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Bioactive compounds and medicinal usefulness of edible leaves of *Vernonia amygdalina, Ocimum gratissimum, Piper guineense* and *Gongronema latifolium*

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Abstract

The therapeutic actions of plants rely solely on the bioactive compounds contained in such plants. Bioactive compounds are synthesized basically from plant primary metabolites such as amino acids, carbohydrates and lipids. Bioactive compounds can be isolated, identified and characterized using standard analytical protocols. Edible leaves of *Vernonia amygdalina*, *Ocimum gratissimum*, *Piper guineense* and *Gongronema latifolium* are used traditionally in various parts of the world, especially in Africa and Asia, for the alleviation of pathologic conditions. The present review highlighted the medicinal usefulness of edible leaves of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* in connection with the diverse bioactive compounds that are linked to their therapeutic potencies. Herbal therapeutics are preferred to synthetic drugs by many people worldwide due to their ease of accessibility, low cost of usage and low incidences of side effects associated with the use of herbs as well as cultural consideration. Thus, the leaves of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* should be subjected to more extensive and rigorous medicinal evaluation as well as consider the use of bioactive compounds from these plant materials for the design and development of novel drugs.

Keywords: Bioactive Compounds; Medicinal; *Vernonia Amygdalina*; *Ocimum gratissimum*; *Piper Guineense*; *Gongronema latifolium*

Introduction

The use of plants-based therapeutics requires the incorporation of various pharmacological experiences and practices, as well as ancient methods of medicinal applications, that serve as a guide in the course of identification, selection, formulation and use of herbs for the cure of diseases. The use of herbs for therapeutic purposes remains the oldest and well-known healthcare practice globally [1].

Bioactive compounds from plants or phytochemicals, which are also known as secondary plant metabolites, are plant active compounds that occur naturally and exhibit diverse biological functions in humans and plants. These secondary plant metabolites are synthesized primarily to protect the plants from diseases and herbivores [2,3]. Bioactive compounds can be separated into various pharmacologically active components, using standardized extraction protocols, for analytical purposes and production of herbal remedies [4,5].

Herbal remedies are more accessible and affordable in comparison with synthetic drugs [5]. Additionally, herbal medicines are preferred to synthetic drugs by many people worldwide due to their low cost of usage, low incidences of side effects associated with the use of herbal therapeutics and cultural consideration [6-8]. According to the WHO, approximately 80% of the inhabitants of some countries in Africa and Asia make use of medicinal plants as therapeutics [9]. Nevertheless, some of these phytochemicals equally exhibit certain deleterious effects in living organisms [10].

Plant bioactive compounds modulates certain physiological events in the human system in health and disease [11]; combating various diseases such as malaria, tissue inflammation, microbial infections, cancer, diabetes mellitus, lipidemia as well as control and protection against tissue oxidative damage [12]. The knowledge of the pharmacological relevance of the bioactive components in plants has led to the evolution of new drugs. For example, Paclitaxel (Taxol), which is an anti-cancer chemotherapy, was developed from *Taxus brevifolia* Nutt [13-15].

The present review highlighted the medicinal usefulness of edible leaves of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* in connection with the diverse bioactive compounds that are linked to their therapeutic potencies, which are of relevance to the alternative medicine practitioners and providers as well as the nutritionist.

Methods

This review work was carried out by collecting information from scientific articles using keywords, namely; 'Bioactive compounds', 'medicinal plants', '*Vernonia amygdalina*', '*Ocimum gratissimum*', '*Piper guineense*', '*Gongronema latifolium*'. Search engines such as Google scholar, PubMed, ScienceDirect, SpringerLink, Pubget and back searches through references were used to acquire relevant online published articles between 1972 and 2020. A total of 168 references were cited in this review article.

Biosynthesis and medicinal importance of bioactive compounds in plants

Bioactive compounds are diverse chemical components whose biosynthetic pathways are offshoot of photosynthesis and basically linked to primary metabolic pathways of amino acids, carbohydrates and lipids (Figure 1). The shikimic acid pathway (Figure 2) plays major role in the biosynthesis of bioactive compounds from aromatic amino acids precursors, namely; phenylalanine, tryptophan and tyrosine [15,16]. Bioactive compounds are also referred to as plant secondary metabolites and confer many medicinal values and benefits to plants and animals [17-19].

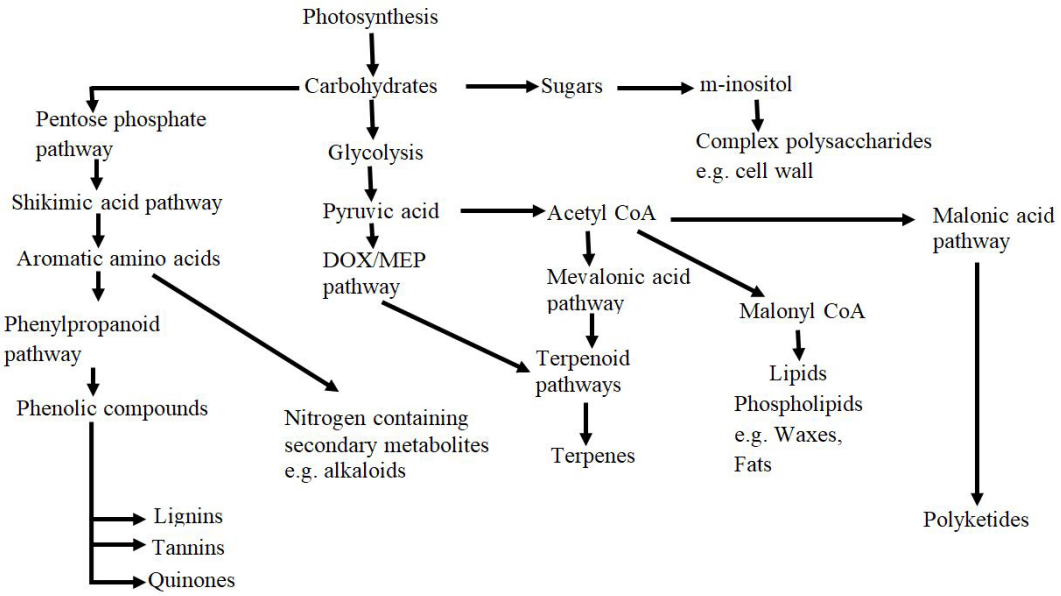

Figure 1: Biosynthetic pathways of bioactive compounds [15,16]
DOX: 1-deoxy-D-xylulose; MEP: methylerythriol-4-phosphate

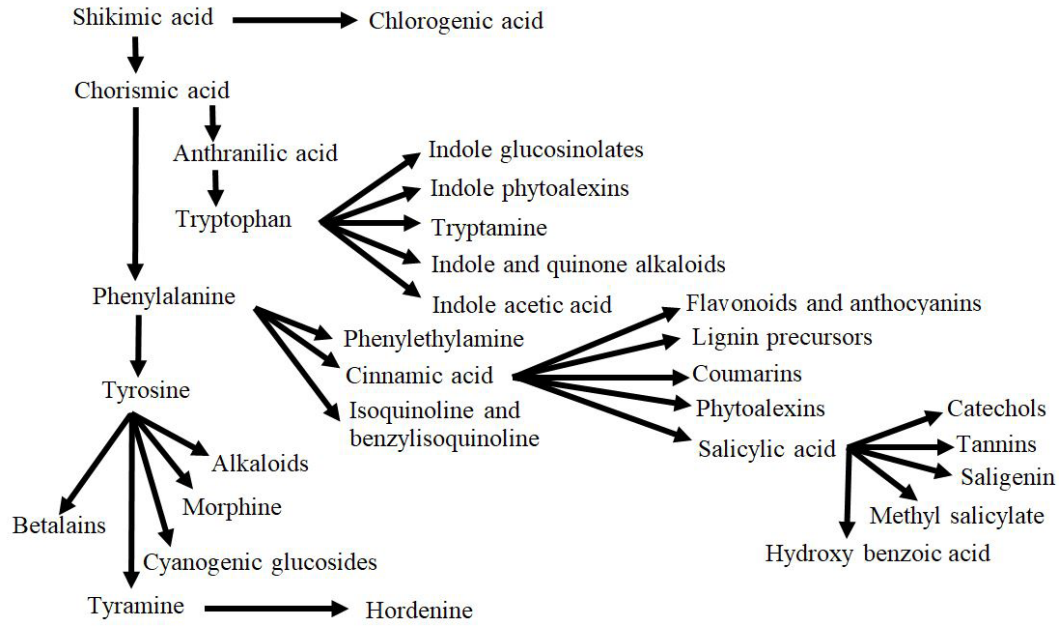

Figure 2: Shikimic acid pathway for the biosynthesis of bioactive compounds [15,16]

