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Full Length Research Paper

*Ginkgo biloba*L.: Phytochemical components and antioxidant activity

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Curative effects of *Ginkgo biloba* L. have been recognized for centuries, dating back to traditional Chinese medicine which used crushed leaves to treat several health problems. Although *G. biloba* L. has several known and investigated activities, the antioxidant activity of its extract (EGb 761) is particularly relevant because reactive oxygen (ROS) and reactive nitrogen (RNS) species are constantly produced in aerobic organisms. Currently, the exploitation of the antioxidant activity of *G. biloba* extract Egb 761 has been of particular pharmacological importance because oxidative stress may be harmful to cells and may trigger the development of many disorders. The antioxidant activity of the EGb extract against oxidative stress has been associated with several therapeutic effects and currently, Egb761 is indicated to treat labyrinthitis, headache, memory disturbance, intermittent claudication, dementia, Alzheimer's disease, glaucoma, cardiovascular disorders, cerebral ischemia, increased libido and sexual activity, and psychiatric diseases, such as depression. This study is a review of basic and clinical studies related to antioxidant properties of *G. biloba* L.

Key words: *Ginkgo biloba* L., EGb 761, antioxidant activity, phytotherapic drug.

INTRODUCTION

Although medicinal plants have provided biologically relevant products for centuries, they still serve as a source for new medicines (Czelusniak et al., 2012; Albuquerque and Hanazaki, 2006). *Ginkgo biloba* L. is a widely used plant in popular medicine; its popular names are Ginkgo Japan, tree-fern, or simply *ginkgo.* Traditional Chinese medicine uses dry and mashed leaves of ginkgo to treat health problems such as asthma, bronchitis, hearing loss, tuberculosis, cognitive dysfunction, stomach pain, skin problems, and anxiety (Almeida, 2009).

Other current uses, such as arteriosclerosis, thrombus formation, ischemic heart disease, and the prevention of diabetes mellitus have also been reported (D'ippolito et al., 2005; Zhao e al., 2015). Recently, *G. biloba* extract associated with extracts from grape seed and skin, green tea, resveratrol, quercetin and bilberry

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was reported to decrease diastolic pressure in hypertensive subjects (Biesinger et al., 2015).

Several authors (Kose et al., 1997; He et al., 2014; Sarikcioglu et al., 2004) have reported that the *G. biloba* L.(EGb 761) extract has antioxidant action. Because reactive oxygen (ROs) and reactive nitrogen (RNs) are constantly produced in aerobic organisms, the ability of EGb 761 to act as a free radical scavenger is significantly relevant (Vasconcelos et al., 2007; Boligon et al., 2013). Of potential therapeutic significance, the combination of EGb 761 with other plant extracts can increase synergistically the antioxidant properties of the combinations (Wang et al., 2015).

Free radical species (FRs) are highly unstable and can react with cellular components. Under normal conditions, the production of these species is balanced by the presence of a sophisticated defense mechanism consisting of enzymatic and non-enzymatic components (Barbosa et al., 2006; Imai and Nakagawa, 2006) such as superoxide dismutases (SOD), catalases (CAT), glutathione peroxidases (GPx), and other components (Spadiene et al., 2012).

Eventually, however, some endogenous or exogenous factors can induce an increased production of ROs and RNs, or trigger depletion in antioxidant mechanisms, leading to an unbalance known as oxidative stress. This condition affects biomolecules and cellular structures and leads to several harmful effects on cells (Rover et al., 2001). These effects may lead to the development of several diseases, particularly pathologies related to the central nervous system (Alok et al., 2014; Pereira et al., 2014). Because the EGb 761 extract has known antioxidant activity against oxidative stress, it may be effective in both treatments and prophylaxis of chornic degenerative diseases (Diamond et al., 2000; Puppo and Silva, 2008; Jager et al., 2006; Berigan and Page, 2000; Forlenza, 2003; Gauthier and Schlaefke, 2014; Siegel et al., 2014; Cheng et al., 2015; Montes et al., 2015; Solfrizzi and Panza, 2015).

This article reviews information related to antioxidant properties of *G. biloba* L. described in basic and clinical studies.

MATERIALS AND METHODS

This study is an integrative literature review of the effects related to the antioxidant properties of *G. biloba* L. in studies published between 1991 and 2015, surveyed in Pubmed, Scientific Eletronic Library Online (SciELO) and Sience Direct.

Ginkgo biloba L. characterization

G. biloba L. is a species from the Ginkgoaceae family cited in Chinese therapeutics around 2,800 years B.C. This is a primitive, deciduous, high and robust plant, with fan-shaped disposed leaves and irregularly lobed; these plants can reach up to 40 m in height (Almeida, 2009; Lorenzi and Matos, 2000; Lorenzi et al., 2003). *G. biloba* L. was the first species to germinate after the atomic bomb explosion in Hiroshima, in 1946. The species is highly resistant to insects, microorganisms, and environmental toxins and conditions (Lima and David, 2006; Raven et al., 2001).

