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Review

Landolphia (P. Beauv.) genus: Ethnobotanical, phytochemical and pharmacological studies

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ABSTRACT

The genus *Landolphia* (P. Beauv.) belongs to the Apocynaceae family with over 65 species distributed all over the tropical regions. This genus has a considerable number of documented medicinal, industrial, and ecologically beneficial effects. Therefore, this review is tailored towards the appraisal of the traditional significance, phytochemistry, and pharmacological activities of the genus *Landolphia*. This will help researchers understand future research trends by bridging the gaps between documented literature and contemporary uses. Relevant information was obtained from selection of scientific databases such as Web of Science, PubMed, Scopus, Google Scholar, ScienceDirect and Wiley. From documented literature, different parts of *Landolphia* have been used to improve fertility, lessen menstrual pain, boost sex libido, cure malaria and typhoid. Several classes of bioactive constituents such as terpenoids, phenolics, flavonoids, steroids, fatty acids, saponins, phytosterol and phenylpropanoid, volatile compounds, lignans and coumarins have been isolated from this genus. These secondary metabolites could be responsible for the reported antimicrobial, antimalarial, aphrodisiac, antioxidant, anti-inflammatory, antidiabetic and anticancer activities exhibited by this genus. The leaves, flower, bark and root of this genus have a wide range of essential nutrients and antinutrients which are essential for normal growth and development in living organisms. Despite all findings indicating the economical, industrial and pharmacological activities of *Landolphia* species, secondary metabolites and pharmacological potency of *Landolphia* of this genus are not adequately documented. Therefore, bioassay-guided isolation on the *Landolphia* extracts with proven biological activities should be prioritised in order to isolate pharmacophores with unique structural frameworks.

1. Introduction

The genus *Landolphia* (P. Beauv.) belongs to the Apocynaceae family, which is broadly distributed in tropical Africa. It represents one of the therapeutically significant genera in folk medicine, with over 60 plant species and 40 genera (Aliyu et al., 2010). The genus *Landolphia* displayed immense adaptability ranging from shrubs, perennial herbs, evergreen or deciduous trees. In recent years, some *Landolphia* species are widely used in rubber production (Aliyu et al., 2010). The genus folkloric uses in the treatment of several diseases are documented (Mitsuo, 2001). Different parts of the *Landolphia* plants exhibited immense therapeutic potentials against early or established infections. In Ghana, the root is used in the treatment of vermifuge, stomach cramps and gastric ulcers (Mireku et al., 2017). In Nigeria, the dried leaves are used in the treatment of bacterial aetiology, constipation, typhoid fever, diarrhoea, gastrointestinal disorders, malaria, ulcer and dermal infections (Okeke et al., 2001, Nwogu et al., 2008; Aliyu et al., 2010).

About 150 phytochemicals belonging to phyto-classes such as alkaloids, anthraquinones, aromadendranes, steroids, reducing sugars, saponins and tannin, cyanogenic glycosides, triterpenes, and flavonoids have been reported from the *Landolphia* genus (Matemu et al., 2017; Nweze et al., 2018; Siombor and Anyam, 2015). These compounds could

Abbreviations: HPLC, High Performance Liquid Chromatography; FAMEs, Fatty acid methyl esters; ATM, Africa traditional medical system; MBD, macro-broth dilution; AWD, agar-well diffusion assay; MIC, minimum inhibitory concentration; DHA, Decosahexanoic acid assay; ZOI, zone of inhibition; LOEE, *L. owariensis* ethanolic extract; LOEF, *L. owariensis* ethyl acetate; LOMF, *L. owariensis* methanolic fraction; LOHF, *L. owariensis* hexane fraction; DPPH, 2,2-diphenyl-1-picrylhydrazyl; TAC, Total antioxidant capacity; ABTs, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid; FRAP, ferrulic reducing antioxidant potential.

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Table 1
Geographical distribution of Landolphia in tropical and Saharan Africa (Persoon et al., 1992).