Saponins

The saponins are secondary plant metabolites, consisting of compounds typical of the triterpenoids, steroid alkaloids and glycosylated steroids (Figure 3). The saponins form stable foam-like matter when suspended in aqueous solution and shaken vigorously [20]. They are classified as monodesmoside and bidesmoside saponins depending on the number of sugar moiety attached to the C-3 and C-22 positions. The monodesmoside saponins refer to saponins with one sugar moiety attached to the C-3 position, whereas the bidesmoside saponins are those that have at least two sugar molecules with one sugar moiety linked to the C-22 and the other with the C-3 positions [21].

The saponins have the potentials of mitigating elevated lipid levels in the plasma and liver as well as promote fecal removal of bile acids and cholesterol [22]. The hypoglycemic, antioxidant and anti-peroxidative activities of the saponins have also been reported [23,24]. The steroidal saponin-charantin has been reported to promote the secretion of insulin into circulation [25,26]. The immune system stimulating activities of the saponins have been reported elsewhere [27].

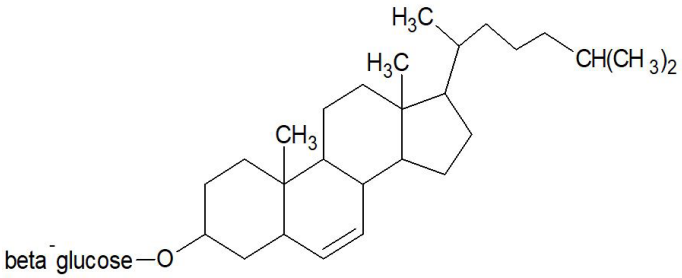

Figure 3: Pharmacological important saponin-charantin

Flavonoids

The flavonoids belong to the class of polyphenols that occur in high quantities in vascular plants in the form of glycosides, aglycones and methylated derivatives. The flavonoids include the flavanones, flavones, anthocyanins, flavan-3-ols and the isoflavones, with each made up of different phytocomponents (Figure 4) [28]. Naturally, the flavonoids are linked with sugar, and can be grouped as monoglycosidic, diglycosidic, etc. with the glycosidic linkage at the C-3 or C-7 positions [29].

The flavonoids exhibit antioxidant capabilities owing to their molecular structure, especially the positioning of their hydroxyl groups [18,30]. Flavonoids have also been reported to exert anti-inflammatory, anticancer and antimicrobial effects. These compounds are also inhibitors of enzyme activities, anti-allergens and also possess estrogenic properties [31].

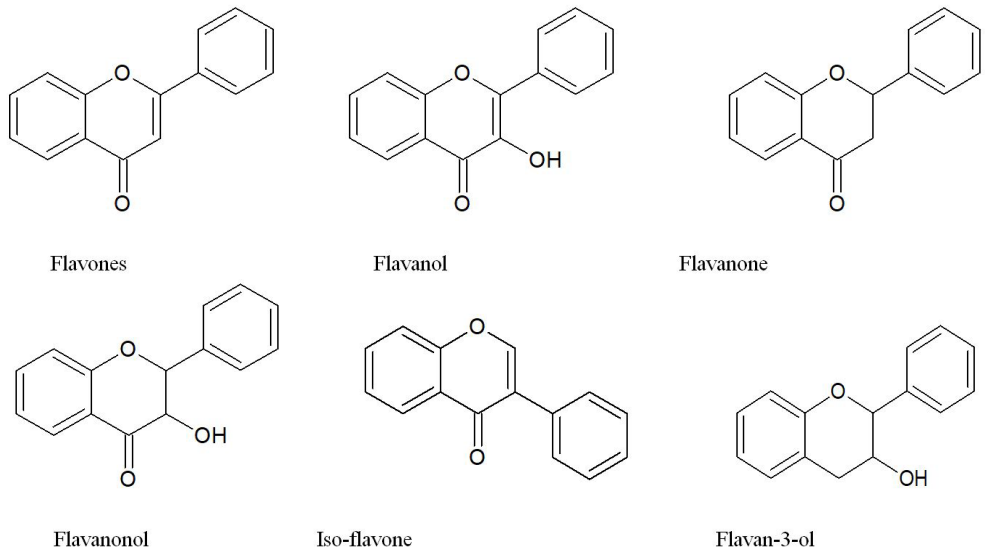

Figure 4: Chemical structures of pharmacological important flavonoids

Glycosides

The glycosides refer to natural products composed of a D-glucose and related sugar molecules (L-rhamnose and L-fructose) linked with an aglycone moiety (Figure 5) [32]. They are colourless, bitter and water soluble compounds that are largely deposited in the cell sap of plants. The glycosides easily undergo hydrolysis and the members of this group of secondary metabolites are classified based on their sugar composition, medicinal relevance and molecular composition of the aglycone component [33,34].

The tannic acid components of the glycosides are responsible for astringent character of the glycosides, and therefore are used as anti-protozoan preparations. The cardiac glycosides promote cardiac outputs and efficacy, chalcone glycosides are effective anticancer agents and the anthracene glycosides have shown efficacy in the treatment of skin infections [35]. Aglycone anthraquinones have antimicrobial potentials, which mitigate proliferation of the renal tubule and inflammation by inhibiting the cyclooxygenase pathway [36].

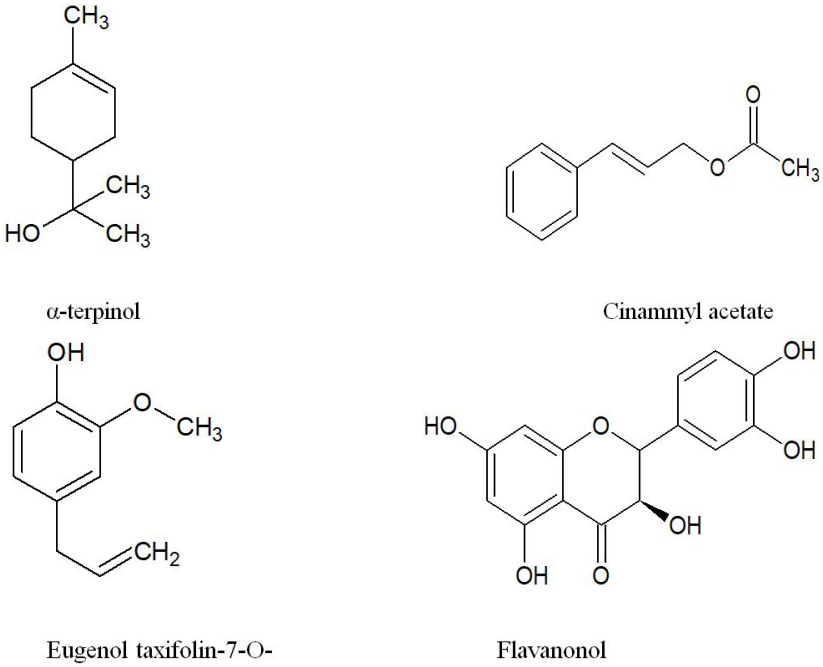

Figure 5: Molecular structures of pharmacological important aglycone moieties of glycosides

Alkaloids

The alkaloids are the largest members of secondary metabolites, mostly ammonium compound derivatives, and therefore exhibit the properties of a base. The basicity of the alkaloids was attributed to the presence of 1°, 2° or 3° amines and the molecular structure and functional group position (Figure 6) [17].