Ginkgo biloba L. phytochemistry

G. biloba L. therapeutic uses were based on macerated plant leaves, which contain known active compounds (Table 1). However, not all these components were useful as therapeutic compounds; Western medicine started using *Ginkgo* extracts in 1965 (Lima and David, 2006). The percentage of each constituent in the extract can vary according to the country where it was produced and the season in which the plant was harvested (Silva et al., 2010). In an effort to standardize this product that has been sold for more than two decades (Kock, 2005; Schulz et al., 2002), Egb761 was extracted from dry and mashed leaves. The flavonoid fraction in this extract stops lipid peroxidation, acting as free-radical scavenger, and helping in the prevention of oxidative stress (Silva et al., 2002). In addition, flavonoids increase the release and reuptake of serotonin (Ahlemeyer and Kriegelsteins, 1998), stop the reduction of cholinergic muscarinic receptors related to age, and stimulate its reuptake in the hippocampus (Defeudis, 1991; Blumenthal et al., 1998). Ginkgolide B is another important active principle in the EGb 761 extract that acts as an antagonist of the platelet-activating factor (PAF) receptor, and thus, inhibits platelet aggregation and improves cognitive and memory function (Luo, 2001; Smith and Luo, 2004). The active compounds, bilobalide (1), ginkgolide A (2), and ginkgolide B (3) (Figure 1) found in the EGb 761 extract have been reported to induce the reduction of peripheral benzodiazepine receptors, that are involved in many biological processes, however, with unknown functions (Amri et al., 1996).

Antioxidant activity

The antioxidant activity in the *G. biloba* L. extract is played by its flavonoids (Mckenna et al., 2001; Macarenco et al., 2001) protecting cellular membranes from oxygen reactive species, chelating transition metals, and acting on the expression of protein antioxidant molecules or leading to an increase in antioxidant metabolites (Smith and Luo, 2004). The literature reports several studies with *G. biloba* L. demonstrating its antioxidant activity. Yoshikawa et al. (1999) showed that the EGb 761 extract has a relaxing effect on vascular walls improving microcirculation and blood flow. Therefore, it could be used in the prevention and treatment of chronic oxidative damage, ischemic heart disease, cerebral infarction, and chronic inflammation (Yoshikawa et al., 1999). Beek (2000) reports that the extract inhibits the activity of xanthine oxidase, which uses molecular oxygen as an electron acceptor to produce superoxide ions and hydrogen peroxide. Hence, the extract activity inhibits the formation of these oxygen reactive species and prevents cellular damages. In the same vein, EGb 761 has been reported to blunt the high-glucose-induced oxidative DNA damage in human umbilical vein endothelial cells (HUVECs) (He et al., 2014) and to inhibit the aggregation of β-amyloid peptide *in vitro* (Xie et al., 2014). Moreover, the EGb 761 extract has the capacity to directly minimize FRs or recycling tocopherol radicals in both cases, sparing the vitamin E present in the membrane. The presence of tocopherol in membranes is important beyond the protection of phospholipids in the lipid bilayer of membrane units against the attack of reactive oxygen species. In addition to antioxidant activity, the EGb 761 extract inhibits the phospholipase A2, which hydrolyzes the ester bonds in phospholipids releasing the substrate for the cyclooxygenase that catalyzes the formation of endoperoxides and giving an

Table 1. Main chemical constituents of *Ginkgo biloba L*.

Metabolite class	Substance	Reference
Flavonoids	Quercetin Kaempferol Isorhamnetin Glycosides	He et al. (2008)
Terpenoids	Bilobalide	He et al. (2008)
	Ginkgolide Ginkgolide B Ginkgolide C Ginkgolide J	Banov et al. (2006)
Biflavones	Bilobetina Ginkgetina	Schneider et al. (2007)
	Ginkgolic acid	Banov et al. (2006)
Organic acids	Shikimic acid Kynurenic acid Ascorbic Acetate 3-Methoxy-4-acid hydroxybenzoic acid 4-hydroxybenzoic acid 3,4-diidroxibenzoic 6-hydroxyquinurenic acid	Schneider et al. (2007)
Other substances	Glucose Ramanose Sterols Aliphaticketones Alcohols Diterpenes Phenylpropanoids Carotenoids	Schneider et al. (2007)

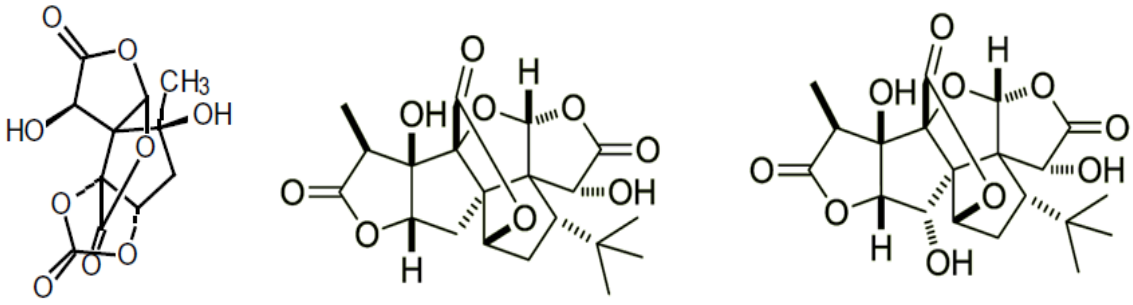

Figure 1. Chemical structure of some active compounds found in *Ginkgo biloba L*.: bilobalide (1) ginkgolide A (2), and ginkgolide B (3).

antithrombotic activity to the plant (Kusmic et al., 2004).

Other studies investigated the neuroprotective effects of *G. biloba* L. in mice through treatment with EGb 761 extract, before or after the administration of MPTP (1-metil-4-fenil- 1,2,3,6-tetrahydropiridine), which is a substance that causes irreversible symptoms of Parkinson disease. According to these authors, mice pre-treated with the EGb 761 extract showed protection against the MPTP toxicity. Protection against oxidized substances occurs through the inhibition of the MAO B enzyme that is responsible for the conversion of MPTP in MPP+. It was concluded that the extract prevents the entrance of oxidized MPTP in the dopaminergic tract obstructing the formation of FRs and, consequently, providing antioxidant protection (Wu and Zhu, 1999).