Species	Local name (s)	Location (s)
Landolphia breviloba J.G.M. Pers.	Ndam Koukoi (Gabon)	Gabon, Congo.
Landolphia bruneelii (De Wild.) Pichon	Mfum (Cameroon), Indongoselele (Zaire)	Congo, Gabon, Cameroon, Zaire
Landolphia buchananii (Hallier f.) Stapf	Magi (Sudan), Gedo, Ghebo, Hobi, Yebo (Ethiopia), Abeli (Zaire), kakopa (Uganda), Mogogowa (Kenya), Mbungo (Tanzania)	Angola, Ethiopia, Sudan, South-east Nigeria
Landolphia calabarica (Stapf) E.A.Bruce	Bonjema (Sierra Leone), Hamah (Ghana), Autopoi (Nigeria)	Nigeria, Sierra Leone, Togo, Ghana
Landolphia camptoloba (K. Schum.) Pichon	Mumbungu, Vinvongo (Angola), Dinsania (Zaire), Bwengenena (Zambia)	Angola, Zaire, Zambia
Landolphia congolensis (Stapf) Pichon	Koldamba (Cameroun), Manguila (Gabon), Bantake (Zaire),	Nigeria, Cameroon, Gabon
Landolphia dulcis (Sabine ex G.Don) Pichon	Katimini (Mali), Ibo, Aro, Akwerri (Nigeria), Agbotro (Bennin), Ongam (Cameroon), Dalonk, Kondoo, Eyontoni (Sierra Leone)	Angola, Gabon, Nigeria, Sierra Leone
Landolphia foretiana (Pierre ex Jum.) Pichon	Ugbo Nikwa (Nigeria), Avom (Cameroon), N'Lombo (Angola), Abutadjamba (Zaire)	Liberia, Cote ́dIvoire
Landolphia glabra (Pierre ex Stapf) Pichon	Janese (Cameroun), Ilandi (Zaire), Anchine (Gabon)	Cameroun, Gabon, Nigeria
Landolphia gossweileri (Stapf) Pichon	Muhuni (Angola)	Angola
Landolphia heudelotii A.DC.	Pempen (Ghana), Gohine (Burkina Faso), Gohine (Mali), Baracan (Senegal)	Burkina Faso, Ghana, Nigeria, Senegal
Landolphia hirsuta (Hua) Pichon	Bunka (Guinea), Eboi, E-Mar (Sierra Leone), Balwa (Liberia), Ajamama (Ghana), Alubuda, Ate, Atomi (Nigeria),	Senegal, Nigeria, guinea, Sierra Leone
Landolphia incerta (K. Schum.) J.G.M.Pers.	Gawe (Sierra Leone), Ugbognikwi (Nigeria), Danga (Cameroon), Equateur (Zaire)	West and western Central Africa, Angola, Zaire, Guinea-bissau
Landolphia jumellei (Pierre ex Jum.) Pichon	Acia, Avoum, Ivogue (Gabon)	Cameroun and Gabon.
Landolphia kirkii Dyer	Bulundu, Mabungo (Zaire), Dabeh (Bom), Giriam (Kenya), Mabwungu (Tanzania), Babungua (Mozambique)	Zaire, Kenya, Zambia, South Africa, Mozambique
Landolphia lanceolata (K. Schum.) Pichon	Malombo, Mamboulou (Congo), Otarampa (Angola), Bankaka (Zaire)	Zaire, Congo, Angola
Landolphia landolphioides (Hallier f.) A.Chev.	Aquatayan (Cameroon), Batuka (Sudan)	Cameroon, Sudan
Landolphia lecomtei Dewèvre	Binntouba (Congo), Bobo (Zaire)	Congo, Zaire
Landolphia membranacea (Stapf) Pichon	Elonk, Finste (Sierra Leone)	Cote ́dIvoire, Sierra Leone, Liberia
Landolphia togolana (Hallier f.) Pichon	Agba (Nigeria).	Nigeria, Ghana, Togo, Benin

Table 2
The traditional relevance of *Landolphia* in Africa.

Country/ region	Plant name	Plant part	Ethnopharmacological activities	Reference (s)
West and East Africa	*L. heudelotti*	Stem and root	Treatment of gastric ulcers, stomach cramp, to cure eye conjunctivitis and cataracts, alleviate leprosy, rheumatism, pains and arthritis	Nthiga et al., 2016; Kareru et al., 2017
Côte d' Ivoire	*L. owariensis*	Unripe fruits and roots	Decoction is used to treat fever	Burkill, 2000
West and East Africa	*L. owariensis*	Leaves	Decoction as antidote for malaria and acts as purgative	Burkill, 2000
West and East Africa	*L. heudelotti, L. owariensis, L. dulcis*	Root, bark and stem	For treating wounds, therapies for constipation, typhoid, food poisoning, diarrhoea and other related gastrointestinal disorders	Odugbemi and Akinsulere, 2006
Equatorial Africa	*L. owariensis*	Latex	Treatment of intestinal worms and preservative	Nwaogu et al., 2007
Senegal, Upper Nile and North Central Africa,	*L. owariensis*	Leaf and root	Used in local beverages and beer production the pulverized root immersed in local gin for 14 days is used for gonorrhoea therapy	Okonkwo and Osadebe, 2013
Southwest Nigeria,	*L. owerrience*	Leaves	The decoction is used to treat ulcers, bacterial infections, purgative and to cure malaria	Olaleye et al., 2008; Ilesanmi et al., 2011
Nigeria,	*L. owerrience*	Root	The infused in local gin is used to treat gonorrhoea	Obute, 2005
Northern and Southern Nigeria	*L. dulcis*	Root	To enhance sexual performance	Ilodigwe et al., 2010
West Africa	*L. buchananii*	Root and bark	Decoction is used in to relieve joint and body pains	Nthiga et al., 2016; Kareru et al., 2017
In Congo and Ghana	*L. owerrience* and *L. dulcis*	Root, stem and bark	To treat giddiness and epilepsy and as food seasoning	NRC, 2008; Saini, 2016
In Africa	*L. dulcis*	Leaves, root and bark	The decoction is an effective antidote for bacterial infections in wounds, for enhancing breast milk glucose	Nthiga et al., 2016; Kareru et al., 2017

be linked to the antibacterial (Nwaogu et al., 2007; Akharaiyi and Boboye, 2009; Nwokonkwo, 2014), antioxidant (Mireku et al., 2017), anti-inflammatory (Owoyele et al., 2001), analgesic (Owoyele et al., 2001), aphrodisiac (Illodigwe et al., 2010), anti-malarial (Bero et al., 2009; Ezike et al., 2016), antipyretic and angiotensin (Nwaji et al., 2016) properties exhibited by this genus. *Landolphia* has exhibited significant drug discovery roles in traditional and contemporary medicine. However, there are no thorough facts on the secondary metabolites and pharmacological activities of crude extracts and isolated compounds from this genus. Hence, this review is targeted towards comprehensive connection between the folkloric significance, phytochemical profile and pharmacological activities of genus *Landolphia* in order to uncover their therapeutic potency, explore the present-day information, and evaluate future research prospects which could contribute to the discovery of new pharmacophores.