The alkaloids are used clinically as major components of drugs. The alkaloids: codeine and morphine are used as analgesics; berberine and sanguinarine are antibiotics; vinblastine exhibits anticancer activity; atropine is essential for the dilation of the pupil; scopolamine is a sedative; caffeine, ergotamine and cocaine are additive stimulants [16,37,38].

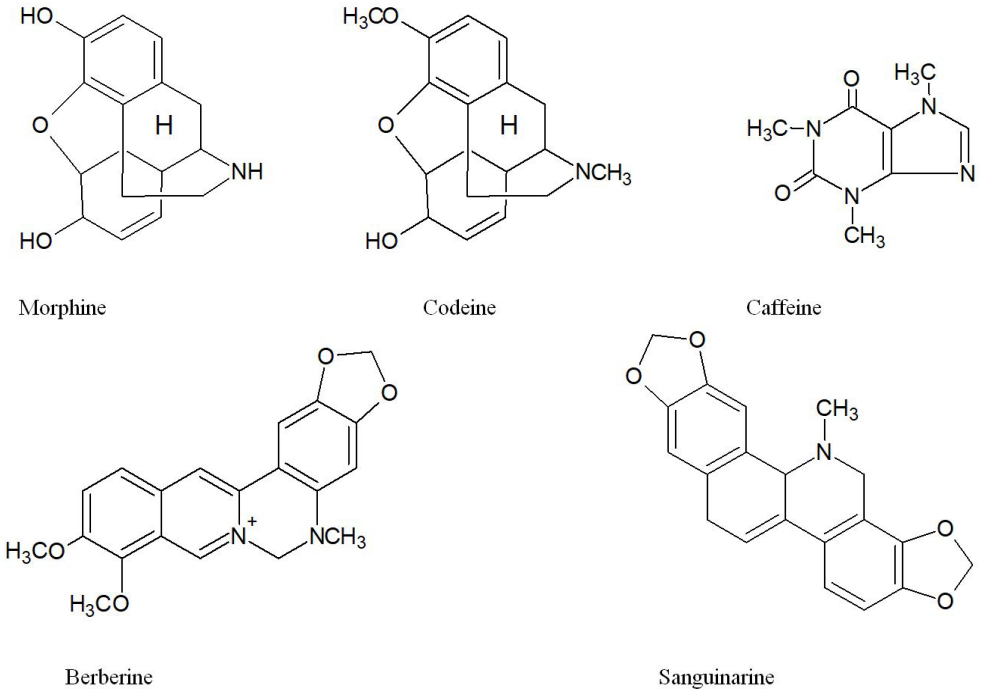

Figure 6: Chemical structures of some pharmacological important alkaloids

Phenolics

Phenolic compounds are characterized by -OH group bonded to one or more aromatic rings (Figure 7). Phenol is the simplest compound of this group, with a chemical formula of C_6H_5OH. The phenolics consist of low molecular weight and complex structured compounds. Some of these compounds include coumarins, phenylpropanoids, flavonoids, tannins, stilbenes and benzoic acid derivatives [39,40]. Phenolpropanoids are among the phenolics characterized by a C_6C_3 carbon skeleton, and connects with quinic acid to generate chlorogenic acid [16].

The phenolics are used for combating pathogenic diseases in humans. The compounds possess antioxidant, anti-inflammatory and anticancer activities [17,41]. This group of bioactive compounds is also known to prevent coronary diseases and myocardial infarction [42,43].