In addition to the neuroprotection against the natural production of FRs EROS, there are studies that link the protective activity of *G. biloba* L. against the induced production of these oxygen species. Ilhan et al. (2004) induced oxidative stress in mice using a system created with mobile phones and anechoic cameras; the treatment of these mice with dry powder of *G. biloba* L.showed that the SOD and GPx enzyme activities were preserved in the brain tissue.

Another study evaluated the activities of catalase, superoxide dismutase, and glutathione peroxidase in cerebral structures (hippocampus, striatum, and substantia nigra) in mice. The animals were orally treated with *G. biloba* L. extract in the dose of 100 mg/kg of body weight during 14 days. The results showed a meaningful increase in the activities of catalase and superoxide dismutase, decreased lipoperoxidation in the hippocampus, and no alterations in the activity of glutathione peroxidase. The authors emphasize that this protective effect might exploited in the development of new drugs to prevent, delay, or improve symptoms related to neurodegenerative diseases such as Alzheimer's disease (Bridi et al., 2001).

Toxicity in the EGb 761 extract

It is noteworthy to emphasize that tests performed with the EGb 761 extract revealed low toxicity to chronic or acute administration (Blumenthal et al., 1998; Blumenthal, 2000) but no mutagenic or teratogenic effects (Mills and Bone, 2000), or negative effects on the reproduction and development in the tested Wistar mice (Castro et al., 2005). Currently, there are many marketed phytotherapeutic products from *G. biloba* L. with indicated use for disorders and symptoms related to impaired cerebral blood flow, such as memory problems, cognitive function, dizziness, headache, vertigo, tinnitus, early stages of dementia, peripheral circulatory disorders, and retina problems. These medicinal products are in compliance with the current legislation (Colombo, 2011).

RESULTS AND DISCUSSION

A significant increase in the use of medicinal plants and herbal medicines has been observed as the result of new scientific information about the molecular mechanisms underlying the therapeutic action of some natural products. Natural products are mainly used by adults and elderly people who have chronic diseases and seek for alternative phytotherapeutic treatment options. These usages are often based on self-medication and in popular and traditional use of the plant extracts, generally without scientific support (Ekor, 2014). In the case of *G. biloba,* fortunately, the traditional use of the plant extracts has been supported by both experimental and epidemiological studies (Yang et al., 2014; Alok et al., 2014; Chen et al., 2015; Montes et al., 2015; Siegel et al., 2014). Of particular importance, *G. biloba* extracts have been proven to be safe for human consumption, particularly the EGb 761 standardize extract. It now is clear that *G. biloba* has antioxidant properties in a variety of *in vitro* and *in vivo* models and that the antioxidant components of the EGb 761 extract can be involved in the therapeutic efficacy of this secular plant. However, we still have scanty information if the modulation of oxidative stress by *G. biloba* extracts is the primary mechanism of the therapeutic properties of this plant. Thus, more studies are needed to establish if oxidative stress is the cause or the consequence of therapeutic properties of *G. biloba* extracts. For instance, *G. biloba* extracts have anti-inflammatory properties in different *in vitro* and *in vivo* models (Apetz et al., 2014; Siegel et al., 2014; Tisato et al., 2013; Chen et al., 2014; Hirata et al., 2015) and the inhibition of inflammatory response can decrease the oxidative stress. In short, the complex interplay between primary cellular responses and oxidative stress in chronic degenerative diseases and the modulation of this interaction by plant extracts need more detailed studies.

Conclusion

There are many studies in the literature demonstrating the powerful antioxidant action and the low toxicity of the EGb 761 extract, confirming the efficiency and the safety of *G. biloba* extracts secular use by the population worldwide.

Conflicts of interest

Authors have none to declare.

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Medicinal plants used in the treatment of neurodegenerative disorders in some parts of Southwest Nigeria

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An ethnobotanical survey of plants used in the treatment of neurodegenerative diseases was carried out in three local government areas (LGA) of Ibadan, Oyo State, South Western Nigeria. Twenty-eight respondents, which comprised traditional medicine practitioners (TMPs), herbalists, herb sellers and the elderly were interviewed using semi-structured questionnaires. Focused group discussion was used to interview the TMPs during one of their associations meetings. Several free interviews were also conducted. Some herb sellers (all women) were interviewed in some of the herbs markets visited. Information was obtained on names of plants constituting the recipes, plant parts used, source of plants, methods of preparation of herbs and mode of administration. Twenty two plant species belonging to 19 Angiosperm families were found to be useful for the treatment of neurodegenerative diseases. The most prominent among these plant families are Fabaceae, Musaceae and Piperaceae with two species each. The leaves constitute the most frequently used parts. Other parts such as root, fruit and stem bark are occasionally used. The modes of preparations are infusion, decoction and concoction which are administered orally, mostly three times daily. Most of the herbs are sourced from the wild; only a negligible number of practitioners have home gardens where plants are grown. It is therefore imperative to encourage the cultivation and proper documentation of some of the plants which may become endangered over long use. All the plants identified in this work have been used regularly by the herbalists and adjudged to be efficacious.

Key words: Ethnobotanical survey, neurodegenerative diseases, medicinal plants, Ibadan, Nigeria.

