SCHOOL OF PHARMACY, UNIVERSITY COLLEGE LONDON

Medicinal plants use in Nigeria for the management of hypertension and diabetes

Master of Philosophy

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Rosemary Alexandra Sylver-Francis

I, Rosemary Alexandra Sylver-Francis, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Worldwide, people constantly embrace alternative and/or complementary therapies, which include traditional medicinal plants (TMPs), for management of their health conditions. Two non-communicable diseases, hypertension and diabetes, evoke growing concerns over the escalating health threat which they pose to humanity globally. Over the past decade these conditions have become two of the biggest healthcare issues in Africa, rivalling communicable diseases. This study focuses on the use of TMPs for the management of hypertension and diabetes in Nigeria, Africa's most populous country. The aim is to determine using questionnaire, the extent of the usage of these TMPs. The high prevalence of hypertension and diabetes in Nigeria is a national health problem. The impact of poor management due mainly to unaffordable healthcare costs makes it more burdensome on the patients. These factors, combined with disease complications, exacerbate the financial plight of individual families. Hence the search for alternatives. This study considers the drive behind TMP use. A survey among HTN and DM patients in two South Eastern Nigeria hospitals was run based on a structured/semi-structured questionnaire administered over 600 patients. The results of this study show high prevalence in the use of TMPs for the management of hypertension and diabetes. Approximately, 75% of the participants use TMPs. All of them use TMPs concurrently with their prescription medicines, predisposing them to severe hypotension or hypoglycaemia, possibilities of drug interactions, direct toxicities, as well as adulteration with active pharmaceutical agents. Also, the poor quality of herbal medicines raises safety concerns. Directions for use of these TMPs are scanty or anecdotal. Consequently, fifty (50) plants commonly used by these patients were recorded with known pharmacokinetic parameters. Most of these TMPs have been proven to possess therapeutic properties and pharmacological effects, thus providing a baseline for investigation into their uses by patients. *Vernonia amygdalina* (bitter leaf), *Ocimum gratissimum* (sweet basil/scent leaf) and *Gongronema latifolium* (bush buck) were three of the most commonly used medicinal plants identified from this work. Quantitative statistical cross-analysis was used to make statistical inferences using data from this study. It was ascertained that there were some associations between the use of TMPs by patients, their conditions and demographics. This study is important as it forms the basis of a future study - survey to be conducted on Nigerian doctors – to ascertain their views on alternative medicine and its integration into the national healthcare system.

Keywords: Hypertension; Diabetes mellitus; Traditional medicines; Medicinal plants; Nigeria; South Eastern Nigeria; CAM; ethnobotany; ethnopharmacology; Antihypertensive, herbs, herbal remedies; hypertension/diabetes and medicinal plant.

Impact Statement

A survey of patients attending hospital in South Eastern Nigeria for the management of hypertension and diabetes showed that the majority used traditional medicinal plants (TMP) alongside conventional drugs. A literature review of these medicinal plants indicated that many have a long tradition of use without known toxicity, and for some, there are pre-clinical data to support their traditional uses. This study provides background information that can aid the Nigerian healthcare professionals in the management of their patients. Specifically, the documentation of ethnomedicinal information identifying which TMPs patients are taking can be used to monitor the potential of herb drug interactions. The production of a guide for clinicians to use in patient management is an important outcome of this project. The fact that 75% of hypertensive and diabetic patients visiting hospitals in Nigeria were using herbal medicines but did not always inform their clinicians is an important factor that supports the need for these guidelines. Another notable finding is that all patients recorded as using TMPs knew their names. Therefore, another output from this study is the need to inform the public about the general safety of TMPs, their toxicity and potential for drug herb interactions. This study has collated data that can be used to provide broad public health awareness of the use of TMPs by patients being treated for hypertension and diabetes. This resource will be available as an open access paper for a global impact, reaching individuals, communities, academics, and non-academics. It will prompt and help local researchers into further work in this direction. Its findings will also be disseminated through scholarly journals, mainstream media, and public engagements featuring public policy makers. It is feasible, too, that with a targeted push, the substance of this study may become incorporated in the curricula of medical schools. Thus, this resource should serve to harness the need for further research into the therapeutic benefits of these medicinal plants alongside conventional drugs, as a first step towards the possible integration of traditional medicine into the Nigerian healthcare system. Finally, a critical finding in this study is the patients' non-disclosure of their use of TMPs to their healthcare professionals, for fear of being scolded and being refused treatment by their doctors. By helping to bring awareness of this gulf between the professionals and their patients and its negative impact on the management of these patients, it is hoped that healthcare professionals will be encouraged to handle their patients in a non-judgemental manner and to open up easy communication with their patients.

Dedication

To God Almighty

Yours the Inspiration

Yours the Glory

Ours the Hope and Trust

Acknowledgement

I wish to thank unreservedly Professor Monique Simmonds, Professor Steve Brocchini, Professor James Barker and Dr Dehbi Hakim-Moulay for their invaluable advice and guidance. I treasure the advice of Professor Sara Randall. Without their advice, professionalism and support this journey might have faltered. My profound gratitude to the entire crew of the Nnamdi Azikiwe Teaching Hospital, Nnewi, Anambra State, Nigeria. Sadly, an attempt at listing individuals here would be fraught with dangers of incompleteness. However, each of you knows the depth of the sincerity of my gratitude. Certainly, too, my thanks would not be complete without acknowledging the roles of my husband and children. Your unwavering support and patience throughout this period demand for your recognition as 'silent contributors' to this successful outcome.

Table of Contents

List of Tables

List of Figures

ABBREVIATIONS

ABPM Ambulatory Blood Pressure Monitoring

ADME Absorption, Distribution, Metabolism and Excretion

AT1 Angiotensin 1 receptors

ACE inhibitor Angiotensin-converting enzyme inhibitor

ARB Angiotensin II Receptor Blocker

BNF British National Formulary

BP Blood Pressure

CCB Calcium Channel Blocker

CAM Complementary and alternative medicine

CM Conventional Medicine

CYP Cytochrome

DBP Diastolic Blood Pressure

DM Diabetes

FDA Food and Drug Administration

GBD Global Burden of Disease

GIP Glucose-dependent Insulinotropic Peptide

GLP-1 Glucagon-like peptide 1

GLP1-RA Glucagon-like Peptide-1 Receptor Agonists

HCT Hydrochlorothiazide

HDI Herb Drug Interaction

HDL High Density Lipoprotein

HTN Hypertension

IDF International Diabetes Federation

IFG Impaired fasting glucose

IGT Impaired glucose tolerance

JNC Joint National Committee

LDL Low Density Lipoprotein

LMICs Low and Middle Income Countries

Na/Cl Sodium Chloride channels

NCD Non Communicable Disease

NICE National Institute for Health and Care Excellence

PD Pharmacodynamic

P-gp P-glycoprotein

PK Pharmacokinetic

RAAS Renin-Angiotensin-Aldosterone System inhibitors

ROS Reactive oxygen specie

SBP Systolic Blood Pressure

SGLT2 Sodium glucose co-transporter 2 inhibitors

SHEP Systolic Hypertension in the Elderly Program

SHR Spontaneously Hypertensive Rat

SJW St John's Wort

TMP Traditional Medicinal Plants

VLDL Very Low Density Lipoprotein

VSM Vascular Smooth Muscle

WHO World Health Organisation

1.0 Introduction

1.1 Alternative and/or Complementary Medicines

Currently, many people in developed and developing countries are turning to alternative and/or complementary medicines, which include traditional medicinal plants (TMPs) for treatment and management of their health conditions (Chintamunnee and Mahomoodally, 2012; Mahomoodally, 2013; Boardman et al., 2020). These conditions range from minor ailments such as coughs and colds to major communicable and non-communicable diseases. The United Nations and other major public health stakeholders have declared Non Communicable Diseases (NCDs) a cause for global concern (Beaglehole et al., 2011; Adeloye et al., 2015; WHO, 2021). Hypertension and Diabetes are two of the non-communicable chronic diseases managed with complementary and alternative medicines (CAM) by their sufferers. There is growing concern about the escalating health threat posed by hypertension and diabetes to the global population (Beran, et al., 2019). The African region has the highest prevalence of hypertension of the WHO's six regions, estimated at 46% of adults aged 25 years and above (WHO, 2020). Diabetes is projected to increase with the numbers rising from 19.8 million in 2013 to 41.5 million in 2035, representing a 110% absolute increase (Peer et al., 2013). These diseases come with very high management costs. There is a high economic burden resulting from hypertension and associated cardiovascular complications in Nigeria (Abegunde, et al., 2007; Adeniji, 2021). This adversely affects developing countries such as Nigeria due to its limited healthcare budgets. Patients, therefore, turn to alternative and/or complementary therapies seeking affordable healing. Large numbers of diabetic and hypertensive patients use them in addition to their prescription drugs for management of their diseases (Argáez-López et al., 2003; Kumar et al., 2006; Hasan et al., 2009; Adeniyi et al., 2021). Hypertension and diabetes in most cases require polytherapy, and the sufferers often have co-morbidities. Consequently, the use of TMPs concurrently with orthodox medicines poses health risks, such as herbal drug interactions (HDIs), hypoglycaemia and hypotension, among others. The study on diabetes by Ezuruike and Prieto demonstrated that over 50% of patients take their conventional medicines concurrently with their TMPs. This number constitutes a large proportion – hence the exposure to HDIs (Ezuruike and Prieto, 2016). Similarly, another study on hypertension reported that co-administration of ginkgo with diuretic thiazide resulted in high blood pressure (Izzo et al., 2005; Brinkley et al., 2010).

1.1.1 What Is CAM?

CAM refers to a broad set of health care practices that are not part of a country's

conventional medicine and are not integrated into the dominant health care system. In addition, WHO indicates that in some countries they can be part of the countries' traditional medicine (WHO, 2019). There are other CAM definitions by various organizations as shown in Table 1.1. Complementary and alternative medicine is an increasing feature of health-care practice; but considerable confusion remains about exactly what it is and what position the disciplines included under this term should hold in relation to conventional medicine (Zollman and Vickers, 1999). Despite these irregularities, its global use is on the rise. Studies have shown that about 42% of global populations use complementary and alternative medicine (CAM) (Josefson et al., 1996; Margolin et al., 1998; WHO, 2019). There is evidence of substantial CAM use across the globe, including Europe (Fisher and Ward, 1994; Fjær et al., 2020); Australia (Maclennan et al., 2002; Steel et al., 2018); China (Ergil, 1996; Xin et al., 2020) and Israel (Shmueli et al., 2011). The use of CAM has increased dramatically throughout the Western world (Lewith et al.,2000; Fjær et al., 2020). The terms "complementary medicine" or "alternative medicine" are used interchangeably with traditional medicine in some countries (WHO, 2019). CAM is grouped within five major domains: alternative medical systems, mind-body interventions, natural and biologically based treatments, manipulative and body-based methods and energy therapies (NCCAM, 2004; Fan, 2005; Tabish, 2008;) which includes but not limited to the following: Herbal medicine, Acupuncture, Ayurveda, Homeopathy, Naturopathy, Chinese or Oriental medicine, Chiropractic and osteopathic medicine, Massage, Body movement therapies, Tai chi, Yoga, Dietary supplements, Nutrition/diet, Electromagnetic therapy, Reiki, Qigong, Meditation, Biofeedback and Hypnosis. Natural and biologically based practices include traditional medicinal plant use/herbal, dietary supplements, special dietary, orthomolecular and individual biological therapies (Tabish, 2008).

Table 1.1 Tabular representation of CAM definition

References	CAM Definitions
(WHO 2014-2023)	The terms “complementary medicine” or “alternative medicine” refer to a broad set of health care practices that are not part of that country’s own tradition or conventional medicine and are not fully integrated into the dominant health-care system.
(BMA,1993)	'Those forms of treatment which are not widely used by the conventional healthcare professions, and the skills of which are not taught as part of the undergraduate curriculum of conventional medical and paramedical healthcare courses.

(Zollman and Vickers,1999; Wieland, 2011 as adopted by Cochrane Collaboration)	"Complementary and alternative medicine (CAM) is a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period. CAM includes all such practices and ideas self-defined by their users as preventing or treating illness or promoting health and well-being. Boundaries within CAM and between the CAM domain and that of the dominant system are not always sharp or fixed."
(House of Lords Select Committee on Science and Technology, 2000)	CAM is a title used to refer to a diverse group of health-related therapies and disciplines which are not considered to be a part of mainstream medical care.
(NCCAM, 2007)	'CAM is a group of diverse medical health care systems, practices, and products that are not generally considered to be part of conventional medicine'
(NHS, 2016)	CAM are treatments that fall outside of mainstream healthcare.

1.2 Context of Healthcare

Health care can broadly be divided into modern (conventional, orthodox, Western, or allopathic) and traditional (indigenous, complementary, alternative or integrative) (WHO, 2000; Xue, 2008). Nigeria's official healthcare system is the modern system. The country's healthcare system uses conventional medicines in the management/treatment of their patients in all their hospitals. Their healthcare professionals are also trained with conventional medicines. However, a significant percentage of Nigerians (about 70%), choose to use traditional health care (Adefolaju, 2014; Aina et al., 2020).

1.2.1 Modern Healthcare system

This system is clearly defined, though with minor regional variations in its underlying philosophy and clinical methods. In modern medicine, knowledge expansion is achieved through scientific research, which can involve global collaboration and commitment. Such research is well supported financially by industries, governments and philanthropic organizations. This is in sharp contrast to the situation with traditional healthcare system (WHO, 2000; VonAchen et al., 2021).

1.2.2 Traditional Healthcare system

Traditional healthcare is a system of healing dating back to 200 B.C. in written form (Tabish,

2008). The discovery of pollen clusters of different kinds of flowers in the Neanderthal grave at Shanidar cave, Iraq, suggests that knowledge of the medicinal properties of plants dates back at least 60,000 years (Solecki, 1975). Traditional medication involves the use of herbal medicines, animal parts and minerals; but this study deals with only herbal medicines. WHO defined traditional medicine as the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness (WHO, 2013). WHO reported that the long historical use of many practices of traditional medicine, including experience passed on from generation to generation, has demonstrated the safety and efficacy of traditional medicine. They stressed the importance of the need for scientific research in order to provide additional evidence of its safety and efficacy. In conducting research and evaluating traditional medicine, knowledge and experience obtained through the long history of established practices should be respected (WHO, 2013).

Many studies have demonstrated and shown evidence of the global historical existence of medicinal plants and their use by the early physicians in the treatment and management of diseases (Oubré et al., 1997). Despite existing in Africa and globally for thousands of years, traditional medicine practice has been neglected or outlawed due to pressure from practitioners of modern medical practice. Furthermore, the unscientific background of its method of operation counts against it and in some cases, it is regarded as fake (Winslow and Kroll, 1998; Okujagu, 2005), and considered as quackery (Jonas, 1998). The practice of traditional medicine varies greatly from country to country and from region to region, influenced by such factors as culture, history, personal attitudes and philosophy (WHO, 2000). The increasingly widespread use of traditional medicines has prompted WHO to promote the integration of traditional medicines, TM, and Complementary and Alternative medicines, CAM, into the national health care systems of some countries. They have also encouraged the development of national policies and regulations as essential indicators of the level of integration of such medicines within the national health care systems (WHO, 2005; WHO, 2011). Despite this, it is still a slow process as the orthodox practitioners have reservations and resentments against alternative traditional medicine practice and use (Nevin, 2001; Ebomoyi, 2009; Ahlberg, 2017).

Prior to the advent of orthodox medicine, traditional medicine practice was the dominant medical system in Africa. It was the only source of treatment for the greater proportion of the population (Romero-Daza, 2002; Abdullahi, 2011). It has been widely reported in studies that the impact of colonialism on indigenous knowledge systems (Mapara, 2009), especially knowledge of medicine (Paul, 1977; Feierman, 2002; Millar, 2004; Konadu, 2008), had a negative effect on African healthcare systems. These studies emphasise the negative impact

of colonialism on indigenous medicine, giving rise to a 'cultural-ideological clash' creating an unequal power-relationship that practically undermined and stigmatised the traditional health care system in Africa. The post-independence period in Africa has seen a rise in the use of traditional medicinal plants (TMPs) (Wada, et al., 2019; Kolawole, et al., 2019). These TMPs are mostly sourced from the wild, and the tropical rain forests face becoming extinct due to overexploitation and lack of conservation programmes aimed at sustaining these plant resources (Obute, 2005).

There is an urgent need for the preservation of the tropical rain forests, the source of these medicinal plants, and for the comprehensive documentation of the pharmacologically medicinal plants. These plants are not sufficiently recorded and documented (Gbile and Adesina, 1986). Several studies have reported rapid depletion of this natural resource, spurred by the pressures from degradation, unsustainable arable land use, urbanization and industrialization (Obute and Osuji, 2002; Ayodele, 2005).

The aspects of CAM commonly practiced and used in Nigeria are mostly the solitary prayer/spiritual practices and the traditional medicinal plants (TMPs). Over 80% of the populations in some Asian and African countries depend on traditional medicine for primary health care (WHO, 2008). WHO estimates that in many developed countries, about 80% of the population has used some form of alternative or complementary medicine, including Ayurvedic, homeopathic, naturopathic, traditional oriental, and Native American Indian medicine (WHO, 2002; WHO, 2019).

Traditional medicine in Nigeria is the oldest medical practice in the country and it preceded the country's conquest by the British (Okujagu, 2005). As reported by Eke in 1999, in traditional African societies phytotherapy was valued more than orthodox medicine until the disruption of this practice with the coming of the colonialists who considered it crude, ineffective and barbaric (Eke, 1999). The early practice of these medicines was in adherence to African religions. Many herbalists, formerly called 'native doctors', still retain their traditional beliefs; some worship a wide range of deities. This constitutes a major reason why many Christians avoid trying out medicinal plants, especially if they must obtain them from this group of practitioners. Furthermore, the practice was believed to protect the people from the menace of wild animals, evil spirits, accidents, and promoting bountiful harvest, good luck and other human activities in addition to curing their diseases (Obute, 2005; Adefolaju, 2014). Some modern herbalists are Christians, but there is a stigma associated with this practice. There are also environmental factors affecting health which are commonly overlooked in this set up. It is important that standards of conduct are established for traditional practice to be carried out in an environmentally safe manner (Obute, 2005).

Also, there is a secrecy surrounding TMPs. The herbalists do not want their clients/patients

to know the names of the medicinal plants they give for fear of the knowledge becoming public, resulting in loss of income (Obute, 2005; Ogbera et al., 2010; Willcox and Bodeker, 2010). However, all this has changed with the emergence of social media through which people are becoming more widely informed. But the quality of this information can be troubling, especially regarding directions for use, dosage, duration of treatment, side effects and herb-drug interaction, if any.

1.3 Hypertension

1.3.1 Hypertension Overview

Hypertension is defined as a systolic blood pressure equal to or above 140 mm Hg and/or diastolic blood pressure equal to or above 90 mm Hg (WHO, 2013''b''). It has three stages. The National Institute for Health and Care Excellence (NICE) classification of hypertension is widely adopted in the treatment and management of the disease. This defines Stage 1 hypertension as Clinic blood pressure ranging from 140/90 mmHg to 159/99 mmHg, and subsequent ABPM (ambulatory blood pressure monitoring) daytime average or HBPM (home blood pressure monitoring) average blood pressure ranging from 135/85 mmHg to 149/94 mmHg. Stage 2 is Clinic blood pressure of 160/100 mmHg or higher, but less than 180/120 mmHg, and subsequent ABPM daytime average or HBPM average blood pressure of 150/95 mmHg or higher. Stage 3 or severe hypertension is Clinic systolic blood pressure of 180 mmHg or higher, or clinic diastolic blood pressure of 120 mmHg or higher (NICE, 2019).

Hypertension is a global public health problem with high prevalence and resulting cardiovascular disease and chronic kidney disease (Kearney et al., 2005; Lawes et al 2008). Hypertension is the leading preventable risk factor for premature death and disability worldwide (Mills et al., 2016). It contributes to the burden of heart disease, stroke, kidney failure, and premature mortality and disability (WHO, 2013''b''; Feigin et al., 2015). It was estimated that 26.4% (972 million) of the global adult population suffered from hypertension in 2000 (Kearney, et al., 2005). Since 2000, the prevalence of hypertension has been shown to be increasing in low and middle income countries, while decreasing or unvarying in high income countries (Danaei et al., 2011; Sarki et al., 2015). It is on the decline in the following countries: Finland (Kastarinen et al., 2009); Czech Republic (Cifkova et al., 2010); USA (Egan et al., 2010). Hypertension prevalence was reported to be higher in urban than rural areas of Africa and India by Addo and colleagues, and Devi and colleagues respectively (Addo et al., 2007; Devi et al., 2013). It was also shown by previous work that Africa is worst hit (Beaglehole et al., 2013). Globally, cardiovascular disease (CVD) accounts for approximately 17.9 million NCD deaths annually, 75% of which occurred in Low- and Middle-Income Countries (LMICs) including in Africa. This increase in NCDs seen in LMICs, may

result from “rapid, unplanned and unmanaged” urbanisation (Juma et al., 2019), often associated with an increase in CVD risk factors such as dietary changes, increasingly sedentary lifestyles, increasing obesity, tobacco use and exposure to air pollutants (Juma et al., 2019; Pranata et al., 2020). High systolic blood pressure, the leading risk for deaths in Africa, resulted in nearly 900,000 deaths (10% of the total deaths on the continent) in 2016 and has increased by 82% since 1990 (GBD, 2018). The prevalence of hypertension is highest in Africa (46% of adults) while the lowest prevalence is found in the Americas (35% of adults). Overall, high-income countries have a lower prevalence of hypertension (35% of adults) than low and middle income groups (40% of adults), An estimated 1.28 billion adults aged 30-79 years worldwide have hypertension, most (two-thirds) living in low- and middle-income countries (WHO, 2021). Hypertension is a major risk factor for coronary heart disease, ischemic and haemorrhagic stroke. In addition to coronary heart diseases and stroke, complications of raised blood pressure include heart failure, peripheral vascular disease, renal impairment, retinal haemorrhage and visual impairment. In their work in 2019, Paciorek and colleagues reported that over 1 billion people with hypertension (82% of all people with hypertension in the world) lived in low-income and middle-income regions. The global age-standardised prevalence of hypertension in adults aged 30–79 years was 32% and 34% in women and in men, respectively. Nationally, prevalence of hypertension in 2019 was lowest in Canada and Peru for both men and women; in Taiwan, South Korea, Japan, and some countries in western Europe for women; and in some low-income and middle-income countries for men. Hypertension prevalence was highest throughout central and eastern Europe, central Asia, Oceania, southern Africa, and some countries in Latin America and the Caribbean (Paciorek et al., 2021).

The treatment and control of hypertension are critically important for the prevention of these consequent cardiovascular and kidney diseases (Pereira et al., 2009). Hypertension is asymptomatic in the early stages, hence the danger of it remaining undiagnosed. Access to treatment for those diagnosed among these populations is almost impossible, therefore, hindering its management and control. Non-management of hypertension may lead to complications and even death. The WHO paper, ‘A global brief on hypertension: Silent killer, global public health crises’, reported that there are significant health and economic gains attached to early detection, adequate treatment and good control of hypertension. Treating the complications of hypertension entails costly interventions such as cardiac bypass surgery, carotid artery surgery and dialysis; these drain individual and government budgets (WHO, 2013a). It is projected that the annual number of deaths due to cardiovascular disease will increase from 17 million in 2008 to 25 million in 2030 (World Health Statistics, 2012). Studies have shown that the proportions of hypertension awareness, treatment, and control as reported across many countries does vary substantially (Rampal et al., 2007; Esteghamati et al., 2009; Pereira et al., 2009; Aekplakorn et al., 2012; Banegas et al., 2012;

Li et al., 2012; Chow, 2013).

Nigeria is the most populous African country, with a population of approximately two hundred and six million (World Bank Data, Nigeria, 2020). This has risen to 214,563,041 in 2022 (World population review, 2022). The prevalence of hypertension contributes to the overall burden in Africa. This prevalence of hypertension in Nigeria was estimated to be 42.8% in 2008 by WHO (WHO, 2011). In 2020, Adeloye and colleagues' work covering the six (6) geopolitical regions of Nigeria reported that absolute cases of hypertension increased by 540% among individuals aged ≥20 years from approximately 4.3 million in 1995 to 27.5 million 2020. Their findings show evidence of substantial regional variation in the prevalence of HTN in Nigeria, which ranged from 25% to 33% across the geopolitical zones. The highest were South-east and North-central at 33.3% and 32.2%, respectively. Additionally, their studies showed that despite the enhanced awareness of HTN, over half of hypertensive individuals in Nigeria are untreated and/or have poorly controlled blood pressure (Adeloye et al., 2021). Some studies attributed this magnitude to the increasing adult population, rapid urbanization and adoption of Western lifestyles, including the high consumption of processed foods (with high salts and fats), tobacco and alcohol products (Bello, 2013; Mezue, 2013; Adeloye et al., 2021). Murthy and colleagues' work showed that women had a higher prevalence of hypertension than men in Nigeria (Murthy et al., 2013). This observation corroborates the findings of many studies in Africa (Van der Sande et al., 2000; Opie, 2005; Addo et al., 2007; Seedat, 2007; Oladapo et al., 2010). The results from a national survey on the prevalence and risk factors for hypertension and its association with ethnicity in Nigeria showed prevalence at 44.9%. Increased age, gender, urban residence and body mass index were independent risk factors, with the Kanuri ethnic group in northern Nigeria ranking the highest, at 77.5% in the prevalence of hypertension. The findings of a systematic review and meta-analysis of Adeloye and colleagues' work showed an estimated hypertension prevalence of 28.9%, with a 29.5% and 25.0% for men and women respectively. Furthermore, prevalence rates of 30.6% and 26.4% were estimated for the urban and rural dwellers, respectively (Adeloye et al., 2015). In 2019, the leading Level 2 risk factor globally for attributable deaths was high systolic blood pressure, which accounted for 10·8 million (95% uncertainty interval [UI] 9·51–12·1) deaths (19·2% [16·9–21·3] of all deaths in 2019), followed by tobacco (smoked, second-hand, and chewing), which accounted for 8·71 million (8·12–9·31) deaths (15·4% [14·6–16·2] of all deaths in 2019) (GBD, 2020). The importance of lowering raised blood pressure cannot be overstated because it decreases the risk of stroke, coronary events, heart failure, and renal impairment (Murthy et al., 2013).

1.3.2 Treatment of Hypertension

The treatment option recommendation depends on the severity of blood pressure readings and other health risk factors, such as stroke and heart attack. Clinical and home blood

pressures consistently above 140/90mmHg or 135/85mmHg, respectively, and with low risk or no risk of other cardiovascular problems, will be advised on the use of non-pharmacological treatment, termed 'lifestyle modifications.' These include, weight loss, increased physical activity, limited alcohol consumption, reduced sodium intake and the Dietary Approaches to Stop Hypertension (DASH) diet (Chobanian et al., 2003).

Epidemiologic Studies have shown overweight (body mass index > 25 kg/m2) to be an important risk factor for higher blood pressure and has a linear relationship between body weight and blood pressure (Doll et al., 2002). Similarly, findings from clinical trials and meta-analysis show that weight loss decreases blood pressure in hypertensive patients (Trials of Hypertension Prevention Collaborative Research Group, 1992; He et al., 2000; Wolf-Maier, et al., 2003; Esler, et al., 2006). Increased physical activities such as brisk walking, jogging, swimming or bicycling have been shown to lower BP (Kohno et al., 1997; Higashi et al., 1999; Fagard, 2000; Rhıaume et al., 2002; Whelton et al., 2002). Alcohol consumption has both acute and chronically harmful effects on blood pressure as have been demonstrated in many epidemiologic studies, clinical trials and other notable works (Cushman et al., 1998; Xin et al., 2001; Chobanian et al., 2003; Franco et al., 2004). A reduction of salt or sodium intake to approximately 100 mmol/day (2.4g/day) can prevent hypertension (Trials of Hypertension Prevention Collaborative Research Group, 1997); it can facilitate blood pressure control in elderly patients on antihypertensive medication (Whelton et al., 2002); also, it can potentially prevent cardiovascular events in overweight individuals (He et al., 1999). The study on the Dietary Approaches to Stop Hypertension (DASH) showed that lower intake of sodium, approximately 60 mmol/day, further reduces BP in both normotensives and hypertensives (Sacks et al., 2001). Therapeutic options can be introduced in addition to lifestyle changes, if the latter are insufficient in lowering the BP.

Drug therapy is needed if non-pharmacological treatment is inadequate in the management of high blood pressure. Clinical and home BPs consistently above 140/90mmHg or 135/85mmHg, and with attending high risk of other cardiovascular problems, medications and lifestyle changes will be the preferred therapeutic option. The same treatment is adopted for blood pressures that are consistently above 160/100mmHg. The choice of medication given depends on several factors: ethnicity, age, other cardiovascular risk factors. Some may require polytherapy in the management of their hypertension. Figure 1.1 shows a flow chart for the treatment/management of people with hypertension. There are four steps for hypertension treatment as clearly shown in Figure 1.1 below.

Step 1 treatment shows that ACE inhibitor and ARB cannot be given as dual treatment. If an ACE inhibitor is not tolerated, an ARB should be used to treat hypertension. ACE inhibitor and ARB are also not recommended for adults of Black African or African–Caribbean family

origin. CCB are recommended for this group and all other groups. Where a CCB is not tolerated, thiazide-like diuretic should be used. Before considering the next step of treatment, adherence should be checked to be sure that patients are taking their medicines as recommended by NICE guidelines on medicines. (NICE guidelines on medicines adherence, 2019). If hypertension is not controlled despite patient's adherence, a CCB or a thiazide-like diuretic should be added to patients on ACE inhibitor or ARB. An ACE inhibitor or an ARB or a thiazide-like diuretic should be added to patients on CCB (Table 1.2). If BP is still not controlled and adherence met by patient, step 3 should be offered by giving optimal tolerated doses of an ACE inhibitor or an ARB plus a CCB and a thiazide-like diuretic. Patients who are not controlled by step 3 are considered to suffer from resistant hypertension. Adherence should be checked and BP readings using ABPM or HBPM confirmed and postural hypotension assessed. A fourth antihypertensive drug should be offered as step 4 treatment or specialist advice sought (NICE, 2019). A diuretic therapy with low-dose spironolactone and a blood potassium level of 4.5 mmol/l or less should be offered. An alpha-blocker or beta-blocker for adults with resistant hypertension starting step 4 treatment who have a blood potassium level of more than 4.5 mmol/l should be offered. NICE advised using caution in people with a reduced estimated glomerular filtration rate because they have an increased risk of hyperkalaemia (NICE, 2019). Blood sodium, potassium and renal function should be monitored within 1 month of starting treatment and should be repeated as needed thereafter. Specialist advice should be sought if blood pressure remains uncontrolled in people with resistant hypertension taking the optimal tolerated doses of 4 drugs (NICE, 2019).