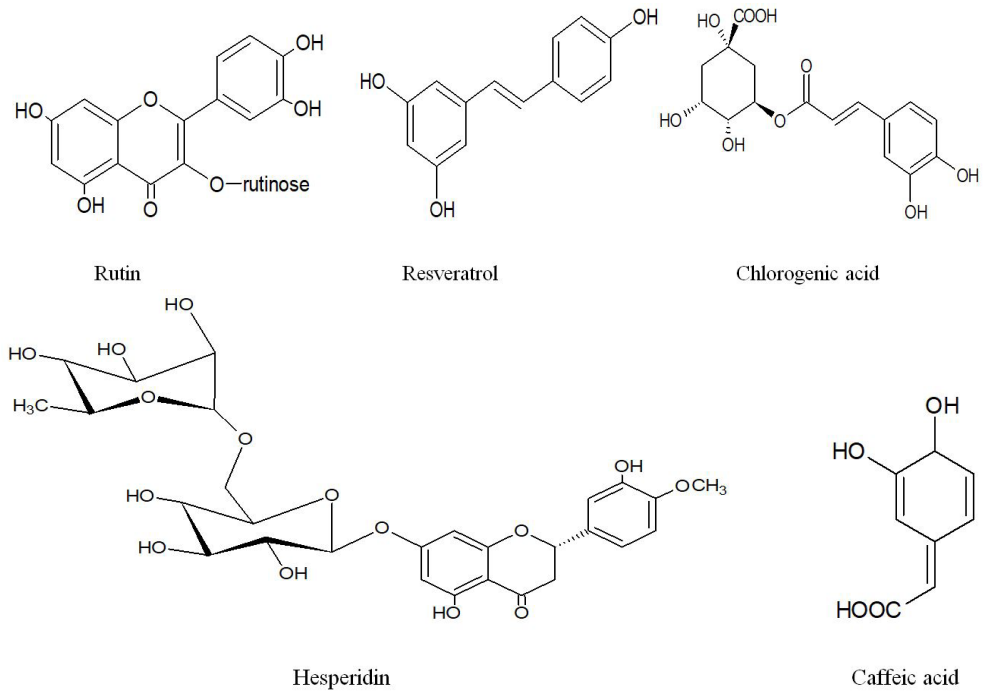

Figure 7: Chemical structures of some pharmacological important phenolics

Tannins

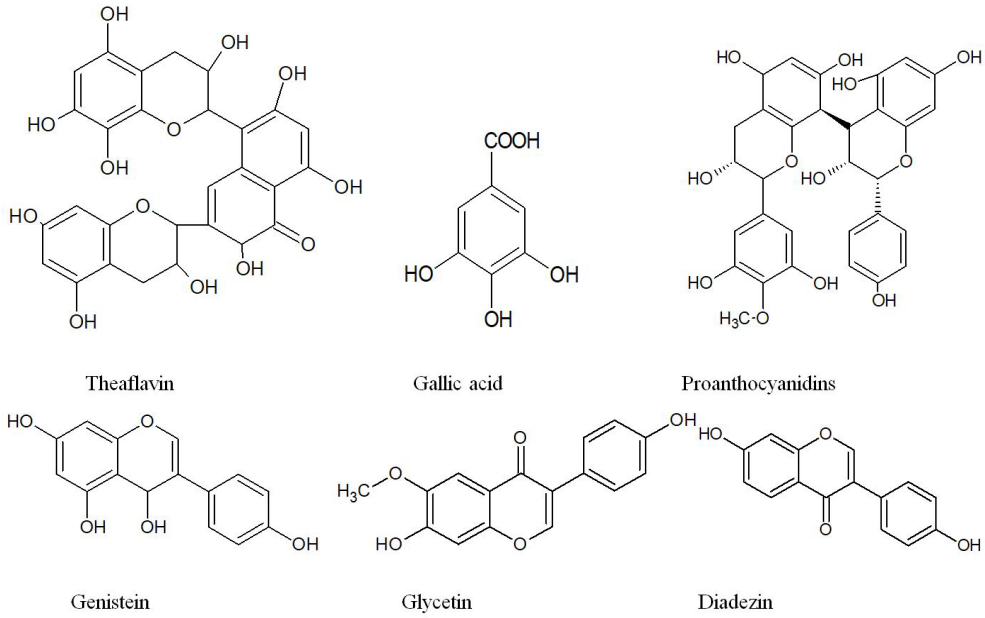

Figure 8: Molecular structures of pharmacological important tannins

The tannins represent a group of bioactive compounds whose molecular configurations are made up of large members of phenolic ring structures (Figure 8) [33]. The tannins release pyrogallic acid when heated. There are two main classes of tannins, namely; condensed tannins and hydrolyzable tannins. The hydrolyzable form of the tannins is composed of different simple phenols linked to each other through various ester bonds [44]. The hydrolyzable tannins undergo hydrolysis yielding ellagic acid and gallic acid by the actions of several factors such as enzymes, alkaline compounds and mineral acids. Thus, hydrolyzable tannins are also known as egallitannins and gallotannins. The condensed tannins are made up of flavonoids components at different levels of condensation [45].

The phenolic group in tannins is responsible for their antiseptic property. Diseases such as diarrhea, leucorrhoea and rhinnorhoea have been successfully treated using herbal medicine, such as Ayurveda, formulated from plants rich in tannins [17]. The tannins such as proanthocyanidins exhibit antioxidant property [46]. According to Velayutham et al., [47] the tannins have been confirmed to exhibit hypoglycemic and hypolipidemic actions.

Phytochemical screening techniques

The use of non-standardized protocols for screening and quantification of plant secondary metabolites causes decomposition of metabolites, variations in experimental results and poor analytical reproducibility [48]. Thus, efforts should be made to follow the appropriate guidelines to obtain appropriate results and standardized outcomes.

Selection of plant materials

There are various approaches available for selection of plant materials for phytochemical screening. Plant species can be selected randomly for phytochemical screening, although this option is not a preferable approach [15,49].

It has been observed that researchers usually select plant materials for phytochemistry and pharmacological analyses based on their established ethno-medicinal uses. Plants used traditionally for the alleviation and amelioration of certain ailments are likely to be composed of bioactive compounds that posses such medicinal efficacy [6,50,51].

The use of chemo-taxonomical data is another approach to plant species selection. In this approach, the knowledge that plants in the same taxonomical group are made up of similar natural products lead to the prediction that such plants being investigated have similar or closely related bioactive compounds with the plant species of established chemo-taxonomical data [51].

Plants are also selected based on their ability to survive in adverse environments enriched with pathogens. The ability of the plants to thrive in such environments is a possible indication that bioactive compounds from such plants can exhibit antimicrobial activities [15]. Plant materials can also be selected based on the reported biological activities of such plants in literature including their chemical, toxicological, veterinary, ecological records [48].

Collection and identification of plant materials

The part of the plant material to be collected for analysis should be such that contains appreciable accumulation of the bioactive compounds of interest. Various parts of the plant such as the leaves, root, seed, tuber, fruit, etc. can be used for analytical investigations. The harvest and collection of the plant material should be done in a manner that will not cause substantial harm to the vegetation and impact negatively on the ecosystem. For the identification of the plant, a plant taxonomist or a botanist must be involved in the authentication of the plant. The plant's name, part collected as well as the geographical location and date of collection should be recorded and deposited as a voucher in the herbarium for future use [15,52].

Drying and grinding of plant materials

Temperatures more than 40 °C should not be used for drying of plant materials in order to prevent the decomposition of thermolabile compounds, and the plant materials should be cut into pieces in order to ensure a homogenous drying of the plant part. It is also not advisable to use sunlight for the drying of plant materials due to ultraviolet radiation, which may cause transformation of certain chemical components. During the drying process, the buildup of heat and moisture should be avoided as much as possible [48,53].

The dried plant materials can be shredded into powder using a blender or grinder, or a mortar and pestle. Grinding of the plant materials is essential for the extraction process because it increases the plant material's surface area, and therefore allows the free and homogenous flow of solvent in all parts of the plant material to be used for analyses [48].

Extraction of plant materials

Various contemporary and conventional procedures are employed in the extraction of plant materials [15,54]. The extraction protocols of the plant materials and polarity of the extractant employed play a crucial role in the identification and characterization of bioactive compounds. Accordingly, the choice of the solvent to be used for extraction, for the most part, depends on the polarity and solubility of the bioactive compounds desired. Water and various organic solvents are more frequently employed in the extraction of bioactive compounds [54,55]. The extraction protocol is influenced by the type of bioactive compounds to be isolated, as well as the nature of the source material. The solvents used for the extraction protocols and the possible extractable bioactive compounds are summarized in Table 1.

Solvents							
Ethanol	Chloroform	Aqueous	Methanol	Ether	Acetone	n-Hexane	Dichloromethane
Flavonoids	Terpenoids	Terpenoids	Tannins	Terpenoids	Flavonoids	Terpenoids	Terpenoids
Terpenoids	Fatty acids	Saponins	Polyphenols	Coumarins	Phenols	Fatty acids	Flavonoids
Sterols	Waxes	Anthocyanins	Lactones	Alkaloids	Terpenes	Waxes	Tannins
Polyacetylenes	Flavonoids	Polypeptides	Phenones	Fatty acids	Terpenoids		
Alkaloids		Tannins	Quassinods		Glycosides		
Polyphenols		Lectins	Saponins				
Tannins		Polysaccharides	Terpenoids				
Saponins		Alkaloids	Anthocyanins				
			Xanthoxylines				
			Totarols				
			Phenones				
			Alkaloids				

Table 1: Solvents used for extraction and the possible bioactive compounds extracted [15,48]

Isolation, identification and characterization of bioactive compounds

Vast combinations of diverse bioactive compounds are contained in medicinal plants, and therefore expertise is required in their isolation, identification and characterization procedures. The frequently used methods for the isolation of bioactive compounds, which have been shown to be efficient, include immunoassay, phytochemical screening assay, and chromatographic techniques such as column chromatography, high-pressure liquid chromatography (HPLC), thin-layer chromatography (TLC), flash chromatography and Sephadex chromatography [56,57]. After the isolation of bioactive compounds, they are identified, quantified and characterized using Fourier transform infrared (FTIR) spectroscopy and gas chromatography-mass spectrometry (GC-MS) [58-64]. Other techniques such as ultra-violet (UV) spectroscopy and infrared (IR) spectroscopy, in conjunction with allied and ancillary instruments are used for structure elucidation of bioactive compounds [15]. Colorimetric and gravimetric methods have also been reported to be relevant in the identification, characterization and quantification of bioactive compounds [65-67].