INTRODUCTION

Neurodegenerative disease is a term applied to a variety of conditions which result from a chronic breakdown and deterioration of neurons, particularly, those of central nervous system (CNS) (Adewusi et al., 2010). Alzheimer's disease (AD), Parkison's disease, multiple sclerosis, amyotrophic lateral sclerosis and spongiform encephalopathy are some of the examples of neurodegenerative diseases (Chiba et al., 2007). AD is the most common of all neurodegenerative diseases (Citron, 2004; Tedeschi et al., 2008). These diseases are commonly found in elderly people. They are a major cause of morbidity, mortality and impose severe strains

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on the social welfare systems, and as a result are gaining increased recognition by the World Health Organisation (WHO) (Houghton and Howes, 2005).

Neurodegenerative diseases are characterized by a gradual onset of progressive symptoms including loss of memory and tremor, difficulty in learning or retaining information, inability to handle complex tasks, impaired spatial orientation and abilities, language deficits and behavioural changes (Adewusi et al., 2010). These symptoms have been recognized as a feature of increasing age for a long time and are acknowledged in many traditional medical systems. However, it is only recently that they have been recognized and received attention from mainstream medicine as distinctive diseases (Houghton and Howes, 2005).

The drugs currently available in the market for the treatment of various learning and memory disorders are associated with several side effects indicating need of substitute medication from alternative system of medicine (Pattewar et al., 2011). Plant materials have been a major source of natural therapeutic remedies and are used to treat various infectious diseases in many developing countries (Beverly and Sudarsanam, 2011; Dike et al., 2012). Medicinal plants have demonstrated their contribution to the treatment of diseases, such as HIV/AIDS, malaria, diabetes, sickle-cell anaemia, mental disorders (Elujoba et al., 2005) and microbial infections (Okigbo et al., 2005). According to the World Health Organization (WHO, 2001), 80% of the world population use medicinal plants in the treatment of diseases and in African countries, this rate is much higher. It has been estimated that up to 90% of the population in developing countries rely on the use of medicinal plants to help meet their primary health care needs (WHO, 2002). The use of traditional medicine is not restricted to the developing countries (Jimoh, 2006). According to Dike et al. (2012), a vast majority of prescription drugs used in the world contain compounds that are directly or indirectly, via semi-synthesis, derived from plants. A variety of plants has been reported to show AChE inhibitory activity and so may be relevant to the treatment of neurodegenerative disorders, such as AD (Mukherjee et al., 2007). Cyril–Olutayo et al. (2012) reported that in traditional practices of medicine, numerous plants have been used to treat cognitive disorders, including neurodegenerative diseases, such as AD and other memory related disorders. According to different cultural traditions, the use of complementary medicines such as plant extracts in dementia therapy varies (Cyril–Olutayo et al., 2012).

Celastrus paniculata Willd. seeds and oil have been used in Ayurvedic medicine for stimulating intellect and sharpening memory (Lekha et al., 2010). The roots of the Indian medicinal plant *Clitoria ternatea* L. have been reported to promote intellect (Taranalli and Cheeramkuzhy, 2003). Aqueous and ethanol extracts of several plants including *Malvia parviflora* L., *Albizia adianthifolia* (Schumach.) W.F. Wight, *Albizia suluensis* Gerstner and *Crinum moorei* Hook. F. have been used in southern Africa to treat memory loss (Risa et al., 2004; Stafford et al., 2008). *Ginkgo biloba* L. has been used widely for the improvement of memory loss associated with abnormalities in blood circulation (Samuelsson, 2004). *Galanthus* species have been used traditionally in Bulgaria and Turkey for neurodegenerative conditions (Mukherjee et al., 2007). Galanthamine is an Amaryllidaceae alkaloid first isolated in the 1950s from *Galanthus nivalis* L. (Shu, 1998). It also occurs in other genera of the Amaryllidaceae family, *Narcissus* and *Lycoris* species.

Nigeria as one of the most important countries in West Africa is richly blessed with great diversity of medicinal plants. However, some of these plants are becoming threatened and endangered (Sonibare and Abegunde, 2012). Hence, there is the need to document and research into various medicinal plants used in treating diseases in different parts of Nigeria. Ethnobotanical surveys of other diseases in the Southwestern part of Nigeria similar to the one presented in this work have been carried out by some researchers (Erinoso and Aworinde, 2012; Sonibare et al., 2009; Soladoye et al., 2010). The Yoruba traditional system of medicine also offers a number of safe treatments for CNS related disorders. Cyril–Olutayo et al. (2012) reported some of the plants used as memory enhancer and anti ageing in Ondo State, Nigeria. Elufioye et al. (2012) also reported some plants used for memory enhancement and antiaging in Sagamu, Nigeria. Some of these plants include *Bryophyllum pinnatum* (Lam) Kurz., *Dioscorea mangenotiana* Meige., *Ficus exasperata* Vahl., *Jatropha curcas* L., *Carica papaya* L., *cola acuminata* (P. Beav) Schott and End. These plant species can be used for the development of drugs for managing AD. This work was undertaken to document indigenous knowledge on the use of medicinal plants in the treatment of neurodegenerative disorders by the people of three local government areas (LGA) of Oyo state in South Western part of Nigeria with a view to promoting further studies on the biological activity of the plants.