2. Research methodology

This review was comprehensively prepared by a broad assessment of published articles or literature using major scientific collections such as Scopus, Science Direct, PubMed, SciFinder and Google Scholar. Furthermore, relevant information was obtained from Tropicos (http://www.tropicos.org), the Plant List (https://www.theplantlist.org), and the Floras books. Search keywords include *Landolphia*, phytochemistry, pharmacology, ethnopharmacology and toxicology of the

Table 3
Secondary metabolites appraised in *Landolphia*.

No	Compounds	Plant species	Plant part	Extraction methods	References
1	Gallic acid	*L. owerienssis*	Leaves	Maceration	Nwaji et al., 2016
2	Vanillic acid	*L. owerienssis*	Leaves		
3	Caffeic acid	*L. owerienssis*	Leaves		
4	p- coumaric acid	*L. owerienssis*	Leaves		
5	Catechin	*L. owerienssis*	Leaves		
6	Apigenin	*L. owerienssis*	Leaves		
7	Quercetin	*L. owerienssis*	Leaves		
8	Protocatechuic acid	*L. owerienssis*	Leaves	Maceration	Ogbuagu et al 2012
9	Cortisone	*L. owerienssis*	Leaves		
10	Isofistularin	*L. owerienssis*	Leaves		
11	Septicine	*L. owerienssis*	Leaves		
12	Asteoside	*L. owerienssis*	Leaves		
13	Quercetin-3-o- galactopyranoside	*L. owerienssis*	Leaves		
14	Hydroxyanthranilic acid	*L. owerienssis*	Leaves		
15	Aloesin	*L. owerienssis*	Leaves		
16	Querce-3-orarab-furano	*L. owerienssis*	Leaves		
17	Citeodrimene	*L. owerienssis*	Leaves		
18	Isorhamnetin-diglycoside	*L. owerienssis*	Leaves		
19	Caulerpin	*L. owerienssis*	Leaves		
20	Epicatechin-o-3,4-dimethylgallate	*L. owerienssis*	Leaves		
21	Catechin-*o*-3,4-dimethylgallate	*L. owerienssis*	Leaves		
22	3,4-o- dimethyl gallic acid	*L. owerienssis*	Leaves		
23	Pyranopyrrol	*L. owerienssis*	Leaves		
24	Vermistatin	*L. owerienssis*	Leaves		
25	Kaempferol	*L. owerienssis*	Leaves		
26	Aloeresin	*L. owerienssis*	Leaves		
27	Quercetrin	*L. owerienssis*	Leaves		
28	Fasilculatin	*L. owerienssis*	Leaves		
29	Piperchabanide	*L. owerienssis*	Leaves		Matemu et al., 2017
30	Hexadecanoic acid	*L. kirkii*	Fruit	Maceration	
31	9- octadecanoic acid	*L. kirkii*	Fruit		
32	Tetradecanoic acid	*L. kirkii*	Fruit		
33	9,12-octadecanoic acid	*L. kirkii*	Fruit		
34	9,12,15- octadecatrienoic acid	*L. kirkii*	Fruit		
35	Capric acid	*L. owerienssis*	Seed pulp	Maceration	Okonkwo et al., 2014
36	Myristic acid	*L. owerienssis*	Seed pulp		
37	Pentadecanoic acid	*L. owerienssis*	Seed pulp		
38	Linoleic acid	*L. owerienssis*	Seed pulp		
39	Palmitoleic acid	*L. owerienssis*	Seed pulp		
40	Undecanoic acid	*L. owerienssis*	Seed pulp		
41	Stearic arid	*L. owerienssis*	Seed pulp		
42	Lauric acid	*L. owerienssis*	Seed pulp		
43	Linoleic acid	*L. owerienssis*	Seed pulp		
44	Heptadecanoic acid	*L. owerienssis*	Seed pulp		
45	α- farnesene	*L. owerienssis*	Leaves	Maceration	Saini, 2016
46	1-Dodecanol	*L. owerienssis*	Leaves		
47	Supraene	*L. owerienssis*	Leaves		
48	α-lonone	*L. owerienssis*	Leaves		
49	β- lonone	*L. owerienssis*	Leaves		
50	Tridecane	*L. owerienssis*	Leaves		
51	Citronellyl acetate	*L. owerienssis*	Leaves		
52	Caryophyllene oxide	*L. owerienssis*	Leaves		
53	4-α- methyldecalin-1-yl-acetate	*L. owerienssis*	Leaves		
54	β-nerolidol	*L. owerienssis*	Leaves		
55	n- tridecan-1-ol	*L. owerienssis*	Leaves		
56	6- phenyldodecane	*L. owerienssis*	Leaves		
57	Cis- geranylacetone	*L. owerienssis*	Leaves		
58	Squalone	*L. owerienssis*	Leaves		
59	6- phenyl- tridecane	*L. owerienssis*	Leaves		
60	Ecosane	*L. owerienssis*	Leaves		
61	2-Phenyldodecane	*L. owerienssis*	Leaves		
62	Benzyl salicylate	*L. owerienssis*	Leaves		
63	Hexahydrofarnesyl acetone	*L. owerienssis*	Leaves		
64	Cis-9-octadecanoic acid	*L. owerienssis*	Leaves	Maceration	Garba and Garba, 2017
65	3-β-sitosterol	*L. owerienssis*	Leaves	Maceration	Okonkwo et al., 2016
66	E-chlorogenic acid	*L. owerienssis*	Leaves		
67	chlorogenic acid methyl ester	*L. owerienssis*	Leaves		
68	Pinoresinol	*L. owerienssis*	Leaves		
69	Erythro/threoguaragylcerol-8-	*L. owerienssis*	Leaves		
70	2-(4,4- dihydroxy	*L. owerienssis*	Leaves		
71	Capstemol	*L. owerienssis*	Leaves		
72	Scopoletin	*L. owerienssis*	Leaves		
73	Picrasmalignon A	*L. owerienssis*	Leaves		