Description of *V. amygdalina*

V. amygdalina originated from Maryland. This perennial shrub is a member of the Asteraceae family (Table 2), and can grow up to a height of 10 m (Figure 9). *V. amygdalina* is commonly called bitter leaf owing to the bitter nature of its leaves when tasted, although it has other local names in various parts of the world (Table 2) [68-70]. The presence of bioactive principles such as saponins, steroids, alkaloids, tannins, cardiac glycosides, flavonoids and phenols are responsible for the bitter taste of *V. amygdalina* leaf [71,72]. The leaf blades of the herb measures about 4 – 15 cm x 1 – 4 cm with oval and lance-like shape. The leaf base is wedge shaped and the margins are saw-toothed and finely denticulate, whereas the leaf apex is sharply cuspidate [70,73].

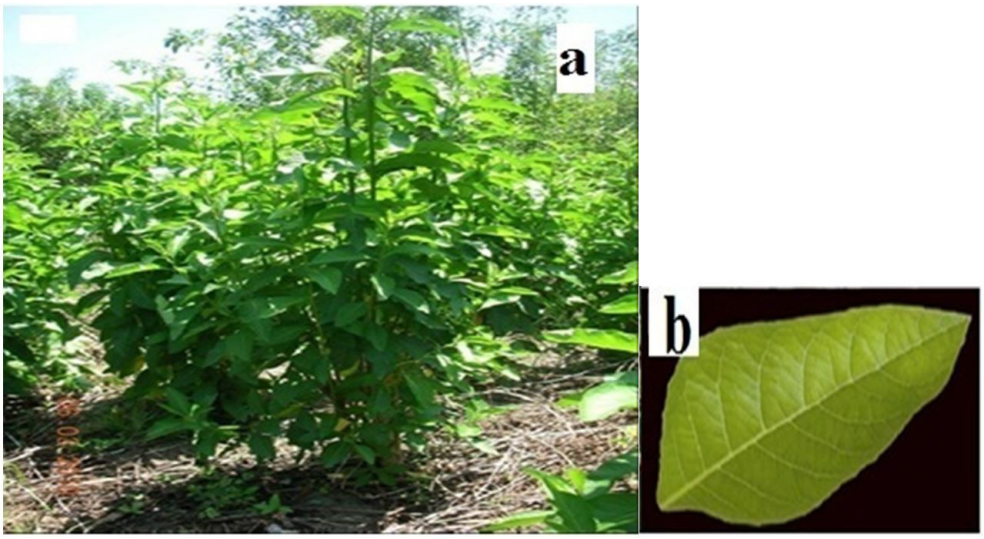

Figure 9: (a) *V. amygdalina* plants (b) *V. amygdalina* leaf [73]

Description of *O. gratissimum*

O. gratissimum is a tropical plant and a native of Africa and Southern Asia [74,75]. The order and family to which this herb belongs are Lamiales and Lamiaceae, respectively (Table 2) [76,77]. *O. gratissimum*, popularly called scent leaf as a result of its pleasant leaf fragrance, is characterized by ovate-shaped leaves with saw-like leaf margins (Figure 10); and has various native names in different regions and countries (Table 2). It is a perennial shrub that is 1 – 3 m tall and is widely used in the preparation of delicacies especially in West Africa due to its palatable aromatic tasty leaves [78]. It is widely distributed in Asia, Africa and India [79].

Figure 10: (a) *O. gratissimum* plants (b) *O. gratissimum* leaf [80][73]

Description of *P. guineense*

P. guineense is a climbing plant that grows widely in the tropical regions (Figure 11). It can grow to a height of 20 m. The fruits of *P. guineense* occur in clusters, peppering to teaste and berry-like in nature [81]. *P. guineense* is a member of the Piperaceae family (Table 2) that is made up of over 700 species [82]. The leaves are 12 cm long with shapes similar to that of heart, which is ellipsoidal. *P. guineense* is prone in areas with constant rainfall or regular supply of water [83].

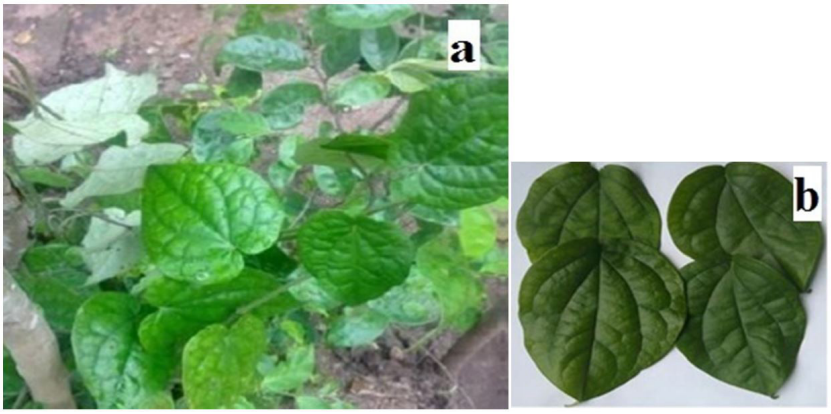

Figure 11: (a) *P. guineense* plant (b) *P. guineense* leaves [84,85]

Description of *G. latifolium*

Figure 12: (a) *G. latifolium* plant [88]. (b) *G. latifolium* leaves [91]

G. latifolium is a perennial climbing shrub with a characteristic bitter leaf taste especially when fresh (Figure 12). The leaves of *G. latifolium* are broad and have shapes similar to that of heart [86]. The plant grows widely in the tropical and sub-tropical regions and sparingly in the south-eastern and northern regions of Asia [87]. The leaves of the plant are widely used in the preparation of delicacies and traditional medicines [88]. The stem is typically smooth, hairy, woody and hollow [89]. This herbal plant grows as long as 5 m [90]. The family, other names and places of origin of *G. latifolium* are summarized in Table 2.

Medicinal plants	Family	Other names	Places of origin
V. amygdalina	Asteraceae	Bitter Leaf, Olubu, Kiriolugbo, Pokok, Bismillah, Ewuro, Shikawa	Maryland
O.gratissimum	Lamiaceae	Scent Leaf, Nchanwu, Efinrin, Daidoya, Basil Fever, Tea Bush, Tanmotswangi-Wawagi, Alfavaca, Clove Basil, Lemon Basil, Ornamental Basil	South Asia, Africa, Polynesia, Bismarck, Archipelago, West Indies
P. guineense	Piperaceae	Uziza, Iyere, Benin Pepper, Guinea Pepper, False Cubeb, Ashanti Pepper, Odusa, Kale	Guinea, Kenya, Zambia
G. latifolium	Asclepiadaceae	Utazi, Akan-Asante Aborode, Sever Gasule, Amaranth Globe, Arokeke, Utasi	Senegal, Chad DR Congo, Nigeria

Table 2: The family, other names and places of origin of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium*

Composition of bioactive compounds in *V. amgdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* leaves

V. amgdalina, *O. gratissimum*, *P. guineense* and *G. latifolium* leaves have been reported by several authors to contain bioactive compounds such as the flavonoids, alkaloids, saponins, tannins, cyanogenic glycosides, phenols [71,72,92-100]. These bioactive compounds are soluble in solvents, namely; acetone, ethanol, methanol, and water, which are used for their extraction protocols. Table 3 showed that 3 major methods, namely; gravimetric, spectrophotometric and colorimetric methods, were used by the various authors for the quantitation of bioactive compounds from leaf extracts of *V. amgdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium*. The percentage composition of bioactive compounds from leaf extracts of *V. amgdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* are summarized in Table 3.