MATERIALS AND METHODS

Study area

The study area Oluyole LGA comprises 5 locations, namely Adebayo, Idi-Ayunre, CRIN (Cocoa Research Institute), Alaho and Ibusogboro. Ibadan South-East LGA comprises of Molete, Bode Market, Idi Arere, Challenge, Orita and Eyini. Akinyele LGA comprises Orogun, Ajibode, Ojoo, Idi-Ose, Moniya, Onidundu, Iroko and Ijaye. The three LGA are part of the 11 LGAs of Ibadan, Oyo State with latitude 7°22′N and longitude 3°55′E. The climate in the region is tropical with two distinct seasons: dry and wet. The dry season is usually between November and February. Rainfall occurs almost throughout the year with an average annual rainfall of 250 cm. The indigenes encountered in this region are Yorubas and they are farmers by occupation, some of them are traders. The areas still have many villages without access to modern health care and

Table 1. Demographic data of respondent.

Parameter	Category	Number of respondent (N)	%
Practice specification	Herbalist	5	18
	Herb-seller	8	29
	Traditional medical practitioners	9	32
	Elderly	6	21
Age (years)	1 -20	0	0
	21-40	8	29
	41 -60	15	54
	>60	5	18
Sex	Male	19	68
	Female	9	32
Religion	Christianity	5	18
	Islam	18	64
	Traditional	5	18

thereby wholly relying on traditionalists and TMPs for solutions to their health challenges.

Data collection

The survey was carried out between June, 2012 and February, 2013. People that were interviewed, include Traditional Medicine Practitioners (TMPs), herb sellers, herbalists and the elderly who possess knowledge of medicinal plant use. Their ages ranged between 28 and 70. Village heads were consulted and LGA secretariats were visited to get information on where and how the TMPs could be met. The village heads gave the description of the residents or the herbalists and the elderly who had knowledge about the medicinal uses of plants. The LGA secretariats were visited and information about the TMPs were obtained. They usually meet fortnightly for their association meeting. Focused group discussion method was used here. The association of TMPs at Oluyole local government of Ibadan comprises both male and female, five members were in attendance on the day of the interview. During the interview, questions were thrown to the whole house and one person responded to the questions at different times. In another local government; four people were in attendance. Special markets designated for the sales of herbs were also visited and the herb sellers who were all women were interviewed. The interview was briefly interrupted by customers who came to buy herbs. Informed consent was obtained orally from all participants before the commencement of the interview.

The use of semi-structured questionnaire and oral interview were adopted to obtain the relevant ethno medicinal data. The questionnaire was administered to the respondents. Some of the questions they responded to include the name and the part of the medicinal plant used to treat neurodegenerative disorders, the preparation of the recipe, etc. (Appendix 1). Field note was taken during the survey and some of the herbalists showed us some of the plants around their house. In most cases, the vernacular names of the plants were given; text books and research journals were consulted to verify the botanical names. Furthermore, the use-mentions index (UMi) was calculated for all plants (Andrade-cetto, 2009). The UMi was taken as the number of use mentioned for a particular plant divided by the total number of informants interviewed.

Collection and authentication of plants

Plant samples were collected from the TMPs and herb sellers and were identified and authenticated at Forest Herbariun Ibadan (FHI) and voucher specimen were deposited at the Department of Pharmacognosy Herbariun, University of Ibadan (DPHUI).

RESULTS

Demographic data

The population of the respondents is made up of TMPs (32%), herbalists (18%), herb sellers (29%) and the elderly (21%) out of which 19 are males and 9 are females. Most of them were between ages 28 and 70 years. All the respondents were Nigerians from the Yoruba ethnic group with 18% practicing Christianity, 18% practicing traditional religion and the rest Islamic religion (Table 1).

Plant information and their families

Data from the survey revealed that neurodegenerative disorders are not only common among the aged, TMPs claimed that the disease is now rampant among the youths due to poor diet, taking of hard drugs, smoking and stress. Different symptoms of neurodegenerative disorders are known by different local names, such as,

'iyerira', 'aagana', 'olodeori' and many TMPs encountered in the course of the survey claimed to have treated some of them with some herbs especially when discovered at the early stage. The plants mentioned include *J. curcas* L., *Talinum triangulare* (Jacq.) Willd., *A. adianthifolia* (Schumach.) W.F. Wight, and *Bacopa floribunda* (R.Br.) Wettst. Many of these plants are obtained from the forest, while some of them are collected from the garden around the house. For the free interviews, each of the respondents especially the herb sellers (4) mentioned three plants which should be prepared as concoction; leaves of *B. floribunda, Spondias mombin* L. and *Digitaria horizontalis* Willd. The other herb sellers (4) mentioned root of *Rauvolfia vormitoria* Afzel. and fruits of *Piper guineense* Schum. and Thonn. apart from the ones mentioned earlier. Herb sellers usually grow some of the herbs and they also work hand in hand with the herbalist to source for some other species in the forest. The other respondents, herbalists (5) and elderly (6) mentioned other plant species as shown in Table 1.

A total of 22 plant species (Table 2) belonging to 19 families were identified. Table 2 shows the list of identified plant species, families, local names and plant parts used. The most prominent among these plant families are the Fabaceae and the Musaceae with two species each. Other plant families, include Apocynaceae, Portulaceae, Srophuliaceae, Poaceae, Olacaceae, Zingiberaceae, Papilionaceae, Arecaceae, Piperaceae and Euphorbiaceae with one species each. In all, the most frequently mentioned species are *B. floribunda* (0.357), mentioned 10 times, *S. mombin* (0.214) mentioned 6 times, *Aframomum melegueta* (0.179) mentioned 5 times, *D. horizontalis* (0.143) mentioned 4 times, and *R. vormitoria* (0.107) mentioned 3 times by the respondents. The species distribution according to the ethnobotanical survey with UMi is given in Table 4. Different plant parts are used, but the predominant parts used are the leaves. Some of the herbs are prepared in combination with other herbs. During the interactions with the respondents, many of them claimed that a mixture of certain plants (*B. floribunda, S. mombin* and *D. horizontalis*) would be efficacious. Many of these plant species have some other ethnomedicinal uses like *Musa sapientum* is often used for ulcer, *Allium cepa* is used for hypertension, *A. melegueta* is used for cough and malaria, *S. mombin* is used for dysentery and as a purgative, *J. curcas* is used for pain relief and *R. vormitoria* is used for stomach disorder and tooth ache.

