescens,* *P. aeruginosa* and *K. pneumonia.* This implies that the activity reported for the extracts of VA against *E. coli* and *P. aeruginosa* by Ijeh *et al.**, and *P. aeruginosa* and *K. pneumoniae* by Akinpelu may be mediated by other phytochemicals other than the Sesquiterpene lactone vernolide and vernodalol.

The aqueous extracts of the leaves of VA have been shown to be potent against plant fungal pathogens, while not affecting the growth of the plant negatively. On the other hand, Akinpelu (1999) reports that a 60% methanol extract of the leaves of VA had no effect against *Candida albicans*–a popular opportunistic pathogen of humans. Vernolide and vernodalol have however been shown to have activity against the fungi *Aspergillus flavus,* *mucor hiemalis,* *Penicillium notatumand Aspergillus niger* in a manner that is comparable (at 0.1 mg/ml and above) to the standard drug Nystatin.

Malaria is said to be responsible for approximately the million infant deaths every year in sub-Saharan Africa. What is worrisome is that the parasite is becoming resistant to a number of the current drugs for malaria treatment available in the market. Abosi and Raseroka (2003) reported that the ethanol extract of the leaves and root-bark of *V. amygdalina* suppressed parasitemia induced by inoculation with *Plasmodium berghei* in mice by 67 and 54% respectively in four days. The aqueous extract of the leaves of the plant has also been shown to reduce the load of *P. berghei* in mice by 73% when given intraperitoneally for 4 days. Iwalokun (2008) and other researchers have also corroborated the effectiveness of the aqueous extract of *V. amygdalina* in managing malaria. These data and the reports by
Ijeh et al., Ejike and Njan et al., that the extracts of *V. amygdalina* may have central and peripheral analgesic properties lend credence to the use of the plant in the folk-loric management of malaria fever. It is thought that the flavonoids, saponins and alkaloids and Sesquiterpene and Steroidal constituents are responsible for the antiplasmodial properties of *V. amygdalina*.\(^ {11,55,57}\)

**Anti-cancer/Tumor properties of *V. amygdalina Del***

The burden of cancer has become a serious global problem. Prostate cancer and breast cancer are the most diagnosed non-skin cancers in men and women respectively. Breast cancer represents 15% of new cases of all cancers, while prostate cancer represents 15.3% of all cancers in men in the developed countries. There is therefore an urgent need to develop chemicals/phytotherapeutics that are effective against different cancers. *V. amygdalina* Del is increasingly becoming a strong candidate for cancer management. It is thought that coumarins, flavonoids, sesquiterpene lactones and edolides may be the principles in *V. amygdalina* that are responsible for its anticancer activity.\(^ {58,59}\)

**Antioxidant properties of *V. amygdalina Del***

Many chronic diseases and causes of food spoilage are linked to pro-oxidants. Antioxidant principles are therefore useful in food preservation and drug formulations. Synthetic antioxidants like butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) are suspected to be tumorigenic.\(^ {60}\) Therefore, there is a need to search for potential antioxidant principles, especially from herbs, that can replace their synthetic counterparts. Flavonoids are known to be good antioxidants, and luteolin (a flavonoid found in *V. amygdalina*) has been reported to be a strong antioxidant. However, Igile et al., (1994) confirmed that luteolin is a more potent antioxidant than BHT, and reported that its glucosides—luteolin 7-0-β-glucoroniside and luteolin 7-0-β-glucoside also have antioxidant activities.\(^ {38,61}\)