Bioactive compounds	Medicinal plants	Extractants	Method of analyses	Composition of bioactive compounds (%)	References
Flavonoids	*O. gratissimum*	Methanol	Calorimetric	6.27	101
	P. guineense	Ethanol	Gravimetric	0.22	102
	P. guineense	Methanol	Gravimetric	6.15	103
	V. amygdalina	Acetone	Gravimetric	32.54	104
	O. gratissimum	Aqueous	Gravimetric	1.55	85
	G. latifolium	Ethanol	Spectrophotometric	0.37	86
	V. amygdalina	Ethanol	Gravimetric	2.32	105
	G. latifolium	Methanol	Gravimetric	0.39	103
	O. gratissimum	Ethanol	Gravimetric	2.50	85
	O. gratissimum	Aqueous	Gravimetric	2.70	75
	P. guineense	Ethanol	Spectrophotometric	0.23	86
	V. amygdalina	Methanol	Gravimetric	1.10	106
	G. latifolium	Aqueous	Gravimetric	0.45	89
	O. gratissimum	Aqueous	Gravimetric	9.15	107
	V. amygdalina	Aqueous	Gravimetric	ND	105
	P. guineense	Ethanol	Gravimetric	7.86	108
	O. gratissimum	Ethanol	Gravimetric	1.88	105
	G. latifolium	Ethanol	Gravimetric	0.49	89
	O. gratissimum	Ethanol	Gravimetric	1.90	109
	P. guineense	Ethanol	Gravimetric	2.07	85
	O. gratissimum	Ethanol	Gravimetric	0.31	102
	G. latifolium	Ethanol	Gravimetric	0.80	109
	P. guineense	Aqueous	Spectrophotometric	0.84	110
	G. latifolium	Ethanol	Gravimetric	0.29	102
	G. latifolium	Aqueous	Gravimetric	0.42	107
	P. guineense	Aqueous	Gravimetric	1.07	85

Bioactive compounds	Medicinal plants	Extractants	Method of analyses	Composition of bioactive compounds (%)	References
Tannins	*G. latifolium*	Ethanol	Spectrophotometric	0.37	86
	O. gratissimum	Methanol	Calorimetric	0.77	101
	V. amygdalina	Acetone	Gravimetric	16.62	104
	P. guineense	Ethanol	Spectrophotometric	1.88	85
	G. latifolium	Ethanol	Gravimetric	0.77	89
	G. latifolium	Aqueous	Gravimetric	0.48	107
	O. gratissimum	Ethanol	Gravimetric	0.13	102
	G. latifolium	Ethanol	Colorimetric	0.69	109
	P. guineense	Ethanol	Colometric	0.30	102
	O. gratissimum	Aqueous	Spectrophotometric	2.82	75
	G. latifolium	Aqueous	Gravimetric	0.71	89
	O. gratissimum	Aqueous	Spectrophotometric	1.63	85
	P. guineense	Aqueous	Spectrophotometric	1.06	85
	G. latifolium	Ethanol	Colorimetric	0.26	102
	O. gratissimum	Ethanol	Colorimetric	0.79	109
	O. gratissimum	Aqueous	Gravimetric	0.012	111
	P. guineense	Aqueous	Spectrophotometric	1.22	110
	P. guineense	Ethanol	Spectrophotometric	0.18	86
	O. gratissimum	Aqueous	Gravimetric	0.96	107
	O. gratissimum	Ethanol	Spectrophotometric	3.98	85
Saponins	*V. amygdalina*	Acetone	Gravimetric	3.97	104
	P. guineense	Methanol	Gravimetric	0.73	103
	O. gratissimum	Aqueous	Gravimetric	0.30	75
	G. latifolium	Ethanol	Spectrophotometric	0.52	86
	V. amygdalina	Aqueous	Gravimetric	7.92	112
	G. latifolium	Methanol	Gravimetric	0.41	103
	P. guineense	Ethanol	Gravimetric	1.69	108
	O. gratissimum	Aqueous	Gravimetric	1.07	85
	G. latifolium	Ethanol	Gravimetric	0.63	89
	P. guineense	Ethanol	Gravimetric	1.82	85
	O. gratissimum	Aqueous	Gravimetric	0.05	107
	G. latifolium	Ethanol	Gravimetric	2.12	109
	P. guineense	Aqueous	Spectrophotometric	1.36	110
	G. latifolium	Aqueous	Gravimetric	0.63	89
	O. gratissimum	Ethanol	Gravimetric	2.10	85
	O. gratissimum	Aqueous	Spectrophotometric	0.23	111
	P. guineense	Ethanol	Spectrophotometric	0.31	86
	G. latifolium	Aqueous	Gravimetric	0.79	107
	O. gratissimum	Ethanol	Gravimetric	0.67	109
	P. guineense	Aqueous	Gravimetric	1.82	85
Alkaloids	*G. latifolium*	Methanol	Gravimetric	0.32	103
	P. guineense	Methanol	Gravimetric	0.25	103
	P. guineense	Aqueous	Spectrophotometric	0.03	110
	G. latifolium	Ethanol	Spectrophotometric	1.39	86
	P. guineense	Ethanol	Gravimetric	0.14	102
	O. gratissimum	Ethanol	Gravimetric	2.82	109
	V. amygdalina	Acetone	Gravimetric	10.09	104
	G. latifolium	Ethanol	Gravimetric	1.64	102
	G. latifolium	Aqueous	Gravimetric	0.78	89

Bioactive compounds	Medicinal plants	Extractants	Method of analyses	Composition of bioactive compounds (%)	References
Alkaloids	*P. guineense*	Ethanol	Spectrophotometric	0.46	86
	V. amygdalina	Methanol	Gravimetric	9.30	106
	V. amygdalina	Ethanol	Gravimetric	2.93	105
	O. gratissimum	Ethanol	Gravimetric	4.03	85
	G. latifolium	Aqueous	Gravimetric	2.34	107
	O. gratissimum	Ethanol	Gravimetric	2.56	105
	V. amygdalina	Aqueous	Gravimetric	4.407	112
	G. latifolium	Ethanol	Gravimetric	0.83	89
	P. guineense	Ethanol	Gravimetric	2.24	108
	G. latifolium	Ethanol	Gravimetric	2.01	109
	V. amygdalina	Aqueous	Gravimetric	6.83	105
	O. gratissimum	Aqueous	Gravimetric	1.43	105
	P. guineense	Ethanol	Gravimetric	3.58	85
	O. gratissimum	Aqueous	Gravimetric	3.10	85
	P. guineense	Aqueous	Gravimetric	2.17	85
	O. gratissimum	Aqueous	Gravimetric	9.84	107
	O. gratissimum	Aqueous	Gravimetric	0.29	111
	O. gratissimum	Aqueous	Gravimetric	4.10	75
Phenols	*P. guineense*	Ethanol	Spectrophotometric	0.16	102
	P. guineense	Aqueous	Colometric	1.60	85
	O. gratissimum	Methanol	Calorimetric	0.67	101
	O. gratissimum	Aqueous	Gravimetric	0.04	107
	P. guineense	Ethanol	Colometric	2.55	85
	G. latifolium	Ethanol	Spectrophotometric	1.66	86
	O. gratissimum	Aqueous	Colometric	3.03	85
	O. gratissimum	Ethanol	Spectrophotometric	0.32	102
	G. latifolium	Ethanol	Gravimetric	0.04	89
	P. guineense	Aqueous	Gravimetric	0.04	110
	O. gratissimum	Ethanol	Colometric	0.54	85
	G. latifolium	Aqueous	Gravimetric	0.03	89
	P. guineense	Ethanol	Spectrophotometric	0.37	86
	O. gratissimum	Aqueous	Spectrophotometric	2.14	75
	G. latifolium	Ethanol	Spectrophotometric	0.22	102
	G. latifolium	Aqueous	Gravimetric	0.28	107

Table 3: Summary of the percentage composition of some bioactive compounds in the leaf extracts of *V. amgdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium*

Medicinal usefulness of *V. amgdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* leaves

Herbs are known for their medicinal relevance and potentials. The healing capabilities of herbs are attributed to their bioactive compounds, which exert biological, physiological and pharmacological activities in the body system. Over the years, *V. amgdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* leaves have been used traditionally, especially in the African region, for the cure or amelioration of diseases in human.