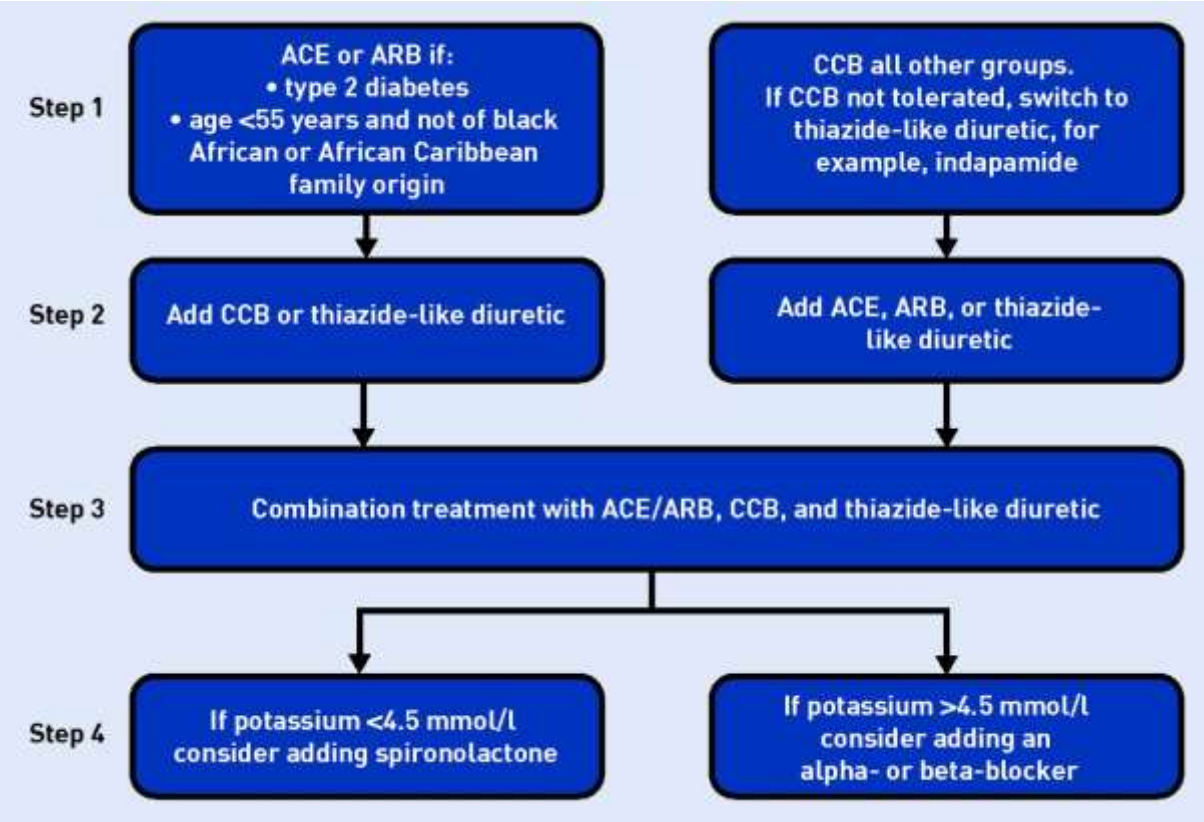

Figure 1.1 Diagnosis and management of hypertension in adults: NICE guideline update 2019

Treatment flow chart. At each step optimise medication dose and check adherence. At step 4, consider confirming the blood pressure measurement is accurate with home or ambulatory readings. ACE (angiotensin converting enzyme). ARB (angiotensin receptor blocker. CCB (calcium channel blocker) (Jones, et al., 2020).

Hypertension is one of the leading causes of cardiovascular disease and death, hence the need for proper treatment. Lowering blood pressure reduces cardiovascular risks. Also, maintaining systolic blood pressure at less than 130 mm Hg has been shown to prevent complications in patients with coronary artery disease, heart failure, stroke, diabetes and other cardiovascular diseases (Ettehad, et al., 2016). Table 1.2 shows the class, mechanism of action and the indication of the conventional or orthodox medicines used in the treatment of hypertension. Angiotensin-converting enzyme (ACE) inhibitors, Angiotensin-2 receptor blockers (ARBs), Calcium channel blockers (CCB), Diuretics and Beta blockers are the major classes of antihypertensive medicines used in the treatment of hypertension (see Table 1.2).

Table 1.2 Conventional medicines used in the treatment of hypertension

Class	Mechanism Of Action	Indication(s)
Angiotensin-converting enzyme inhibitors (ACE inhibitors) [enalapril, lisinopril, perindopril and ramipril]. (Armstrong, 2014; Rajaram, 2021)	ACE inhibitors decrease the blood pressure by inhibiting the angiotensin-converting enzyme; this causes a decline in the production of angiotensin II and increases the bradykinin level by inhibiting its degeneration, which leads to vasodilation	Antihypertensive of choice for patients with heart failure and chronic kidney disease
Angiotensin-2 receptor blockers (ARBs) [candesartan, irbesartan, losartan, valsartan, telmisartan and Olmesartan] (Armstrong, 2014).	ARBs work by blocking the binding of angiotensin II to the angiotensin 1 AT1 receptors, which inhibit the angiotensin II effect. In contrast to ACE inhibitors, ARBs do not affect the kinin levels	Antihypertensive of choice for patients with heart failure and chronic kidney disease
Calcium channel blockers [amlodipine, felodipine, nifedipine. diltiazem, felodipine, nicardipine and verapamil (Armstrong, 2014; Whelton, 2018).	The mechanism of action of CCBs is related to inhibition of Ca2+ entry to the cells; this occurs by binding to the L-type voltage-gated calcium channels located in the heart muscle. This effect can cause peripheral vasodilation, which is seen mainly in dihydropyridines, or negative inotropic effect on the heart muscle in non-dihydropyridines, inhibiting the sinoatrial and atrioventricular nodes leading to slow cardiac contractility and conduction	First-line treatment, to be used alone or in combination with other antihypertensives in all patients with HTN regardless of age and race, with the exception of patients with chronic kidney disease where ACE inhibitors or ARBs are the recommended first-line treatment
Diuretics: Thiazide (Bendroflumethiazide, hydrochlorothiazide);	Diuretics work by flushing excess water and salt from the body. Thiazide diuretics act on the proximal part of the distal tubule to inhibit sodium and chloride reabsorption,	Thiazide diuretics can be used as the first-line treatment for HTN (either alone or in combination with other

and and thiazide-like (chlortalidone, indapamide); Loop (Furosemide, bumetanide); Potassium sparing/ aldosterone antagonist (Amiloride, spironolactone) (Armstrong, 2014; Jackson and Bellamy, 2015)	with resultant reduction in water reabsorption leading to diuresis. Thiazides inhibit sodium transport in the distal tubule; this occurs by blocking the Na/Cl channels	antihypertensives) in all age groups regardless of race unless the patient has evidence of chronic kidney disease where ACE inhibitor or ARB is indicated
Beta blockers [atenolol, bisoprolol, acebutolol, metoprolol, nadolol, nebivolol and propranolol] (Khan and McAlister, 2006; Thomopoulos, et al., 2018; Oliver, 2019)	Beta-blockers work by inhibiting the catecholamines from binding to the Beta 1,2, and 3 receptors. Beta-1 receptors are found primarily in the heart muscle, beta-2 receptors are located in the bronchial and peripheral vascular smooth muscles, and beta-3 receptors appear in adipose tissue of the heart	Not indicated as primary treatment for hypertension unless there is a specific indication of heart failure and myocardial infarction

1.4 Hypertension in Diabetes

1.4.1 Hypertension in Diabetes Overview

Hypertension is a very common comorbid condition in diabetes and vice versa (Lee et al., 2017). The clinic blood pressure target of patients with diabetes is below 140/80 mmHg (below 130/80 mmHg is advised if kidney, eye, or cerebrovascular disease are also present) (NICE, 2019). Hypertension is a component of the metabolic syndrome, common in patients with type 2 diabetes. Hypertension predisposes the patients to microvascular complications, strokes, myocardial infarctions, and total mortality (Fisher M, 2016). Patients with diabetes and hypertension are at an increased risk of macrovascular and microvascular complications (Long and Dagogo-Jack, 2011). The importance of reducing blood pressure in this group cannot be overstated and achieving this requires polytherapy. The complexities and complications posed by these diseases renders it critical that the physiology and pathology of diabetes and hypertension be examined.

Blood pressure is controlled by the relationship between circulatory fluid volume and peripheral vascular resistance (Shimamoto et al., 2014). The circulatory fluid volume is regulated by blood fluid volume and cardiac contractile force. Peripheral vascular resistance is regulated by vascular tone, which is influenced by both vascular remodeling and vasoactive agents including the renin-angiotensin system (Ohishi 2018). The close relationship between hypertension and dietary sodium intake is widely recognised and supported by several studies for decades. High salt intake may result in elevated blood pressure as exemplified by Guyton's pressure natriuresis relationship curve, (Guyton, et al., 1984), which showed sodium excretion at a blood pressure level higher than the threshold in the kidney. A higher blood pressure is required in urinary sodium excretion. In addition, the work of Guyton and colleagues showed that blood pressure regulation was linked with fluid volume regulation and not by the vascular resistance (Guyton et al., 1984). Studies have shown that consumption of diet with high salt content and in combination with salt sensitivity causes nocturnal hypertension (Uzu et al., 1997). Furthermore, patients with diabetes and nocturnal high blood pressure reportedly have a 16-fold higher risk of cardiovascular events (Eguchi et al., 2008). Mente and colleague's study showed a direct relationship between salt intake and elevated high BP (Mente et al., 2014). A reduction in dietary sodium does not only decrease the blood pressure and the incidence of hypertension, but it also decreases the morbidity and mortality from cardiovascular diseases (Grillo et al., 2019). Prolonged modest reduction in salt intake induces a relevant fall in blood pressure in both hypertensive and normotensive individuals, irrespective of sex and ethnic group, with larger falls in systolic blood pressure for larger reductions in dietary salt (Grillo et al., 2019).

Insulin plays an important role in the relationship between diabetes and high blood pressure. It is a peptide hormone secreted by the β cells of the pancreatic islets of Langerhans and maintains normal blood glucose levels by facilitating cellular glucose uptake, regulating carbohydrate, lipid and protein metabolism, and promoting cell division and growth through its mitogenic effects (Wilcox, 2005). Its functions include the following: facilitation of glucose uptake by organs, promotion of glycogen storage in liver and muscle tissue; control of the breakdown of stored glycogen, promotion of adipose tissue development, and control of fat resolution (Saltiel et al., 2015). Insulin also stimulates vascular smooth muscle cell migration and proliferation (Arnqvist et al., 1995). Insulin resistance induces hyperinsulinemia causing the sodium reabsorption from renal tubules to increase, leading to high blood pressure (Martínez and Sancho-Rof, 1993). Furthermore, studies have shown that hyperglycaemia elevates systemic blood pressure by increasing the circulatory fluid volume. In addition, hyperinsulinemia was reported to stimulate sympathetic nervous activity, thereby increasing renin excretion (Seravalle and Grassi, 2016). Kishida and colleagues reported that the increase in renin activates the sympathetic nervous system and increases cardiac output

and peripheral vascular resistance; this elevates blood pressure by increasing both the circulatory fluid volume and peripheral vascular resistance (Kishida, et al., 2012). Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin-II receptor antagonists (ARB) are first-line medicines used in reducing acute cardiovascular events and diabetic nephropathy through the addition of either a calcium-channel blocker or a diuretic. Studies carried out in older patients with isolated systolic hypertension showed clear evidence that lowering of blood pressure is beneficial in diabetics. The Systolic Hypertension in the Elderly Program (SHEP) study examined the use of chlortalidone compared to placebo in systolic hypertension (Fisher M, 2012). Significant reductions in major cardiovascular events, with a greater absolute risk reduction in the diabetic subgroup was reported. “Meta-analyses of available trials show that, in diabetes, all major antihypertensive drug classes protect against cardiovascular complications, probably because of the protective effect of BP lowering per se” (Perk et al., 2012).

The mechanism or the link between insulin resistance and hypertension could be attributed to several possible explanations such as, insulin-stimulated sodium and water retention through the distal renal tubules; increased contractility and vascular resistance; increased sympathetic stimulation, vascular smooth muscle proliferation and impaired insulin-mediated vasodilation (Fisher, 2012). The dysregulation of neurohumoral and neuro-immune systems is involved in the pathophysiology of both insulin resistance and hypertension (Mancusi, 2020). The mechanism involved in the development of hypertension in type 2 diabetes mellitus is a deficiency of insulin at the cellular level. They reported that the impaired cellular response to insulin predisposes to increased vascular smooth muscle (VSM) tone, the hallmark of hypertension in the diabetic state (Sowers, 1991). Untreated hypertension in diabetes increases the risk of cardiovascular disease (myocardial infarction, congestive cardiac failure, stroke) and microvascular disease (retinopathy, nephropathy). If the definition of hypertension of a blood pressure greater than 140/90 mmHg is adopted, then at least 40% of patients with type 2 diabetes will have hypertension (Fisher M, 2012). He noted that the risk of vascular events in people with diabetes increases even within the normal range, hence blood pressure is a continuous risk factor. Blood pressure lowering in patients with type 2 diabetes has been associated with decreased cardiovascular events and mortality (UKPDS, 1998a; UKPDS, 1998b; Fowler, M. J., 2008).

1.4.2 Treatment of hypertension in diabetes

NICE guidelines recommended measurement of BP annually in adults with type 2 diabetes without previously diagnosed hypertension or renal disease as shown in the flow chart (Figure 1.2). The targets should be adhered to for proper management of the disease. If BP

is above target, lifestyle measures should be offered. If BP target is uncontrolled, a titrated dose of ACE inhibitor or ARB should be offered. For people of African-Caribbean origin, ACE inhibitor should be offered in addition to diuretic or CCB. In diabetic hypertensives, ACE inhibitors are the first line in the treatment of hypertension and can be replaced by angiotensin II receptor blockers (ARBs) if patients are intolerant of them. The flow chart should be strictly adhered to until the BP is within target (Figure 1.2).

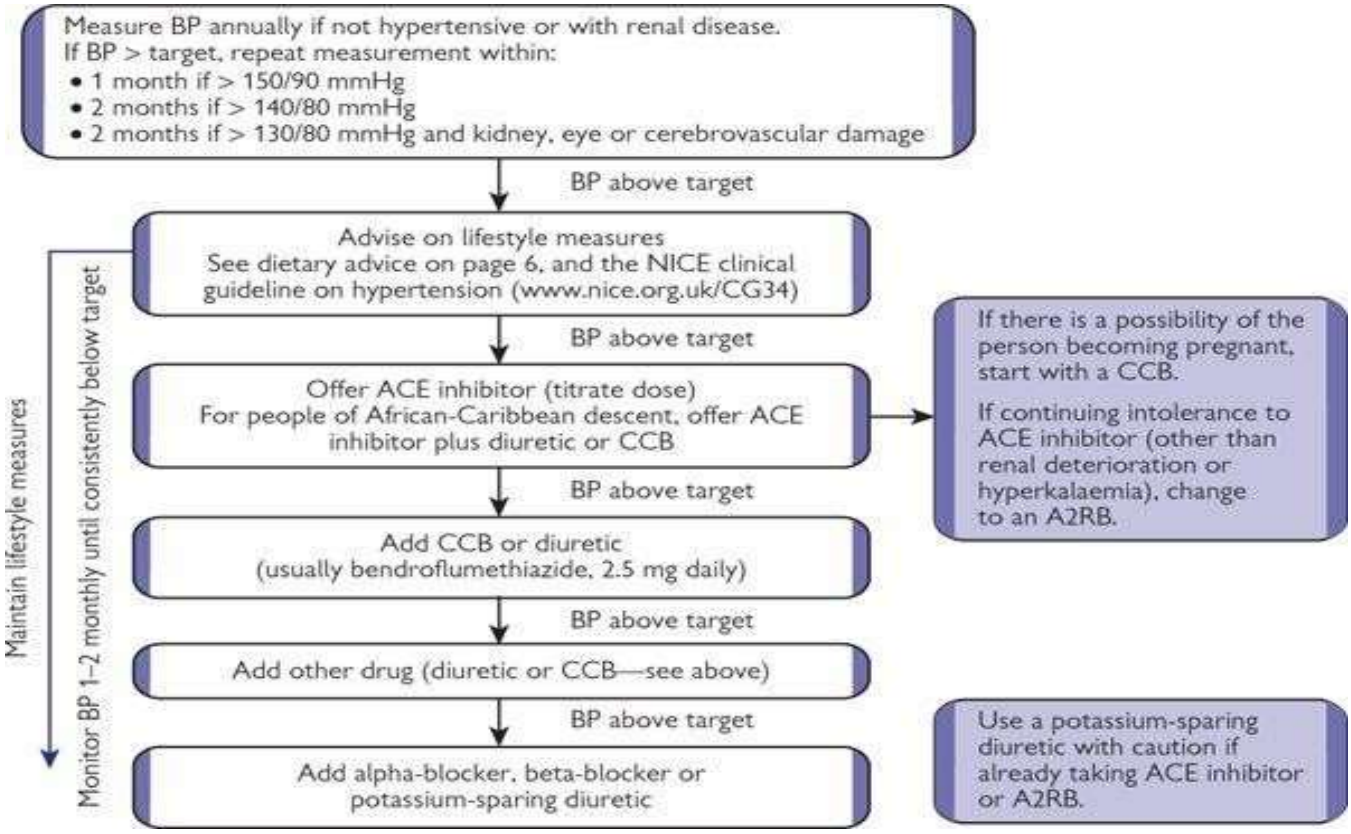

Figure 1.2 Management of hypertension in people with diabetes (NICE guidelines)

Algorithm for the management of hypertension in patients with diabetes. ACE (angiotensin converting enzyme); ARB (angiotensin receptor blocker); BP (blood pressure); CCB (calcium channel blocker) (NICE Clinical Guidelines 66 Type 2 diabetes (Update) 2008).

1.5 Diabetes mellitus

1.5.1 Diabetes mellitus overview

Diabetes is one of the components of metabolic syndrome. Metabolic syndrome is the medical term for a combination of diabetes, high blood pressure (hypertension) and obesity. Researchers have varying descriptions of metabolic syndrome. In 1923, Studien described it as a clustering of hypertension, hyperglycaemia and gout (Studien, 1923); Syndrome X

(Reaven, 1988); The Deadly Quartet (Kaplan, 1989). This 'clustering' although known, did not receive much attention for several decades until Reaven in 1988 described it as syndrome X (insulin resistance, hyperglycaemia, hypertension, low HDL-cholesterol, and raised VLDL-triglycerides). The International Diabetes Federation (IDF) has defined metabolic syndrome as a cluster of the most dangerous heart attack risk factors, high blood pressure (hypertension), diabetes and raised fasting plasma glucose, abdominal obesity (visceral obesity) and high cholesterol (dyslipidaemia) (Alberti et al., 2005; IDF, 2005; Alberti et al., 2006). A quarter of the world's adults have metabolic syndrome (Saklayen, 2018). People with metabolic syndrome have a five-fold greater risk of developing type 2 diabetes.

Diabetes is a metabolic disease characterised by elevated levels of blood glucose (or blood sugar). Generally, the following are ideal ranges, 4-7 mmol/L before meals; 8-9 mmol/L two hours after meals and 6-10 mmol/L at bedtime. Poorly managed diabetes will over time result in serious damage to the heart, blood vessels, eyes, kidneys, and nerves. It is one of the elements of metabolic syndrome, characterised by persistent hyperglycaemia caused by deficient insulin secretion or resistance to the action of insulin. Diabetes is a condition primarily defined by the level of hyperglycaemia giving rise to risk of microvascular damage (nephropathy, neuropathy and retinopathy) (Fowler, 2011). International Diabetes Federation (IDF) reported that 463 million people have diabetes in the world and more than 19 million people in the African region. This number will rise to 47 million by 2045. (IDF, 2020). Diabetes is associated with reduced life expectancy, significant morbidity due to specific diabetes-related microvascular complications, increased risk of macrovascular complications (ischaemic heart disease, stroke and peripheral vascular disease), and diminished quality of life (Fowler, 2011; Stehouwer, 2018). WHO describes it as a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces (WHO, 2016). There are four different types of diabetes, types 1 and 2 diabetes (the most widely used distinction); gestational (develops during pregnancy and mostly, resolves after pregnancy); and secondary diabetes resulting from some pharmacological treatments, such as antiviral, antipsychotic or endocrine drugs, and also, by pancreatic damage, hepatic cirrhosis, or endocrine disease.

Type 2 diabetes affects 90-95% of people with diabetes and is the most common type of this condition in adults. Type 2 diabetes occurs due to the body's resistance to insulin or inability to produce enough insulin. It is commonly associated with obesity, physical inactivity, raised blood pressure, and dyslipidaemia – hence it is predisposed to cardiovascular risk. Type 2 diabetes typically develops later in life but is increasingly diagnosed in children despite previously being considered a disease of adulthood.

Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, affects 5% of the people with diabetes. It is a chronic condition in which the pancreas produces little or

no insulin (WHO, 2016). The absolute insulin deficiency is attributed to be the result of destruction of insulin-producing beta-cells in the pancreatic islets of Langerhans. Type 1 diabetes is an auto-immune disease affecting mostly children but can occur at any age usually under 50 years. In adults, it presents with the following features such as ketosis, sudden high plasma- glucose concentration above 11mmol/litre, rapid weight loss, a body mass index below 25 kg/m2 and a family history of autoimmune disease.

1.5.2 Treatment of Diabetes mellitus

Treatment is aimed at minimising the risk of long-term microvascular and macrovascular complications by effective blood-glucose control and maintenance of HbA1c at or below the target value set for each individual patient. The six major classes of antidiabetic medicines used in the management/treatment of diabetes are tabulated below on Table 1.3 as indicated by the British National Formulary (BNF). The BNF is a joint publication of the British Medical Association and the Royal Pharmaceutical Society. It aims to provide prescribers, pharmacists, and other healthcare professionals with sound up-to-date information about the use of medicines. The BNF includes key information on the selection, prescribing, dispensing and administration of medicines. The mechanisms of action and the indication of these six (6) classes of antidiabetic medicines are also stipulated in Table 1.3 below.

Table 1.3 Conventional medicines used in the treatment of type 2 diabetes mellitus (BNF, British National Formulary)

Class	Mechanism Of Action	Indication(s)
Sulfonylureas [glibenclamide, gliclazide, glimepiride, glipizide, tolbutamide] and the Glinides [meglitinides, nateglinide and repaglinide] (Nathan et al., 2006; Sola, et al., 2015)	Increase insulin secretion	Insulinopenia
Biguanides - Metformin hydrochloride (Goodarzi and Bryer-Ash, 2005; Unger, 2012)	Decrease hepatic gluconeogenesis.	Obesity and insulin Resistance
Thiazolidenediones [pioglitazone] (Bailey and Day, 2004)	Decrease peripheral insulin resistance	Insulin resistance
α-glucosidase inhibitors (Acabose) (Martin, 1996; Fallah et al., 2022)	Inhibition of α-glucosidase delay the release of glucose therefore slow absorption of carbohydrates (reduces	Postprandial hyperglycemia

	fatty acid)	
Dipeptidylpeptidase-4 (DPP-4) inhibitors (gliptins) [alogliptin, linagliptin, sitagliptin, saxagliptin, and vildagliptin] (Nathan et al., 2006; Ahren, 2019)	Inhibit the degradation of the incretins, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP)	Glycemic control enhancement
Sodium glucose co-transporter 2 inhibitors, SGLT2, [canagliflozin, dapagliflozin, and empagliflozin] (Wright, 2001; Lee and Han, 2007; Brown, 2019)	Work by helping the kidneys to lower blood glucose levels	May be suitable for some patients when first-line options are not Appropriate
The glucagon-like peptide-1 receptor agonists [albiglutide, dulaglutide, exenatide, liraglutide and lixisenatide] (White and Campbell, 2008; Di Ienno et al., 2021)	Stimulates insulin and suppresses glucagon secretion, inhibits gastric emptying, and reduces appetite and food intake	Reserved for combination therapy when other treatment options have failed

1.6 Emergence of Alternative medicines

In the present era, the highest priority is given to evidence-based medicine (orthodox medicine), in which standardization and health care are shown by research to produce benefits. This contrasts with alternative medicine which is less rule-bound, self-regulated, unauthorised, and backed by very limited scientific evidence. These facts have not prevented the global popularity of alternative medicine, as demonstrated by several researchers: some users find them more congruent with their own values, beliefs, and philosophical orientations toward health and life (Astin, 1998; Wiles and Rosenberg, 2001; Parasuman et al., 2014; Pedersen et al., 2016); some others want to be in control of their own health (NCCAM, 2001-2005); use of CAM is sometimes associated with poor self-reported health (Hansen et al., 2005; Baarts and Pedersen, 2009; Kristoffersen et al, 2018). Expenditures increased 45.2% between 1990 and 1997 and were conservatively estimated at $21.2 billion in 1997, with at least $12.2 billion paid out-of-pocket (Eisenberg et al., 1998); its cost is exhorbitant (Ernst, 2000; Thomas et al., 2001) and many use alternatives in addition to conventional medicines (Ni et al., 2002; Tindle et al., 2005; Li et al., 2020). Ong and Banks' summary of British studies found that CAM is typically used for long-standing illnesses such as hypertension, diabetes, asthma, and conditions recognised to be markedly less responsive to conventional treatment (Ong and Banks, 2003).

In addition, the World Health Organisation, institutional and individual researchers have shown hypertension and diabetes to be non-communicable chronic diseases which can devastate lives if not treated urgently and effectively. Therefore, these diseases pose global challenges and compel the need to search into their urgent treatment and/or management. This puts in perspective the heightened, even frantic search for any form of treatment to address them. The tempo cuts across both developed and developing parts of the world, though the developing countries such as Nigeria are most severely affected. Complementary or unconventional treatments are used by many doctors and other therapists throughout Europe and in western culture. The relative popularity of therapies differs between countries, but public demand is strong and growing (Fisher and Ward, 1994 Kaptchuk et al., 1998; Li et al., 2020). Some studies reported that the prevalence of CAM use among Indians was similar to findings in other parts of the world (Singh et al., 2004; Nailwal and Gupta, 2021); the same was reported in Morocco where phytotherapy of diabetes mellitus, hypertension and cardiac disorders is highly developed (Eddouks et al., 2002); and Jamaica (Delgoda et al., 2004). The threat to life is especially rife in Africa and specifically Nigeria, Africa's most populous nation where there is no national health care. The sufferers of these diseases are left to fend for themselves with little or no capacity to pay their way. For example, the Nigerian budget for health often falls much lower than the level recommended by the International Monetary Fund (IMF) and World Health Organization (WHO, 2015). In 2012,

the per capita health expenditure in Nigeria was US$161 (compared to the United States' US$8895), and the total expenditure on health as a percentage of the GDP was 6.1% (compared to 17.9% in the USA) (WHO, 2015). In 2019, the per capita health expenditure in Nigeria was US $71.47 (World Bank Data, 2022). Therefore, in despair, many people now seek alternative treatment options. These problems among others have fuelled the nationwide surge towards the search for alternative medicines.

1.6.1 Drives behind search for alternative and/or complementary medicines

Many factors have led to a great number of people seeking and using alternative and/or complementary medicine globally. These varying factors include the following: patients' rehabilitation and the minimising of risk and pain (Ahn and Kaptchuk, 2005; Arman and Rehnsfeldt, 2003; Baer et al., 2008); bad experiences with conventional medicine, a general belief in the alternative paradigm (Boon et al. 1999; Welz et al., 2018); dissatisfaction with conventional health care systems and the failure of such treatments to cure chronic diseases and disability (Avina and Schneiderman, 1978; Jensen, 1990; Foote-Ardah 2004; Welz et al., 2018); unpleasant side effects of conventional medicines (Cassileth et al.; 1984 Jensen, 1990; Welz et al., 2018). Additional factors encouraging the trend towards alternative medicine include these: conventional medicine is seen as impersonal, very technologically oriented and with high medication costs (Marquis, 1983; Cassileth et al., 1984; Jensen, 1990; Murray and Rubel, 1992; Furnham and Bhagrath, 1993; Furnham and Forey, 1994; Sutherland and Verhoef, 1994); patients gain easy accessibility and control over their health care decisions (Duggan, 1995; Vincent and Furnham, 1996); and alternative medicines are seen by patients to align with their spiritual/religious beliefs and their perception of nature (Fairfoot, 1986; Levin and Coreil, 1986; Warner, 1990; Charlton, 1993; Vincent and Furnham, 1996; Ray, 1997).

At the onset of a chronic disease such as hypertension, the tendency was to use a conventional treatment. But when complications set in with no cure in sight, there is a shift towards alternative treatment. Also, when the conventional treatment has no success, patients seek alternative and/or complementary medicines (Yeh et al., 2002; Alzahrani et al., 2021). Egede and colleagues' study showed that TMP usage was more prevalent with older people (≥65 years) and those with higher education (Egede et al., 2002). Their study also showed that people in United States of America (USA) with chronic disease such as diabetes were more likely to use CAM compared to those without diabetes. This assertion was demonstrated by several other studies. Higher rates of CAM use were reported among patients with various chronic conditions including 42% of patients with asthma/rhinosinusitis (Blanc et al., 2001; Mazur et al., 2001); 80% with cancer patients (Bernstein and Grasso, 2001); 68% of those with HIV (Fairfield et al., 1998); and 54% among those with amyotrophic lateral sclerosis (Wasner et al., 2001). A high percentage (84%) of the respondents reported

that plants are safe and with fewer side effects; at the same time about 80% believed that they are more effective than conventional medicines and about 50% said that TMPs have no herb drug interactions (Chintamunnee and Mahomoodally, 2012). Medicinal plant use is embedded into Mauritius culture. Over 75% of interviewees said that they use TMPs to treat DM, HTN and cardiac diseases because they are cheaper, more effective and better than conventional medicines. A total of ninety-two (92) TMPs were used for the treatment of DM, HTN and cardiac diseases, 37 for DM, 73 for HTN and cardiac diseases (16 of which are also used for DM treatment). The study concluded that the use of TMPs for the treatment of DM, HTN and cardiac diseases is highly developed (Mootoosamy and Mahomoodally, 2014).

1.6.2 Complementing CMs with TMPs and the use of solitary prayers

The review carried out by Ezuruike and Prieto stated the need to address potential toxicities or possible herb-drug interactions, and significant risks resulting from the concurrent use of both CMs and TMPs (Ezuruike and Prieto, 2016). Several studies have shown that people use CMs and TMPs concurrently (Argáez-López et al., 2003; Kumar et al., 2006; Hasan et al., 2009; Alzahrani et al., 2018). Similarly, Mootoosamy and colleague stated that herb drug interactions (HDIs) occurred when some plants with hypoglycaemic effect were taken with conventional oral antidiabetic drugs by Mauritians (Mootoosamy and Mahomoodally, 2014). Hypertension and diabetes are conditions managed with more than one prescription (conventional) medicine; risk of drug interactions increases with the number of drugs given to a patient (Fakeye et al., 2008). In addition, the risk of herbal drug interactions (HDIs) increases with patients on polypharmacy (Patsalos et al., 2002). These complications of HDIs will impose strain on countries such as Nigeria which have poor healthcare systems (Ezuruike and Prieto, 2014). People find alternative medicines which are in harmony with their personal values, religious and health philosophies (Warner, 1990; Levin and Coreil, 1986; Fairfoot, 1986; Ray, 1997). In their study of complementary and alternative medicine (CAM) use among persons with diabetes mellitus residing in the United States, using 1997–1998 national survey data, Yeh and colleagues reported that 57% of the study population use CAM to treat diabetes. However, when solitary/spiritual practice was excluded, the rate dropped to 20%, showing that more people used solitary prayer only (Yeh et al., 2002). This study's findings on solitary prayer are similar to those of Hunt and colleagues who carried out a survey among the Mexican Americans with type 2 diabetes. It was found that many Mexican Americans used solitary prayers in combination with the conventional medicines. They believed that prayers helped their medication to work well (Hunt et al., 2000). Similarly, too, Yeh and colleagues' findings showed that, regardless of condition, solitary prayer was used as a form of therapy (Yeh et al., 2002). Previous studies supporting these findings suggest that a high percentage of patients, and physicians, believe that personal spiritual practices play important role in health and illness (Zaldivar and Smolowitz, 1994; Aviles et

al., 2001). It should be noted that some researchers do not consider solitary prayer a CAM therapy, and thus exclude it from their analyses (Eisenberg et al., 1998).