Sources of plant, mode of treatment

From the survey, 36% of the respondents employed plant and animal parts in their therapies, while 21% use herbs only (be it in fresh or dry forms). About 43% claimed that the treatment is accompanied with divination or incantation (Table 3). Many of the respondents claimed that the treatment has no side effects and when there is, it is usually mild like vomiting, headache, nausea and sleeping for long hours. It is generally observed that administration of plant decoctions rarely elicit noticeable side effects compared with orthodox drugs, because they are considered as nature cure (Morris, 2002).

Half of the respondents confirmed regular supply of their plant remedies from the forest, others (29%) usually sourced for plants either from the home gardens or markets. The TMPs especially and the herbalists usually source for plants in the forest and many of them grow herbs around their houses. The herb sellers usually grow some of the herbs and they also work hand in hand with the herbalist to source for some other species in the forest. Only very few (18%) claimed that the plants are not always available. This development supports the clamour for biodiversity preservation through cultivation and afforestation programmes (Ogbole et al., 2010). Knowledge of herbal treatment was mainly acquired either by ancestral means or by training or both, while the duration of treatment ranged from 2 to 3 weeks, 3-5 to 5-12 weeks as reported by 21, 29 and 14% of the respondents, respectively. 80% of the respondents claimed the use of verbal instructions in administering herbal recipes to their patients. This is believed to enhance the understanding of the dosage and methods of application of the remedies. In orthodox practice, written label instructions usually accompany prescriptions dispensed in the pharmacies or bought from the community pharmacies.

Method of preparation

Herbal remedies can either be prepared from dry plants from markets or freshly collected samples around homes or home gardens. However, respondents affirmed that both forms of plant materials are efficient in herbal preparation except in some cases where freshly collected samples are preferred. The main method of preparation is decoction (boiling in water). Others are infusion and concoction. Preference was shown for decoction. The time required for boiling varied and is dependent on plant parts or nature of plant. In all cases the preparation is to be taken orally.

Enumeration of recipes

The dried leaves of *B. floribunda, S.mombin* and *D. horizontalis* are boiled with water and made into a decoction. A cup ful is to be taken three times daily. The dried leaves of *B. floribunda, S. mombin* and *D. horizontalis* are grinded together and mixed with pap and should be taken regularly. The leaves of *T. triangulare* and *A. adianthifolia* are mixed with snail and ash and then burnt. The residue is then mixed with pap and

Table 2. Medicinal plants used in the treatment of neurodegenerative disorders.

S/N	Botanical name	Family	Local name	Part(s) used
1	*Abrus precatorius* L.	Fabaceae	Omisinmisin	Leaves
2	*Aframomum melegueta* K. Schum.	Zingiberaceae	Atare	Seed
3	*Albizia adianthifolia* (Schumach.) W.F. Wight	Fabaceae	Ayunrebonabona	Leaves
4	*Allium cepa* L.	Liliaceae	Alubosaelewe	Leaves
5	*Angraecum eichlerianus* Bory.	Orchidaceae	Ewe ela	Leaves
6	*Bacopa floribunda* (R.Br) Wettst.	Scrophuliaceae	Oniyemiye	Leaves
7	*Baphia nitida* Lodd.	Papilinionaceae	Iyereosun	Leaves
8	*Bombax buonopozense* P. Beauv.	Bombacaceae	Eso	Leaves
9	*Digitaria horizontalis* Willd.	Poaceae	Eeran	Whole plant
10	*Elaeis guineensis* Jacq.	Arecaceae	Imo ope	Leaves
11	*Flueggea virosa* (Roxb. ex Willd.)	Phyllantaceae	Ewe iranje	Leaves, root
12	*Jatropha curcas* L.	Euphorbiaceae	Lapalapa	Fruits
13	*Justicia schimperi* (Hochst.) Dandy	Acanthaceae	Esisi	Leaves, root
14	*Musa paradisiacal* L.	Musaceae	Ogede agbagba	Leaves
15	*Musa sapientum* L.	Musaceae	Ogedewewe	Fruits
16	*Olax subscorpioidea* Oliv.	Olacaceae	Igionifon	Stem bark
17	*Piper guineense* Schum. And Thonn.	Piperaceae	Iyere	Leaves, fruit
18	*Rauvolfia vomitoria* Afzel.	Apocynaceae	Asofeyeje	Root
19	*Rinorea dentata* Kuntze	Violaceae	Oloborowo	Leaves
20	*Spondias mombin* L.	Anacardiaceae	Iyeye	Leaves
21	*Talinum triangulare* (Jacq.) Willd.	Portulaceae	Gbure	Leaves
22	*Piper* spp.	Piperaceae	Atareaja	Seed

Table 3. Mode of treatment of neurodegenerative disease.