(*continued on next page*)

Table 3 (*continued*)

No	Compounds	Plant species	Plant part	Extraction methods	References
74	Halanophonin	*L. oweriensis*	Leaves		
75	Linalool	*L. heudelotti*	Fruit	Maceration	Pelissier et al., 1996
76	p-farnesene	*L. heudelotti*	Fruit		
77	p-cymene	*L. heudelotti*	Fruit		
78	1,8- Cineole	*L. heudelotti*	Fruit		
79	Limonene	*L. heudelotti*	Fruit		
80	Amyl isobutyrate	*L. heudelotti*	Fruit		
81	2-acetyl-4-methylfuran	*L. heudelotti*	Fruit		
82	Cis-linalool oxide	*L. heudelotti*	Fruit		
83	Phenylacetronitrile	*L. heudelotti*	Fruit		
84	Camphor	*L. heudelotti*	Fruit		
85	Amyl isovalerate	*L. heudelotti*	Fruit		
86	Methone	*L. heudelotti*	Fruit		
87	Iso amylvalerate	*L. heudelotti*	Fruit		
88	Terpinen-44	*L. heudelotti*	Fruit		
89	α-terpineol	*L. heudelotti*	Fruit		
90	Pulegone	*L. heudelotti*	Fruit		
91	Geranial	*L. heudelotti*	Fruit		
92	Indole	*L. heudelotti*	Fruit		
93	Thymol	*L. heudelotti*	Fruit		
94	4-heptyl-γ-lactone	*L. heudelotti*	Fruit		
95	β- damascenone	*L. heudelotti*	Fruit		
96	ρ- caryophyllene	*L. heudelotti*	Fruit		
97	Nerolidol	*L. heudelotti*	Fruit		
98	Bisabolol	*L. heudelotti*	Fruit		
99	Geranyl acetone	*L. heudelotti*	Fruit		
100	Phenyl acetaldehyde	*L. heudelotti*	Fruit		
101	Benzyl alcohol	*L. senegalensis*	fruit		
102	Myrcenol	*L. senegalensis*	fruit		
103	2-phenyl acetate	*L. senegalensis*	fruit		
104	α-terpinyl acetate	*L. senegalensis*	fruit		

genus *Landolphia*.

3. Botanical description

3.1. Morphological characterization

According to the botanical classification, the genus *Landolphia* belongs to Gentianales (order), Rauvolfioideae (subfamily) and Apocynaceae (family). The genus has distinctive corolla tube thickened directly above the glabrous fruits, anthers and typically dense inflorescences (Persoon et al., 1992). Most *Landolphia* species are huge lianas with large curled terminal tendrils. There are two auxiliary branches with one of it partially forming the extension, thus resulting to sympodial growth. Auxiliary buds besides the tendril concurrently open, leaflets sprout, branch formed and grows slowly while the other produced inflorescences. The second branch shapes the next apical tendril subsequently producing leaf pairs and the process is repeated. Hence, these plants grow in the prototypical of Koriba (Halle and Oldeman, 1970).

3.2. Geographical distribution

The genus *Landolphia* consists of about 75 accepted species which are widely distributed in the tropical and Saharan Africa, from Guinea to Cameroon, including Central Africa, Uganda, Southern Tanganyika and Sudan (Table 1). *L. owarrensis* (vine rubber) is found in Madagascar, South Africa, and Nigeria (Ilesanmi et al., 2011), *L. dulcis* in tropical forest of Nigeria, Guinea and spreading to Congo (Ilodigwe et al., 2013), *L. buchananii*in Angola, Sudan, Nigeria, Ethiopia, Mozambique, Zambia, Cameroun and Democratic Republic of Congo, and *L. heudelotti* is widely dispersed in Western tropical Africa (Kini et al., 2012).

3.3. Ethnopharmacological significance of Landolphia genus

Medicinal plants since time immemorial played significant roles as the safest and accessible therapeutic means in primary and communal health care systems (Oladeji et al., 2020,2022). The folkloric uses or ethnopharmacological significance of different parts of the genus *Landolphia* are well documented and acknowledged by the locals especially people in tropical regions. Up to date, about fifteen *Landolphia* species have been widely used or documented for the treatment of innumerable ailments and diseases (Table 2) (Owoyele et al., 2002).

4. Phytochemistry

The extensive appraisals of secondary metabolites from the genus *Landolphia* have immensely aided the identification of a wide range of compounds characterized by structural diversity (Table 3). Despite the numbers of species in this genus, quite a few secondary metabolites were isolated from the leaves, barks, stem, roots, flowers and seeds via spectroscopic assays. These secondary metabolites are reported to be responsible for the marked pharmacological activities demonstrated by this genus (Oladeji et al., 2019). Currently, about 107 compounds have been isolated from the genus *Landolphia*. The documented compounds include twenty-nine phenolic compounds **(1–29)**, thirty-three fatty acids **(30–63)**, three triterpenoids **(65–67)**, seven lignans and coumarins derivatives **(68–74)** and thirty-three volatile constituents **(75–104)** (Table 3) (Figs. 1–3).