It is worth noting, also, that some patients use alternative medicines in addition to their conventional medicines – and not as a replacement. This therefore shows the importance of the conventional practitioners acknowledging the fact that their patients use alternative medicines, and the need for integration (Egede et al., 2002).

Documentation of Traditional Medicinal Plants (TMPs)

Africa's vast biodiversity resources are estimated at between 40,000 and 45,000 species of plants of which 5,000 species are used medicinally (Manach et al., 2004). Africa is a tropical continent with strong ultraviolet rays and numerous pathogenic microbes such as bacteria, fungi, and viruses, indicating accumulation of more chemopreventive substances in African plants than plants from the northern hemisphere (Farnsworth et al., 1985; Abegaz et al., 2004; Manach et al., 2004). Africa has the highest rate of endemism, with the Republic of Madagascar topping the list at 82%, and Africa contributing about 25% of the world trade in biodiversity (Gurib-Fakim, 2006). Despite this huge potential and diversity, the African continent has only few drugs commercialised globally from her flora (Gurib-Fakim, 2006; Atawodi, 2005). Mahomoodally states in his work that the scientific literature has witnessed a growing number of publications geared towards evaluating the efficacy of medicinal plants from Africa which are believed to offer an important contribution in the maintenance of health and in the introduction of new treatments (Mahomoodally, 2013). But he also notes the dearth of updated comprehensive compilations of promising medicinal plants from the African continent. Researchers from Nigeria share similar concerns, reporting that although the knowledge of traditional medicinal plants has been with the Nigerian people for generations, it has not been duly recorded. This knowledge remains mostly with the traditional medical practitioners who are now old; such knowledge needs to be documented and passed down to the younger generations. (Gbolade, 2012). The pharmacological screening of the identified plants used in the treatment of hypertension and diabetes should be conducted to ascertain the effectiveness of these plants (Karou et al., 2011). The TMPs commonly used against non-communicable diseases (NCDs) such as diabetes, hypertension, cardiovascular and gastrointestinal diseases in the tropical island of Mauritius have no database (Chintamunnee and Mahomoodally, 2012). Their study was, therefore, directed towards identifying different TMPs frequently used by Mauritians. In their effort to initiate novel antidiabetic drugs discovery, Mootoosamy and colleague focused on the documentation of orally transmitted ethnopharmacological knowledge on commonly used anti-diabetic TMPs in a group of diabetic patients and traditional medicine practitioners in Mauritius. Their study shows that native remedies (NRs) are an integral part of the therapy for diabetic patients in Mauritius; hence the reason for their documentation. The knowledge

gathered and described in this work avails new opportunities for the discovery of novel antidiabetic drugs based on the active constituents of the documented medicinal remedies (Mootoosamy and Mahomoodally, 2014). Many researchers have carried out surveys, collected names of medicinal plants, their cures and even the HDIs; but that is as far as the studies go. Nothing further is done with these findings with a view to harmonising understanding and coordination among HCPs, institutions and patients. There is, currently, no evaluated comprehensive database on medicinal plant use by hypertensive, hypertension in diabetics and diabetics in Nigeria. The plant genetic resources of Nigeria are a veritable fount of pharmaceuticals and therapeutics, but the plants are not adequately documented (Gbile and Adesina, 1986; Lawal, et al., 2022). It is therefore very important that the ethnopharmacology of these plants are investigated, critically assessed and documented to provide easy accessibility for all concerned.

2.0 Aim of Study

The aim of this study is to determine using a questionnaire, the extent of the usage of traditional medicinal plants (TMPs) for the treatment and management of diabetes and hypertension in South Eastern Nigeria.

Research Strategy

The aim was addressed by two (2) objectives.

- To examine and understand at community level the traditional medicines used by hypertensive and diabetic patients in South Eastern Nigeria. A field work study was conducted in South Eastern Nigeria with the aim of identifying medicinal plants that are commonly used by hypertensive and diabetic patients in the management of their conditions. This was conducted via patients' interview using questionnaires.
- To critically appraise the ethnopharmacology of the medicinal plants that are traditionally used in the treatment and/or management of hypertension and diabetes in Nigeria. A literature review on the evidence of TMPs' pharmacology and therapeutic potentials was carried out. An assessment of available published scientific data on the pharmacology and toxicology of plants traditionally used for hypertension and diabetes management in Nigeria was conducted using electronic databases such as Web of Science, Scopus, PubMed, and Google Scholar.

3.0 Materials and Methods

3.1 The Fieldwork Site

Nigeria is situated in the western part of Africa and is the richest and most populous country in Africa. The country is endowed with fertile vegetation and with numerous minerals, especially petroleum. Nigeria consists of thirty-six (36) states, plus Abuja, its Federal Capital Territory (FCT). It has six (6) geopolitical zones, South-east, South-south, South-west, North-east, North-central and North-west (Figure 1). The country is inhabited by 250 ethnic groups of which Igbos, Yorubas and Hausas are the three (3) major ones.

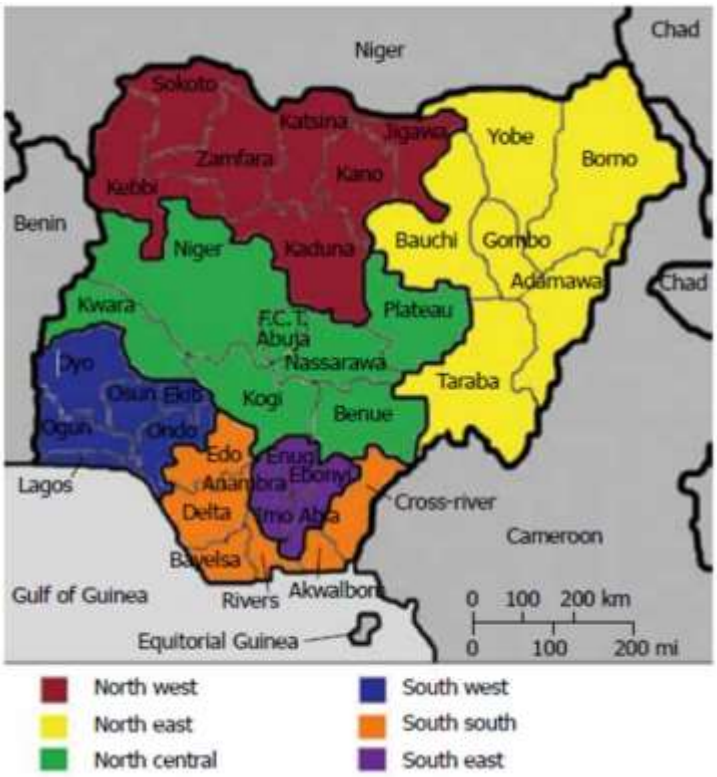

Figure 3.1 Map of Nigeria showing the 6 geo-political zones, 36 states and Federal Capital Territory (Ogah et al., 2012).

Nigeria is a sub-Saharan tropical country with a damp and very humid climate in the South, and Sahelian or tropical dry climate in the North. The regional climate features vegetation which varies considerably, with the semi-arid Sahelian landscape in the North, the savannah in the Centre, the forests in the South, and the mangroves in the Niger Delta and the coastal areas. Nigeria boasts of natural vegetation regulated by the effects of temperature, humidity and rainfall (Falola, et al., 2020). This contributes immensely to the indigenous plants that grow throughout the country. The Igbos inhabit the South-east and parts of South-south,

originally known as South Eastern Nigeria, a region spanning through eight heavily populated states of the country. South Eastern Nigeria's forest flora is very diverse and is the richest. The vegetation consists of mangrove, freshwater swamp, rain forest and woodland, and tall grass savanna (Figure 2.2). The fieldwork for this study was carried out in this South Eastern part of Nigeria, where the population consists of the Igbos, Efik, Ibibio, Annang, and Ijaw (Falola et al., 2020).

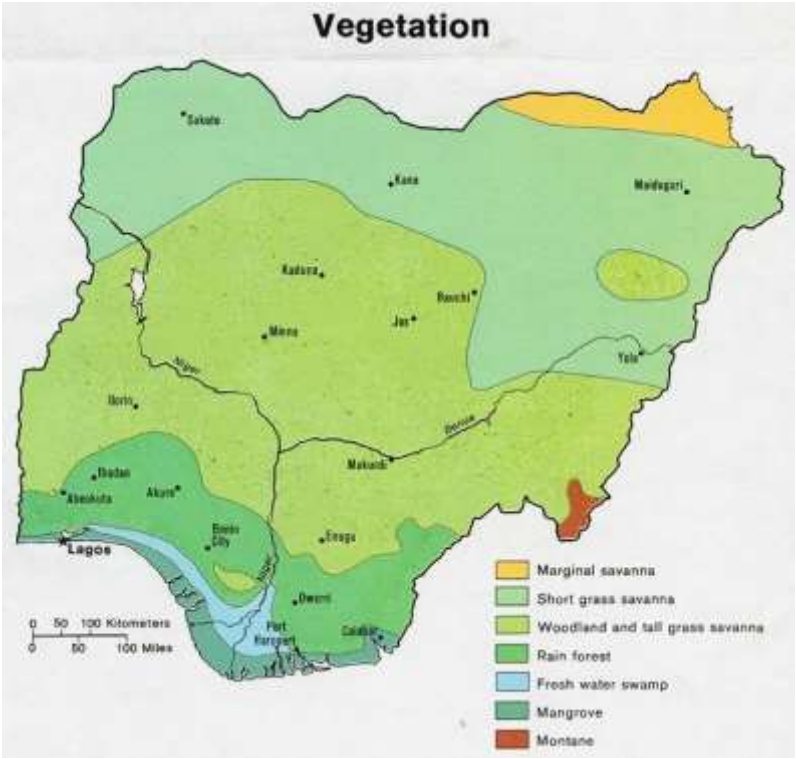

Figure 3.2 Map of Nigeria showing the main vegetation types (Oni et al., 2014)

3.2 Ethical approval

Ethical Approvals for fieldwork in Nigeria were obtained from these three institutions: University College London, 11257/001; Nnamdi Azikiwe Teaching Hospital Nnewi, Anambra State, Nigeria; and University of Nigeria Teaching Hospital, Enugu, Enugu State, Nigeria NHREC/05/01/2008B- FWA00002458-1RB00002323. The Ethics Committee required participants' confidentiality and anonymity of the survey questionnaires, with no record of identifiable data and that was observed by all concerned. All the participants gave their consent before any interview proceeded. The researcher sought and obtained verbal consent from each participant prior to their interview. Interviews were conducted in both English and the participant's native language, at the choice of each participant. Translators were offered but were not needed as the researcher spoke both English and the participants'

native language, Ibo.

3.3 Development of the instruments and data-collection methods

Armed with this study's aim, objectives and research questions, the next task was the selection of a research instrument that would best fit this project.

A three-part questionnaire was the instrument chosen for this study (see Appendix 1).
Part 1 dealt with patient demographics (age, gender, ethnicity/race, level of education, religion and marital status).
Part 2 assessed basic knowledge of their conditions, (time since diagnosis, type of disease, type of treatment, regularity on medication, and cost of medication among others).
Part 3 dealt with their treatment of choice, reasons behind it, the sources of information and other chronic conditions.
The questionnaire was carefully chosen by the researcher as the most suitable tool for the type of statistical analyses that will be required for this work. The constructed questionnaire encompassed all the necessary questions that enabled the investigator to elicit the required information from hypertensive and diabetic patients who use TMPs for the management of their diseases. In constructing the questionnaire, the following criteria were born in mind: the questionnaire must translate the research questions into very concise, clear and simple language enabling the respondents to understand and provide accurate answers (Salant and Dillman, 1994; Bowling, 2005; Bowling, 2014); After designing and constructing the survey, the researcher assured its practical success by seeking the advice and due approval of professionals whose knowledge and expertise encompassed other disciplines such as statistics, anthropology and pharmacy. The research ideas and topics were also discussed with this group. Meetings with experts in survey design and fieldwork were held. The investigator also had several discussions, via internet, with the relevant health professionals involved in the management of the target group (the diabetic and hypertensive patients) at both NAUTH and UNTH. These created an awareness and interest which, subsequently, resulted in the collaboration between the researcher and relevant doctors at the said Hospitals. The researcher attended a two-week course on statistics covering a wide range of statistical tools required for the analysis of this project before embarking on the fieldwork trip. This was to prepare the researcher beforehand with ideas of relevant statistical analysis that would be required in carrying out the analysis of the study findings.

The investigator then sought out the most appropriate way to collect information from a sample of the population of interest. The face-to-face personal interview was the most suitable option considering that this population consisted of sick people of varying status including the frail, elderly and uneducated, among others (Bowling, 2014; Fink, 2016). The varying demographic characteristics, comprising of all levels of educational status along with

other participants' features, were also considered. These would consequently impact positively on the validity and reliability of this study. Closed and open ended style of questions were used in the questionnaire design. Closed ended enabled respondents to choose from specific response options for each question. In close-ended questions, carefully chosen response options allow for the same frame of reference for all participants when choosing an answer. "If an educator knows the specific information needed to answer a question – and requires a single frame of reference among respondents, closed-ended responses are preferred (Converse and Presser, 1986, p.33). Open ended questions, on the other hand, were used when the aim was to exhaust all possible responses and where one could not be sure of the full range of possible responses. The interview was considered and used especially for the open ended questions. Although the questions were scripted in the questionnaire the interviewer would usually not know the extent of the contents of the response from open ended questions. They allow the respondents to reply in their own words and are effective where the range of responses is unknown or cannot easily be categorised (Bowling, 2014, p.279).

3.4 Fieldwork Data collection and Piloting

In order to document the use of the traditional medicinal plants over the broader region of South Eastern Nigeria, an exhaustive survey was carried out from November 2017 to the end of January 2018 (3 months). This specific timeframe was strategically chosen under the advice of the local coordinators of this fieldwork at Nnamdi Azikiwe Teaching Hospital, Nnewi (NAUTH), and those at University Teaching Hospital, Enugu (UNTH). This was intended to cover the Christmas season and enable the researcher to reach more people; it was considered the optimum time for gathering maximum information. It was explained that at Christmas time, the indigenous people of this zone traditionally travel home en-masse to the South-east from other parts of Nigeria and from all over the world. Most of these indigenes are registered patients at both NAUTH and UNTH. Those visiting for the first time are registered before treatment is received. Interviews were carried out using structured questionnaire consisting of both structured and semi-structured questions (see Appendix 1). The fieldwork of this cross-sectional study was conducted via face-to-face interviews, with data being collected from patients who had agreed to participate. The participants were interviewed while attending their regular clinics in the endocrinology and cardiology departments of the Nnamdi Azikiwe Teaching Hospital, Nnewi, in Anambra State and University of Nigeria Teaching Hospital, Enugu, in Enugu State, Nigeria. Both institutions are two of the nation's most popular federal teaching/research hospitals in Nigeria. The major part of the fieldwork was conducted at NAUTH. The interview was performed inside the consultation clinical rooms of the doctors. The researcher was provided with a desk and two chairs. So, participants were seen by the researcher after their consultation with their

doctors. All folders were made available to the researcher, thereby greatly facilitating the accurate recording of names of medications prescribed by the doctors, as well as changes made over a period of one year with respect to dosage and prescription information. These arrangements also enabled the remarkable number of patients processed in the short period of three months. The questionnaire (see Appendix 1) allowed for descriptive responses regarding information about the plants, such as the part(s) of the plant used, medicinal uses, mode of preparation (i.e., decoction, maceration, paste, powder and juice). Also, of interest were details on their administration: the form of usage (whether fresh or dried), mixtures of other plants used, the source of the plant, route of application, approximate dosage, and side effects, if any. All ages over 18 years were included in this study. In recording the information of diseases, although many spoke English, care was taken and their native language was used to "translate" this into medical terms, so as to avoid the information being in any way erroneous. The names of the TMPs were provided by the participants in their vernacular, English or in both languages.

A pilot study was carried out to test-run the questions on a small number of patients representing the sampled population (Salant and Dillman, 1994, p.120-121; Fink, 2009, p.6). Thirty (30) patients in total were interviewed; ten from each of the three groups – the diabetics, hypertensive and patients with both hypertension and diabetes. The sampling method used in choosing these patients was non randomised convenience method; this was also the method used for the rest of the entire participants. These 30 participants used for the pilot study were seen during their regular check up visits to the Hospital. The researcher personally interviewed the patients in order to assure validity of the questionnaire data which would depend on participants' proper understanding of the questions for correct responses. The researcher in asking the questions aimed at making sure that the questions were understood by the patients and interpreted accordingly; that the wording was understood by all respondents. It was observed throughout this process that the participants understood the questions and responded accordingly. Having tested the questionnaire via the pilot study, no changes were made to the questionnaire as it was deemed suitable. The researcher embarked on interviewing the rest of the participants.

3.5 Sampling strategy and procedures

The sampling units of this study are the diabetic and hypertensive patients, and a non-randomised convenience sampling method was used (Dorofeev and Grant, 2006; Bowling, 2014). Every patient aged 18 years or over, with the above-mentioned conditions willing to be interviewed was included in the survey. The risk of developing hypertension and type 2 diabetes increases with age. The lower age limit of 18 has been shown to be an age to start testing for these diseases. There is no upper age limit because these diseases increase

steadily with age and the elderly have been found by research to depend mainly on TMPs for their treatment, hence the reason for not stipulating a cut off age.

The observation during the fieldwork was contrasted with the actual number of target population of both diabetes and hypertension. The researcher noted that hypertension was alarmingly high while diabetes was at its lowest levels; this observation was supported by the physicians. Patients' medical records showed their absences from regular clinic visits. The total number of interviews were 823. While there were 823 interviews there were only 601 patients (285 HTN; 94 DM; 222 HTN and DM). The HTN and DM patients were interviewed twice (once for each disease).

Although the total target population was inconsequential in the sample determination, we chose a higher sample size in order to enhance the findings' validity and reliability in making statistical inferences, achieving a representative sample, and in minimising sampling bias, among other advantages. Statistics have shown that for a population of 1,000,000 members, evenly (50/50) split on the characteristics in which we are interested, we need a sample of 384 to make an estimate with a sampling error of no more than +/-5%, at the 95% confidence level. The same sample of 384 will be chosen for 100,000,000 study population (Salant and Dillman, 1994).

3.6 Recruitment of participants

The researcher used existing professional networks and an internet search to identify public healthcare services in Nigeria and their functions. In order to reflect a cross-sectional scope of services, the sampling frame included a diversity of patient populations and service types (community-based medical centres and hospitals), and a geographic range covering eight South Eastern states of Nigeria. Initial contact was made by telephone call and email to the Vice Chancellor (a medical doctor), and the Chief Medical Director of University of Nigeria and Nnamdi Azikiwe University Teaching Hospital, respectively. The departments of endocrinology and cardiology of both hospitals were then informed, and potential participants were mapped out – hypertensives, diabetics, and those with both conditions. The participants in this study were diabetics and hypertensive patients who were attending their normal clinical check-up at the Teaching Hospitals. They were registered patients of the Teaching Hospitals. This study's proposal had been sent to the relevant doctors of these Hospitals prior to the arrival of the researcher. The researcher introduced herself at the beginning of each clinic session, stating clearly what the mission constituted. The researcher explained to the patients the details of this work, its procedures and the benefits to the patients. The role, functions and the responsibilities of the researcher were also communicated to the participants. The information sheets were then personally administered to them by the researcher. The information sheet was fully explained to them and those who

were willing to take part were interviewed using the questionnaires. It was clearly stated and explained that participation was voluntary and that it was up to each person to decide whether or not to take part. Also, that if they did decide to take part, they may withdraw at any time without giving a reason and without it affecting any benefits to which they were entitled.

3.7 Data processing and analysis

The collected clinical data of the patient survey, which was recorded on questionnaire were inputted and analysed using Microsoft Excel 2016. A preliminary representation of the data was done using tables and column charts for this report. The results of this study consisted of both descriptive and non-descriptive data. The statistical software, Statistical Package for Social Sciences (SPSS) 25, was used for this study's data analysis. The analysis comprised of descriptive statistics of baseline characteristics using tabulations and charts as well as measures of associations to investigate associations between variables, and for explaining the use of herbal medicines in patients with diabetes, hypertension or those with both conditions. Descriptive statistics were used for frequency counts and percentages of participants' characteristics. A difference was considered significant at an alpha level of 0.05. It helped in determining whether there were significant differences between TMP use in relation to gender, religious affiliation and other characteristics of the patients. Chi square test was used for measures of association in the comparison of demographic characteristics (age, education status, gender, marital status and religion) of participants and their use of TMPs.

4.0 Results and Discussion

This study investigates and reports on the use of TMPs among diabetic and hypertensive patients attending tertiary clinics in South Eastern Nigeria. All the patients who took part in this study had analysable and completed questionnaires. This achievement may be linked to the fact that the researcher physically performed virtually all the interviews, supervising the few that were executed by doctors, and making sure that all questions were answered by the participants. Also worthy of note is the fact that every questionnaire was filled in by the researcher and a few by doctors.

Socio-demographic characteristics of Participants and TMP usage

The results in Table 4.1 summarise the demographic characteristics (gender, age, marital status, education level and religion) recorded from the diabetic and hypertensive participants during the fieldwork study. In addition, their conditions are relayed. This study found some significant associations between some of the demographic characteristics of participants and the use of plant remedies. These associations were found between the two demographic characteristics of age and marital status, versus the use of plant remedies (P=0.006 and P=0.007 respectively). The three age categories are under 40 years, 40 – 65 years and those above 65 years. The participants in the 40 - 65 year group ranked highest in TMP usage with two hundred and eighty five (78.5%) compared to 78 (21.5%) of non users. This group was followed by the oldest group of participants, those above 65 years of age with one hundred and thirty five participants (74%) against forty seven (26%) non users. This study shows that the youngest group, under 40 years of age, has the smallest percentage of TMP usage at 59% (33 participants) versus 41% (23 participants) non usage.

Barner and colleagues' study also show that older adults use TMPs more than the younger generation. Medicinal plants have been traditionally used for thousands of years and the older population is more prone to accept the use of traditional remedies given their deeper knowledge in traditional medicines compared to the younger population (Barner et al. 2010). Their study showed that old people were reported to be the most frequent users of traditional medicines. This current study also showed that the participants have knowledge of medicinal plants. In the marital status category, married participants were the highest TMP users with a rate of 78% to 22% of non users. This group was followed by widows with a rate of 68.5% against 31.5% of non users; singles were the least with rates of 58% compared to 42% for non users. This finding was also supported by Barner and colleagues' work. Marital status was found to have an impact on usage of TMPs, with a greater number of married people using TMP than any other group in this category (Barner et al. 2010).

Chi square test was used for measures of association in the comparison of demographic

characteristics (age, education status, gender, marital status and religion) of participants and their use of TMPs. The findings showed no association between participants' gender, level of education or religion and their usage of TMPs (P=0.636; P=0.533; P=0.419 respectively). The findings also showed that the majority of the participants are Christians, solely due to the location of the study – South Eastern Nigeria, which is dominated by Christians (Table 4.1). It should be noted that there were no agnostics, atheists or traditional beliefs/believers encountered during interviews. Therefore, any inferences relating to religion and TMPs relate solely to Christianity (Catholics, Anglicans and Evangelicals) which constituted 99% of the participants and one percent comprising other religions (Judaism, Sabbath and Islam). This study's findings demonstrated that there was no significant relationship between participants' religion and their use of medicinal remedies (P=0.419). The use of TMPs was more common among females, 258 (76.1%) users versus 81 (23.9%) non users; males were 195 (74.4%) users versus 67 (25.6%) non users (see Table 4.1). This study also shows a significant relationship between the use of plants and the diseases the participants suffer (P=0.003). Its findings show that the participants' conditions have resulted in their search for an alternative to their CMs or the need to use additional help alongside their prescribed medicines. This was supported by a related study conducted by Ezuruike and Prieto on management of diabetes in Nigeria (Ezuruike and Prieto, 2014). Those who suffer from both diseases tend towards TMP use more than those with just diabetes or hypertension alone. In addition, Singh and colleagues' study show that people with chronic diseases including diabetes, hypertension, cancer, asthma among others seek alternatives to their orthodox medicines (Singh et al., 2004). Similarly, some studies in developed countries show that women have higher prevalence of CAM use than men (MacLennan et al., 1996; Astin, 1998). The findings of this study are similar to those of the American and Australian studies, in which both found several associations between demographic factors and alternative and/or medicinal use (MacLennan et al., 1996; Eisenberg, et al., 1998). In this current study, participants' level of education played no part in their use of plants; hence the association/relationship between the level of education and their use of TMPs was not statistically significant (P=0.533) (see Table 4.1). It is worthy of note that all 601 patients recorded in Table 4.1 were visiting the hospital for treatment when interviewed. A significant number of them (75.4%), who visited the hospital still made use of traditional medicine, while 24.6% use only conventional medicines to manage their diseases. Almost all participants in this latter group stated that the lack of clear directions for use associated with TMPs was the reason for not using them. All six hundred and one participants reported using prayers in addition to their prescribed medications.

Table 4.1 Demographic characteristic of Participants

Parameters	TMP Users	Non TMP Users	Total	Chi Square (P<0.05)
Participants	453 (75.4%)	148 (24.6%)	(N = 601)	
Sex				P=0.636
Male	195 (74.4%)	67 (25.6%)	262 (43.6%)	
Female	258 (76.1%)	81 (23.9%)	339 (56.4%)	
Age				P=0.006
Under 40	33 (58.9%)	23 (41.1%)	56 (9.3%)	
40 - 65	285 (78.5%)	78 (21.5%)	363 (60.4%)	
Above 65	135 (74.2%)	47 (25.8%)	182 (30.3%)	
Mean Age	59 years	59 years		
Minimum age	22 years	19 years		
Maximum age	95 years	93 years		
Marital Status				P=0.007
Married	367 (78.3%)	102 (21.7%)	469 (78.0%)	
Single	25 (58.1%)	18 (41.9%)	43 (7.2%)	
Widowed	61 (68.5%)	28 (31.5%)	89 (14.8%)	
Level of Education				P=0.533
No Formal Education	38 (82.6%)	8 (17.4%)	46 (7.7%)	
Primary	149 (76.4%)	46 (23.6%)	195 (32.4%)	
Secondary	104 (72.2%)	40 (27.8%)	144 (24.0%)	

College/University	162 (75.0%)	54 (25.0%)	216 (35.9%)	
Religion				P=0.419
Catholic	320 (77.3%)	94 (22.7%)	414 (68.9%)	
Anglican	84 (74.3%)	29 (25.7%)	113 (18.8%)	
Evangelicals	44 (64.7%)	24 (35.3%)	68 (11.3%)	
Others (Judaism, Sabbath and Islam)	5 (83.3%)	1 (16.7%)	6 (1.0%)	
Conditions				P=0.003
Diabetes	71 (75.5%)	23 (24.5%)	94 (15.6%)	
Hypertension	202 (70.9%)	83 (29.1%)	285 (47.4%)	
Diabetes and Hypertension	180 (81.1%)	42 (18.9%)	222 (37.0%)	

Table 4.2 shows the participants' state of birth, the state where they reside and their ethnicity. 387 (64.4%) of the entire 601 participants were born in Anambra State, where this study was carried out. 214 (35.6%) were born outside Anambra State. 478 (approximately 80%) of the participants reside in Anambra state while the rest of them, 123 (20%) live outside the State. South Eastern Nigeria is home to the Ibos; 586 (97.5%) of the six hundred and one participants are Ibos, while a combination of other tribes comprising of Yoruba and Hausas accounted for the other 15 (2.5%). Clearly, these numbers reflect the location of the fieldwork, being in the heart of Ibo land within an Ibo State.

Table 4.2 Participants' State of Birth, State of Residence and Ethnicity

Parameters	Number of Participants
State of Birth	
Anambra State	387 (64.4%)
Outside Anambra State	214 (35.6%)
Total	601 (100%)
State of residence	
Anambra State	478 (79.5%)
Outside Anambra State	123 (20.5%)

Total	601 (100%)
Ethnic Origin	
Ibo	586 (97.5%)
Hausa	3 (0.5%)
Yoruba	11 (1.8%)
Other	1 (0.2%)
Total	601 (100%)

4.1 Preference for Healthcare

Figures 4.1 to 4.3 illustrate the different health facilities or places where the study's participants' conditions were diagnosed. The vast proportion of the respondents reported seeking care for their condition from the hospital followed by doctor's clinic. Other choices were health centres, followed closely by pharmacy and chemist. Others use a combination of these facilities. It should be noted that in Nigeria, the pharmacist is a qualified personnel who obtained a 5 or 6 year Bachelor or Doctor of Pharmacy degree from an accredited University within or outside Nigeria. The chemists are however not pharmacists. They are self-acclaimed chemists who sell drugs in stalls/kiosks. In some cases these individuals have no University degrees whatsoever. This study's findings showed that most of the participants' first port of call when sick was the hospital. This was closely followed by doctor's clinic and then pharmacy. It is noteworthy that none of the respondents reported using a traditional healer; but one stated that their brother is a traditional medicinal practitioner.

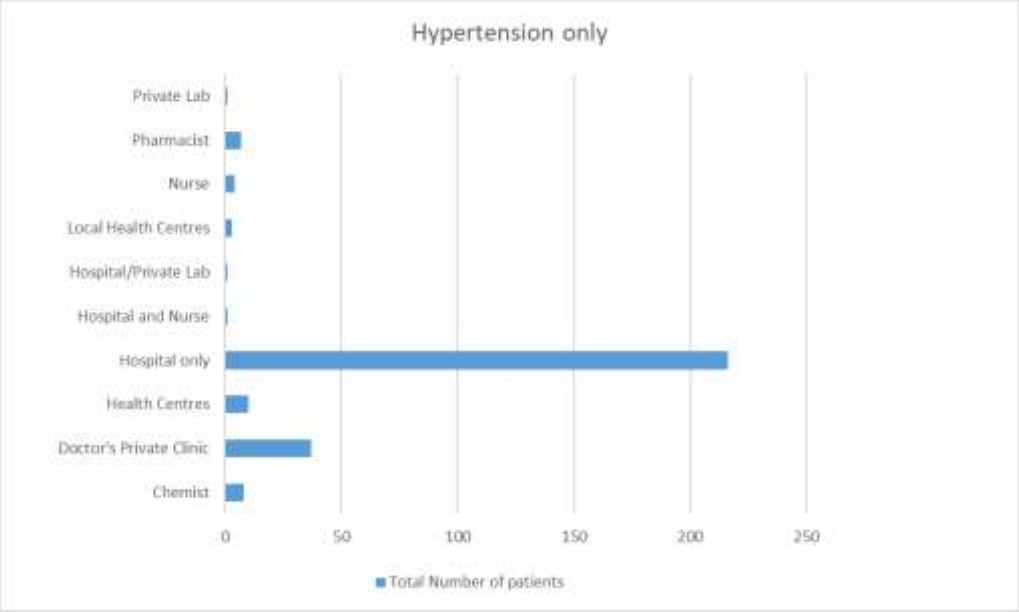

Figure 4.1 Place of Diagnosis for hypertension only Patients (Y-axis show the places where the hypertensive participants were first diagnosed of their diseases).