Question	Category	Number of response (N)	%
Frequency of treatment	Regular	22	80
	Irregular	6	20
	No treatment	0	0
Other treatment apart from herbs	None	6	21
	Animal part	10	36
	Divination/Oracle/ Incantation	12	43
Source(s) of knowledge of herbal treatment	Ancestral	11	39
	Training	8	29
	Ancestral and training	9	32
Duration of treatment	2-3 weeks	6	21
	3-5 weeks	8	29
	5-12 weeks	4	14
	No response	10	36
Accompanied side effect(s)	None	7	25
	Nausea and vomiting	15	54
	others	6	21
Accompanied verbal instructions	Yes	22	80
	No	4	15
	No response	2	5

Table 4. Species distribution according to the ethnobotanical survey with Use Mention Index.

S/N	Species	Number of times mentioned	Use mention index (UMI)
1	*Abrus precatorius* L.	1	0.036
2	*Aframomum melegueta* K. Schum.	5	0.179
3	*Albizia adianthifolia Schumach. W.F. Wight*	1	0.036
4	*Allium cepa* L.	2	0.071
5	*Angraecum eichlerianus* Bory.	2	0.071
6	*Bacopa floribunda (R. Br.) Wettst.*	10	0.357
7	*Baphia nitida* Lodd.	1	0.036
8	*Bombax buonopozense* P. Beauv.	1	0.036
9	*Digitaria horizontalis* Willd.	4	0.143
10	*Elaeis guineensis Jacq.*	3	0.107
11	*Flueggea virosa (Roxb. ex. Willd.)*	1	0.036
12	*Jatropha curcas* L.	2	0.071
13	*Justicia schimperi* (Hochst.) Dandy	1	0.036
14	*Musa paradisiaca* L.	1	0.036
15	*Musa sapientum L.*	2	0.071
16	*Olax subscorpioidea* Oliv.	1	0.036
17	*Piper guineense Schum. and Thonn.*	1	0.036
18	*Rauvolfia vomitoria Afzel.*	3	0.107
19	*Rinorea dentata (P. Beauv.) O Ktze.*	1	0.036
20	*Spondias mombin* L.	6	0.214
21	*Talinum triangulare (Jacq.) Willd.*	1	0.036
22	*Piper* spp	2	0.071

should be taken regularly. The bark of *Olax subscorpioidea* Oliv. is cut into pieces and mixed with the leaves of *Alium cepa*; the mixture is put in a bottle and then water is added. The infusion is to be taken regularly. The fruit of *M. sapientum*, the leaves of *Elaeis guineensis*, fruit of *A. melegueta* and fish was cooked with rain water and eaten as soup. The leaves of *B. floribunda*, fruit of *A. melegueta* and the leaves of *Abrus precatorius* L. were sun dried and ground together or burnt together. The powder is then taken with pap regularly. The root bark of *R. vormitoria* is scrapped and dried. It is then ground into powder and taken with pap, a table spoonful of the powdered root for half a cup of pap. The fruit of *J. curcas* is dried and ground into powder and taken with pap. The leaves of *Bombax buonopozense* P. Beauv. are burnt with snail and taken. The leaves of *Angraecum eichlerianus* Bory is cooked as soup with fish and eaten. The leaves of *Rinorea dentata (P. Beauv.) O Ktze.* is cooked with snail and eaten. Dried leaves of *B. floribunda* and *S. mombin* are ground together and taken with pap or mixed with honey. The root of *R. vormitoria*, fruits of *P. guineense* and the leaves of *A. cepa* are ground together and taken with pap. The leaves of *Angraecum eichlerianus*is dried and ground into powder. The powder is poured into a hoe and the person licks the powder from the hoe with his mouth. The leaves of *E. guineense*, *M. sapientum*, *A. melegueta* and the feather of a cock is burnt together and taken with palm oil in the morning.

DISCUSSION

Neurodegenerative disorders primarily affect the elderly population but from this survey, many of the respondents claimed that it is also common among the youths due to poor eating habit, taking of alcohol, stress and smoking. They have different local names for the different symptoms of neurodegenerative disorders e.g ‘iyerira, ‘aagana, ‘olodeori and they claimed to have treated some of them with some herbs, especially when discovered at the early stage. Numerous herbal extracts, containing several active constituents and often more than one plant species, have been used to treat neurodegenerative disorders. Amongst these are the *Salvia* species (*Salvia officinalis* L. and *Salvia lavandulaefolia* Vahl., *Salvia miltiorrhiza* Bung.) (Howes et al., 2003; Perry et al., 2000a, b), *Cymbopogon schoenanthus* (L.) Spreng. (Khadri et al., 2010), *Terminalia chebula* Retz. (Sancheti et al., 2009).

The findings from this survey revealed some plant families with the highest occurrence of species which include Fabaceae, Musaceae and Piperaceae with two species. Other plant families include Apocynaceae, Portulaceae, Srophuliaceae, Poaceae, Anarcadiaceae, Phyllantaceae, Orchidaceae, Olacaceae, Liliaceae,

Zingiberaceae, Papilinionaceae, Arecaceae, Bombaceae, and Euphorbiaceae with one species each. This suggests that these families can be explored scientifically for AD drug development. Results also revealed that quite a number of plant parts especially the leaves, roots, fruits, seeds and very rarely the whole plants have been found efficient in the treatment of the disease. The most prominent plant species in the recipes according to the UMi were *B. floribunda* (Scrophuliaceae), *S. mombin* (Anarcadiaceae), *D. horizontalis* (Poaceae), *A. melegueta* (Zingiberaceae), *R. vormitoria* (Apocynaceae), *M. sapientum*, *A. cepa* (Liliaceae), *E. guineense* showing that they possess potential anticholinesterase and neuroproctective actions. Investigations on the plant parts used and the mode of preparation and administration indicated that irrespective of the plant part(s) or combinations used, water was the main medium for all the medicinal preparations. In addition to pure herbal preparations, in some cases the drug was administered along with honey, hot pap or palm oil. These supplement ingredients may be used to enhance the effect of the herbal preparations or are simply used to make the preparations palatable. Many scientific researchers have reported the anticholinesterase activity of some of the plants or other species of the families identified in this study. Some of these are *B. buonopozense* (Bombacaceae), *J. curcas* (Euphorbiaceae), *S. mombin* (Anarcadiaceae), *B. monniera* (Scrophuliaceae) and *A. adianthifolia* (Fabaceae) (Elufioye et al., 2010; Adewusi et al., 2010).