**Hepato-and nephro-protective properties of *V. amygdalina Del***

Liver diseases are serious medical problems, especially because of the central role of the liver in metabolic homestasis and xenobiotic transformations. The search for alternative drugs for the treatment of liver diseases has produced some ‘botanical chief’ among which is *V. amygdalina del* compounds of the sesquiterpene family have been shown to have antihepatoxic activity in tetrachloromethane-induced hepatic damage in rats.\(^ {62}\) A study by Ijeh and Obidoa (2004) found that a diet incorporated with *V. amygdalina* protected weanling
albino rats against aflatoxin B1-induced hepatotoxicity.\cite{63} Data published by Ejere et al., 2015, and obarisiagbon et al., 2019, support the hepatoprotective effect of \textit{V. amygdalina} in rats. Dietary incorporation of the leaves of \textit{V. amygdalina} resulted in no significant difference in the mean weight of the liver and kidneys of weanling rats, implying an absence of acute toxicity.\cite{63,64} A study on the impact of an ethanolic extract of \textit{V. amygdalina} on some indices of kidney function in rats concluded that the extract can protect against kidney impairment, but may induce dilutional hyponatremia. The same team subsequently published findings that the combined administration of \textit{V. amygdalina} extract and another plant extract was nephroprotective, and also reversed dilutional hyponatremia, but this time, amplified diabetes-induced hypophosphatemia.\cite{65,66}

\textbf{The role of \textit{vernonia amygdalina} in the management of diabetes mellitus}

There are many forms of treatment in the African region. Most times, the patients visit the local traditional healers before coming to the hospital.\cite{67} Many traditional healers had heard of diabetes and knew at least the disease was characterized by excessive thirst and urination. The frequency of utilization of traditional medicine, in this case \textit{Vernonia amygdalina}, is increasing worldwide and is well documented in both African and global populations to be between 20 to 80%. Multiple therapy practices involving combined use of traditional herbal medicine and prescription medications has also been identified as prevalent in some populations.\cite{68} Diabetes mellitus is a metabolic disease with severe socio-economic importance characterized by hyperglycemia and glycosuria due to absolute or relative lack of insulin. Treatment is usually directed towards the relief of depressing symptoms. Management of protocol of the disease involves non-pharmacological (diet, exercise and surgery) and or pharmacological means (insulin and oral hypoglycemic agents). \textit{V. amygdalina} known as bitter leaf possesses hypoglycemic effect and is capable of normalizing other biochemical and hematological abnormalities associated with diabetes mellitus and thus could be used as main therapy for diabetes mellitus. The fact that it is commonly used for edible purposes and has antidiabetic properties suggests possibility of therapeutic interaction when used with an antidiabetic agent either consciously or inadvertently.

\textbf{The role of herbal medicine in tradomedicinal management of diabetes}

Herbal medicine involves herbs which are plants or plant parts used for its scent, flavor or therapeutic properties, sold as tablets, capsules, powders, teas, extracts and fresh or dried plants. People use herbal medicine to try to maintain or improve their health. Herbal medicine
do not have to go through testing that drugs go through and which is not essentially safe, some herbs can interact with prescription or over-the-counter (OTC) medicines. One of the regulatory requirements for an investigational new drug (IND) approval is preclinical pharmacokinetics of the new drug entity. However, for the majority of herbal remedies used in ethnomedical or conventional medical practice, data on their disposition and biological fate in humans are lacking or inadequate. It is vital in the drug development chain, to understand the disposition of these herbal products and how they interact with conventional drugs before their launch in the market, in order to ensure the rational use of herbal medicines.

Increasing number of patients and consumers are using plant-based therapeutic products as complementary therapy in the treatment and management of chronic ailments such as tuberculosis, diabetes, hypertension, HIV/AIDS, cancer and diseases of endemicity and high recrudescence especially malaria, as well as other social conditions like obesity, cigarette smoking and drug abuse. This upsurge in the use of phytomedicines is a global phenomenon, with more than 80% of people in Africa and Asia using herbal medicines and an increasing number in Western world. It is estimated that 60%-70% of the American population is taking botanical products.[69,70] The therapeutic superiority of many plant extracts over single isolated constituents, as well as the bioequivalence of many phytopharmaceuticals with synthetic chemotherapeutics is well documented. The gradual transition from the long-standing use of monodrug therapy in classical medicine to the new concept of a multidrug and multitarget therapy is greatly promoting phytotherapeutics. There is a gradual shift from the orthodox use of mono-substance therapy and an increasing transition to multidrug therapy of patients with drug combinations, such as is done presently for the treatment of diabetes, cancer, acquired immune deficiency syndrome (AIDS), malaria, tuberculosis or hypertension.