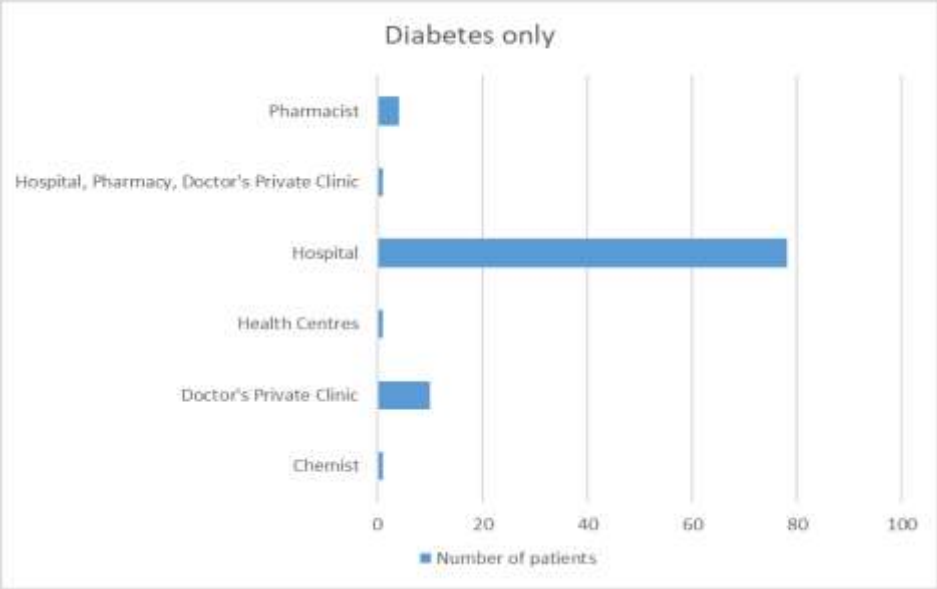

Figure 4.2 Place of Diagnosis for Diabetes only Patients (Y-axis show the places where the diabetic participants were first diagnosed of their diseases).

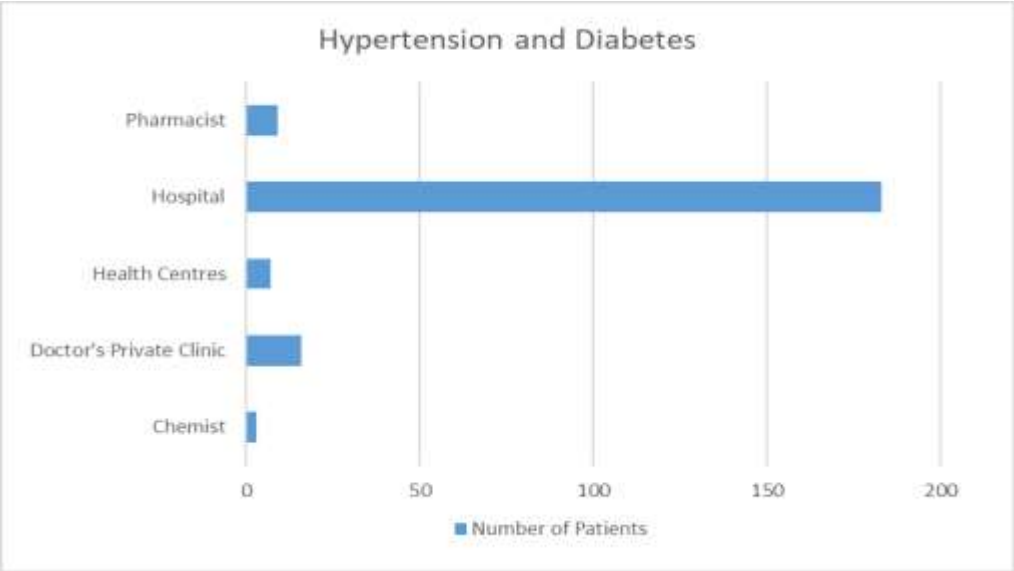

Figure 4.3 Place of Diagnosis for Patients with both diabetes and hypertension (Y-axis show the places where participants suffering from both diseases were first diagnosed of their diseases).

The recorded findings in Figure 4.4 show the pattern of drug prescription given by endocrinologists for the management of these diseases. All (100%) of the diabetics

interviewed were prescribed with metformin either as a monotherapy or in combination with other medication(s). Insulin is the least prescribed due to the difficulty in its preservation as Nigeria lacks steady electricity supply. In addition to suffering from diabetes, 32% of these patients had co-morbidities such as hypercholesterolaemia, arthritis, cancer, and prostate problems among others.

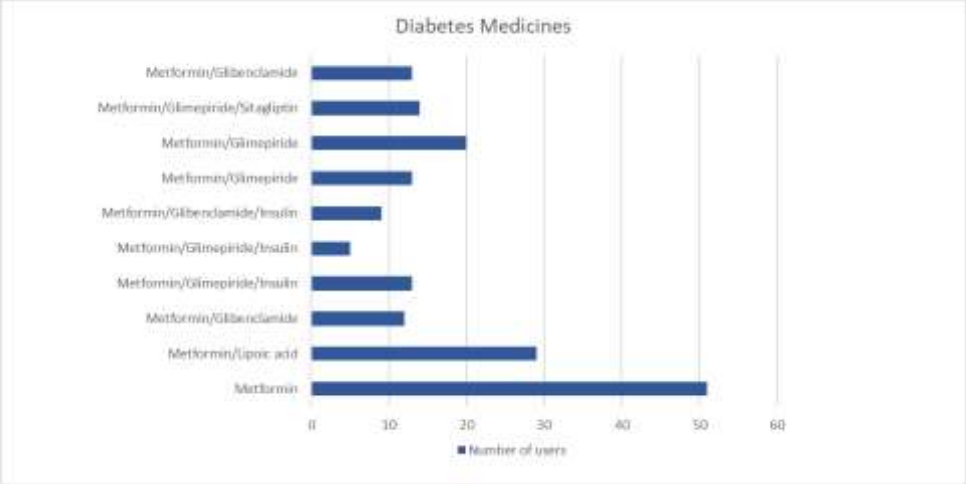

Figure 4.4 Drugs used by diabetic patients for disease management (Diabetic medicines prescribed for diabetic patients by their doctors).

In the hypertensive group of participants, as shown in fig 4.5 below, Amlodipine was the most prescribed medicine. This can be explained by the fact that amlodipine, a calcium channel blocker, is the first-line drug for the treatment of hypertension for the African descents (see Figure 1.1). Two of the antihypertensive medicines prescribed by their doctors are combination drugs, namely vasoprin (aspirin and isosorbide) and moduretic (amiloride and HCT). In addition to suffering from hypertension, 52% of these patients have co-morbidities such as hypercholesterolaemia, arthritis, cancer, and prostate problems among others. Almost all the diabetic and hypertensive patients were treated with polytherapy.

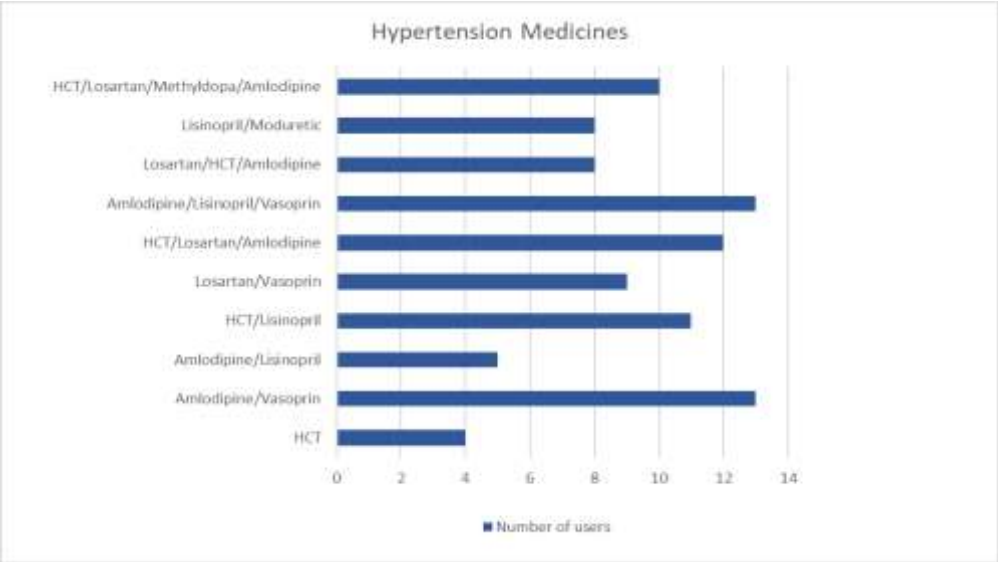

Figure 4.5 Drugs used by hypertensive patients for disease management (Hypertensive medicines prescribed for hypertensive patients by their doctors).

4.2 Herbal Drug Interaction (HDI)

The hazardous public belief that herbal medicines are safe simply because they are natural is one of the reasons for its wider scope of use (Kaufman et al., 2002; Brantley et al., 2014). But this assertion has been reported by studies to be non-factual; many herb-drug-interactions have been reported (Zhou et al., 2007; Izzo and Ernst, 2009; Kennedy and Seely, 2010; Tengku et al., 2020). A "possible interaction" refers to the possibility that one substance may alter the bioavailability or the clinical effectiveness of another substance, when two or more substances are taken concurrently (see Interaction/toxicity studies section in Table 4.7). These interactions are classified in two major categories, pharmacokinetic and pharmacodynamic interactions. Pharmacokinetic interactions occur when herbs change the absorption, distribution, metabolism, protein binding, or excretion of a drug that results in altered levels of the drug or its metabolites (Chavez et al.,2006). Pharmacodynamic interaction are related to the pharmacologic activity of the interacting agents and can affect organ systems, receptor sites, or enzymes (Natural Medicine Comprehensive Database, 2005). Herbal medicines usually have a variety of constituents exerting polypharmacological roles against multiple targets (Chen et al., 2017; Table 4.7 of this study). Furthermore, herbal medicines are mixtures of more than one active ingredient, hence increasing the likelihood of interactions occurring. As demonstrated in the findings of this study, approximately 75% of 601 respondents who were managed at the Hospitals with prescription drugs, made use of herbal therapies concurrently (see Table 4.1).

Most of the participants are on multiple prescription medications, with some experiencing some side effects from their prescription medicines. A great number of patients on orthodox

medicines are known to concomitantly take herbal remedies as shown by several researchers (Briskin, 2000, Willcox and Bodeker, 2004, Reddy et al., 2005, Singh and Levine, 2007; Onaku et al., 2011; Ameade et al., 2018). This practice increases the consequences of drug-herb interactions and the finding is supported by similar studies (Patsalos et al., 2002; Peter and Smet, 2007; Fakeye et al., 2008). The remainder of this current study's participants, about 24%, use only conventional medicines to manage their diseases. Almost all this latter group stated that the non-availability of clear directions for use associated with TMPs was the reason for not using them.

As represented in table 4.5, all four hundred and fifty three (453) TMP users reported that their doctors did not know that they use TMPs. All the respondents reported not informing their doctors of their use of TMPs. A few stated that their doctors inquired, but that they had denied the use of medicinal therapies for fear of being scolded and of being refused treatment by their doctors. Worryingly, 99% of them obtained their TMPs' information from sources outside verified medical/scientific sources, including friends, family, internet and social media. These findings are consistent with other studies from West Africa (Olisa and Oyelola, 2009; Kretchy et al., 2014). This behaviour poses higher risk of herb-drug interaction since their healthcare givers cannot possibly provide any form of guidance or advice.

Interestingly, only five of the respondents reported experiencing side effects from TMP usage compared to the several hundreds who reported having side effects from their prescription or conventional medicines. This low occurrence of side effects with the use of TMPs could be as result of high usage of leaves. The findings show that most of the respondents use leaves, which are widely reported by related studies to be void of these side effects (Ezuruike and Prieto, 2014). Most side effects are experienced from the use of medicinal plants' bark and root. There are few documented cases of herbal interactions with diabetic and or hypertensive drugs (DiPiro et al., 2004; Ezuruike and Prieto, 2016).

Herbal medicines share the same drug metabolising enzymes and drug transporters, including cytochrome P450 enzymes (CYPs), glucuronosyltransferases (UGTs), and P-glycoprotein, with several clinically important drugs (Venkataramanan et al., 2006; Mohamed and Frye, 2011; Na et al., 2011). Several studies have reported interactions of commonly used herbal therapies with orthodox medicines. This have included anticoagulants (warfarin, aspirin, and phenprocoumon) (Skalli et al., 2007; Zhou et al., 2007; Yang et al., 2010; Leite et al., 2021); sedatives and antidepressants (midazolam, alprazolam, amitriptyline, and trazodone) (Zhou et al., 2007); anti-human immunodeficiency virus (HIV) agents (indinavir and saquinavir); cardiovascular drugs (digoxin, nifedipine and propranolol); immunosuppressants (cyclosporine and tacrolimus) (Ioannides, 2002; Pal and Mitra, 2006).

Also anticancer drugs, (irinotecan and imatinib) in humans have been extensively reviewed (Izzo and Ernst, 2009; Shord et al., 2009; Colalto, 2010).

Most of the respondents of this study suffer from other conditions in addition to diabetes and hypertension. This study's findings include most of the above-mentioned medications including Garlic, *Vernonia amygdalina* among others, with therapeutic drugs such as warfarin, hydrochlorothiazide, digoxin, nifedipine, midazolam, alprazolam, indinavir, tacrolimus, and cyclosporine. Most of these drugs have very narrow therapeutic indices. The following combinations of cocktails of medicines (TMPs and CMs) were reported by some of the participants in this current study. One participant, patient 'X', suffers from both hypertension and diabetes and is on Lisinopril (10mg), Vasoprin (Aspirin) (75mg), Losartan (50mg) for Hypertension, and on Glucophage (Metformin) (500mg) and Daonil (Glibenclamide) (5mg) for diabetes management. All these medications are taken daily alongside TMPs, *Vernonia amygdalina*, Garlic and *Ocimum gratissimum.*

Another respondent, 'Y' with both hypertension and diabetes is on Digoxin (0.25mg), Daonil (10mg), Warfarin (5mg), Losartan (25mg) and Aldactone (25mg) for his hypertension, and on Galvusmet (50/500mg) for diabetes, in addition to *Vernonia amygdalina, Gongronema latifolium,* Garlic, Greens, Fluted pumpkin and Kava. Some of these herbs, such as garlic, contain compounds with antagonistic properties (allicin), which are likely to reduce drug efficacy and produce therapeutic failure. The anticoagulant action of warfarin, enhanced by garlic, may produce such effects. Several studies have supported this assertion (Zhou et al., 2007; Mohammad et al., 2009; Leite et al., 2021). Another hypertensive participant on hydrochlorothiazide and felodipine reported taking garlic and grapefruit alongside her prescribed medication. Garlic is known to interact with hydrochlorothiazide; it increases the bioavailability and half-life of hydrochlorothiazide along with a decrease in the clearance and elimination rate constant (Shaw et al., 1997; Asdaq and Inamdar, 2009). Grapefruit juice has been reported to inhibit intestinal CYP3A4 and only slightly affects hepatic CYP3A4. The sensitivity of the interaction with Grapefruit juice may be related to the oral bioavailability of the calcium- channel blocker. It was reported that Amlodipine and Diltiazem, with high bioavailability, are least affected; Nifedipine is intermediate; Felodipine and Nisoldipine, which have lower bioavailability, are most sensitive to the activity of Grapefruit juice (Baxter, 2010).

One respondent, suffering from both hypertension and diabetes, had Aldactone (25mg), Losartan (25mg), Vasoprin (75mg) and Digoxin (0.25mg) for hypertension, and Glucophage (500mg) for diabetes on his hospital prescription. He takes them concomitantly with his herbal therapies, bush buck leaves, bitter leaves, bitter kola, ginger and garlic. Oga and colleagues reported *Vernonia amygdalina*'s interaction with P-glycoprotein (P-gp). Their

study demonstrated that *V. amygdalina* significantly ($p<0.01$) inhibited p-gp at 1–20 mg/mL with inhibition to Digoxin (a p-gp substrate drug) transport of 59–73% (Oga et al., 2012). Their findings show that extracts of V. amygdalina significantly inhibit p-gp in vitro and interactions with conventional p-gp substrate drugs are likely to occur on co-administration and may alter therapeutic outcomes. Furthermore, conventional antidiabetic drugs such as glyburide, sitagliptin, saxagliptin and Glibenclamide, which are p-gp substrates, may be concomitantly used with V. amygdalina (Oga et al., 2012).

All the respondents suffering from diabetes have metformin in their prescription (see Figure 4.4), and 75% of this number use TMPs concurrently with their prescription medicines (see Table 4.1). Several of their commonly used herbal therapies, which have been reported in other studies to interact with metformin, are used by this group (Khatun et al., 2011). Amongst the TMPs used by these participants is *Abelmoschus esculentus* (okro) which has been reported to have herb-drug interaction. Water soluble fractions of *Abelmoschus esculentus* inhibits metformin absorption in vivo (Khatun et al., 2011). Atorvastatin, which has been extensively prescribed for hypertensive participants is a known P-gp substrate metabolized by CYP3A4 enzymes to active metabolites (Lennernäs, 2003). CYP3A4 is the most abundant CYP enzyme and is responsible for the metabolism of 50-60% of drugs in use (Pelkonen et al., 2008). *Vernonia amygdalina* inhibits P-gp efflux activity (Oga et al., 2012). A combination of the inhibitory effects of *Vernonia amygdalina* on P-gp efflux activity and the ability of metformin to decrease P-gp expression could bring about an increase in the plasma concentration of atorvastatin beyond normal level. If the activity of CYP3A4 is significantly inhibited by Vernonia amygdalina, the effects of atorvastatin will be hindered despite its high plasma concentration, as the metabolite is the pharmacologically active entity (Ezuruike and Prieto, 2016). Their work also stated that the identified 'potential' herb-drug interaction may or may not translate to a clinical effect; but it may provide very useful preliminary information that would enable clinicians to undertake better clinical monitoring of a patient's disease management. Thus, it may be more likely to identify clinically relevant herb-drug interactions if encountered.

Summarised in Table 4.3 is a plethora of medicinal plants that are commonly used by the hypertensives and diabetics in South Eastern Nigeria for the management/treatment of their conditions. A total of fifty medicinal plants distributed among 34 families were documented during the fieldwork study for the management/treatment of diabetes and hypertension. Some of these plants were used alone or in combination with other TMPs. This study showed that all the fifty TMPs grow in southern region of the country. These TMPs are used by these patients in addition to their conventional medicines. The most commonly used TMPs are of Cucurbitaceae, Malvaceae, Poaceae, Rutaceae and Salicaceae families of plants (See Table 4.3). Our findings showed that most of the medicinal products were readily available as they were cultivated in their farms or purchased locally. When asked about the source of procurement of the TMPs,

participants responded that they were obtained from their farms. Almost all the plants and herbal products used for diabetes and hypertension were grown by these participants, in their farms or gardens. Plants like *Moringa* and *Aloe vera* were also grown by most participants. Those TMPs that were not grown in their own farms were sourced from their local markets. All the participants interviewed reported that they got their information of the plants from friends, family or social media - hence their ability to buy what they require either from local or herbal markets.

Table 4.3 Ethnobotanical survey of medicinal plants used in the South Eastern Nigeria by hypertensive and diabetic patients in the management of their diseases

S/ No	Scientific Name	Family	Plants' usage frequency	Common name	Local Nigerian name(s)	Plant part(s) used	Disease	Traditional preparation method	Pictorial representation of Plant
1	*Abelmoschus esculentus* (L.) Moench	Malvaceae	2	Okro/Okra, Lady's fingers	Okweje (I); Kubewa (H); Ila (Y)	Fruit, Seed	DM, HTN	Decoction, Maceration, used as vegetable for food	
2	*Aframomum melegueta* K. Schum.	Zingiberaceae	1	Alligator pepper, Grains of paradise, Guinea grain	Ose-orji (I); Citta (H); Atare (Y)	Seed, Fruits, Leaves	DM, HTN	Maceration, Tincture	
3	*Allium cepa* L	Amaryllidaceae	2	Onion	Alubasa (I); Yabasi (H); Alubosa(Y)	Bulb	DM, HTN	Mince 10 bulbs with a bottle of honey. Take 4tbsp thrice daily	
4	*Allium sativum* L	Amaryllidaceae	10	Garlic	Ayo-ishi (I); Tafarunua (H); Aayu (Y)	Cloves	DM, HTN	Cloves are minced (5 - 10), and blended with honey, three spoons are taken three times daily. Or Boil & take liquid 2-3 times daily	

5	*Aloe vera* (L.) Burm.f. syn. *Aloe barbadensis* Mill.	Asphodelaceae	11	Barbados aloe, Curaçao aloe, Aloe barbadensis Mill, Aloe vera	Ibube agu (I); Tinya, Zaboo (H); Alon Erin, Eti-erin (Y)	Leaves	DM, HTN	Juice extract, Decoction	
6	*Anacardium occidentale* L.	Anacardiaceae	1	Cashew	Kachu (I); Jambe, Kadinnia (H); Kaju, Kantonoyo (Y)	Cashew fruit, nuts and leaf extract and bark	DM, HTN	Eat the Cashew fruit, nuts and drink leaf and 2bark extract	
7	*Ananas comosus* L.	Bromeliaceae	1	Pineapple	Akwumbe, Akwu olu (I); Nkwu aba, Abara (H); Ope oyinbo (Y)	Unriped fruit, Stem and fruit	HTN	Eat the fruit Decoction of stem, maceration of fruit, Infusion of leaves	
8	*Annona muricata* L. Merrill	Annonaceae	9	Soursop	Sawansop (I); Tuwon biri (H); Sapi sapi, Ebo (Y)	Leaves, Fruit, seeds, Bark, Root	DM, HTN	Infusion, Decoction, Fruit juice	

9	*Annona senegalensis* Pers.	Annonaceae	1	Wild Custard apple	Ubunu-ocha (I); Gwandar daji (H); Abo, Abobo (Y)	Leaves, Stem bark and Root	DM, HTN	Eat raw, Decoction	
10	*Beta vulgaris* subsp. maritima	Amaranthaceae	1	Wild Spinach, Lamb's quarter spinach, Goosefoot, Fat-hen and Pigweed	Okazi, Ukazị (I), Ajáàbalè, Ajakobale, Ewe Abamoda, Odundun (Y); Afang (Ibibio); Afàng, Afiayo (Efik);	Entire plant	DM, HTN	The entire plant, including the stems, is edible. It can be cooked slightly or eaten fresh.	
11	*Bryophyllum pinnatum* (Lam.) Oken	Crassulaceae	2	Africa never die, Life plant, Resurrection plant; Wonder of the world, Life plant	Abomoda (H); Eru-odundun (Y)	Leaves, Flower, roots, leaf sap; whole plant	DM, HTN	Juice extract from its leaves, Decoction	

12	*Camellia sinensis* (L.) Kuntze	Theaceae	2	Tea plant, Tea shrub, Tea tree and Tea	Ndeme (I); Garafun (H); Ejirin wewe (Y)	Leaves	DM, HTN	Use as tea – infused in hot water	
13	*Carica papaya* L. syn. *Carica mamaya* Vell., *Carica hermaphrodita* Blanco, Carica cubensis Solms.	Caricaceae	4	Paw paw	Okworo-gbogbo, Okworo bekee, Okwere (I); Gwanda, Gonada (H); Ibepe, sayinbo (Y)	Leaves, fruits	DM, HTN	Eat fruits; Dry leaf and use as tea or boil leaf and drink the juice	
14	*Chrysanthelum Americanum* L.	Asteraceae	1	Grass flower gold, Marigold	Agádī-ísí-awo (I); Goshin, Baana, Ganshin, Gona, Raáriyár,	Whole plant	HTN	whole plant harvested after flowering and dried in the sun or in a well ventilated place protected from moisture. Used as supplement	

					Kása (H); Abilẹrẹ, Ayigi/oyigi (Y)				
15	*Citrullus lanatus* (Thunb.) Matsum. & Nakai	Cucurbitaceae.	3	Watermelon	Anyu (I); Kankana guna (H); Eso bara, Elegede (Y)	Fruit, Leaves, Seeds	DM, HTN	Eat as fruit, Decoction	
16	*Citrus aurantiifolia* (Christm.) Swingle	Rutaceae	1	Lime	Oroma ịlụ ịlụ, Oroma nkirisi (I); Lemun, Tsami, Dankabuya (H); Orombo, Wewe, Osan wewe (Y)	Fruit	DM, HTN	Juice extract	

17	*Citrus limon* (L.) Osbeck Syn. Citrus limonum	Rutaceae	3	Lemon	Oloma-ogbe (I); Leemu (H); Osam-laimu, Osan orombo nla (Y)	Fruit, leaves, stem bark, and root	DM, HTN	Blend whole fruit with a glass of water and use first thing in the morning daily Fruit extraction, infusion, decoction	
18	*Citrus paradisi* Macf. Syn. *Citrus aurantium* L.	Rutaceae	2	Bitter orange, Sour orange, Grapefruit	Mkpụrụ osisi grepu (I); Lemun tsami, Dankabuya (H); Orombo wewe, Osan wewe (Y)	Fruit stem, root and leaves	DM, HTN	Eat the fruit Juice extraction, decoction, infusion	
19	*Cucumis sativus* L.	Cucurbitaceae	11	Cucumber	Alo-ose (I); Kakayi (H); Ejinrinw (Y)	Fruit	DM, HTN	Eat Fruit raw	
20	*Cucurbita pepo* L.	Cucurbitaceae	2	Pumpkin	Ukọrọ, ụgbọ̀gụ̀lụ̀, Anyụ̄ (I); Akwato, Bàkánùwaà (H); Apala, élégédé (Y) Eyèn (Edo);	Seed	DM, HTN	Seed oil extract; use as salad spread; do not use for frying	

					Mfrì ǹdìsè (Efik); Agbàdù (Tiv)				
21	*Cymbopogon citratus* (DC) Stapf. syn. *Andropogon citratus*, A. ceriferus Heckel, A. nardus L. var. Ceriferus(L) Rendle	Poaceae	1	Lemon grass, Fever grass, Citronelle(Fr.)	Nche awuta, Ahihia tii (I); Kokoba, Koriko oyibo (Y)	Root, stem and leaves	DM, HTN	Decoction	
22	*Cyperus esculentus* L.	Cyperaceae	1	Tiger nuts, Yellow nutsedge, Zulu nut, Yellow nutgrass, Ground	Aki awusa (I); Haya, Aya (H); Imumu, Ofio omu (Y)	Seeds	DM, HTN	It can be eaten raw, dried, roasted, or grated and can be subjected to further processing.	

				almond, Chufa, Rush nut					
23	*Dioscorea dumetorum* (Kunth) Pax.	Dioscoreaceae	3	Yellow yam, Air potato, Air yam, Bitter yam, Cheeky yam, Potato yam, Cluster yam	Ona, Ji abana, Ji ilu (I); Haushi (H); Ewura, Kikoroisu (Y); Igie'wa (Bini), Abeghe (Efik)	Tuber	DM, HTN	Cook yam and eat with vegetables or tomato sauce	
24	*Garcinia kola* Heckel	Clusiaceae	7	Bitter cola, False cola, Male cola	Aku-ilu or Ugolo, Aki-inu, Adi (I); Cida goro (H), Orogbo (Y); Edun (Bini); Efiari (Efik); Efiat (Ibibio)	Seed	DM, HTN	Chew 3-4 seeds a day; Maceration	

25	*Gongronema latifolium* Benth Syn. *Marsdenia latifolia* (Benth.) K.Schum.	Apocynaceae	257	Bush buck	Utazi (I); Arokeke (Y); Urasi (Efik; Ibibio)	Leaves	DM; HTN	Chew a handful a day or eat with bitter leaf and scent leaf mixed together for a more effective result	
26	*Hibiscus sabdariffa* L.	Malvaceae	3	Rose Mallow, Roselle, Jamaica sorrel or Red sorrel, Zobo, Hibiscus flower	Okworo-ozo (I); Abin kan iyaka, Zobo (H); Amukan (Y)	Fruits, seeds, Calyx	HTN	Decoction of the seeds; eat fruit raw	
27	*Irvingia gabonensis* (Aubry-Lecomte ex O'Rorke) Baill.	Irvingiaceae	1	African bush mango, Wild mango, Native mango, Sweet bush mango, Dika nut tree, Dika	Ogbono, Ugili, Odika (I); Goron, Biri (H); Oro, Apon (Y)	Fruit, seed	DM, HTN	Eat raw fruit; Break off the kernel and remove seeds, crush it into fine powder and make soup	

				bread tree.					
28	*Mangifera indica* L.	Anacardiaceae	1	Mango	Mangolo (I); Mangwaro (H); Mangoro (Y)	Leaves, Stem, bark, Kernel , Fruits	DM, HTN	Decoction is taken once daily	
29	*Manihot esculenta* Crantz	Euphorbiaceae	1	Cassava	Abacha, Akpu (I); Rogo (H); Ege, Gbaguda (Y)	Tubers, Leaves	DM, HTN	Soak tubers for days, wash, and cook for very long time and use as food or prepare as tapioca	
30	*Mentha pi perita* L.	Lamiaceae	1	Mint leaves	Akwukwo mint(I); Na'a naa (H); Ewe mint (Y)	Leaves	DM, HTN	Use as tea	
31	*Moringa stenopetala* (Baker f.) Cufod. *Syn. Moringa oleifera*	Moringaceae	33	Ben oil tree, Horseradish tree, Drumstick tree, African moringa	Odudu oyibo, Okochi egbu, Okwe olu, Okwe oyibo, Okughara ite, Uhe, Ikwe beke (I);	Leaves, seeds Pods	DM, HTN	Infusion with dried leaves; powder from seed and use in food; chew leaves and swallow Boil the leaves and drink the water	