V. amygdalina

Bioactive compounds from *V. amygdalina* leaves have been reported to exhibit antioxidant activity [93,113-115]. Antioxidants hinder the deleterious actions of reactive oxygen and nitrogen species (RONS) and, in the process, protect the target tissues and cellular components from oxidative damage. This feat is achieved by the entrapment and quenching actions of RONS by antioxidants, and thereby prevents oxidative damage and associated complications [70]. The ethanol leaf extract of *V. amygdalina* exhibits antioxidant activities, demonstrated by DPPH radical scavenging activity *in vitro*, which was attributed to its flavonoid content [93]. A related study showed that the antioxidant activity of ethanol extract of *V. amygdalina* was significantly more effective than vernodalol and vernolide (250 µg/mL), in terms of their DPPH radical scavenging capacities [114]. Furthermore,

methanol extract of *V. amygdalina* leaves was reported to exhibit higher antioxidant potential than the corresponding aqueous and acetone extracts [115]. The comparative higher antioxidant potential was attributed to the capability of methanol extract of *V. amygdalina* to maintain membrane stability against the damaging actions of RONS [113].

The antimicrobial capabilities of ethanol and aqueous leaf extracts of *V. amygdalina* against *Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans, Klebsiella spp.* and *Escherichia coli* has been reported [116]. The study showed that the minimum inhibitory concentration (MIC) values were within the range of 12.5 – 50 µg/mL. A related study showed that higher MIC values between the range of 25 and 55 µg/mL were registered when Streptococcus mutants were challenged with ethanol and aqueous leaf extracts of *V. amygdalina* [117]. The antimicrobial activity of leaf extract of *V. amygdalina* was attributed to the presence and actions of saponins, sesquiterpene lactones and flavonoids [96]. Warm water extract of *V. amygdalina* leaves suspended in honey exhibited antimicrobial effect on septic wounds. The aqueous leaf extract of *V. amygdalina* has been demonstrated *in vitro* to inhibit the growth of *Proteus mirabilis, Klebsiella pneumonia, C. albicans, E. coli, S. aureus* and *P. aeruginosa*, which are antimicrobial agents associated with sepsis [118,121].

The steroids, tannins, flavonoids and alkaloids contents of ethanol extracts of *V. amygdalina* leaves have been reported to exhibit antipyretic and analgesic activities [100]. Extracts of *V. amygdalina* are administered in form of folklore medicine for the treatment of malaria. Accordingly, report showed that 80% methanolic leaf extract of *V. amygdalina* was demonstrated to possess antimalarial activity [120]. Another study carried out by Egedigwe et al., [121] reported that methanolic and aqueous leaf extracts of *V. amygdalina* altered certain critical enzyme activities and hormonal actions in obese rats subjected to high fat diet such that it was effective in the treatment of obesity. The anxiolytic, detoxification and anti-cancer activities of methanol leaf extract of *V. amygdalina* have been reported [122,123].

In most African countries, especially Nigeria, *V. amygdalina* leaves are used traditionally for anti-helminthic purposes. The modes of actions of the herbal recipe include paralyzing the worms by disrupting energy production as a result of poor nutrient uptake as well as disrupting reproductive processes in the worms [124].

O. gratissimum

Edible leaves of *O. gratissimum* have been extensively used for the treatment of malaria and convulsion, as well as applied as an antimicrobial agent and mosquito repellant in regions of West Africa [125]. The leaves of *O. gratissimum* are widely applied in the treatment of headache, dysentery, cough, skin infections, and respiratory infections as well as inflammation of the lungs, hearing impairments, abdominal pains, pyrexia, eye infections and conjunctivitis [79,126].

The aqueous leaf extract of *O. gratissimum* has been reported to avert the growth of tumor cells and prevent angiogenesis, disrupt the proliferation of tumor cells, differentiation, stromal apoptosis, and stimulates inducible COX-2 [127,128]. Dichloromethane leaf extract of *O. gratissimum* suppresses myeloid leukemia *in vitro*, which was an indication of possible anticancer activity in human [129]. The antimicrobial potentials of *O. gratissimum* have been extensively described [130]. The antimicrobial capabilities of edible leaves of *O. gratissimum* have been reported to inhibit dehydrogenases activities in *E. coli* and *S. aureus* [131,132]. The flavonoid content of ethanolic leaf extract of *O. gratissimum* was reported to be responsible for the antimicrobial activity against various bacterial and fungal species [94,95].

The aqueous extract of *O. gratissimum* inhibits the unconstrained pendular movement of jejunum in rabbits and exhibits analgesic activity in mice [133]. Methanolic leaf extract of *O. gratissimum* reduces the generation of free radicals and hinders lipid-protein interactions of murine peritoneal macrophages in mice and *in vitro* models. Additionally, aqueous extract of *O. gratissimum* is a pharmacological agent for the mitigation of nicotine toxicity [134]. The mosquitocidal effect of chloroform leaf extract of *O. gratissimum* has been reported [135], and was attributed to the phenolic content of the leaves. The essential oil extract from *O. gratissimum* leaves is effective in the treatment of diarrhea [136].

P. guineense

The leaves of *P. guineense* are used as local therapy for respiratory infections and rheumatism [137]. The leaves are also used for the relief of discomfort caused by excess gas in the gastrointestinal tract, and therefore are aperitif, carminative and eupeptic agents [138]. The aseptic nature of these leaves makes it a suitable candidate for the relief of flatulence [139]. In local medicine, the leaves of *P. guineense* are utilized for the alleviation of fertility and sexually related problems such as female infertility, low sperm count and syphilis [140]. *P. guineense* is a food supplement for pregnant, postpartum women and nursing mothers as well as a medicinal spice [141]. There is a report on the antimicrobial activity of leaf extracts of *P. guineense* against five Gram-negative and three Gram-positive bacteria [142]. The screenings were done using an agar well diffusion and micro-dilution methods. The results showed that leaf extracts of *P. guinnense* inhibited the growth of all the microbial isolate tested. According to Mgbeahuruike [142], n-hexane leaf extract gave the lowest MIC value of 19 µg/mL against *Sarcina spp*. and growth inhibitory effects against *S. aureus* and *Enterobacter aerogenes* (MIC = 78 µg/mL). Growth inhibition was also reported in the presence of chloroform leaf extract of *P. guineense* against *P. aeruginosa* with a MIC value of 78 µg/mL. Antimicrobial activity of the leaf extract of *P. guinnense* was observed against *E. aerogenes*, *S. aureus*, *E. coli, S. enterica, P. mirabilis* and *Bacillus cereus* with MIC values ranging between 39 – 1250 µg/mL.

The antimicrobial activity of *P. guineense* extract was attributed to its bioactive compounds. Majority of the bioactive compounds are the piperamide alkaloids, piperine and piperlongumine which are known for their antimicrobial properties. Another study had reported anti-mycobacterial activity of leaf extract of *P. guineense* [102]. The antifungal activity of *P. guineense* against fungal strains gave MIC values within the range of 39 – 2500 µg/mL [143]. The lowest MIC value of 39 µg/mL was reported for methanol leaf extract of *P. guineense* against *C. albicans*, *Candida glabrata* and *C. tropicalis*. In addition, ethanol and n-hexane extracts were effective against the growth of *C. albicans* and *C. glabrata*, (MIC = 78 µg/mL), respectively. The antifungal property was also attributed to the piperamide alkaloids, piperlongumine and piperine.