The survey revealed that majority of the plant species used for the treatment of neurodegenerative disorders are sourced from the wild. Regardless of how medicinally important the plants are, only very few cultivate them. The assessment reveals that little or no conservation strategies are in place to safeguard these plants. Awoyemi et al. (2012) reported that although, medicinal plants are necessary in deciding a programme of action for primary health care, most of the practitioners have not imbibed conservation techniques as most of these genetic resources are for now largely undocumented and the indigenous knowledge of their relevance are steadily being lost due to unsustained harvesting of plants from the wild. Sonibare and Abegunde (2012) reported that there are many cases of unsustainable harvesting of various medicinal plants in different communities in Africa and other continents of the world. In order to have a considerable long term effect on the environment, health care and economy, the use of important medicinal plants in a way and at a rate that does not threaten or endanger the plants must be ensured (Wong et al., 2001). It is therefore imperative to encourage cultivation and proper documentation of these plants, some of which have become endangered so as to conserve them and prevent them from going into extinction.

The result of this survey showed that majority (80%) of the herb sellers/ TMPs/herbalists claimed no occurrence of side effects following patients' use of herbal preparations. However, some of the traditional healers said that patients may have some nausea feeling like vomiting after taking the recipe; some of them may sleep for a very long time.

With this information on the local uses of these medicinal plants, subsequent isolation of the biologically active compounds from the plants can be carried out. The isolation, identification and purification of the bioactive compounds will certainly form the basis for future drug discovery and design from these indigenous medicinal plants. Conservation of the traditional knowledge and these medicinal plants is greatly advocated for. In this context, more detailed studies about the anticholinesterase activity of the medicinal plants identified in this survey are currently being carried out in our research laboratory, and the biological activity of the most promising plants will be further investigated, evaluated and elucidated.

Conclusion

This study revealed twenty two medicinal plants used to treat memory related disorders in three LGAs in Ibadan, South Western part of Nigeria. The documentation is ethnopharmacologically relevant in view of the scarcity of information on plants used to treat neurodegenerative disorders in the area, where traditional healers claimed to have been managing and curing associated diseases with appreciable success. The results of this study therefore provide the basis for further studies on the phyto-constituents and compounds responsible for the treatment of neurodegenerative disorders. The study plays an important role in documenting and conserving traditional knowledge of plants for future use.

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Conflicts of interest

Authors have none to declare.

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Appendix 1: Questionnaire

DEPARTMENT OF PHARMACOGNOSY

FACULTY OF PHARMACY

UNIVERSITY OF IBADAN, IBADAN

QUESTIONAIRE FOR FIELD WORK SURVEILLANCE

1. Name:_____

2. Practice specification

Herbalist ☐ Herb seller ☐ Traditional ☐ Medical Practitioner ☐ Others ☐

3. Age (years) 1-20 ☐ 21- 40 ☐ 41- 60 ☐ > 60 ☐

4. Religion Christianity ☐ Islam ☐ Traditional ☐

5. Sex Male ☐ Female ☐

6. Do you know any medicinal plants used to treat neurological disorders? Yes ☐ No ☐

7. How often do you treat diseases related to neurological disorders? .....

Irregular ☐ Regular ☐ Not at all ☐

8. Give local names of the plant and the plant parts used for treating neurological disorders.

Plants used	Plant part used
a._____	_____
b._____	_____
c._____	_____
d._____	_____
e._____	_____

9. Which of the plants listed above is the most used?

10. What are the other medicinal uses of the most used plants?

_____

_____

_____

11. State the method of preparation of the plant: _____

12. What other treatment do you use apart from herbs? .....

None ☐ animal parts ☐ divination/ oracle/incantation ☐

13. What are the types of dementia diseases that have been treated before? .....

14. What are the side effects of the treatment? None ☐ Nausea/vomiting ☐ others ☐

15. What is the duration of the treatment? 2 -3 weeks ☐ 3 – 5 weeks ☐ 5 – 12 weeks ☐

> 12 weeks ☐

16. Are the plants readily available? Yes ☐ No ☐

17. What are the various locations of the plants in the study area? …….

In the forest only ☐ other places (Market, around the house) ☐ Not always available ☐

18. What are your sources of knowledge of herbal treatment?

Ancestral ☐ Training ☐ Ancestral and training ☐

19. Do you give verbal instructions during treatment? Yes ☐ No ☐

Related Journals Published by Academic Journals

- *Journal of Medicinal Plant Research*
- *African Journal of Pharmacy and Pharmacology*
- *Journal of Dentistry and Oral Hygiene*
- *International Journal of Nursing and Midwifery*
- *Journal of Parasitology and Vector Biology*
- *Journal of Pharmacognosy and Phytotherapy*
- *Journal of Toxicology and Environmental Health Sciences*

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