	Lam				Gawara, Habiwal (H); Ewe ile, Ewe igbale, Idagbo monoye (Y)				
32	*Musa paradisiaca* L. Syn: *Musa sapientum* L.,	Musaceae	1	Banana	Ule/uneri/ unele (I); Ayaba, agade (H); Ogede wewe (Y)	Fruit	HTN	Eat the fruit; Juice extract	
33	*Plantago major* L.	Musaceae	1	Plantain	Abrika (I); Okamu/ayaba (H); Ogede agagba (Y)	Fruit	HTN	Boil with water and eat with vegetables or tomato sauce	
34	*Ocimum basilicum* L	Lamiaceae	102	Scent leaf, Basil	Nchuanwu, Arigbe (I); Dai doya ta gida (H); Efirin (Y)	Leaves	DM, HTN	Wash with warm water and eat; mix a handful of scent leaf, bitter leaf and bush buck, macerate with a litre of water and drink about	

								half a cup a day.	
35	*Olea europaea* L.	Oleaceae	1	Olive oil Olive tree, Olea	Mmanụ oliv (I); Man zaitun (H); Olifi epo (Y);	Fruit, Leaves, Stem bark	DM, HTN	Already made oil Decoction, Extraction	
36	*Pentaclethra Macrophylla* Bentham	Mimosaceae	2	African oil bean	Ukpaka, Ugba (I); Ukana (Efiks)	Seeds	HTN	Fermented oil bean seeds is consumed with tapioca, stock fish and garden eggs and leaves. Take 2 seeds a day	
37	*Persea Americana* Mill	Lauraceae	1	Avocado, Avocado-pear, Alligator pear, Butter fruit	Ube-beke, Ube Oyibo (I); Igba/apoka (Y); Olumue Bo (Esan/Benin); Eban Mbakara (Efik)	Fruits, Leaves, flowers and seeds	DM, HTN	Decoction 3x daily, fruit is eaten; Seed powder added to drinks; Leaves are made into shreds, dried and taken as infusion	

38	*Piper guineense* Schumach. & Thonn	Piperaceae	1	Black pepper, Climbing black pepper, West African black pepper, Benin pepper, Ashanti pepper, Bush pepper, Guinea pepper	Uziza (I); Masoro (H); Ata-iyere, Iyere (Y); Ngolo imassoro (Kanuri); Chitta masoro (Fulani); Eti-nkeni (Efik)	Leaves Seeds	DM, HTN	Leaves and seeds are prepared as soup. Food: sauces, condiments, spices, flavourings	
39	*Populus alba* L.	Salicaceae	1	Abele, Gin-doro, Silver-leaf poplar, Silver poplar, White poplar	Abele, Gin-doro	Leaf	DM, HTN	Dried leaves used as tea	
40	*Psidium guajava* L.	Myrtaceae	1	Guava	Ugwoba (I); Gwaaba (H); Guafa (Y)	Leaves	DM, HTN	Guajava leaf aqueous extract; Infusion	

41	*Saccharum officinarum* L.	Poaceae	1	Sugar cane	Okpètè, Achàrà mmako (I); Aràkké, Gwalagwaji, Kárán sárkíí, Kuburu (H); Ireke (Y); Mbọ̀kọ̀ (Ibibio); Iyelegh (TIV)	Stem	DM, HTN	Chew stem and suck the juice	
42	*Solanum aethiopicum* L.	Solanaceae	10	Garden egg, Egg plant, African eggplant, Scarlet eggplant, Bitter tomato	Aghara, afufa (I); Gauta (H); Igbagba, Ikan, Osun, Aka igba, Ikanin (Y)	Roots, fruits and leaves	DM, HTN	Infusion; Juice extract; eat raw	
43	*Solanum lycopersicum* L. Syn. Lycopersicon esculentu	Solanaceae	4	Tomato	Tomato (I); Tomati (H); Tomati (Y)	Fruit	DM, HTN	Eat raw or blend, cook and use as sauce; decoction	

	m Mill								
44	*Talinum fruticosum* (L.) Juss. Syn. *Talinum triangulare* (Jacq.) Willd. .	Portulacaceae	1	Water leaf	Gborondi (I); Gbure (Y); Ebe-dondo (Esan)/Benin)	Leaves and Roots	DM, HTN	Leaf infusion is taken as tea or cut roots into pieces and made as decoction	
45	*Tapinanthus bangwensis* (Engl. & K.Krause) Danser; syn *Loranthus bangwensis* Engl. and K.Krause, often misnamed *Loranthus*	Loranthaceae	3	African mistletoe	Awuruse (I); Bokondoro (H); Afomo (Y)	Whole aerial plant	DM, HTN	Make decoction and take as needed; Infusion, taken as tea	

	micranthus Hook.f								
46	*Treculia africana* Decne. ex Trécul	Moraceae	1	Africa breadfruit	Ukwa (I); Afon (Y)	Seed, decoction of its leaves	DM, HTN	Remove shells and cook seeds and eat	
47	*Vernonia amygdalina* Delile	Asteraceae	240	Bitter leaf	Onugbu(I); Ewuro(Y); Shiwaka, Chusar doki, fatefate (H); Etidot (Ibibio); Oriwo (Bini); Ityuna (Tiv); Oriwo (Edo)	Leaves and roots	DM, HTN	Leaf decoctions, infusion or maceration	
48	*Xanthosoma sagittifolium* (L.) Schott	Araceae	1	Cocoyam, Wild taro	Akaso, Ede (I); Gwamba (H); Koko, Kokof-un, Kokoibile (Y)	Tuber, leaves	HTN	Cook and eat as food	

49	*Zea mays* subsp. mays	Poaceae	1	Maize, Corn	Oka (I); Masara (H); Agbado (Y)	Corn Silk	DM, HTN	Dry the silk and use as tea; can be drunk with fresh or dried corn silk Decoction	
50	*Zingiber officinale* Roscoe	Zingiberaceae	4	Ginger	Jinja (I); Chita, Sankanjabir, Citaraho (H); Ata ile, Ata le, Jinja (Y)	Rhizomes, whole plant	DM, HTN	Remove skin and eat; Powder	

Decoction: A concentrated liquor resulting from heating or boiling a substance, especially a medicinal preparation made from a plant. Infusion: A drink, remedy, or extract prepared by soaking plant leaves or herbs in liquid. Juice Extract: a preparation containing the active ingredient of a substance in concentrated form e.g. natural plant extracts. Maceration: the act of softening leaves, fruits or seeds by soaking in a liquid. Mince: to cut up fruits, leaves or seeds into very small pieces, typically in a machine. Paste: A thick, soft, moist substance typically produced by mixing dry ingredients with a liquid. Tinctures - are concentrated herbal extracts made by soaking the bark, berries, leaves (dried or fresh), or roots from one or more plants in alcohol or vinegar.
(Local Nigerian name(s): I, H, Y, stand for Ibo, Hausa, Yoruba respectively).

The review carried out by the researcher showed that all fifty TMPs have some level of pharmacological effects (see Appendix 3: Table 4.7, experimental evidence section). The findings showed that all the plants recorded from the fieldwork were already in use in Nigeria by diabetics and hypertensives in the management of their diseases. Most of these plants have been used for centuries as vegetables, usually in cooked form. For medicinal effect, most of them are used in their raw forms (see Appendix 3: Table 4.7).

The result also showed that almost every patient interviewed knew the names of both their conventional and medicinal plants, contrary to the widely circulated opinion that stated otherwise. The patients knew exactly what TMPs they were using, and their sources; so, there was virtually no need for the traditional medicine practitioners. It was noted that the respondents in this study do not visit herbalists anymore as shown by previous studies (Ezuruike and Prieto, 2014), since information about these plants are widely circulated by social media, family, friends, radio, blogs and the internet in general. The most frequently used CAM was prayer/faith healing. One hundred percent of the participants employed this medium. Religion has always been commonly and widely used by Africans from of old. Prayer and Healing is also favoured in other parts of the world (Yeh et al., 2002; Levin, 2016; South and McDowell, 2018). This was followed next by TMPs.

Among those reporting use of TMPs, *Vernonia amygdalina* (bitter leaf), *Ocimum gratissimum* (sweet basil/scent leaf) and *Gongronema latifolium* (bush buck) were three of the most commonly used medicinal plants identified from this work (see Table 4.3). The reasons behind these choices of TMPs may be as a result of the phytoconstituents identified in the plants, and which have been scientifically proven to have both antihypertensive and antidiabetic effects as reported previously by researchers. For contractility investigation, the aortic smooth muscle maximum relaxation of 31.3 +/- 3.1% was observed with extract concentration of 2.7 mg/ml of *Vernonia amygdalina* (Taiwo et al., 2010). Infusion of the leaves of *Vernonia amygdalina*f showed significant ($p < 0.05$) inhibitory activity against α-glucosidase and pancreatic lipase. It also inhibited intestinal glucose absorption and enhanced muscle glucose uptake, respectively (Erukainure et al., 2019). Chronic intake of 400 mg/kg ethanolic extract of the fresh leaves of *Vernonia amygdalina* significantly decreased fasting blood glucose levels, increased serum and pancreatic insulin levels, increased the activity of liver antioxidant enzymes, and also increased the expression and distribution of Glut 4 receptors in STZ-induced diabetic rats (Ong et al., 2011). Decoction of the leaves of Vernonia amygdalina (bitter leaf), *Ocimum gratissimum* (scent leaf) and *Gongronema latifolium* (bush buck) tested in humans decreased their baseline blood glucose levels (Ejike et al., 2013).

Vernonia amygdalina was reported to possess potent pharmacological activities such as

antidiabetic, anthelminthic, antiplasmodial, antimicrobial, antioxidant and antianaemic activities (Ezeadila et al., 2015; Udochukwu et al., 2015; Danladi et al., 2018; Alara et al., 2020). Leaf extract of *V. amygdalina* reduced fasting blood sugar from 96 mg% to 48 mg% in 4 h when given to normoglycaemic rabbits. Administration of the leaf extract to alloxan induced rats showed significant reduction in blood and serum glucose (Danladi et al., 2018). It was also reported that the crude *Vernonia amygdalina extract* consists of multiple chemical components which could exhibit a strong vasorelaxant effect on isolated aortic rings due to its employment of multiple signalling pathways (Yung et al., 2017).

Ocimum gratissimum crude extract was reported to decrease BP level (Umar et al, 2010). *O. gratissimum* was also reported to inhibit renovascular hypertension-induced hypertrophy of heart and increased in ET-1 and Ang II levels (Umar et al, 2010). *Ocimum gratissimum* water extract exhibited an in vitro ACE-inhibition activity, with the 50% inhibition concentration (IC50) value being 56.3 µg/mL. *Ocimum gratissimum* extract has a significant blood pressure lowering effect in spontaneous hypertension rats (SHRs) (Huey-Mei et al., 2017). *Ocimum gratissimum* was found to have vasorelaxant effect, although the mechanism for this relaxation was not determined. It was suggested that one potential mechanism could be due to *Ocimum gratissimum*'s potent Reactive Oxygen Species' (ROS) scavenging ability (Kaurinovic et al, 2011). The aqueous extract of the leaves was found to improve glucose tolerance (Oguanobi et al., 2012). The methanol extract of the leaves was reported to decrease blood glucose levels (Aguiyi et al., 2000; Erukainure et al., 2019).

Ethanol extract of the leaves of *Gongronema latifolium* was found to decrease the blood glucose levels and increase the activity of glucose metabolizing enzymes (Ugochukwu and Babady, 2003). The methanol extract of *Gongronema latifolium* has hypoglycaemic effect (Ugochukwu and Babady, 2002; Fasakin et al., 2011). The use of its crude leaf extract in maintaining healthy blood glucose levels has been reported. *G latifolium* modulates glucose homeostasis as well as inhibiting redox imbalance and inflammation in diabetic rats (Ojo et al., 2020). Administeration of hydro-alcoholic leaf extracts of *G. latifolium* at moderate doses, reduces blood glucose through modulation of the gut microbiome (Chukwudozie et al., 2021). The extract of *Gongronema latifolium* is likely to be of biological significance in cardiovascular complication of diabetic and non-diabetic users (Edet et al., 2009). The findings of their investigation showed that the application of *Gongronema latifolium* crude leaf extract in the treatment of hypertension may have significant effects in moderating the incidence of myocardial infarction (Edet et al., 2009). *Gongronema latifolium* was reported to have hypotensive properties mediated by the synergistic activity of the compounds, probably via the β-adrenergic blockade mechanism (Beshel et al., 2019). The hypoglycemic and antihypertensive activities of the following plants identified in this study have also been

demonstrated experimentally (see Appendix 3: Table 4.7).

The antihypertensive effect of aqueous extract of *Psidium guajava* leaf was demonstrated in Dahl salt-sensitive rats, resulting in significant decrease in the systemic arterial blood pressures and heart rates of hypertensives (Ojewole, 2005). *G. latifolium* was reported to have hypotensive properties mediated by the synergistic activity of the compounds, probably via the β-adrenergic blockade mechanism (Ademiluyi et al., 2016).

The aqueous and methanol leaf extracts of the *Bryophyllum pinnatum* administered intravenously produced a decrease in arterial blood pressures and heart rates of both anaesthetised normotensive and hypertensive rats (Ojewole, 2005). The *Bryophyllum pinnatum* leaf extract used on isolated guinea pigs caused a decrease on their cardiac contractility and heart rate and inhibited contractions stimulated by electrical field stimulation provoked (Ojewole, 2005).

Allium cepa has been reported to reduce BP anesthetized normotensive rats (Brankovic et al., 2011). Aqueous extracts of *Allium cepa* increase expression of endothelial nitric oxide synthase (eNOS) but decrease that of vascular cell adhesion molecule 1 (VCAM-1) (Vazquez-Prieto et al., 2011). Galavi and colleagues' study concluded that onion can be helpful in the prevention and treatment of high blood pressure, diabetes mellitus, dyslipidaemia, and obesity (Galavi et al., 2021). The antidiabetic effect of aqueous extract of *Allium cepa* was also demonstrated on streptozotocin-induced diabetic rats (Ozougwu, 2011).

Persea americana extract used to test hypertensive and naïve rats resulted in decreased mean arterial pressure (MAP). *P.americana* leaf extract doses showed hypotensive effects (Adeboye et al, 1999).

Throughout Nigeria, *Hibiscus sabdariffa*'s calyces is brewed locally for beer. The acclaimed antihypertensive effect of the aqueous extracts of the calyx of *H. sabdariffa* was investigated by Adegunloye and colleagues (Adegunloye et al., 1996. Their findings suggested that mechanism of antihypertensive effect of the *H. sabdariffa* calyces was a result of the involvement of acetylcholine-like and histamine-like mechanisms as well as direct vasorelaxant effects (Adegunloye et al, 1996). Roselle's blood pressure lowering effects have been extensively reported in both animal (Ali et al., 2005; Mojiminiyi et al., 2007; McKay et al., 2010; Inuwa et al., 2012; Hopkins et al., 2013) and human studies (Herrera-Arellano et al., 2004; Mojiminiyi et al., 2007; Mozaffari-Khosravi et al., 2009; Inuwa et al., 2012; Hopkins et al., 2013). Furthermore, *Hibiscus Sabdariffa* was reported to lower blood pressure in patients with stage 1 hypertension (Jalalyazdi et al., 2019). (See Table 4.7 for

phytoconstituents identified in the plants).

*Allium sativum'*s blood pressure lowering properties come mainly from allicin, a vasodilating agent that inhibits angiotensin-converting enzymes and consequently reduces blood pressure (Stabler et al 2012; Wang et al., 2015). Evidence from meta-analysis studies indicated that aged garlic extract (AGE) produces consistent lowering of blood pressure compared to other forms of garlic. A recent meta-analysis of randomised, controlled trials concluded that garlic supplements induce a significant reduction in both SBP and DBP (Wang et al., 2015).

The antioxidant, carpain, identified in *Carica papaya,* when given in small doses, slows down the heart and thus reduces the blood pressure. Higher doses produce vasoconstriction and lower blood glucose (Akinloye and Solanke, 2011). The methanolic extract of C. papaya elicited angiotensin converting enzyme inhibitory activity (Brasil et al., 2014). The researchers stated that the antihypertensive effects elicited by the methanolic extract of *C. papaya* were similar to those of enalapril, and the baroreflex sensitivity was normalised in treated spontaneously hypertensive rats (Brasil et al., 2014). In addition, Wahdi and colleagues concluded in their findings that *Carica papaya* decreased blood pressure in adult patient (Wahdi et al., 2020).

Extract of *Solanum lycopersicum* (tomato) modestly reduces BP in patients with mild, untreated hypertension (Engelhard et al, 2006). Another study reported a significant correlation between systolic BP and lycopene levels. Dutta-Roy and colleagues in 2001 reported that (20-50 microl of 100% juice) of tomato extract, tested for their anti-platelet property, inhibited both ADP- and collagen-induced aggregation by up to 70%, but could not inhibit arachidonic acid-induced platelet aggregation and concomitant thromboxane synthesis under similar experimental conditions (Dutta-Roy et al, 2001). Their work demonstrated that the anti-platelet components (MW <1000 Da) in tomatoes are water soluble, heat stable and are concentrated in the yellow fluid around the seeds. These results indicate that tomatoes contain anti-platelet compounds in addition to adenosine (Dutta-Roy et al, 2001). The researchers stated that unlike aspirin, the tomato-derived compounds inhibit thrombin-induced platelet aggregation. They also noted that the data indicate that tomato contains very potent anti-platelet components, and consuming tomatoes might be beneficial both as a preventive and therapeutic regime for cardiovascular disease (Dutta-Roy et al, 2001). Similarly, the results of the study carried out by Marcolongo and colleagues showed that *Solanum lycopersicum* lowers blood pressure (Marcolongo et al., 2020). Fuethermore, *Solanum lycopersicum was reported to lower blood glucose level* (Banihani, 2018).

The aqueous extract of ginger has also been reported to inhibit lipid peroxidation as well as ACE in rat hearts (Akinyemi et al., 2013). It was found that ginger not only reduces levels of total cholesterol, triglyceride, LDL, and vLDL, but can also inhibit ACE-1 activity (Akinyemi et al., 2014). The systematic review and meta-analysis carried out by Zhu and colleagues provided evidence for the effects of ginger on glucose control, insulin sensitivity, and improvement of blood lipid profile (Zhu et al., 2018).

The leaves of *Mangifera indica* have been reported to increase the resistance and decrease the permeability of capillary vessels; and they have been successfully used for over 20 years in treating vascular problems. The three amino phenols are sympathomimetic and in other plants (*Surothamnus scoparius* Koch.) have proved to have marked vasoconstrictive properties and to be hypertensive (Oliver-Bever, 1986). Dichloromethanic fraction of M. indica leaf produced antihypertensive effect, most likely by ACE inhibition, with benefits in baroreflex sensitivity and cardiac hypertrophy (Ronchi et al., 2015). After two and four weeks of treatment, the leaf extract of Mangifera indica significantly reduced blood glucose levels, exceeding glibenclamide effects (Villas Boas et al., 2020). The aqueous extract of Mangifera indica leaves was effective in maintaining the long-term hypoglycemic effect, as well as, significantly increased the sensitivity of diabetic animals to insulin and the plasma insulin level (Villas Boas et al., 2020).

This study also observed that the most common method of preparation was decoction. A hundred percent of these recipes were administered via oral route. This is supported by one of the studies carried out in Nigeria (Gbolade, 2009), in which the researcher recorded decoction as the most cited method of preparation. In another study, similar to the current one, an ethnopharmacological survey conducted in Kisangani City (Democratic Republic of Congo), 83% of herbal remedies were prepared by aqueous decoction, while 97% of recipes were administered to patients by oral route. All plant parts are used fresh, with water as the sole solvent. Leaves are the most used plant parts (Katemo et al., 2012). This was followed by fruit, then seeds.

4.3 Determinants for the use of Medicinal Plants

Table 4.4 illustrates the reasons behind the use of medicinal plants by the participants. A good proportion of the respondents reported that they were trying out their effectiveness as reported by others. Other categories claimed that the TMPs helped in lowering their glucose level, BP reduction, lowering both BP and glucose levels. Most of the patients monitor their glucose and blood pressure levels by visiting the pharmacies for the measurements.

Pharmacies are readily available and they are walk-ins. Some of the patients have the equipment and measure themselves at home. Other respondents reported that TMPs have no side effects, are cheaper than CMs and are convenient. In addition, some of the participants reported that they were seeking for cure and they believe that TMP is the answer. Furthermore, some reported that TMPs are more effective than CMs. Various reasons cited by the participants for using TMPs mirrored those ascertained by other researchers for the increased prevalence of medicinal plants utilisation. There were numerous other medicinal plants recorded and used by the participants of this study. This study's findings showed that most diabetic and hypertensive patients believe in and seek alternative and or complementary medicines for the treatment/management or the cure of their diseases. Furthermore, the participants who have both diabetes and hypertension ranked highest among all TMP users. This may be attributed to the fact that they suffer from two debilitating diseases – hence, are desperate for relief or even cure. Perhaps, due to the nature and seriousness of these diseases, the participants are inclined to seek resolution for them. This belief is echoed in related studies (Oke and Bandele, 2004). In their work titled Misconceptions of Hypertension, "Sixty-five percent of subjects feel that they will require no more medication once they achieve control of their blood pressure. Twenty-one percent of respondents are of the opinion that they will achieve a permanent cure only from alternative medical practitioners and will consider using alternative medicine in future". Other reasons reported include absence of side effects associated with TMPs, and their low cost (Eddouks, 2002). In this study, very few respondents (five in total) experienced side effects; and these occurred at the onset of usage. All five reported feeling somewhat dizzy; and that it happened only once. They attributed it to the large quantities of the TMPs (dosage) they consumed but that they got used to it. Others are searching for a cure for their diseases (Kaptchuk et al., 1998). A significant number of respondents reported that TMPs are natural and hence promote and maintain health. This study's findings are echoed by other studies that reported similar preferences for TMPs (Fisher and Ward, 1994). The poor economic state in Nigeria and the increasing costs of conventional medicines are also influencing this decision. About 70% of Nigerians live in the rural areas with no national healthcare and life expectancy of 54.7 years at birth. 40.1% live below income poverty line (UNDP, 2020). Some other attraction to alternative therapies may be related to the power of the underlying philosophies they share, which involve closeness to nature, spirituality, and cultural beliefs of the people (Kaptchuk et al., 1998; Astin, 1998). One of the major hurdles with TMPs is the lack of dosage standardisation.

Table 4.4 Patients' Reasons for use of medicinal plants in each condition

Drives behind TMP use	Diabetes	Hypertension	Hypertension and Diabetes	Total
Effectiveness	41	180	99	320
To lower BP level	N/A	82	5	87
To lower BP and Blood glucose levels	N/A	N/A	69	69
Cure	17	21	31	69
To lower blood glucose level	31	N/A	14	45
Low cost	4	2	2	8
No side effects	0	0	2	2
Convenience	1	0	0	1
Total	94	285	222	601

In Table 4.5, the participants widely reported that their doctors did not ask them whether they use the TMPs. Of the three groups, hypertensives, diabetics and those under both conditions, higher numbers of hypertensives and those with both conditions reported that their doctors did not inquire as to their usage of TMPs; meanwhile, more diabetics reported being asked, in comparison to the other groups. Interestingly, when all the TMP users from all the 3 groups, diabetes, hypertension, and those suffering from both conditions, were asked whether their doctors knew that they used medicinal plants, the answer was 'No' in all cases. Healthcare professionals do not know what their patients are taking daily because their patients take TMPs in addition to their prescription medicines without their knowledge. The patients' reasons for non-disclosure of their use of TMPs was the fear of being scolded and being refused treatment by their doctors. 100% of those patients interviewed who use alternative medicines use them in addition to their orthodox medicines. This matches the findings reported by other studies (Eddouks et al., 2002; Shafiq et al., 2003; Delgoda et al., 2004). Several studies had shown that the chemical constituents of some of these medicinal plants are indicated to have herb-drug interaction (Ezuruike and Prieto 2016). Their study showed that the use of herbal medicines is one of the self-management practices adopted

by diabetic patients in Nigeria. They stated that this practice is often without the knowledge of their healthcare practitioners. It also assessed the potential for pharmacokinetic herb-drug interactions (HDIs) amongst Nigerian adult diabetic patients. One of their key findings was that over 50% of diabetic patients in Nigeria use herbal medicines alongside their conventional drugs for their disease management, which highlights the large number of patients at risk of HDI and the need for such assessments. This predisposes these patients to herb-drug interaction (HDI) (Ezuruike and Prieto 2016). TMPs like garlic can adversely affect concurrently administered drugs (Awang and Fugh-Berman, 2002). TMPs may mimic, decrease, or increase the action of prescribed drugs (Awang and Fugh-Berman, 2002). This can be especially important for drugs with narrow therapeutic windows and in sensitive patient populations, such as older adults, the chronically ill, and those with compromised immune systems. Also, adversely affected when used concurrently, is the interaction between garlic and thiazide diuretics (Izzo and Ernst 2009). Interactions between TMPs and cardiovascular drugs could also increase the toxicological effects of cardiovascular drugs, such as the interaction between garlic and warfarin (Fugh-Berman, 2000; Mansoor, 2001; Kupiec and Raj, 2005).

It was noted by the researcher that though a few of the participants acknowledged that their doctors asked whether they use TMPs, they nevertheless denied using them for fear of being scolded or denied treatment. These findings are consistent with other studies from West Africa (Olisa and Oyelola, 2009; Kretchy et al., 2014). This assertion coupled with the high prevalence of TMPs among diabetics and hypertensive patients, is as important as it is necessary that clinicians must inquire about such health practices from their patients. This should be done in a non-judgmental and tempered way which encourages patients not to conceal use. Patients should be educated on the importance of informing their healthcare professionals of their TMP use, the attending benefits and harm. The importance of more research into the study of alternative and/or complementary medicines cannot be overstated. When asked where they obtain the information about the medicinal plants they use, family members, friends and social media topped the list. It is noteworthy that only a handful of them stated pharmacy. Similar study carried out by Alzweiri and colleagues (Alzweiri et al. 2011) reported that traditional knowledge of the younger generation is greatly influenced by what they hear from television and other media outlets. This is disturbing as we are dealing with medicinal plants which are, in effect, medicines. From these reports, it is evident that hypertension and diabetes are major public health problems in Nigeria and demand more serious attention towards their management and treatment, and most importantly, their prevention.

Table 4.5 Awareness of conventional healthcare practitioners in patient use of TMPs

Parameters	Yes	No	Total
Did your doctor ask if you use TMP?			
Diabetes	7 (7.4%)	87 (92.6%)	94
Hypertension	9 (3.2%)	276 (96.8%)	285
Diabetes and Hypertension	7 (3.2%)	215 (96.8%)	222
Did your doctor know that you use TMP?			
Diabetes	0 (0%)	71 (100%)	71
Hypertension	0 (0%)	202 (100%)	202
Diabetes and Hypertension	0 (0%)	180 (100%)	180

4.4 Preference of Treatment

As summarised in Table 4.6, there are two major groups of the participants with regards to their choice for treatment – those with preference for conventional medicines alone, and those who prefer TMPs. A few others prefer to complement their CMs with medicinal therapies while a very marginal number of the respondents were undecided. The results of this study show that a wide range of traditional medicinal plants (TMPs) are commonly used against diabetes and hypertension in the South Eastern Nigeria. The percentage of the use of TMPs by respondents in this study is over 75% against 25% of non users. This equates the results of related studies from Nigeria and other African countries. In Morocco 80% of patients with hypertension and diabetes was reported using medicinal plants (Eddouks, 2002). Chi square test showed that there is association between participants' choice of treatment and the conditions they suffer (P=0.003). It is worthy of note that though 75% of the participants use TMPs, some of this group still prefer conventional medicines as shown on Table 4.6 below. The data represented in table 4.6 demonstrates that TMPs are the treatment most preferred by the participants generally. Although hypertensive patients prefer conventional medicines, diabetic and those suffering from both conditions prefer TMPs.

Table 4.6 Preference for Treatment versus conditions

Which treatment do you prefer	Diabetes	Hypertension	Hypertension and Diabetes	Total
Conventional	30 (32%)	156 (55%)	53 (24%)	239 (40%)

TMPs	58 (62%)	104 (37%)	140 (63%)	302 (50%)
TMPs and Conventional	3 (3%)	21 (7%)	25 (11%)	49 (8%)
Undecided	3 (3%)	4 (1%)	4 (2%)	11 (2%)
Total	94	285	222	601

4.5 Strengths and Weaknesses of the fieldwork study

4.5.1 Strengths

The period of this fieldwork was strategically planned to cover the Christmas season in order to maximise our target population who return home en masse during this season from all over Nigeria and the world at large. Using a structured questionnaire encompassing both semi-structured and structured questions for this study was designed to yield highly accurate data.

Structured questions enabled the interviewer to collect unambiguous and easy-to-count answers, leading to quantitative data for analysis. Due to the ease of data collection and analysis, it was very economical, and a larger target population was reached within the time-constraint of the fieldwork research. Open and closed-ended questions enabled respondents to give their opinions in full, enhancing the reliability and validity of the findings (see Appendix 1). The fieldwork of this cross-sectional study was conducted through face-to-face interviews, thereby presenting the opportunities to probe fully for responses as intended by the questions, for clarification of any ambiguities that the participants might have had, and for answering any questions they found complicated. Inconsistencies and misinterpretations were checked using this method. Questions were asked and answered in the predetermined order. The participants' response rate was very high, therefore improving the quality of research data because it maintained the effective sample size; this enhanced the findings' general applicability and reliability. The participants were interviewed during their regular clinical check-ups, thus minimising safety risks. These interviews were carried out at Teaching Hospitals which serve as an umbrella institution covering more than one hundred local Hospitals and private clinics in south-eastern Nigeria; this was beneficial because it saved time, money, and other resources by eliminating the need to travel to several locations to interview participants. Interpreter/translational errors were avoided since the researcher is bilingual; it also bypassed an additional cost. All ages 18 years and over were included in this study enhancing the validity of age coverage.

4.5.2 Weaknesses

The fieldwork study only covered one of the three major regions of Nigeria due to the security status of some areas of the country. Therefore, comparison with the other two parts was hindered. The Face-to-Face interviews also has the potential for interviewer bias. Non randomised convenience sampling method was used for this study. There is possibility of sample bias in this method. Sampling bias occurs as a result of a sampling procedure where some members of a population of interest are systematically more likely to be selected in a sample than others. In order to avoid this bias, this study's sample was collected from Teaching Hospitals so as to collect a representative sample to avoid skewing the results of this study. Generally, teaching hospitals work in larger teams than general hospitals and manage a greater variety of patients. Participants of this study came from all walks of life and spanning through 8 states. The fieldwork was carried out in the busiest season in the South Eastern Nigeria where people converge from across the globe for Christmas celebration. Although non randomised convenience sampling method was used for this study, every diabetic or hypertensive patient was invited and have equal chance to be included. And the fieldwork lasted for three (3) months giving a large number of patients an equal chance to participate. Every patient that came for the study was interviewed and included.