4.1. Phenolic compounds and alkaloids

To date, about twenty-nine flavonoids and phenolic compounds (**1–29**) have been reported from five species of the genus *Landolphia* (*L. kirkii, L. owariensis, L. dulcis, L. heudelotti, L.membranace*) (Fig. 1) (Nwaji et al., 2016). Compounds (**1–7**) were obtained from ethanolic leaves extract of *L. Owariensis* using High Performance Liquid Chromatography (HPLC). However, compounds **2** and **5** were obtained from non-polar extracts, that is, n-hexane and acetone solvent extracts (Nwaji et al., 2016). Compounds **16, 22** and **24** were obtained for the first time in leaves extract of *L. Owariensis*. Aside these novel compounds, other compounds **(8–29)** have been reported in other *Landolphia* species (Ogbuagu et al., 2012; Garba and Garba, 2017; Matemu et al., 2017).

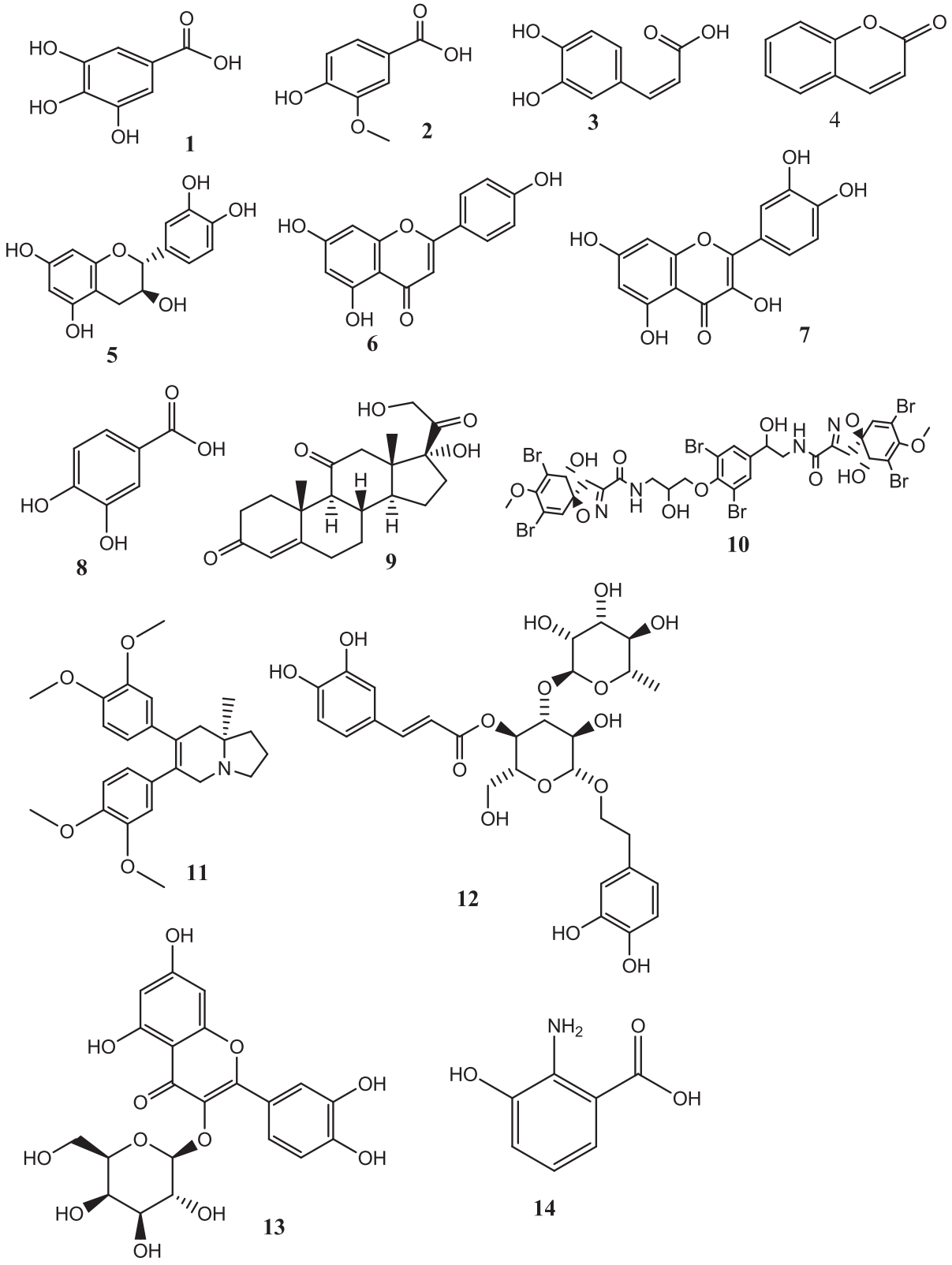

Fig. 1. Phenolic compounds and alkaloids in *Landolphia*.