Status of herbal medicine in Nigeria; Nigeria has a rich tradition of herbal medicine with its diverse cultures and traditions. Nigeria is rich in traditions. Nigeria is rich in traditional medicine and has eminent and respected traditional healers involved in taking care of the teeming population. In Nigeria, traditional medicine practices are a main source of livelihood for a significant number of populations who depend on it as a source of their income. High population growth rate (2.8%) and poverty coupled with dwindling economic reserves in the country make Nigerians move to the more affordable sources for their immediate health needs; and as the population increases, demand for traditional medicine would increase. In order to provide affordable health care services especially to those who cannot afford orthodox medicine. Several state governments through their traditional medicine boards have
tried to institutionalize the use of traditional medicine. They attempt to do this through tradomedicine fairs and exhibition which seeks to enlighten the public on the possible cures from the kind of traditional medicine. Herbalists are being encouraged to register their proven and efficacious standardized herbal preparations with the National Agency for Food and Drug Administration and Control (NAFDAC).

Traditional medicine programme of the WHO defines traditional medicine as the sum total of all knowledge and practices whether explicable or inexplicable use in diagnosis, prevention and elimination of physical, mental or social imbalance and relying exclusively on practical experience and observation handed down from generation to generation whether verbally or written.\textsuperscript{71} According to the World Health Organization (2008)\textsuperscript{72}, about three quarters of the world population depends on traditional remedies mainly herbs for the health care of its people. Historians from around the world have produced evidence showing that apparently all primitive peoples used plants often in a sophisticated way. Quinine from Cinchona bark was used to manage the symptoms of malaria long before the disease was identified and the raw ingredients of a common aspirin tablet have been a popular pain killer for longer than we have had access to tablet making machinery.

CONCLUSION

The growing popularity of herbal remedies is fuelling the interest in herbal medicine by scientists. Scientific evidence of efficacy is beginning to emerge from random controlled trials in which herbs compare favorably with placebo. Another reason for popularity of herbal medicine is that many people believe they are safer and more natural than pharmaceuticals. It is believed that herbal products in the market today have not been subjected to critical drug approval process to demonstrate their safety and effectiveness. Many users of herbal medicine however consider that these products are safer for consumption based on prior extensive field experience. Orthodox medical practitioners are to be convinced of the efficacy of plant extract. There is the opinion of some traditional herbalists who believe that unprocessed natural products have an innate superiority and mystical aura surrounding the herbs, and these will somehow be destroyed by extraction and standardization. The vision of the role of traditional medicine and natural product science for the future should continually be evolved for the future when the pressures on available resources including land use, water and oil etc, becomes too high. All the available technologies should be completely integrated into developing the societal role of traditional medicine in global health care. It is the duty to
create these visions and maintain them for creative growth of the health care individuals and for the security and stabilities of societies. Innovative strategies employing all the associated sciences and technologies must be created in order that the natural product sciences including traditional medicine can help in the development of sustainable foods and the health care products including drugs for a dramatically expanding population.

Finally, the development of multidisciplinary national collaborative research programme should be encouraged to motivate the local and global scientific development of natural resources. A team work amongst ethnobotanist, ethnopharmacologist, physician, pharmaceutical chemist and phytochemist is a must for the fruitful outcome on medicinal plants research. While the ethnopharmacologist have a greater role in the rationalization of combination of activities, the phytochemist’s role will slightly shift towards standardization of herbal medicines. Pharmaceutical research must go beyond focusing on pharmacological efficacy of botanicals, but also in studies that improve their effectiveness in order for humanity to fully benefit from their inherent therapeutic potentials. *Vernonia amygdalina* has proven that the various characteristics and properties would give the glimpse of hope needed and required for the effective maintenance and or treatment of Diabetes mellitus. Traditional medicine has more possibilities now than ever and it is the pharmacist, herbalist, botanist and chemist that need to be aware and more advancely broadened on the possibilities of *Vernonia amygdalina* in the treatment of this chronic disease (s) and more studies should be done on clinical trials on humans to finally confirm the potentials of this novel plant.

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