5 Conclusion

A great deal of research has gone into complementary and alternative medicines. It is important to state that this practice has come to stay, and interest has grown so widely with no end in sight. As the use of alternative and/or complementary medicines increases, there is a dire need to separate 'the wheat from the chaff'. The aim of this study is to determine using a questionnaire, the extent of the usage of this TMPs. This study has shown quite clearly that a large proportion (75.4%) of patients are taking TMPs, all of whom use them concurrently with conventional medicines. This study also showed that the use of TMPs constitutes a major part of the healthcare management of HTN and DM in Nigeria. Despite the fact that Nigeria's medical healthcare system practices orthodox medicines, TMPs play an important role in their primary source of healthcare provision. This study has brought to the fore a gulf between the healthcare professionals and their patients – one which impacts negatively on the management of these patients. Healthcare professionals do not know what their patients are taking daily because their patients take TMPs in addition to their prescription medicines without their knowledge. The finding of this study showed that among patients' reasons for non-disclosure of their use of TMPs, was the fear of being scolded and being refused treatment by their doctors. This study's recommendation is that the healthcare professionals should handle their patients in a non-judgmental manner so as to open up easy communication with their patients. It was discovered in this study that *Vernonia amygdalina* (bitter leaf), *Ocimum gratissimum* (sweet basil/scent leaf) and *Gongronema latifolium* (bush buck) were three of the most commonly used medicinal plants. They were popular amongst all three categories of patients – those with diabetes, hypertension and those suffering from both diseases. Their medical records showed drops in both sugar levels and blood pressure. Finally, it is the researcher's hope that the empirical knowledge described in this study shall encourage more research in search of the pharmacologically effective medicinal therapies for the better health management of the Nigerian people.

Future Work - A second survey should be conducted on medical professionals throughout Nigeria, with an intent on ascertaining their views on alternative medicine and subsequently, their integration into the national healthcare system for better management of their patients.

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7 Appendices

Appendix 1: Patients' questionnaire

for the management of hypertension and diabetes

University College London
RD PBC

Rosemary Sylver-Francis

Demographic characteristics of the participants

1. ID : _____

2. Sex: □ Female □ Male

3. Town of birth Please specify _____

4. _____
Town where you live nowPlease specify

5. How long have you been living here?

6. How old are you? _____

7. Marital Status: □ Single □ Partnered □ Married □ Separated □ Divorced
☐ Widowed

8. Ethnic origin: □ Ibo □ Yoruba □ Hausa

Any other, Please specify _____

9. Please tick the highest year of school completed:

□ No Formal Education □ Primary□ Secondary School □ College/University

10. Religion: □ Catholic □ Catholic charismatic □ Anglican □ Evangelical□Islam

Any other:Please specify

_____

Chronic conditions/Treatment

11. Last time you were sick who did you consult? [tick all that apply in the order you consulted them, 1= 1st consultation]

☐ Chemist ☐ Pharmacy ☐ Doctor's private clinic

☐ Health Centres ☐ Nurse ☐ Traditional practitioner

☐ Hospital ☐ No one

If not listed, please specify _____

12. Thinking back to all the time you have been sick in the last year, which of these have you consulted. Tick all that apply.

☐ Chemist ☐ Pharmacy ☐ Doctor's private clinic

☐ Health Centres ☐ Nurse ☐ Traditional practitioner

☐ Hospital ☐ No one

13. Which of the following do you suffer from? Tick all that apply to you.

☐ Diabetes type 2 ☐ Diabetes type 1 ☐ Hypertension

Now we talk about hypertension:

14. By whom was your hypertension first diagnosed?

☐ Chemist ☐ Pharmacist ☐ Doctor's private clinic

☐ Health Centres ☐ Nurse ☐ Local Health centres

☐ Hospital ☐ Traditional practitioner

If not listed, please specify _____

15. In what year was your Hypertension diagnosed?

Please specify _____

Conventional Medicines Used For Hypertension Over the Last One Year

S/No.	a) What are The names of	b)How much do you take,	c) How often do you take	d)How long have	e)Who gives you these	f)How much does	Have you ever skipped

	hypertensive medicines you take. If you don't know their names, please, can you describe them	that is, the doses?	them, that is, the frequency	you been using them	treatments (Private Pharmacy, Hospital Pharmacy, private clinics, Chemist or other). Indicate all sources.	these therapies Cost you every month	any of your medicines, if yes why (Could not afford to buy it, Side effects, Not working, Pharmacy ran out of stock, Forgot to take them, Preference for traditional herbal medication, please indicate)
1							
2							
3							

16. Have you ever had any side effects from your conventional hypertensive medicines

17. □No □ Yes

If you have ever had any side effects in the last one year, please complete the table below.

s/no.	Name of hypertensive medicine	Side Effects
1		
2		

3		
4		

18. Do you take any herbal medicines or other therapies for hypertension

☐Yes ☐No

If yes, can we talk about those different therapies?

Herbal Medicines/Therapies Used For Hypertension Over the Last One Year

S/No.	a) What Type of Therapy do you use	b)How much do you take?	c)How long have you been using them	d)What part of the plant are you taking	e)How do you use them	f)How often do you use them (monthly, weekly, daily, occasionally)	h)Who gives you these treatments	i)How much does these therapies Cost you every month	j)Have you ever skipped any of your medicines, if yes why
1									
2									
3									
4									

19. Does your doctor know that you are taking herbal medicines for hypertension? Yes ☐ No ☐

20. Did your doctor ask you whether you take herbal medicines for it? ☐Yes ☐No

21. Does your herbalist know that you are taking conventional medicines for hypertension medicines? ☐No ☐Yes

22. Did your herbalist ask you whether you take conventional medicines for Hypertension?

☐Yes ☐No

23. Have you ever had any side effects from your hypertensive herbal medicines ☐ No

☐ Yes

If you have ever had any side effects in the last one year, please complete the table below.

s/no.	Name of Herbal Medicines	Side Effects
1		
2		
3		
4		

Now let's talk about diabetes:

24. By whom was your diabetes first diagnosed?

☐ Chemist ☐ Pharmacist ☐ Doctor's private clinic

☐ Health Centres ☐ Nurse ☐ Local Health centres

☐ Hospital ☐ Traditional practitioner

If not listed, please specify _____

25. In what year was your Diabetes diagnosed?

_____

Please specify

Conventional Medicines Used For Diabetes Over the Last One Year

S/No.	a) What are the names of hypertensive medicines you take. If you don't know their names, please, can	b)How much do you take, that is, the doses?	c) How often do you take them, that is, the frequency	d)How long have you been using them	e)Who gives you these treatments (Private Pharmacy, Hospital Pharmacy, private clinics,	f)How much does these therapies Cost you every month	Have you ever skipped any of your medicines, if yes why (Could not afford to buy it, Side effects, Not

	you describe them				Chemist or other). Indicate all sources.		working, Pharmacy ran out of stock, Forgot to take them, Preference for traditional herbal medication, please indicate)
1							
2							
3							
4							

26. Have you ever had any side effects from your conventional diabetic medicines☐ No

☐ Yes

If you have ever had any side effects in the last one year, please complete the table below.

s/no.	Name of diabetic medicine	Side Effects
1		
2		
3		
4		

27. Do you take any herbal medicines or other therapies for hypertension

☐Yes ☐No

If yes, can we talk about those different therapies?

Herbal Medicines/Therapies Used For Diabetes Over the Last One Year

S/No.	a) What Type of Therapy do you use	b)How much do you take?	c)How long have you been using them	d)What part of the plant are you taking	e)How do you use them	f)How often do you use them (monthly, weekly, daily, occasionally)	h)Who gives you these treatments	i)How much does these therapies Cost you every month	Have you ever skipped any of your medicines, if yes why
1									
2									
3									
4									

28. Does your doctor know that you are taking herbal medicines for diabetes? □ No □ Yes
29. Did your doctor ask you whether you take herbal medicines for diabetes? □Yes ☐No
30. Does your herbalist know that you are taking conventional medicines for your diabetes? ☐No □Yes
31. Did your herbalist ask you whether you taking conventional medicines for your diabetes? □Yes □No
32. Do you use herbal medicines in conjunction with your conventional medicines: □ No ☐ Yes
33. Have you ever had any side effects from your diabetic herbal medicines□ No □Yes
34. If you have ever had any side effects in the last one year, please complete the table below.

s/no.	Name of Herbal Medicines	Side Effects
1		
2		
3		
4		

35. How did you hear about the use of herbal medicines? □ Family □ Friend □ Doctor □

Pharmacists □ Other

If other, Please Specify

_____

34. What is the reason for taking herbal medicine?

Please specify

_____

35. Which treatment do you prefer?

Please specify

_____

36. Why do you prefer that treatment?

Please specify____

_____

37. Do you suffer from any other long term chronic condition?

Please specify:

_____

38. Do you take medications for them □ Yes □ No

If Yes Please specify:

_____

_____

Appendix 2: Analysis of Fieldwork Data – Data analysis 1

Descriptive analyses

- TMPs in hypertensives
    - Tabulations (breakdown + frequency + percentages) of TMPs used for hypertension
- TMPs in diabetics
    - Tabulations (breakdown + frequency + percentages) of TMPs used for diabetes
- Conventional medicines in hypertension
    - Tabulations (breakdown + frequency + percentages) of conventional drugs used for hypertension
- Conventional medicines in diabetes
    - Tabulations (breakdown + frequency + percentages) of conventional drugs used for diabetes
- In patients with both diabetes and hypertension
    - Two-way tabulations (breakdown + frequency + percentages) of TMPs for both hypertension + diabetes
    - Two-way tabulations (breakdown + frequency + percentages) of conventional drugs for both hypertension + diabetes
- In hypertensives, is TMP used as stand-alone or as complement
    - % patients with TMP + conventional versus % with only conventional
- In diabetics, is TMP used as stand-alone or as complement
    - % patients with CAM + conventional versus % with only conventional
- Awareness of conventional health care practitioners in patient use of TMPs
    - % of practitioners aware of use for Hypertension
    - % of practitioners aware of use for Diabetics
- Awareness of traditional health care practitioners in patient use of CMs
    - % of practitioners aware of use for Hypertension
    - % of practitioners aware of use for Diabetics
- In Hypertensives
    - % of patients with preference for TMPs
    - % of patients with preference for CM
- In diabetics
    - % of patients with preference for TMPs

- % of patients with preference for CM?

- In patients with both hypertension and diabetes

  - % of patients with preference for TMPs
  - % of patients with preference for CM

- In hypertensives, drives behind the use of TMPs

- % use of TMPs due to price affordability?
  - % use of TMPs due to Side effects?
  - % use of TMPs due to ineffectiveness of CM?
  - % use of TMPs due to availability?
  - % use of TMPs due to forgetfulness?
  - % use of TMPs due to preference for TMPs?

- In diabetics, drives behind the use of TMPs
  - % use of TMPs due to price affordability?
  - % use of TMPs due to Side effects?
  - % use of TMPs due to ineffectiveness of CM?
  - % use of TMPs due to availability?
  - % use of TMPs due to forgetfulness?
  - % use of TMPs due to preference for TMPs?

- In patients with both diabetes and hypertension, drives behind the use of TMPs
  - % use of TMPs due to price affordability?
  - % use of TMPs due to Side effects?
  - % use of TMPs due to ineffectiveness of CM?
  - % use of TMPs due to availability?
  - % use of TMPs due to forgetfulness?
  - % use of TMPs due to preference for TMPs?

- Side effects in Hypertensive
  - % of patients experiencing side effects from CMs
  - % of patients experiencing side effects from TMPs

- Side effects in Diabetics
  - % of patients experiencing side effects from CMs
  - % of patients experiencing side effects from TMPs

- Side effects in patients with both diabetes and hypertension
  - % of patients experiencing side effects from CMs
  - % of patients experiencing side effects from TMPs

Measures of associations

- Comparison of demographic characteristics (age, education status, ethnicity/race, gender, marital status, religion and occupation) of TMP users and non-users in Hypertension
    - Tabulations (breakdown + frequency+ percentages)
    - p-value for difference between groups (users vs non-users)
- Comparison of demographic characteristics (age, education status, ethnicity/race, gender, marital status, religion and occupation) of TMP user and non-users in Diabetes
    - Tabulations (breakdown + frequency+ percentages) of demographics in diabetics
    - p-value for difference between groups (users vs non-users)
- Comparison of demographic characteristics (age, education status, ethnicity/race, gender, marital status, religion and occupation) of TMP user and non-users in Diabetes+Hypertension
    - Tabulations (breakdown + frequency+ percentages) of demographics in Diabetics + Hypertension
    - p-value for difference between groups (users vs non-users)

Appendix 3: Table 4.7 Ethnopharmacological review of the medicinal plants used in the management of hypertension and diabetes in Nigeria

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
1	*Abelmoschus Esculentus* (L.) Moench	Hypertension: *Abelmoschus esculentus* seed extract in fructose-induced Hypertensive rat model showed a reduction in blood pressure (Kallolika et al., 2017). They reported that the ECG pattern and Heart rate was improved in the ethanolic *Abelmoschus esculentus* seed extract treated Hypertensive rats. Remarkable reduction in the Blood pressure [systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and mean arterial pressure (MAP)] levels were observed along with a significant reduction in the Total cholesterol and Triglyceride levels (Kallolika et al., 2017). Diabetes: It was reported that all parts of the okra fruits showed significant reduction in blood glucose level, glycated hemoglobin and improvement on lipid profile compared with the diabetic nontreated control and comparable with metformin positive control (Abbas et al., 2017); 100 and 200 mg/kg of the seed and peel powder decreased blood glucose in streptozotocin (STZ) induced diabetic rats (Sabitha et al., 2011); antioxidant effects of the aqueous extract of the leaves (Tsumbu et al., 2011); the	*Abelmoschus esculentus* contains many phytoconstituents including, 12,13 epoxy oleic acid; 9-hexadecenoic acid; alanine; alpha tocopherol; ascorbic acid; aspartic acid; calcium; carbohydrates; copper; cyanidin-3-glucoside;cyaniding-4-glucoside; cysteine; folacin; gamma-tocopherol; glutamic acid; glycine; gossypetin; gossypol; histidine; iron; isoleucine; leucine; linoleic acid; lysine; magnesium; manganese; methionine; mono unsaturated fatty acids; myristic acid; niacin; oleic acid; oxalic acid; palmitic acid; pantothenic acid; pectin; pentosans; phenyalanine; phosphorus; phytosterols; potassium; proline; protein; poly unsaturated fatty acids; quercetin; riboflavin; serine; saturated fatty acids; sodium; starch; stearic acid; sugar; sulphur; thiamin; threonine; tryptophan; tyrosine; valine; pyridoxine; zinc (Amin, 2011; Sabitha et al., 2011; Saha et al.,	It was also reported that the water-soluble fraction of the fruits of Abelmoschus Esculentus decreased oral metformin absorption in-vivo (Khatun et al., 2011).

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		Abelmoschus esculentus peel, its seed, its seed and peel were also reported to demonstrate a significant decrease in blood glucose compared to the metformin group (Abi et al., 2017). Several other studies reporting antidiabetic effect of okra (Nguekouo et al., 2018; Majd et al., 2018).	2011).	
2	*Aframomum Melegueta* K. Schum.	Hypertension: The seeds of *Aframomum Melegueta* were reported to have a potent effect on blood pressure in both normotensive and hypertensive subjects (Lawal et al., 2007). Diabetes: Administration of 450 and 1500 mg/kg of *Aframomum Melegueta* extract in male Sprague-Dawley (SD) rats showed a significant decrease in blood glucose (Ilic et al., 2010). Similarly, it was also reported by Adesokan and colleages that administration of 200 and 400mg/kg aqueous seed extract of *A. Melegueta* decreased blood glucose in alloxan-induced diabetic rats (Adesokan et al., 2010).	The seeds of *A. melegueta* contain the benzenoids gingerol, shagaol, and paradol (Smith, 1982). Other constituents of the genus include flavonoids, (Ayafor et al., 1981) monoterpenes, (Eglinton et al., 1965; Biftu, 1981) and quinoids (De Bernadi et al., 1976). The chloroform extract of the seeds contains antiestrogenic diarylheptanoids, named gingerenone D, dihydrogingerenone A, dihydrogingerenone B, and dihydrogingerenone C (El-Halawany Hattori, 2012).	
3	*Allium cepa* L	Hypertension:	*Allium cepa* contains amino acid	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		Allium cepa has been reported to reduce BP in fructose-fed rats (Gharib-Naseri et al., 2008) and anesthetized normotensive rats (Brankovic et al., 2011). 400 mg/kg/day of aqueous extracts of onion increase expression of endothelial nitric oxide synthase (eNOS) but decrease that of vascular cell adhesion molecule 1 (VCAM-1) (Vazquez-Prieto et al., 2011). Administration of 0.06–2.00 mg/ml of alum cepa in rat isolated thoracic aorta, attenuated both phenylephrine- and KCl-induced contractions (Gharib-Naseri et al., 2008). Removal of endothelium or inhibition of NO, cyclic guanosine monophosphate (cGMP), or prostaglandins did not affect the vasorelaxant action of onion which suggests an endothelium-independent mechanism, possibly through the regulation of extracellular Ca2+ levels (Gharib-Naseri et al., 2008). The investigators implied that antioxidants and the polyphenol quercetin may play a role in relaxing the rat aorta (Gharib-Naseri et al., 2008). Ethanol extracts of onion (0.2–6 mg/kg) induced a transient hypotensive effect with ED50 value of 11.43 ± 2.87 mg/kg. Hypotensive effects caused by onion ethanol extract lasted 72.01 ± 9.65 s (Brankovic, 2011). Diabetes:	cysteine and its derivatives; it also contains flavonoids, mainly quercetin; and phenolic compounds (Lee and Mitchel, 2011). Quercetin and its glycosides, Kaempferol, Cepaenes, S-methylcysteine sulfoxide (SMCS), β-chlorogenin (CorzoMartínez et al., 2007); thiosulfinates, volatile sulphur compounds, and polar compounds of phenolic and steroidal origin (Lanzotti, 2006). Tropeosides, scalonicoside, Sitosterol, Amyrin, Oleanolic acid, Taxifolin, Diosgenin, Gitogenin, Apigenin, Luteolin, Myricetin (Lanzotti, 2006).	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		Effect of *A. cepa* (red onion) bulb aqueous extract on membrane stability in diabetic rats was reported by Nwaehujor and colleagues in their study (Nwaehujor et al., 2014). Their work showed that at the dose of 300 mg/kg, a percentage stabilization comparable to the reference diabetic drug (glibenclamide, 2 mg/kg) was obtained (Nwaehujor et al., 2014).		
4	*Allium sativum*	Hypertension: In the study by Nwokocha et al., administration of intravenous injection of 5-20mg/kg of *Allium sativum* resulted in a decrease on MAP and HR. *A.Sativum* caused hypotension and bradycardia which did not involve cholinergic pathway. The investigators therefore deduced that the mechanism of action may involve a peripheral mechanism for hypotension (Nwkocha et al., 2011). A clinical trial carried out by Ashraf et al on three groups receiving atenolol, placebo and *A.Sativum*. Their results showed a significant reduction in systolic and diastolic BP of patients administered with *A. Sativum* in comparison with the other two groups (Qidwai, et al., 2013). An ethanolic extract of garlic (0.8 mg/ml) caused relaxation in rat pulmonary arteries pre-contracted with phenylephrine (Ku et al., 2002). Another study has demonstrated that	Garlic contains largely allicin along with (1)-S-methyl-l-cysteine sulfoxide (methiin) and (1)-S-(trans-1-propenyl)-l-cysteine sulfoxide. Garlic cloves also contain S-(2-carboxypropyl) glutathione, γ-glutamyl-S-allyl-l-cysteine, γ-glutamyl-S-(trans-1-propenyl)-l-cysteine, and γ-glutamyl-S-allyl-mercapto-l-cysteine (Amagase et al., 2001); Sativosides, Proto-desgalactotigonin, Apigenin, Quercetin, Myricetin, N-feruloyl tyrosine, N-feruloyl tyramine (Lanzotti, 2006); S-allylcysteine sulfoxide (SACS), Allyl sulfides, Allicin and its breakdown products, Allixin, Eruboside B, Vitamin B6 and B12	No serious toxicity is associated with garlic when used moderately. But with ingestion of large quantities of garlic allicin yields a degradation product that often causes severe halitosis (Jung, F. 1976). Contact dermatitis to garlic has been reported

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		extracts (150 and 400 mg/kg daily) of garlic not only upregulate eNOS, but also induce an increase in eNOS activity in fructose-fed rats (Vazquez-Prieto et al., 2011). In addition, garlic does not merely increase H2S production, but induces its synthesis for vasorelaxant activity (Benavides et al., 2007). In their study, they demonstrated that red blood cells synthesize H2S from polysulfides that were extracted from garlic. They also reported that garlic (500 µg/ml) and garlic compounds-mediated increase in H2S is correlated with an increase in vasorelaxant activities in rat aortic rings (Benavides et al., 2007). Diabetes: Montasser and colleague investigated the antidiabetic effects of bulbs of garlic *(Allium sativum)* methanolic extract at doses of 250 and 500 mg/kg on Alloxan-induced diabetic male Wistar rats in comparison to Acarbose (as a reference drug). Their findings showed that methanolic extract of *Allium sativum* bulbs demonstrated antihyperglycemic effects by different mechanisms like inhibition of α-glucosidases activities, increase of antioxidant enzymes activities and up regulation of Ins and Glut-4 genes expression (Montasser and Fehresby, 2011). Administration of 200–300 mg/kg aqueous	(Corzo-Martinez, et al., 2007).	(Bleumink, J. et al. 1976). Garlic medication is contraindicated in ambulatory patients taking anticoagulant drugs due to possible prolongation of bleeding time. According to Martindale's Extra Pharmacopoeia, the administration of preparations of garlic to children is dangerous, and fatalities have been recorded (*Martindale Extra Pharmacopoeia*).

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		extract of the cloves of *A. sativuum* decreased blood glucose levels in alloxan-induced diabetic rats after one week (Eyo et al., 2011).		
5	*Aloe vera* (L.) Burm.f.	Hypertension: A. vera is considered a blood pressure lowering agent through its active ingredients, emodin; however, studies are still limited. One of the effective mechanisms of this component is the inhibition of phosphorylation, followed by the reduction of MLC-phosphatase enzyme activity. In addition, emodin can inhibit tumour necrosis factor-α-induced human aortic smooth muscle cells proliferation, thereby causing smooth muscle relaxation (Lim et al., 2014). Diabetes: Oral administration of one tablespoonful of Aloe vera juice, twice a day for at least 2 weeks in patients with diabetes decreased the blood sugar and triglyceride levels (Yongchaiyudha et al., 1996). Similarly, in another study, a dose of 1 mg/ml aloe vera whole gel extract in alloxan-induced diabetic rabbits prevented the onset of hyperglycaemia (Akinmoladun and Akinloye, 2007).	Aloes contain C-glycosides and resins. The gel contains several organic acids and biostimulators. The plant also contains polysaccharides, glycoproteins, sterols, organic acids, and saponins. (Shida et al., 1985; Wren, 1988). Major chemical constituents of Aloe are hydroxyanthrone derivatives, mainly of the aloe-emodin-anthrone 10-C-glucoside type; its major constituent is barbaloin (aloin) (15–40%) (Bradley and British Herbal Medicine Association", 1992; Bruneton, 1995).	When used moderately, no toxicity has been reported in aloe vera usage. But caution was raised by the U.S. National Toxicology Program, which found that rats grew tumors after drinking water spiked with an extract of the plant (Iwu, 2014).

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
6	*Anacarddium occidentale* L.	Hypertension: Ingestion of extracts from the leaves and bark of *Anacarddium occidentale* has been found to reduce hypertension to normal levels. These effects are due to peripheral vasodilation. It was reported that the hypotensive effect was observed first in rats with three different forms of experimental hypertension (Giono et al., 1971). DM: As per Ezuruike and Prieto	Bassorin and true gum, from the bark (Dispensary of U.S.A., 1955 as ref. by Oliver-Bever, B. 1986). Cashew "balsam" is composed of anacardie acid and its decarboxylated derivatives: anacardol, cardol and gingkol, which are aromatic phenols. In the leaves, are polyphenols (chiefly hydrobenzoic) and flavonoids which are heteromonosides (glucoside, rhamnoside, arabinoside or xyloside) of kaempferol and in particular quercetin (Attanasi and Caglioti, 1970; Laurens and Paris, 1976). The seed contains protein and oil. The oil contains oleic acid and linoleic acid. Cashew nutshell liquid (CNSL) contains anacardic acid ($C_{22}H_{32}O_3$) and cardol ($C_{32}H_{27}O_4$). It also yields glycerides; linoleic, palmitic, stearic, and lignoceric acids; and sitosterol. Other constituents include anarcardol, cardanol, quercetin, and kaempferol glycosides. The testa contains α-catechin, β-sitosterol, and 1-	"Allergies to raw cashew nuts and cardol and anacardic acid in CNSL has been reported. Other proteins have been identified as contributing to the allergic reaction to cashew. Cooking often does not remove or change these proteins. These allergic reactions can be life threatening or even fatal; prompt medical attention is necessary. Dermatitis among cashew nut

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
			epicatechin, proanthocyanidin, leucocyanidin and leucopelargonidin. Gum exudates contain arabinose, galactose, rhamnose, and xylose (Iwu, 2014).	workers has been reported in many countries. During processing, care should be taken to ensure that CNSL does not contaminate the kernels" (Iwu, 2014).
7	*Ananas comosus* L.	Hypertension: The crude aqueous extract from stem and fruit of *Ananas comosus*, bromelain, has been reported to decrease blood pressure (Heinicke, et al., 1972). Diabetes: As per Ezuruike and Prieto	Bromelain, Chlorogenic, Caffeic, Coumaroylquinic, P-coumaric and Caffeic acids, Caffeoylglycerols, Coumaroylglycerols, Ferulic acid glucuronide, Hydroferuloylglucose, Ananaflavoside B and C, Ananasate, Dicaffeoyl glycerides, Tricin, Feruloyl glycerols (Heinicke et al., 1972; Ma et al., 2007).	Bromelain has very low toxicity with an LD50 (lethal doses) greater than 10 g/kg in mice, rats, and rabbits (Taussiget al., 1975).
8	*Annona muricata* L.	Hypertension: The leaf extract of the plant lowers an elevated BP by decreasing the peripheral vascular resistance (Hasrat et al,	Reticuline, Coclaurine, Anomurine, Anomuricine, Coreximine (Lannuzel et al., 2002); Scyllitol, Oleic, Linoleic and P-	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		2004; Tabassum and Ahmaad, 2011; Nwokocha et al., 2012). Intravenous administration of 9.17–48.5 mg/kg of *A. muricata's* aqueous leaf extract on Sprague–Dawley rats caused dose-dependent reduction in blood pressure without affecting the heart rates (Nwokocha et al., 2012). The hypotensive effects were unaffected by atropine (2 mg/kg), mepyramine (5 mg/kg), propranolol (1 mg/kg) and L-NAME (5 mg/kg). It was also reported that *A. muricata's* leaf aqueous extract significantly relaxed phenylephrine (10−9–10−4 M) and 80 mM KCl induced contractions in endothelium intact and denuded aortic rings (Nwokocha et al., 2012). Also reported was a significant rightward shift of the Ca2+ dose response curves in Ca2+-free Kreb's solution containing 0.1 mM EGTA. Their study concluded that the hypotensive effects of *A. muricata* were not mediated through muscarinic, histaminergic, adrenergic and nitric oxide pathways, but through peripheral mechanisms involving antagonism of Ca2+ (Nwokocha et al., 2012). The extract of leaves and stems of *A. muricata* has a passing depressive effect on the blood pressure, which has been attributed to r-amino- butyric acid (Durand et al., 1962).	coumaric acid, Procyanidins, Stigmasterol (Leboeuf and Cave, 1980); Annonaine, Asimilobine (Hasrat et al., 1997); Acetogenins (Carmen Zafra-Polo et al., 1998); Alkyl esters, Linalool, β-caryophyllene, Cadinene, Humulene, Caryophyllene oxide, Phellandrene, Cadinol (Fournier et al., 1999); Gallic acid, Epicatechin, Quercetin and itsglycosides, Catechin, Chlorogenic acid, Argentinine, kaempferol and its glycosides (Nawwar et al., 2012).	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
9	*Annona senegalensis* Pers.	The constituents of *A. reticulata* explain the cardiotonic activity of the plant which is inotrope + chronotrope (Forgaes et al., 1981).	The root wood of *Annona senegalensis. A. senegalensis* contains sterols, triterpens, polyphenols, reducing compounds, and flavonoids (Ilboudo et al., 2019); Kaurane diterpenes, Quercetin, Sitosterol, Oleic acid, Linoleic acid, Sitosterol (Leboeuf et al., 1980); Rutin, Epicatechin, Catechin, Isoquercetin (Potchoo et al., 2008); Cadinol, α-phellandrene, Z-ocimene, Limonene, α and β-pinene, Linalool, Myrcene, Caryophyllenol, 1,8-cineole (Fournier et al., 1999). Anthocyanes, glucids, coumarins, and alkaloids. The water and ethanol extract of leaves and roots contains flavonoid, tannis, cardiac glycoside, saponins, alkaloid, steroid, and volatile oils, and negative for saponins, glycoside and antraquinone (Lapornik et al., 2005).	The aqueous extract has a low acute toxicity with an LD50 greater than 5000 mg/kg boody weight (b.w.) (Ilboudo, et al., 2019).
10	*Bryophyllum*	50-800 mg/kg of aqueous and methanol leaf extracts of the	Xanthones, flavonoids, anthraquinones,	The

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
	pinnatum (Lam.)	*Bryophyllum pinnatum* administered intravenously produced a decrease in arterial blood pressures and heart rates of both anaesthetized normotensive and hypertensive rats. The hypotensive impact exhibited by this extract was greater on hypertensive rats than on the normotensive rats (Ojewole, 2002). The *Bryophyllum pinnatum* leaf extract used on isolated guinea pigs caused a decrease on their cardiac contractility and heart rate and inhibited contractions stimulated by electrical field stimulation provoked (Ojewole, 2002).	and traces of alkaloids. Potent cytotoxic bufadienolides bryophyllin A and B have been isolated from the species (Yamagishi et al., 1988; Afzal et al., 2012; Yamagishi et al., 1989). Syringic acid, Caffeic acid, 4-hydroxy-3-methoxy cinnamic acid, 4-hydroxy benzoic acid, Hydroxy cinnamic acid, P-coumaric acid, Protocatechuic acid, Phosphoenolpyruvate, Ferulic acid, Astragalin, Friedelin, Luteolin, Epigallocatechin-3-Osyringate, Kaempferol α- and β-amyrin and their acetates, Glutinol, Bryophollone, Bryophynol, Bryophyllol, Bryotoxin A, B and C (Afzal et al., 2012); Cardiac glycosides, bryotoxins, are also present in the plant (McKenzie et al., 1987).	bufadienolides found in Bryophyllum species are toxic to cattle and other farm stocks (Gwehenberger, et al., 2004). Bryophyllum poisoning causes anorexia, depression, ruminal atony, diarrhea, heart rate and rhythm abnormalities, dyspnea, and death. Myocardial degeneration and necrosis with hemorrhages of the heart and alimentary tract

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
				have been observed (McKenzie, and Dunster, 1986).
11	*Camellia sinensis* (L.) Kuntze	Meta-analysis study of randomized controlled trials demonstrated that green tea reduces both SBP and DBP by 1.98 and 1.92, respectively (Peng et al., 2014). Similarly, other meta-analysis of randomized controlled trials came to the same conclusion that green tea reduces SBP and DBP by 1.8 and 1.4 mmHg, respectively. It was reported that green tea evoked a more powerful hypotensive effect compared to black tea, and that long-term tea consumption produced a more significant SBP and DBP reduction. In a double-blind, placebo-controlled trial, obese hypertensive patients who consumed 379 mg green tea extract for 12 weeks exhibited a significant decrease in SBP and DBP by 4 mmHg each (Bogdanski et al., 2012). Another randomized double-blind, placebo-controlled trial concluded that hypertensive subjects who consumed 4479 mg (3 cups/day, 1493 mg each) of black tea for 24 weeks exhibited a significant reduction in both SBP and DBP by 2 and 2.1 mmHg, respectively (Hodgson et al., 2012).	Catechins, the major flavonoids in tea, include (−)-epicatechin (EC), (−)-epicatechin-3-gallate (ECG), (−)-epigallocatechin (EGC), and (−)-epigallocatechin-3-gallate (Deka and Vita, 2011); alkaloids, benzollicolone, colotropin, calotoxin, uscharin, usharidin, calactin, voruscharine and mudarin (Deka and Vita, 2011).	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		Green tea has been reported to increase CAT antioxidant enzyme while simultaneously blocking AT1 receptors in streptozotocin-treated rats (Thomson et al., 2012). Flavonoids are noted for their vasorelaxant responses, including flow-mediated (Ras et al., 2011), and endothelial-dependent dilation (Oyama et al., 2010). Black tea catechins are converted by an enzymatic (polyphenol oxidase and peroxidase) oxidative polymerization reaction to tannins: theaflavins (benztropolone ring) and thearubigins, both of which are orange-red coloured polyphenolic pigments that are also potent vasodilators (Yang et al., 2011). A couple of clinical studies have reported black tea's positive effect on flow-mediated dilation (FMD), an index of endothelial function (Duffy et al., 2001; Hodgson et al., 2002). Diabetes:		
12	*Carica Papaya* L.	It was reported that when given in small doses, carpaine slows down the heart and thus reduces the blood pressure. In higher doses produce vasoconstriction. Given at doses of 0.01 - 0.02 mg/day orally, or administration of 0.006 -	Papain and chymopapain (Iwu, 1993); Chlorogenic and P-coumaric acids, 5,7-dimethoxy coumarin (Canini et al., 2007); Tannins,	Contraindicated in patients taking warfarin

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		0.01 mg/day subcutaneously, to humans, carpaine hydrochloride has a digitalis-like action and hence its use in hypertension (Noble, 1946 - 47).	Saponins, Cardiac glycosides, Alkaloids, Inulin (Mensah et al., 2009); Caffeoyl and Protocatechuic acid hexoside, Gallic acid deoxyhexoside, Caffeoyl hexose-deoxyhexose, Ferulic and Caffeic acids, Myricetin, Isoharmnetin, Quercetin, Kaempferol, Rutin, Lycophene, β-cryptoxanthin, β-carotene (Rivera-Pastrana et al., 2010). "The crude papain consists of two crystallised enzymes – papain, chymopapain, tryptophan, tyrosine and cysteine. The enzyme has peptidase, coagulase (acting on milk casein), amylase, pectase and lipase action (Kerharo and Adam, 1974). Vitamins and traces of an alkaloid have also been found in the latex. This alkaloid from the pyridine group, called carpaine, has also been reported in other parts of the plant and particularly in young leaves (0.28%) (Bevan and Ogan, 1964). The seeds	as it increased the INR of a patient (Shaw et al., 1997). Aqueous extract of the leaves inhibited P-gp efflux activity in Caco-2 cells (Oga et al., 2012).