4.2. Fatty acids

Several fatty acids have been reported from the genus *Landolphia*. Though, the most common fatty acid is the fatty acid methyl esters and unsaturated fatty acids (Fig. 2). From *L. Kirkii* fruits extract obtained from Limpopo Province, South Africa gave about five fatty acids **(30–34)** (Matemu et al., 2017). Bioactive fatty acid methyl esters (FAMEs) identified as mono-, di- and poly unsaturated fatty acids were isolated from petroleum ether fractions of leaves of *L. Owariensis* to give compounds **(35–44)**. These compounds were subjected to antibacterial

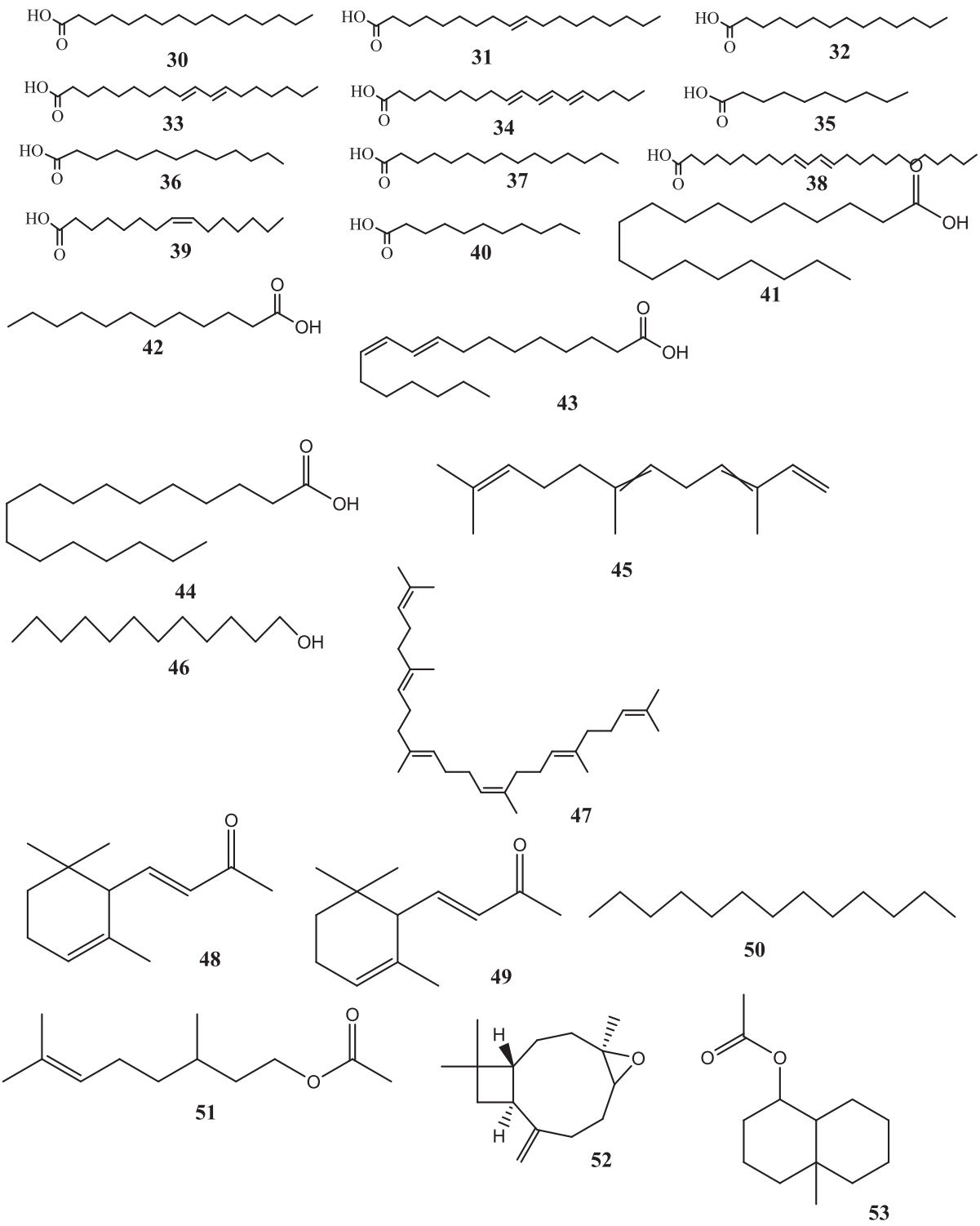

Fig. 2. Some of the fatty acids in *Landolphia* species.

screenings; however, **35, 39, 42** and **43** exhibited prominent antibacterial inhibitory activities (Okonkwo et al., 2014). Similarly, about nineteen aliphatic aldehydes and unsaturated fatty acids compounds **(39–63)** were isolated from leaves of *L. Owariensis* collected in Nigeria. Out of these compounds, **45, 48, 49, 54** and **63** reported to demonstrate considerable therapeutic potency against several diseases caused by microbes or parasitic infections (Saini, 2016). In addition, structural elucidation of compound **64** isolated from leaves of *L. Owariensis* was established using nuclear magnetic resonance (2D). Similarly, compound **64** exhibited significant curative potency against wide range of diseases (Garba and Garba, 2017).