The antioxidant activity of *P. guineense* was reported by Omodamiro and Ekeleme [102], in which they noted that leaf extract of *P. guineense* exhibited free radical scavenging activity. In another study [144], *P. guineense* was observed to rapidly scavenge nitric oxide *in vitro*. This antioxidant activity was attributed to the presence of phenolic compounds in the plant, which is a major group of compounds that act as primary antioxidants or free radical scavengers [99].

Study showed that methanol leaf extract of *P. guineense* promoted increased secretion of follicle stimulating hormone (FSH), luteinizing hormone (LH) and estrogen in non-pregnant Wistar albino rats [145]. Another report according to Memudu et al., [146] showed that crude leaf extract of *P. guineense* improved male reproductive functions in adult Sprague Dawley rats, and further recommended the use of the leaf extract of *P. guineense* to treat male fertility problems especially those associated with dysfunctional hormone secretion.

Tankam and Ito [97], investigations reported the therapeutic potentials of the aroma of *P. guineense* essential oil in mice following inhalation. The results showed significant sedative activity of the aroma of *P. guineense* essential oil with effective dose of 4.0 × 10-5 mg per cage, whereas the potent anxiolytic effective dose was 4.0 × 10-6 mg per cage. Tankam and Ito [97], further proposed that the effective bioactive compounds responsible for the sedative activity of *P. guinnense* were linalool and 3, 5-dimethoxytoluene. Accordingly, the report suggested that inhalation of *P. guineense* essential oil might induce a mild tranquilizing effect.

The anti-atherosclerotic activity of leaf extract of *P. guineense* in atherogenic diet fed hamsters was reported close to a decade ago [147]. The results of the study suggested that *P. guineense* had significant antioxidant and anti-atherogenic activities against deleterious atherogenic diet. In a related study, Nwozo et al., [148] showed that aqueous extract of *P. guineense* was a potent antioxidant preparation that exhibited hepato-protective properties in ethanol-induced liver injury in male albino rats. Additionally, leaf extract of *P. guineense* was effective in the treatment of diabetes mellitus and associated metabolic disorders [149].

G. latifolium

Many pharmacological activities of leaf extract of *G. latifolium* have been reported by several authors. The medicinal usefulness of *G. latifolium*, which stems from specific pharmacological activities of its bioactive compounds includes hypoglycemic, hypolipidemic, nephroprotective, hepato-protective, antioxidant [150,151], anti-inflammatory [152,153], hemostasis [154], anti-ulcer [155], anticancer [129], immunomodulatory [156], antimicrobial [157] as well as tissue regenerative and restorative potentials [158]. The aforementioned therapeutic benefits of *G. latifolium* are associated with the vast array of bioactive compounds present in various parts of the plant [98]. In ethnomedicine, extract of the whole plant of *G. latifolium* infusion is used for the treatment of pathologic conditions associated with digestion such as dyspepsia, anorexia, colic and stomachache, constipation, dysentery and intestinal worms [155] and damaged liver [159] as well as management of postpartum women and nursing mothers and treatment of dental caries [98].

The anti-diabetic activities of aqueous, ethanol, methanol and n-hexane leaf extracts of *G. latifolium*, using alloxan-induced diabetic animal models, have been reported [151,160,161] and were suggested to be effective for the management of diabetes mellitus. Related studies [92,162-164] had demonstrated the anti-hyperglycemic activity of leaf extract of *G. latifolium*.

Studies reported [165,166] showed the capability of aqueous leaf extract of *G. latifolium* to reverse renal tissue damage in carbon tetrachloride (CCl_4)-induced kidney dysfunctional rats. By virtue of the potential nephroprotective activity of leaf extract of *G. latifolium*, these studies suggested the use of bioactive compounds from the plant material for the alleviation of renal dysfunction. Furthermore, the antioxidant and hepato-protective potentials of aqueous and ethanolic leaf extracts of *G. latifolium* in rats have been reported elsewhere [150,167,168]. Related studies have confirmed that perturbed tissue biomarkers levels associated with oxidative stress and liver dysfunction were reversed to normal reference values following the administration of leaf extract of *G. latifolium* [92,98]. The anti-inflammatory potentials and erythrocyte membrane stabilizing activity of methanolic and aqueous leaf extracts of *G. latifolium* in rats have been demonstrated and reported [152,153].

An overview of the medicinal usefulness of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* leaves is summarized in Figure 13.

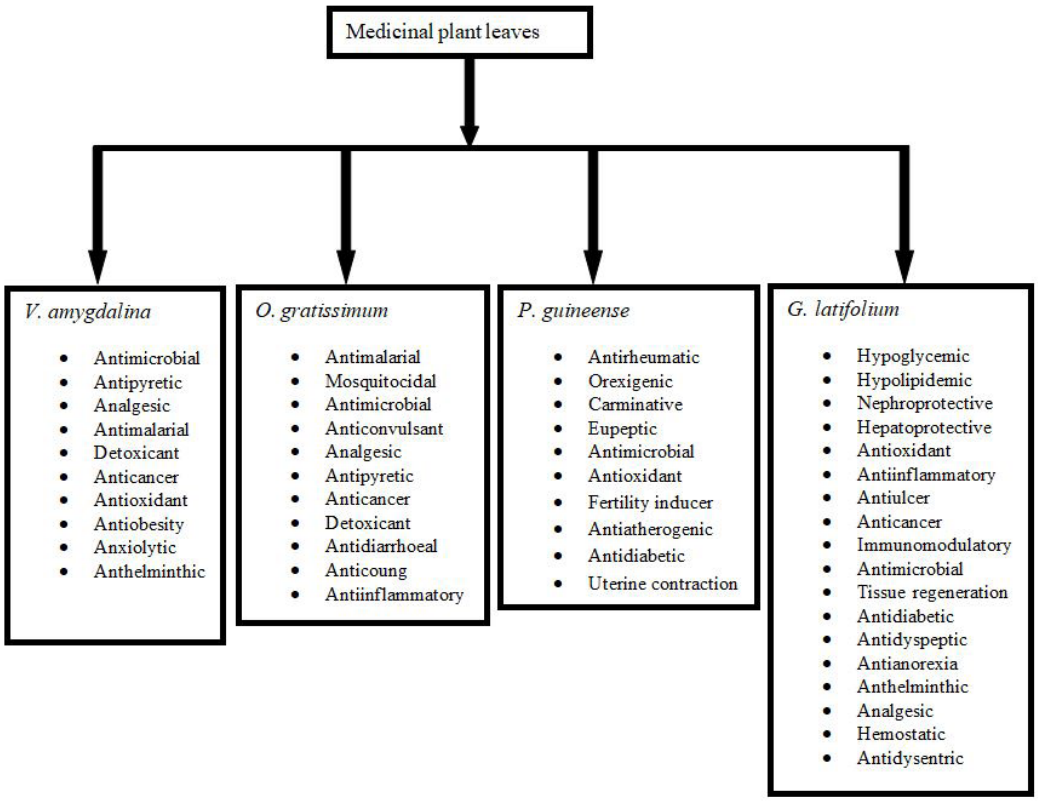

Figure 13: Summary of the medicinal usefulness of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* leaves

Conclusion

The edible leaves of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* are used in various regions of the world, especially in Africa and Asia, for the cure of diseases. The capability of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* to combat diseases was attributed to the presence of bioactive compounds present in these plants in different combinations and quantities. Bioactive compounds can be isolated, identified and characterized for medicinal evaluation using standard methods. Thus, the leaves of *V. amygdalina*, *O. gratissimum*, *P. guineense* and *G. latifolium* should be subjected to more extensive and rigorous medicinal evaluation as well as consider the use of bioactive compounds from these plant materials for the design and development of novel drugs.

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