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			contain fixed oils, carbohydrates, carpasemine (a benzylthiourea), benzyl senevol and a glucoside" (Manske and Holmes, 1950 - 1971; Watt and Breyer-Brandwijk, 1962). [as reported by Oliver-Bever, 1982].	
13	*Chrysanthelum Americanum* L.		Among the active constituents (Becchi et al., 1979, 1980; Honoré-Thorez, 1985) are two saponins (chrysantellins a and b) and five flavonoids: a flavone: luteolin 7-O-glucoside, two flavanones: eriodictyol 7-O-glucoside and isookanin 7-O-glucoside or flavonomarein, a chalcone: okanin 4′-O-glucoside or marein, and an aurone: maritimetin 6-O-glucoside or maritimein.	
14	*Citrullus lanatus* (Thunb.) Matsum & Nakai	Their study on Nigerian *Citrullus Lanatus* Fruit and Seed Juice, showed a reduction in cardiovascular diseases modifiable risk biomarkers in normal experimental rats (Ibrahim et al., 2018). *Citrullus lanatus* fruit and seeds juice significantly decreased the levels of triglycerides, serum creatine kinase, and serum sodium. These markers were implicated in CVDs when elevated. Hence the fruit could	As repoted by Ezuruike and Prieto in 2014, Citrullus lanatus contains Cucurbitacin E (Abdelwahab et al., 2011); Lycophene, Phytofluene, Neurosporene, ζ- and β- carotene, Lutein, Phytoene (Perkins-Veazie et al., 2006); Protocatechuic acid glucosides,	

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		be said to have a cardiovascular risk factors reduction potential in normal albino rats (Ibrahim et al., 2018). It was also that supplementation with 6 g/day of watermelon extract promoted a significant reduction in systolic and diastolic blood pressure in prehypertensive and hypertensive individuals (Massa et al., 2016). Diabetes check Ezuruike and Prieto 2014:	Phloroglucinol glucuronide, Ferulic acid hexosides, Isorhamnetin, Citrulline, Salicylic acid-O- hexoside, p-coumaric acid glucoside, Vanillin hexosides, Rutin, Salicin- 2-benzoate, Sinapic acid glucoside, Feruloyl sugars, Caffeoylshikimic acids, Caffeoylhexose, Luteolin, Calodendroside; Naringenin, Chrysoeriol Apigenin, Kaempferol, Taxifolin, Saligenin and Isolariciresinol glucosides; Hydroquinone, Isovitexin, Aviprins, Shikonine, Icariside, Leachianol G, Glehlinoside C, Ajugol, Dihydrophilonotisflavone, Catalposide, Obtusoside, Picrosides, Quercitrin, Coumarin, Cimifugin (Abu-Reidah et al., 2013).	
15	*Citrus aurantiifolia* (Christm.) Swingle	The methanol extract of *Citrus aurantifolia*, administered at the dose of 0.75mg orally, significantly ($p<0.01$) reduced systolic blood pressure, mean blood pressure, diastolic blood pressure, heart rate and body weight of Sprague-Dawley rats in both normotensive and hypertensive	The preliminary phytochemical analysis of methanol extract of *Citrus aurantifolia* showed the presence of alkaloids, flavonoids, tannins, saponins, steroids, cardiac glycosides, and reducing sugar	The acute toxicity study performed, for lethal and toxic dose indicated that

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		experimental models when compared to control groups (Akhtar, 2013).	(Akhtar, 2013); α- and β-pinene, P-cymene, Limonene and its oxide, Linalool and its oxide, Citral, α- and β-terpineol, Myrtenol (Asnaashari et al., 2010); Isoswertisin, 6-O-α-arabinopyranosides of vitexin and isovitexin (Veitch and Grayer, 2011).	doses up till 3g is safe and 3.5g is toxic dose (Akhtar, 2013). Bergamottin and furanocoumarins found in citrus fruits are inducers and inhibitors of Cyt P450 enzymes (Baumgart et al., 2005).
16	*Citrus aurantium* L. Syn. *Citrus paradisi* Macfad.	In vitro Effect of *Citrus paradisi* peel extract on the Langendorff isolated and perfused heart model Standardized *Citrus paradisi* peel extract, infused at a concentration of 119.3 ± 2.3 µg of total phenolics, showed a coronary vasodilator effect on the Langendorff isolated and perfused heart model, observing a statistically significant decrease in coronary vascular resistance (CVR), when compared with the control group(60 ± 15 × 107dyn s cm−5 vs 100 ± 10 × 107dyn cm−5,respectively) (Díaz-Juárez et al, 2009).	The following phytoconstituents were found in *Citrus aurantium*: flavonoids, furocoumarin, three C-glucosides (lucenin-2, vicenin-2 and lucenin-2, 4′-methyl ether), two O-glycosides (rhoifolin 4′-glucoside and narirutin 4′-glucoside), two 3-hydroxy-3-methylglutaryl flavanone glycosides (melitidin and brutieridin) and a furocoumarin (epoxybergamottin) (Barreca et al.,	

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		When the isolated and perfused rat hearts were pre-treated with100 µM L-NAME, CVR significantly increased (150 ±15 × 107dyn s cm−5), indicating a vasoconstriction due to unspecific nitric oxide synthase inhibition that was not reversed by *C. paradisi* peel extract infusion (145 ±10 × 107dyn s cm−5), suggesting that nitric oxide might mediate this coronary vasodilator effect (Díaz-Juárez et al, 2009). In vivo: In normotensive subjects, the consumption of *C. paradisi* juice showed a statistically significant decrease in diastolic arterial pressure (65 ± 10 mmHg vs 90 ± 15 mmHg, normotensive control values) and systolic arterial pressure (90 ± 10 mmHg vs 120 ± 10 mmHg, normotensive control values) (Fig. 4A and 4B, respectively), an effect that was also observed with hypertensive subjects (Díaz-Juárez et al, 2009). In this group of patients, the diastolic arterial pressure decreased from 90 ± 10 mmHg to 80 ± 10 mmHg, whereas the systolic arterial pressure decreased from 140 ± 15 mmHg to 115 ± 10 mmHg (Fig. 3A and 3B, respectively). The decrease in mean arterial pressure (Fig. 4C) was more evident in patients who received *Citrus paradisi* juice, when compared with the control, *Citrus sinensis*, cowmilk and vitamin C-supplemented beverage	2011).	

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		groups (80 ± 10 mmHg vs 110 ± 15 mmHg, 90 ± 15 mmHg,105 ± 12 mmHg, 107 ± 10 mmHg, respectively) (Díaz-Juárez et al, 2009).		
17	*Citrus limon* (L.) Osbeck Syn. *Citrus limonum*	It was reported that citroflavonoids of *Citrus limonum*, control the permeability of the vessels by decreasing the porosity of the walls hence improving the exchange of liquids and the diffusion of proteins (Paris and Delaveau, 1977; Pourrat, 1977). The increase in the resistance of the capillaries is based on a complex mechanism including the protective action of o-diphenols to catecholamines participating in vascular solidity. When capillary resistance is diminished, citroflavonoids can prevent bleeding in hypertensive patients (Paris and Moury, 1964; Vogel and Stroecker, 1966; Paris, 1977).	The peel of *Citrus limon* fruit contains citroflavonoids. The main constituents are Hesperidoside (rhamnoglucoside of hesperetol), naringoside and eryodictyoside (flavanones). It also contains essential oils and vitamin C. (Horhammer and Wagner, 1962; Ravina, 1964; Paris, 1971; Paris et al., 1972).	
18	*Cucumis sativus* L.	It was reported that a decrease in both the systolic and diastolic blood pressure in participants in groups 1 to 4 was observed. (Group 1 was given 200g *cucumis sativus* juice only, group 2 received 200g *cucumis sativus* juice + 200g (ww) rice meal, group 3 was given 400g *cucumis sativus* juice only, group 4 was given 400g *cucumis sativus* juice + 400g (ww) rice meal) (Bartimaeus et al., 2016). Increasing the quantity of cucumber in the juice resulted in significant	*Cucumis sativus* extract contains alkaloids, flavonoids, carbohydrates, glycosides, proteins, amino acids, phenolic compounds, tannins, oils, fats and saponins. (Beckett and Stanlake, 1986; Gurudeep and Anand, 2003; Kasture et al., 2003; Krishnaswamy et al., 2003; Harborne, 2005; Furniss et al.,	

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		decrease in the blood pressure of hypertensive subjects (Bartimaeus et al., 2016). Furthermore, individual variations and other factors such as the genetic composition of the individuals may have also contributed to the delay in significant reasonable reduction in the blood pressure of the subjects (Pickering et al., 2008; van Berge-Landry et al., 2008). They concluded that an intake of cucumber could have significant effect on blood pressure if taken in higher quantity for a considerable period of time (Bartimaeus et al., 2016).	2005). The presence phytonutrients found in cucumber such as flavonoids and tannins which have been reported to cause regeneration of damaged pancreatic islets, stimulate calcium and glucose uptake may also contribute to the antihyperglycaemic effect of cucumber (Tapas et al., 2008); The phytosterol which is a constituent of cucumber has been shown to improve the control of blood sugar among diabetics (Lee et al., 2003).	
19	*Cucurbita pepo* L.	Treatment of hypertensive rats with felodipine or captopril separately or combined with pumpkin seed oil resulted in improvement of free radical scavengers in the heart and kidney tissues ((Al-Zuhair et al., 2000). Furthermore, pumpkin seed oil was reported to retard the progression of hypertension and reduce hypercholesterolemia (Al-Zuhair et al., 1997).	Pumpkin seeds have the following phytoconstituents: proteins, polyunsaturated fatty acids (Applequist et al., 2006; Sabudak, 2007), phytosterols (Phillips et al., 2005; Ryan et al., 2007), antioxidant vitamins, such as carotenoids and tocopherol (Stevenson et al., 2007) and trace elements, such as selenium and zinc (Glew et al., 2006).	
20	*Cymbopogon*	The relaxant effect of lemongrass has been demonstrated	*Cymbopogon citratus* contains Citral, a	

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	citratus (DC) Stapf.	in several different tissues, including the rabbit ileum (Devi et al., 2011), rat aortic rings (Devi et al., 2012), and the rat mesentery (Bastos et al., 2010). The crude extracts of *C. citratus* (leaves, stems, or roots) generated a dose-dependent vasorelaxation in phenylephrine pre-constricted aortic rings from male WKRs or SHRs (Devi et al., 2012). The underlying mechanism for this relaxation appeared to be mediated by activation of NO and/or the inhibition of calcium channels (Devi et al., 2012). Similarly, administration of an intravenous bolus of Citronellol, an acyclic monoterpenoid isolated from lemongrass to male Wistar rats, produced a hypotensive response. It was also reported that the hypotensive effect was not affected by L-NAME, indomethacin, atropine, or hexamethonium (Bastos et al., 2010). Citronellol also induced relaxation of rat superior mesenteric artery via an endothelium-independent mechanism. The arteries denuded of endothelium were not reliant on tetraethylammonium-dependent potassium channels. Rather, citronellol acted by inhibiting Ca2+-influx through voltage operated calcium channels (VOCCs) as well as regulating IP3- and caffeine-gated intracellular Ca2+ stores (Bastos et al., 2010).	terpene aldehyde. Geraniol, nerol, furfural, citronelle, methyleptenone, myrcene (Metwally and Ekejuba, 1981; Gyllenhaal and Soejarto, 1988); triterpenescynbopogon and cymbopogonol (Hegnauer, 1973; Hanson et al., 1976); Geraniol, myrcene and citral were identified as aldose reductase inhibitors based on an in-silico approach (Vyshali et al., 2011).	

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21	*Cyperus Esculentus* L.	*Cyperus Esculentus*, rich in amino acid arginine, reduces blood pressure. In addition, the body uses arginine to produce nitric oxide, a compound that helps arteries and veins dilate, hence lowering blood pressure (Schneider et al., 2015; Kashyap et al., 2017). Diabetes: *Cyperus Esculentus,* due to its amino acid arginine constituents, is reported to increase insulin production and sensitivity, both of which are important for blood sugar control (Suliburska et al., 2014; Umeda et al., 2015; Carvalho et al., 2016).	*Cyperus Esculentus* contains carbohydrates, flavonoids, minerals, phytosterols, tocopherols, tocotrienols, and various nutrients. The oil is composed of 7 major TAG (triacylglycerol) classes, with C54:3 (29.00%) and C52:2 (27.82%) dominating. Oleoyl chain primarily occupies both sn-1/3 (52.68%) and sn-2 (77.62%) positions in the tiger nut oil. It has a total tocol content of 120.10 µg/g, dominated by α-tocopherol (86.73 µg/g) and β-tocopherol (33.37 µg/g). The total 4-desmethylsterol content is 986 µg/g, dominated by β-sitosterol (517.25 µg/g) and stigmasterol (225.25 µg/g) (Yeboah et al., 2012).	
22	*Dioscorea dumetorum* (Kunth) Pax.	Hypertension In the cat, the extract produces a long-lasting hypotension when injected intravenously in doses of 100 mg/kg. The total extract produces a contraction of the smooth muscle fibres of the intestine both in vivo and in vitro (Bevan et al., 1956). In small doses (30 mg/kg) in the cat or monkey	The dried tubers contain dioscin, the genin of which diosgenin, small quantities of other steroid sapogenins, and a convulsant alkaloid dihydrodioscorine (Bevan et al., 1956). Nigerian yams also contain 83.3% of	

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		Schlag and colleague have noted a desynchronisation of the cortical electrical record lasting over 0.5 h (Schlag et al., 1959). With higher doses (200 mg/kg) there are progressive convulsive impulses preceded each time by increase in the arterial pressure and of the intestinal peristaltis which, according to the authors, indicates an exciting action of the drug on the cerebral cortex (Bevan et al., 1956). Diabetes: Dioscoretine isolated from the aqueous fraction of the methanol extract of *Dioscorea dumetorum* tubers, when administered intra-peritoneally to normal and alloxan diabetic rabbits, produce significant hypoglycaemic effects at a dose of 20 mg/kg (Iwu et al., 1990). It was also reported that the blood sugar levels in rabbits treated with whole tuber extract, WT, or tolbutamide had a clear reduction in the mean blood sugar concentration as compared with initial levels and with water-treated controls (Ashiwel et al., 1986). In addition, the maximum effect which occurred after 8 h was equivalent to a reduction of 51 mg/dl or 41.8% in the level of blood sugar. Tolbutamide also elicited a hypoglycaemic effect as would be expected,	glucides and 9.9% of proteins. Diosgenin has been much used as a starting compound in the synthesis of hormones, corticosteroids (Oliver-Bever, 1972).	

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		and its maximum effect of 37 mg/dl or 29.1% occurred after 4 h. Undie and colleague stated that the comparison shows that the maximum hypoglycaemic effect of 2 ml/kg of extract was one and a half times the activity of tolbutsmide, 250 mg/kg (Undie and Akubue, 1986)		
23	*Garcinia kola* Heckel	This study of Naiho and Ugwu shows that the alcohol extract of *Garcinia kola* contains vasoactive substance that has a blood pressure reducing effect (Naiho and Ugwu, 2009). Their result shows that the systolic blood pressure of treated groups reduced significantly; a dose range of 1 g/kg body weight (bwt) produced a significant fall in mean arterial blood pressure and a significant increase in basal heart rate (Naiho and Ugwu, 2009).	The major pharmacologically active ingredient in *Garcinia kola* is a flavonoid, Kolaviron (Naiho and Ugwu, 2009; Shah et al.,2019). G. kola contains phenolic compounds such as biflavonoids, xanthones, and benzophenones (Locksley, 1973; Rao et al., 1980; Iwu et al., 1982); antimicrobial benzophenone, kolanone (Hussain et al., 1982) and biflavonoids based on eridictoyl/taxifolin moiety GB1, GB2, GB3, kolaflavanone, and garciniflava-none. (Kabangu et al.,1987; Iwu et al., 1982). The seeds also contain the chromanols garcinoic acid and garcinal and their derivatives, as well as tocotrienol (Terashima et al.,1997).	
24	*Gnetum*	Hypertension:The aerial parts of *Gnetum africanum* was	*Gnetum* leaves contain C-	

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	africanum Welw.	reported to have been used in traditional medicine for the treatment of diabetes and high blood pressure (Iwu, 2014) Diabetes: *Gnetum africanum* methanol leaf extract tested on alloxan induced diabetic rats produced significant dose and time-dependent reductions in fasting blood sugar. It was reported that the highest reduction was observed six hours post treatment in rats treated with 1,600 mg/kg of the extract ($p < 0.0001$) (Udeh et al., 2018).	glycosylflavones, 2″-xylosylisoswertisin and 2″-glucosylisoswertisin. Of chemotaxanomic importance is the presence of 2″-O-rhamnoylisoswertisin and apigenin-7-hesperidoside and the absence of vitexin and 2″-O-glycosylvitexin in *Gnetum africanum* (Quabonzi et al., 1983). Stilbenes, as well as their dimeric, polymeric, and hydroxylated derivatives, have been isolated from some *G. africanum* and other *Gnetum* species (Ouabonzi et al., 1983). There is also the presence of the antioxidant compound resveratrol and stilbenes in *Gnetum* (Iliya et al., 2002).	
25	*Gongronema latifolium* Benth	Systolic and diastolic BP levels (128/90 mm Hg; MAP 103 ± 3 mm Hg) and heart rates were all significantly ($p < 0.01$) decreased after *Gongronema latifolium* administration (Beshel et al., 2019). Raised mean arterial pressure (MAP) and heart rate by atropine, L-NAME and methyl blue were also significantly ($p < 0.01$) reduced, while propranolol	The leaves contain preganane glycosides, 17β-marsdenin derivatives, β-sitosterol, lupenyl cinnamate, lupenyl acetate, lupeol, essential oils, and saponins. The main components of the essential oil from the leaves are linalool	Gongronema is considered a nontoxic vegetable. An oral toxicity test on rats gave an

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		significantly ($p < 0.01$) inhibited hypotension caused by *Gongronema latifolium*. Infusion of *Gongronema latifolium* reduced MAP (95 ± 3 mm Hg) comparable with nifedipine (93 ± 2 mm Hg), a calcium channel blocker (Beshel et al., 2019).	(19.5%), (E)-phytol (15.3%), and aromadendrene hydrate (9.8%). The fixed oil contains saturated (50.2%) and unsaturated (39.4%) fatty acids. Palmitic acid accounts for 36% of the total fatty acid content; minor saturated fatty acids are stearic acid (4.6%), behenic acid (3.7%), and arachidic acid (2.8%). The main UFA is linoleic acid (31.1%), followed by oleic acid (7.1%) and linolenic acid (7.1%). The nutritional composition of the dry leaves is crude protein (9.8–27.2%), lipid extract (6.1%), ash (5.8–11.6%), crude fiber (8.7–10.8%), tannin (0.3%), and nitrogen-free extractives (44.3%). The composition of minerals per 100 g dry matter is K 244.8–332.1 mg, Na 110–113 mg, Ca 115.4–154 mg, P 125.5–326.9 mg, Fe 7.8 mg, Zn 13.4 mg, Pb 0.2 mg, Cu 2.3–43.5 mg, Mg 53.8 mg, Cd 0.1 mg, Co 115.9 mg, oxalate 70 mg, and ascorbic acid 187.1 mg. The major essential	LD50 of 1450.5 mg/kg, and an intraperitoneal injection in mice gave an LD50 of 1678.6 mg/kg (Iwu, 2014).

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			amino acids are leucine, valine, phenylalanine, aspartic acid, glutamic acid, and glycine (PROTA, 2013). The phytochemicals identified in *Gongronema latifolium* were 34 compounds, including oleanolic acid derivatives, flavonoids, antioxidant fatty acids, 2 coumarins and 2 iridoids (Beshel et al., 2019).	
26	*Hibiscus sabdariffa*	Throughout Nigeria, *Hibiscus sabdariffa*'s calyces is brewed locally for beer. The acclaimed antihypertensive effect of the aqueous extracts of the calyx of *H. sabdariffa* was investigated by Adegunloye and colleagues (Adegunloye et al., 1996). Their findings suggested that mechanism of antihypertensive effect of the *H. sadariffa* calyces was as a result of the involvement of acetylcholine-like and histamine-like mechanisms as well as direct vaso-relaxant effects (Adegunloye et al., 1996). Intravenous injection of 1-125 mg/kg of aqueous extract of the calyx of *H. sabdariffa* lowers blood pressure and heart rate of hypertensive and normotensive rats suggesting that *H. sabdariffa* possesses anti-hypertensive, hypotensive and negative chronotropic effects. Their results showed	The chemical constituents isolated from the calyx and flowers of roselle include alkaloids, ascorbic acid, β-carotene, anisaldehyde, arachidic acid, citric acid, malic acid, tartaric acid, glycine, betaine, trigonelline; anthocyanins as cyanidin-3-rutinoside, delphinidin, delphinidin-3-glucoxyloside (also known ashibiscin, the major anthocyanin in H. sabdariffa flowers), delphinidin-3-monoglucoside, cyanidin-3-monoglucoside, cyanidin-3-sambubioside, cyanidin-3,5-diglucoside; the flavonols glycosideshibiscetin-3-monoglucoside, gossypetin-3-glucoside,	

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		remarkably lower mean arterial pressure on the hypertensives than on the normotensives (Mojiminiyi et al., 2007). Roselle's blood pressure lowering effects have been extensively reported in both animal (Odigie et al., 2003; Ali et al., 2005; Ajay et al., 2007; Mojiminiyi et al., 2007; McKay et al., 2010; Ojeda et al., 2010; Inuwa et al., 2012; Hopkins et al., 2013) and human studies (Onyenekwe et al., 1999; Herrera-Arellano et al., 2004, 2007; Mojiminiyi et al., 2007; Mozaffari-Khosravi et al., 2009; Inuwa et al., 2012; Hopkins et al., 2013).	gossypetin-7-glucoside, gossypetin-8-glucoside, and sabdaritrin; quercetin, protocatechuic acid (PCA), pectin, polysaccharides, mucopolysaccharides, stearic acid, and wax (Hirunpanich et al., 2005; Maganha et al., 2010). The phytosterols campasterol, stigmasterol, ergosterol, β-sitosterol, and α-spinasterol have been reported from the seed oil (Dnyaneshwar and Ravindra, 2012). The petals yielded 65% (dry weight) of mucilage, which on hydrolysis gave galactose, galacturonic acid, and rhamnose. In addition to these compounds, *Hibiscus sabdariffa* extract (HSE) contains complex polyphenolic acids (1.7% dry weight), flavonoids (1.43% dry weight), and anthocyanins (2.5% dry weight). Organic acids, anthocyanins, polysaccharides and flavonoids (Müller and Franz, 1990).	
27	*Irvingia*	Martínez-Abundis and colleagues work on the Novel	*Irvingia gabonensis* seeds yield fat (40–	

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	gabonensis (Aubry-Lecomte ex O'Rorke) Baill.	nutraceutic therapies for the treatment of metabolic syndrome reported that clinical trials of *Irvingia gabonensis* have shown important effects decreasing glucose and cholesterol concentrations as well decreasing body weight (Martínez-Abundis et al., 2016).	75 g/100 g), called dika fat, which consists of lauric acid (20–59%), myristic acid (33–70%), palmitic acid (2%), stearic acid (1%), and oleic acid (1–11%). The nutritive value of the kernels per 100 g edible portion is water 4 g, energy 2918 kJ (697 kcal), protein 8.5 g, fat 67 g, carbohydrate 15 g, Ca 120 mg, Fe 3.4 mg, thiamin 0.22 mg, riboflavin 0.08 mg, and niacin 0.5 mg. The pulp yields about 75% juice, which is rich in vitamin C, and wine produced from it was found to be of good colour, mouthfeel, flavour, and general acceptability. The pulp contains zingiberene and α-curcumene, ethyl and methyl esters of cinnamic acid, and dodecanal and decanol, which are the main flavour components and are responsible for imparting spicy-earthy, fruity, and wine-yeast flavour notes. The nutritive value of the fruit pulp per 100 g edible portion is water 81 g, energy 255	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
			kJ (61 kcal), protein 0.9 g, fat 0.2 g, carbohydrate 15.7 g, Ca 20 mg, P 40 mg, Fe 1.8 mg, and ascorbic acid 7.4 mg. (Nsour et al., 2000). [As per Iwu, 2014].	
28	*Mangifera indica* L. [Igoli et al, 2005; Gill, 1992; Oliver-Bever 1982)	The leaves of *Mangifera indica* has been reported to increase the resistance and decreased the permeability of capillary vessels and have been successfully used for over 20 years in treating vascular problems (Pourrat, 1977). It was also reported that excellent results were obtained in retinopathy of hypertensive origin (Pourrat, 1977). Similarly, it was noted that injection of an aqueous extract of leaves and stems of *M. indica* produces in dogs a distinct hypotensive action. In rabbits a similar effect was obtained with an alcoholic extract (Feng et al., 1964).	The leaves have four anthocyanidins (3-monosides of delphinidin, petunidin, poeonidin and cyanidin), leucoanthocyanins, catechic and gallic tannins, mangiferin (flavonit heteroside), kaempferol and quercitin (both free and as glycosides) were reported (Jacquemain, 1959). Tannic acid, Gallic acid, Epicatechin, Ellagic acid, Gallocatechin, n-butyl cyanidin (Arogba, 2000); 3,4-dihydroxy benzoic acid, Benzoic acid, Methyl gallate, Propyl gallate, Mangiferin, Catechin, Benzoic acid propyl ester (Núñez Sellés et al., 2002); Violaxanthin dibutyrate, β-Carotene, 9-cis- and transviolaxanthin, Luteoxanthin, Mutatoxanthin,	Absorption of preparations based on the leaves, stems and bark produces irritation of stomach and kidneys, and ingestion of the fruit in large quantities can produce shock reactions (RubIn et al., 1965). Stem bark extract of the plant, mangiferin and its metabolite

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
			Neochrom, Xanthophyllpalmitic and myristic acid esters (Pott et al., 2003); Isomangiferin, Quercetin and its glycosides, Kaempferol-3-Oglucoside, Rhamnetin-3-O-glycoside, Mangiferin and Isomangiferin gallate (Schieber et al., 2003; Berardini et al., 2005).	norathyriol as well as, quercetin, constituents of the plant showed dose-dependent modulation of P-gp activity in HK-2 and Caco-2 cell lines (Chieli et al., 2009). The stem bark extract also showed inhibitory effects for Cyp1A, 2D and 3A4 enzymes of uman liver microsomes (Rodeiro et al., 2009).
29	*Manihot esculenta* Crantz	Administration of 100 mg/kg of Crude juice extracts of *Manihot esculenta* intravenously injected into rats significantly reduced systolic and diastolic pressures as	The root of *Manihot esculenta* contain hydroxycoumarins scopoletin and its glucoside scopolin, trace quantities of	If *Manihot esculenta* is not adequately