4.3. Terpenoids

Few terpenoids have been isolated from the genus *Landolphia*. The documented terpenoids include three compounds (triterpenoids)

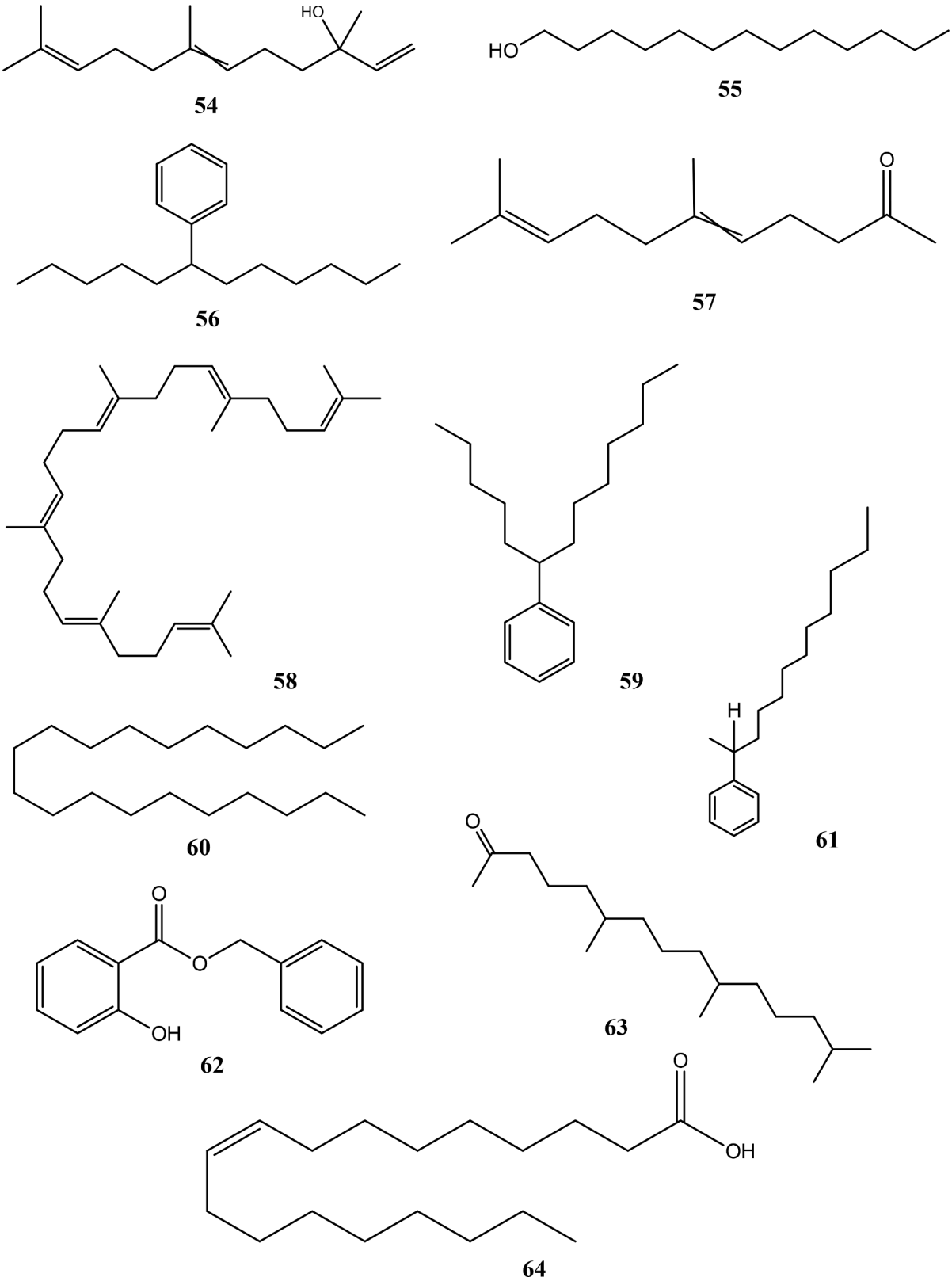

Fig. 2. (*continued*).

elucidated as 3β–Sitosterol **(65),** (E)-Chlorogenic acid **(66)** and (E)-Chlorogenic acid methyl ester **(67)** were isolated from leaves of *L. owariensis*, characterized and structural elucidation was established via spectroscopic and chromatographic assays (Fig. 3) (Wen-yi et al., 2003; Okonkwo et al., 2016).

4.4. Lignans and coumarins derivatives

Aside flavonoids and fatty acids, lignans and coumarins derivatives are two widely documented phytoconstituents in the *Landolphia* genus (Fig. 4). To date, lignans and coumarins have been reported in only five

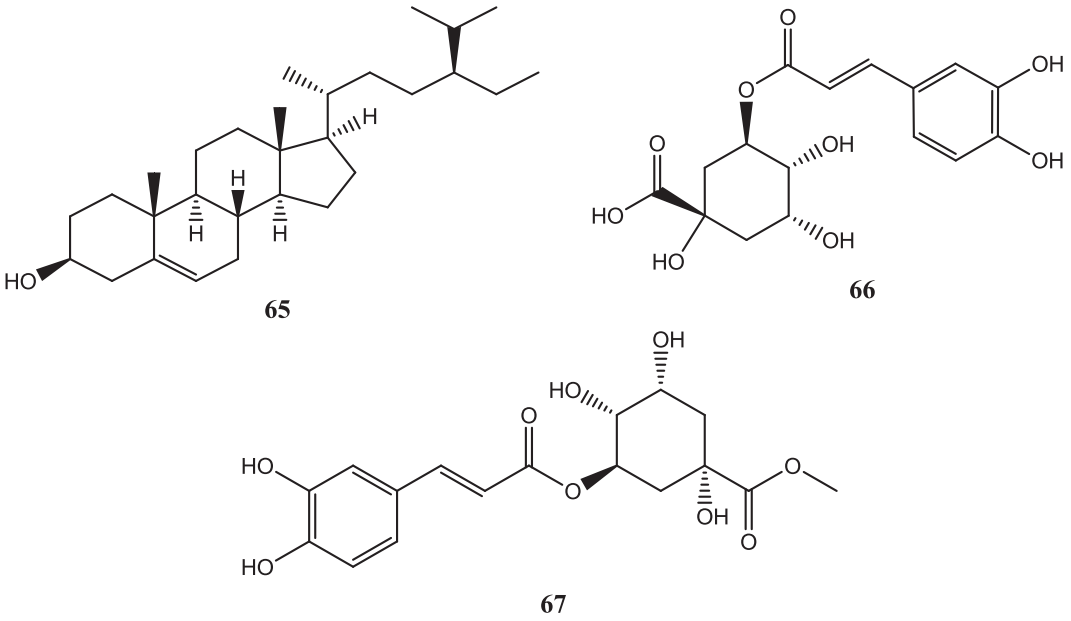

Fig. 3. Some of the terpenoids in *Landolphia* species.