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		well as heart rate (Ozougwu, 2017).	esculetin and its glucoside esculin. (Blagbrough et al., 2010); Cyanogenic glycoside, from cassava root, in which the branched chain pentose, apiose, was linked β1–6 to the glucose unit of lotaustralin (2-((6-O-(β-d-apiofuranosyl)β-d-glucopyranosyl)oxy)-2-methyl butanenitrile) has been reported together with non-cyanogenic glycosides of propan-2-ol and butan-2-ol containing the same disaccharide unit (King and Bradbury, 1995, Prawat et al., 1995); flavonoid glycosides, quercetin-3-O-rutinoside (rutin) and kaempferol-3-O-rutinoside, flavone-3-O-glycosides, were also found in the leaves of the plant (Prawat et al., 1995).	processed or the consumer has nutritional deficiencies, its cyanogenic glycoside (i.e., linamarin and lotaustralin) content makes it potentially neurotoxic (Rivadeneyra-Domínguez et al., 2013).
30	*Mentha piperita* L.	It was reported that the *Mentha piperita* extract exhibits an antihypertensive effect via its antioxidant capacity, vasodilator property, and reduced vascular remodelling (Pakdeechote et al., 2014). The vasorelaxant activity of the *Mentha piperita* extract was determined using the perfused	*Mentha piperita* contain hydroxycinnamic acids (HCAs), in particular, caffeic (CA), p-cumaric (CU), ferulic (FE), and rosmarinic (RS) acids (Alexa et al., 2018).	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		mesenteric vascular bed of normotensive and L-NAME hypertensive rats.		
31	*Moringa stenopetala* (Baker f.) Cufod. (originated from Africa) *Moringa oleifera* Lam (originated from India)	When aqueous crude extract of *Moringa stenopetala* leaf and 70% ethanol fraction was used on experimental rats, it significantly prevented blood pressure increment in a dose-dependent manner and suppressed increment in cholesterol, glucose and triglycerides (Meresa et al., 2017). Their study also showed that the crude aqueous leaf extract of *Moringa stenopetala* caused a significant reduction in SBP, DBP and MABP at doses of 10, 20, 30 and 40 mg/kg in normotensive anaesthetized guinea pigs (Meresa et al., 2017). Moringinine has a sympathomimetic action similar to that of adrenaline; it produces peripheral vasoconstriction, raises the blood pressure and acts as a cardiac stimulant (Chopra et al., 1938). Spirochine accelerates and amplifies the heartbeat in concentrations of 1:10000 and has an opposite effect at a concentration of 1:1000 (Watt and Breyer-Brandwijk, 1962).	The rootbark has sulphurated aminobases moringinine and spirochine, benzylamine (moringine) and glucotropaeoline. The root also contains two antibiotic constituents: athomine and pterygospermine; the latter is probably a condensation product of two benzolisothiocyanate molecules with one benzoquinone molecule (Kurup and Narasimha Rao, 1954; Hegnauer, 1962 - 1968; Kondagbo and Delaveau, 1974). The leaves contain amino acids, aspartic acid, glutamic acid, serine, glycine, threonine, α-alanine, valine, leucine, isoleucine, histidine, lysine, cysteine, methionine, arginine, and tryptophan (Das, 1965); the flowers and the fruits also contain amino acids (Ramiah and Nair, 1977); the root bark yields the sulfurated amino bases moringinine and spirochine, benzylamine and glucotro-	

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			paeline (Adesogan and Okunade, 1979); the seeds contain Beni or Moringa oil. The oil consists of a 60% liquid olein fraction and 40% solid fat. The major constituents of the oil are oleic acid (65%), stearic acid (10.8%), behenic acid (8.9%), myristic acid (7.3%), palmitic acid (4.2%), and lignoacetic acid (3.0%) (Kucera et al., 1973; Rao and George, 1949). The stem bark contains sterols and terpenes (Bhattacharjee and Das, 1969); also 4-hydroxymellin, vanillin, β-sitosterol, β-sitosterone, and octacosanoic acid (Saluja et al., 1978). The roasted seeds contain 4-α-L-rhamnosyloxyphenylacetonitrile, 4-hdroxyphenylacetamide (Villasenor et al.,1989).	
32	*Musa paradisiaca* L., Syn:	The three amino phenols are sympathomimetic and in other plants, *Surothamnus scoparius,* have proved to have marked vasoconstrictive properties and to be hypertensive (Jain, 1968; Oliver-Bever and Zahnd, 1979).	Analysis of the bracts of ten wild species of *Musa paradisiaca* has shown the presence of six anthocyanidins (pelargonidin, cyanidin, delphinidin,	

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	Musa sapientum L., *Musa troglodytarum* L.	It was reported that the administration of aqueous extract of *Musa Paradisiaca* into the aorta and portal veins isolated from rats, produced concentration dependent relaxation in both NA contracted aortic 54.45± 6.63 % and in KCl contracted rings 77.5± 2.52 % of the initial tension developed in response to the contractile agents (Agarwal et al., 2009).	malvidin, paeonidin and petunidin). The ripe and unripe fruit also contains 5 hydroxytryptamine (serotonin) (Hood and Lowburry, 1954; Sinha et al., 1962; Hegnauer 1962 - 1968;). Dopamine and noradrenaline (adrenaline precursors) have also been reported in *M. paradisiaca* plants (Harborne et al., 1974). The three amino phenols are sympathomimetic and in other plants (*Surothamnus scoparius* Koch.) have proved to have marked vasoconstrictive properties and to be hypertensive (Jain, 1968; Oliver-Bever and Zahnd, 1979).	
33	*Ocimum Gratissimum* L	Administration of 100–400 mg/kg of *Ocimum basilicum* crude extract decreased BP level in rats (Umar et al., 2010). It was reported that it inhibited renovascular hypertension-induced hypertrophy of heart and increased in ET-1 and Ang II levels (Umar et al., 2010). It also caused a vasorelaxant effect in rat aortic rings, though the mechanism for this relaxation was not determined (Amrani et al., 2009). A potential mechanism could be due to *Ocimum basilicum's* potent ROS scavenging ability	The plant contains xanthones, terpenes, and lactones (Iwu, 2014); terpenes, sesquiterpenes, thymol, eugenol and *cis*-ocimene (Ogendo et al., 2008).	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		(Kaurinovic et al., 2011).		
34	*Olea europaea* L.	A dose of (50mg/kg) of *Olea europaea* resulted in improvement of blood pressure, antioxidative defence and cardiac performances (Ivanov et al., 2018). Their work showed that medium dose, 25 mg/kg, was revealed as the most effective in reducing cardiovascular risks by improving systemic and regional haemodynamics, oxidative stress and lipid profile (Ivanov et al., 2018). Another study showed that 100mg/kg of *Olea europaea* leaf extract administered on male Wistar rats completely normalised elevated blood pressure and actually suppressed any further increase in blood pressure (Khayyal et al., 2002). The aqueous extract of *Olea europaea* (olive leaves) possess significant hypotensive activity in rats (Lassere et al., 1983). It was reported that the antihypertensive activity of olive leaves may be due to the presence of oleuropein (Weiss, 1988). Extracts of the leaves also exhibited direct relaxant action on smooth muscles, dilated the bronchi, and improved blood circulation (Carpetti et al., 1948 – as reported by Iwu, 2014).	The leaf is rich in tannins. A bitter water-soluble glucoside called oleorepein has been shown to be present in the bark, leaves, and fruits (Esdom, 1954). The seed is the source of the commercially important olive oil, which consists of glycerides of oleic acid (70–80%), with the glycerides of palmitic, stearic, and linoleic acids minor components (Esdom, 1954).	
35	*Pentaclethra Macrophylla*	Okwuonu and colleagues demonstrated in their case report, the potential antihypertensive effect of *Pentaclethra*	*Pentaclethra macrophylla* (African oil bean) seeds and leaves contains crude	

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	Bentham	*Macrophylla* (African oilbean) seed (Okwuonu et al., 2013). A 4-day fermentation of cooked *Pentaclethra Macrophylla* seed reduce the eight component lipids present in the cooked unfermented seed to a more nutriceutical three component lipids (Hexadecanoic acid methyl ester, 9-Octadecenoic acid (Z)-methyl ester and Methyl stearate) (Ohiri and Bassey, 2017). The 9-Octadecenoic acid (Z)-methyl ester (oleic acid) consumption has been associated with an increased concentration of high-density lipoprotein (HDL) and a concomitant decrease in low-density lipoprotein (Martin-Moreno et al., 1994). indicating that fermented *P. macrophylla* Benth seed may be useful in the treatment and management of high blood pressure (Ohiri and Bassey, 2017).	protein, crude fat, crude fibre, moisture and carbohydrate in the leaves and seeds (Osabor et al., 2017). The leaves and seeds also contain macro-minerals calcium, with highest value and magnesium the least. Other minerals include sodium, potassium and phosphorus. The micro-minerals showed the highest value for iron and lowest value for cobalt. Other micro-minerals include copper, zinc, manganese, cadmium for the leaves and seeds. The phytochemicals include saponins, flavonoids, alkaloids, cardiac glycosides, polyphenols and reducing sugar in both water and petroleum ether extract of the plant. Quantitative analysis of the phytochemicals revealed that polyphenols have the highest value and the least value, saponins, occur in the water extract and petroleum extract of the leaves and seeds. Other	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
			phytochemicals found include flavonoids, alkaloids, cardiac glycoside and reducing sugar in the leaves and seeds. The anti-nutrients composition consists of phytate, tannin, hydrocyanide, oxalate for the leaves and seeds (Osabor et al., 2017). *P. Macrophylla* contains citronellol and oxirane, tetradecyl- (hexadecylene oxide) were identified in the extract (Ugbogu et al., 2020).	
36	*Persea Americana* Mill	*Persea americana* extract used to test hypertensive and naïve rats at doses 240, 260, 280 mg/kg with bolus doses of Ach (1, 2, 4 microgram/kg resulted in decreased mean arterial pressure (MAP) from 125+/-11.2 to 92.1+/-8.5 mmHg and Heart Rate (HR) from 274.6 ± 39.3 to 161.6 ±11.6 beats/min (Anaka et al., 2009). Intravenous administration of doses of aqueous and methanol extract of *P. americana* leaf ranging from 6.25 to 50 mg/kg to normotensive anesthetized rats produced dose-related hypotensive effects (Yasir et al., 2010).	The major chemical constituents of the various plant parts of *P. americana* (avocado) are alkanols, terpenoid glycosides, flavonoids and a coumarin (Ding et al., 2007); phytoconstituents of *Persea americana* leaves contain isorhamnetin, luteolin, rutin, quercetin and apigenin (Owolabi et al., 2010); 1,2,4-trihydroxy nonadecane derivatives, 1,2,4-trihydroxy heptadec-16-ene and heptadec-16- yne	Ethanol extract of the leaves inhibited the activity of Cyp3A4, 3A5 and 3A7 enzyme supersomes (Agbonon et al., 2010).

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			derivatives (Abe et al., 2005); Persin ((Z,Z)-1-(acetyloxy) -2-hydroxy- 12,15-heneicosadien-4- one) (Oelrichs et al., 1995); *Persea americana* contains peptone, b-galactoside, glycosylated abscisic acid, alkaloids, cellulose, polygalacto urease, polyuronoids, cytochrome P-450, and volatile oils. 1.0 mg benzyladenine/L, 0-1mg Indole Butyric Acid/L, 0.1 mg Gibberalic Acid 3/L are also present (Yasir et al, 2010); Saponins, Tannins, Flavonoids, Cyanogenic glycosides, Alkaloids (Mensah et al., 2008).	
37	*Piper guineense* Schum. et Thonn. Syn. *P. leonense* DC.,	The amides of *Piper guineense* have been shown to possess antihypertensive properties (Ameh et al., 2011).	Tannins, Saponins, Cardiac glycosides, Alkaloids, Inulin. Fruit constitutes amines piperine, N-isobutyloctadeca-trans-2-trans-4-dienamide, sylvatine, -dihydropiperine, trichostachine and a new naturally occurring amide, P-dihydropiperlonguminine. In the roots,	High doses of the drug have been reported to cause convulsions and hematuria (Paris, and Moyse, 1967).

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
	P.famechonii DC.		piperine, trichostachine, and in the leaves, dihydrocubebin, a new naturally occurring lignane, have been reported. Earlier, 0.2% of a lignane derived from shikimic acid, aschantine and another lignane which has been named yangambine has also been reported (Hanzel et al., 1966). An essential oil composed of terpenes (phellandrene, pinene, limonene) has been obtained from the berries (l-2.4%) (Tackie et al., 1975a; Dwuma-Badu et al., 1975d,1976a; Raina et al., 1976). *Piper guineense* plant has been reported to have lignans, including aschantine and yangambine (Oliver-Bever, 1986). The roots yield piperine, trichostachine, and lignans; the leaves contain the lignin dihydrocubebin (Dwuma Badu et al., 1975d). Its berries' essential oil consists mainly of phellandrene, pinene, and limonene (Tackie et al., 1975a; Dwuma Badu et al., 1976a). The fruits contain	

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			amide piperines, including sylvatine, N-isobutyloctadeca-trans-4-dienamide, Δα,β-ihydropiperlonguminine, Δα,β-dihydropiperine, and trichostachine (Addae-Mensah et al.,1977). The plant also contains the pyrrolidine amide wisanidine, pipreidine amides, dihydrowisanine (Okogun et al., 1977); dihydropiperine (Ameh et al., 2011); wisanine (Addae-Mensah et al.,1976; Okogun et al., 1977) and N-formyl piperine (Debrauwere and Verzele, 1975).	
38	*Plantago major* L.	The leaves and seeds of *Plantago major* have been reported to have biological activities of antihypertensive (Samuelsen, 2000; Nyunt et al., 2007).	*Plantago major* constituents include phytol 13.22%, benzofuranone 10.48%, penthynediol 10.26% and benzene propanoic acid 10.18%; diglycerol 30.31% and glycol 18.91%; glycerine 30.70%, benzene 21.81% and dibuthyl phthalate 16.22%; phtalic acid 24.62%, benzene propanoic acid 16.83% and group of phenol 10.20%; phenol 27.47%,	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
			diathiapentene 14.53%, napthalenone 14.13% and glycerine 12.02% (Jamilah et al., 2012).	
39	*Populus alba* L.		The main constituents of *P. alba* are, 1,8-Cineole (38.02%), βEudesmol (20.58%), δ-Cadinene (8.30%), α-Eudesmol (6.75%) (Belkhodja et al., 2016; Banthrope, 1996). Sixteen compounds were isolated and identified as tremuloidin (1), populin (2), chaenomeloidin (3), 4'-O-benzoylsalicin (4), salicin (5), tremulacin (6), poliothrysin benzoate (7), catechol (8), benzoic acid (9), tremulacinol (10), 6'-O-benzoylsalicin-7-salicylate (11), salicylol (12), salicortin (13), 7-O-acetyl-3'-O-benzoylsalicin (14), 7-O-acetyl-4'-O-benzoylsalicin (15), and 6'-O-acetyl-2'-O-benzoylsalicin (16) (Ma et al., 2013).	
40	*Psidium guajava*	Intravenous administration of 50-800 mg/kg of *P. guajava* leaf aqueous extract in Dahl salt-sensitive rats resulted in significant decrease in the systemic arterial blood	The fruits of *Psidium guajava* are rich in vitamins (A and C), iron, calcium, and phosphorus (Kasturi and Manithomas,	Evaluation of the toxicity markers like SGOT (serum

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		pressures and heart rates of hypertensives (Ojewole, 2005). It has also been reported that nonenzymatic glycosylation (glycation) between reducing sugar and protein results in the formation of advanced glycation end products (AGEs), believed to play an important role in diabetes-associated cardiovascular complications. Agents that inhibit the formation of AGEs are believed to have therapeutic potential against diabetic complications (Soman et al., 2013).	1967). The essential oil from the leaves contains caryophyllene, nerolidiol, β-bisabolene, and β-sitosterol and ursolic, oleanolic, crategolic, and guayavolic acids. The plant contains leukocyanidins, sterols, and gallic acid in the roots (Gyllenhaal and Soejarto, 1988).	glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase) revealed the nontoxic nature of the extract (Soman, et al. 2013).
41	*Saccharum officinarum* L.	The study of Molina Cuevas and colleagues on pharmacological interactions between policosanol (200 mg/kg) and antihypertensive agents revealed that pre-treatment with high doses of policosanol significantly increased propranolol-induced hypotensive effects, while the effects of nifedipine remained unchanged (Molina et al., 1998). Furthermore, their results show that policosanol does not antagonize the hypotensive effect of beta-blockers; but it can increase the hypotensive effect of beta-blockers without modifying cardiac frequency (Arencibia et al., 1995). In another study, Askarpour and colleages	*Saccharum officinarum* contains phenolics, flavonoids, triterpenoids, phytosterols (Feng et al., 2014). Four phytosterols including cholesterol, campesterol, stigmasterol and β-sitosterol were identified (Feng et al., 2014). The phytochemistry of sugarcane wax (obtained from the leaves and stalks of sugarcane), leaves, juice, and its products show the presence of various fatty acid, alcohol, phytosterols, higher	

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		included 19 RCTs with a total of 2289 participants and a follow-up range 3–54 weeks. This meta-analysis indicated that supplementation with the policosanol significantly decreased both SBP (−3.423 mmHg) and DBP (-1.468 mmHg) (Askarpour et al., 2019). Furthermore, the meta-regression analysis showed significant effect of increasing dose on lowering effect of policosanol on SBP (Askarpour et al., 2019).	terpenoids, flavonoids, -O- and -C-glycosides, and phenolic acids (Singh et al., 2015).	
42	*Solanum aethiopicum* L.,	The fruits and roots of *Solanum aethiopicum* have been reported to be used for the treatment of diabetes and hypertension (Iwu, 2014). It was also shown that lyophilized eggplant powder induced significantly lowered acute and chronic blood pressure levels at very low doses of 0.0650 mg/kg body weight (b.w.) and 0.821 mg/kg b.w. per day, respectively (Yamaguchi et al., 2019). In addition, Chronic administration suppressed adrenaline and noradrenaline excretion in the urine, and aorta assays showed that eggplant acted on the M3 muscarinic ACh receptor (M3 mAChR) (Yamaguchi et al., 2019). ACh was conclusively shown to function as the main component of eggplant contributing to antihypertensive activity by suppressing sympathetic nervous activity via M3 mAChR (Yamaguchi et	A 100 g edible portion of Solanum aethiopicum fruits contain water 90.6 g, energy 135 kJ (32 kcal), protein 1.5 g, fat 0.1 g, carbohydrate 7.2 g, fiber 2.0 g, Ca 28 mg, P 47 mg, Fe 1.5 mg, β-carotene 0.35 mg, thiamin 0.07 mg, riboflavin 0.06 mg, niacin 0.8 mg, and ascorbic acid 8 mg (Iwu, 2014). The composition of fresh leaves per 100 g edible portion is water 82.1 g, energy 215 kJ (51 kcal), protein 4.8 g, fat 0.3 g, carbohydrate 10.3 g, fiber 2.4 g, Ca 523 mg, P 94 mg, Fe 6.0 mg, β-carotene 6.40 mg, thiamin 0.23 mg, riboflavin 0.44 mg, niacin 1.8 mg, and ascorbic acid 67	Some members of the Solanaceae family have been reported to contain steroidal alkaloids, some are toxicThe rule of thumb is to avoid very bitter cultivars (Iwu, 2014).

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		al., 2019).	mg (Iwu, 2014). Other constituents of the fruits include the phytosterols betulin and sterolin (sitosterol glucoside), flavonoids, and terpenes. Its bitter taste is attributed to furostanol glycosides (Iwu, 2014). Several sesquiterpenoids, the antifungal agents lubimin and epilubimin, have been found in the roots (PROTA, 2013). The leaves contain oxalate and alkaloids (e.g., solasodine), which has glycocorticoid effects (PROTA, 2013). Their concentration is reduced by cooking.	
43	*Solanum lycopersicum* L.	It was reported that extract of *Solanum lycopersicum* (tomato) modestly reduces BP in patients with mild, untreated hypertension (Engelhard et al., 2006). In another study, a significant correlation was observed between systolic BP and lycopene levels. Addition of *S. lycopersicum* extract with low doses of ACE inhibition, calcium channel blockers, or their combination with low-dose diuretics had a clinically significant effect-reduction of BP on the patients by more than 10 mmHg systolic and more than 5 mmHg diastolic pressures (Paran et al., 2009).	Phenolic compounds (phenolic acids and flavonoids), carotenoids (lycopene, α, and β carotene), vitamins (ascorbic acid and vitamin A) and glycoalkaloids (tomatine) (Chaudhary et al., 2018).	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		It was reported that (20-50 microl of 100% juice) of tomato extract, tested for their anti-platelet property, inhibited both ADP- and collagen-induced aggregation by up to 70%, but could not inhibit arachidonic acid-induced platelet aggregation and concomitant thromboxane synthesis under similar experimental conditions (Dutta-Roy et al., 2001). It was observed that the anti-platelet components (MW <1000 Da) in tomatoes are water soluble, heat stable and are concentrated in the yellow fluid around the seeds. These results indicate that tomatoes contain anti-platelet compounds in addition to adenosine (Dutta-Roy et al., 2001). The researchers stated that, unlike aspirin, the tomato-derived compounds inhibit thrombin-induced platelet aggregation. They also noted that the data indicate that tomato contains very potent anti-platelet components, and consuming tomatoes might be beneficial both as a preventive and therapeutic regime for cardiovascular disease (Dutta-Roy et al., 2001).		
44	*Talinum fruticosum* (L.) Juss. Syn. *Talinum triangulare*	Hypertension: It is also used to treat high blood pressure (Ogunlesi et al., 2010). Diabetes:	*Talinum triangulare* contains carotenoids; moderate benzoic acid derivatives, hydroxycinnamates and flavonoids; and low terpenes, alkaloids, phytosterols, allicins, glycosides,	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
	(Jacq.) Willd.	Results of their study show that administration of *Talinum triangulare* leaf flavonoid extract (TTFE) for 21 days normalized streptozotocin-induced (STZ)-induced hyperglycemia and its associated dyslipidemia by a mechanism involving inhibition of α-amylase and HMG-CoA reductase activities, respectively, in rats (Oluba et al., 2019).	saponins, and lignans contents (Ikewuchi et al., 2017). Ten known carotenoids (mainly 50.42% carotene and 33.30% lycopene), nine benzoic acid derivatives (mainly 84.63% ferulic acid and 11.92% vanillic acid), and six hydroxycinnamates (55.44% p-coumaric acid and 44.46% caffeic acid) were also identified. *T. triangulare* also contains eight lignans (88.02% retusin) and thirty flavonoids (50.35% quercetin and 39.36% kaempferol) (Ikewuchi et al., 2016). Qualitative phytochemical analyses of the T. triangulare plant parts revealed the presence of tannins, flavonoids, cardiac glycosides, alkaloids, saponin and inulins (Mensah, et al., 2009).	
45	*Tapinanthus bangwensis* (Engl. & K.Krause) Danser	The effects of extract of *Tapinanthus bangwensis* (Loranthus Micranthus) was investigated by Obatomi and colleagues. A dose of 1.32 g/kg per day for 8 days considerably decreased the mean arterial pressure and serum total cholesterol (Obatomi et al., 1996). Iwaloku and	The phytochemical analysis of Tapinanthus bangwensis revealed the presence of saponins, flavonoids, tannins and steroidal glycosides (Ekhaise, et al., 2010). Seven new	

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	Syn *Loranthus bangwensis* Engl. and K.Krause, often misnamed *Loranthus micranthus* Hook.f	colleagues' findings concluded that the anti-hypertensive effect of *L. micrathus* entails vasorelaxation, cardiac arginase reduction, anti-artherogenic events and Nitric Oxide elevation (Iwalokun et al., 2011).	pentacyclic triterpenoids, including five oleanane-types designated bangwaoleanenes A–E (1)–(5), and two ursane-types, named bangwaursenes A (6) and B (7) together with eight known compounds: 3b-acetoxy-urs-12,13-ene-11-one (8), 3b-acetoxy-11a-hydroxyurs-12,13-ene (9), 11a,12aoxidotaraxeryl acetate (10), b-amyrin acetate (11), (1R,5S,7S)-7-[2-(4-hydroxyphenyl)ethyl]-2,6- dioxabicyclo[3.3.1]nonan-3-one (12) 1-desoxyribose (13), myo-inisitol (14), sorbitol (15), were isolated from the seeds of Tapinanthus bangwensis (Maza et al., 2017).	
46	*Treculia Africana* Decne. ex Trécul Syn. *Artocarpus Altilis*	*Treculia Africana* was reported to cause significant ($p < 0.05$) hypotensive and bradycardiac responses unaffected by atropine (2 mg/kg) and mepyramine (5 mg/kg) but attenuated by propranolol (1 mg/kg) and N(G)-nitro-L-arginine methyl ester (5 mg/kg) (Nwokocha et al., 2012). The investigators stated that extract (0.71-4.26 mg/mL) significantly ($p < 0.05$) relaxed phenylephrine (10^{-9}-10^{-4} M)	The major constituents of Treculia Africana were α-pinene, myrtenal, limonene, camphene and n-hexanoic acid (Aboaba et al., 2007). Its leaf and root barks essential oils contained ten seequiterpenoid hydrocarbons, alcohols and ketones;	

S/no	Scientific Name	Experimental evidence for its use in hypertension management	Phytoconstituents identified in the plant	Interaction/toxicity studies
		and 80 mM KCl-induced contractions in endothelium intact and denuded aortic rings; and caused a significant ($p < 0.05$) rightward shift of the Ca^{2+} dose-response curves in Ca^{2+}-free Kreb's solution. Their work concluded that *T. Africana* exhibits negative chronotropic and hypotensive effects through α-adrenoceptor and Ca^{2+} channel antagonism (Nwokocha and Williams, 2012).	sesquiterpenoids were αcopaene (0.7%), (E)-β-caryophyllene (0.4%), α-humulene (0.6%), β-acoradiene (0.6%), (E,E)-α-farnesene (1.6%), elemol (0.7%), E-nerolidol (0.8%), spathulenol (0.1%), and αtumerone (2.5%) (Aboaba, et al., 2007). *T. Africana* contains between 13.4 and 23.3% proteins, 53.7 and 62.6% carbohydrates, 10.4 and 18.9% fats, and a wide array of nutritive elements (Ca, Zn, Fe, Mg), and antinutrient components of the seed (phytate, oxalate, tannin, and hydrogen cyanide) (Oyetayo and Oyetayo, 2020).	
47	*Vernonia amygdalina* Del	Intravenous administration of 5 and 10mg/kg of *Vernonia amygdalina* aqueous extract in normotensive Sprague-Dawley rats produced a biphasic alteration of blood pressure, with an initial transient rise in mean arterial pressure and a subsequent fall beyond the basal levels (Eghianruwa et al., 2016). It was noted that this result was more prominent with 10mg/kg. For contractility investigation, the aortic smooth muscle maximum relaxation of 31.3 +/- 3.1% was observed with extract	Active ingredients: vernoniosides, glucosides, flavonoids and antioxidants (Jisaka et al., 1993). Carbohydrates, saponins, alkaloids, tannins, proteins and steroid occurred in very high concentration (+ + +), flavonoids and glycosides occurred in high concentration (++), the concentration of resins was low (+) (Ugwoke et al., 2010).	Aqueous extract of the leaves inhibited P-gp efflux activity in Caco-2 cells (Oga et al., 2012).

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		concentration of 2.7 mg/ml (Taiwo et al, 2012) (Oliver-Bever,1968). When injected intravenously in dogs, vernonin produces hypotension and has an action on the heart comparable to that of digitalin but is much less toxic. The cardiac glycosides similarly had a distinct cardiotonic action but no cardiotoxic action (Patel et al.,1964). Jawalekar reported that a leaf extract of *V. amygdalina* reduces the rate and force of contraction of the isolated frog heart. In cats it causes a marked fall in the blood pressure and reduces the heart rate and conduction block. Further, it strongly stimulates contractions of the isolated rabbit intestine. These effects can be blocked by atropine (Kerharo and Bouquet, 1950;).	Vernodalin, Vernolide, Vernomygdin, Vernolepin (Kupchan et al., 1969). Vernodalol, 11,13- dihydrovernodalin (Ganjian et al., 1983). Luteolin, Luteolin 7-Oglucoside and 7-Oglucuronide (Igile et al., 1994). Vernonioside D and E (Igile et al., 1995).	
48	*Xanthosoma sagittifolium*	The extract of *Xanthosoma sagittifolium* has been shown to be effective in the management of hypertension (Oridupa et al., 2018). Its extracts stopped progression of the haematological and metabolic derangement associated with hypertension. In addition, it reversed renal damage caused by hypertension (Oridupa et al., 2018).	Terpenoids, cardiac glycosides and tannins were highly present (+++), flavonoids and alkaloids were moderately present (++) while saponins and steroids were present in trace (+) amounts in cocoyam inflorescence (Ukpong et al., 2014). Cocoyam leaves contain antioxidants, vitamins, and dietary fiber (Boakye et al.,	

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			2018). Its corms contain Calcium, Phosphorous and Magnesium (Boakye et al., 2018).	
49	*Zea mays*	Martín and colleagues reported that intravenous injection of 1.342 mg/kg boiling dialysate of corn silk decreased diastolic blood pressure by 63.8% ± 33.6% in normotensive anaesthetized dogs (Martin et al., 1991). Similarly, it was also reported in another study that oral administration of 260 mg/kg corn silk aqueous extract reduced the intraocular pressure in eyes with ocular hypertension and lowered the blood pressure in systemic and non-systemic hypertensive subjects. (George and Idu, 2015); Corn silk extract (CSE) significantly reduced systolic blood pressure (SBP) levels in spontaneously hypertensive rats and inhibited the ACE activity (Li et al., 2019). In addition, by proteomics coupled with bioinformatics analyses, we identified a novel ACE inhibitory peptide CSBp5 in CSE. CSBp5 significantly inhibited the ACE activity and decreased SBP levels in a dose-dependent manner (Li et al., 2019).	Zea mays (corn) silk contains dipeptide Ala-Tyr (AY), potassium, zein, an alcohol soluble protein present in corn gluten meal, tripeptide (Leu-Arg-Pro, Leu-Ser-Pro, and Leu-Gln-Pro), identified from thermolysin-hydrolyzed zein (Li, et al., 2019); Chrysoeriol 6-C-β-boivino pyranosyl-7-O-β-glucopyranoside, Alternanthin (Suzuki et al., 2003).	
50	*Zingiber officinale*	In a clinical study, oral (70–140 mg/kg) or intravenous (1.75–3.5 mg/kg) administration of two bioactive	Ginger oil consists mainly of camphene, citral, cineol, linalool, zingiberene,	

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		constituents of ginger, namely (6)-gingerol and (6)-shogoal, produced triphasic blood pressure profiles: initial rapid fall, intermediate rise, and finally a delayed decrease in BP (Suekawa et al., 1984). Iwu also reported that when (6)-shogaol (0.5 mg/kg i.v.) was administered to rats, blood pressure showed a triphasic response, which comprised a rapid fall, followed by a rise and a delayed fall (Iwu, 2014). His work also noted that the rapid fall, which followed immediately after the injection of the compound, disappeared with the use of atropine and vagotomy, whereas the sequential marked rise was not affected by α-adrenoceptor blockade and calcium antagonists and ganglion blockade. Only a combination of the three inhibited this pressor response (Iwu, 2014).	bisbolene, zingiberol, zingibcrenol, and methylheptenone. Its plant ontaiins gingerols and shogaols (Narasirnhan and Govindarajan, 1978; Der Marderosian and Liberti, 1988). 2-(4-Hydroxy-3-methoxy phenyl) ethanol, 2-(4- hydroxy-3-methoxy phenyl) ethanoic acid, 2- (3,4-dimethoxyphenyl) ethanooic acid, 4-(4- hydroxy-3-methoxyphenyl)-2-butanone, (4- hydroxy-3-methoxy phenyl) methanol (Kato et al., 2006); Zingerone, Geraniol (Chen et al., 2007).	