species, these are *L. kirkii, L. owariensis, L. dulcis, L. heudelotti* and *L. membranacea* (Staerk et al., 2004; Mireku et al., 2016). About seven lignans, sesquilignans, neolignans and coumarins compounds **(68–74)** were isolated from leaves of *L. heudelotti* and characterized via spectroscopic techniques. Out of these compounds, **69, 70, 73** and **74** were reported as either novel compounds or compounds isolated for the first time in *L. heudelotti*. These compounds exhibited significant antioxidant (*in vitro*), antidiabetic and anti-inflammatory activities (Mireku et al., 2017). There is a significant difference between inhibitory activities exhibited by **68, 71** and **72,** and this could be linked to solvent polarity used for extraction, geographical location of where plant sample was collected or harvest time or time of sample collection (Mireku et al., 2016; Okonkwo et al., 2016).

4.5. Volatile components

There are a small number of volatile compounds isolated from the genus *Landolphia*, however, about thirty-three compounds were fully documented **(75 – 104)**. The volatile compounds **(75–100)** were obtained from fruit extract of *L. heudelotii*, whereas compounds **75** and **76** were reported as the major volatile constituents (Fig. 5). Despite this, therapeutic or curative potency of these constituents are not fully documented. Similarly, volatile concentrate of fruit of *L. Senegalensis* gave **75** and **89** as major constituents. The volatile constituents **75, 82, 84, 85, 89** and **100** were also obtained from other *Landolphia* species most especially, extracts of similar solvent polarity or time of sample or plant materials collection (Pélissier et al., 1996).

5. Pharmacological properties

Therapeutic potency exhibited by plants or herbal products could be due to the presence of diverse chemical constituents present in different parts (Kalimuthu et al., 2010; Oladeji et al., 2022a; 2022b; Oluyori et al., 2022). In tropical regions, *Landolphia* genus is a commonly used herbal medicine as detoxifier and antidote for malaria. Modern pharmacological appraisals have authenticated its aphrodisiac, anti-microbial, anti-ulcer and gastric anti-secretory, anti-trypanosomal, anti-diarrhoeal, antiplasmodial, antipyretic, anti-inflammatory, analgesic, cytotoxic and antiproliferative activities (Table 4). The distinct therapeutic appraisals are based on the ethnopharmacological beliefs (Liu, 2003). Furthermore, fractions, crude extracts and isolated metabolites from *Landolphia* spp. have been exhibited a wide range of medicinal properties. The therapeutic potencies of an assortment of pharmacological properties are thoroughly investigated (Fig. 5).

5.1. Aphrodisiac activity

The urge to improve sexual performance in mankind has been viewed as enormous tasks that required urgent consideration. Till date, few studies have assessed the effects of different parts of the genus *Landolphia* on sexual performance in animals. The first investigation of aphrodisiac activity of leaves of *L. dulcis* was first reported by Ilodigwe et al., The ethanolic extracts, n-hexane, methanolic and ethyl acetate fractions were orally administered at a daily dose of 500 and 1000 mg/kg body weight in male Swiss albino rats for five consecutive days (group XA_1, to XA_4, YA_5, to YA_8 each containing five male albino rats). Similarly, about forty-five female albino rats were treated with estradiol benzoate and 10 μg/100 g progesterone and distributed into nine groups. After treatment, at $p < 0.05$, the extract and fractions significantly increase the serum testosterone concentration, ejaculation, mount and intromission frequency was observed in group X and Y male albino rats. However, mounting and intromission frequency was dose-dependent with pronounced performance evident in group Y. The decline in intromission and protracted ejaculation was considerably higher in control rats (Ilodigwe et al., 2012).

5.2. Antimicrobial activity

The most assessed pharmacological activity in this genus is the antimicrobial screenings of crude extracts, fractions or isolated compounds of *Landolphia* species. The antibacterial activity of the root of *L. owerienesis* was first assessed by Okeke et al., (2001). The inhibitory (*in vitro*) potential of ethanolic and aqueous root and root-bark extracts were appraised in *Bacillus subtilis* (ATCC 6051), *Pseudomonas aeruginosa* (ATCC 10145), *Staphylococcus aureus* (ATCC 12600) and *Escherichia coli* (ATCC 11775) using macro-broth dilution (MBD) and agar-well diffusion assay (AWD). The extracts exhibited prominent inhibitory activities against *P. Aeruginosa* and *S. aureus,* though, no observable activity was shown against *B. subtilis* and *E. coli.* The minimum inhibitory concentration (MIC) demonstrated by gentamycin (0.125–8.0 g/ml) was significantly lower than that of ethanolic extracts in AWD (0.78–50 mg/ml) and MDB (0.39–50 mg/ml). Furthermore, concentrations (20–2000

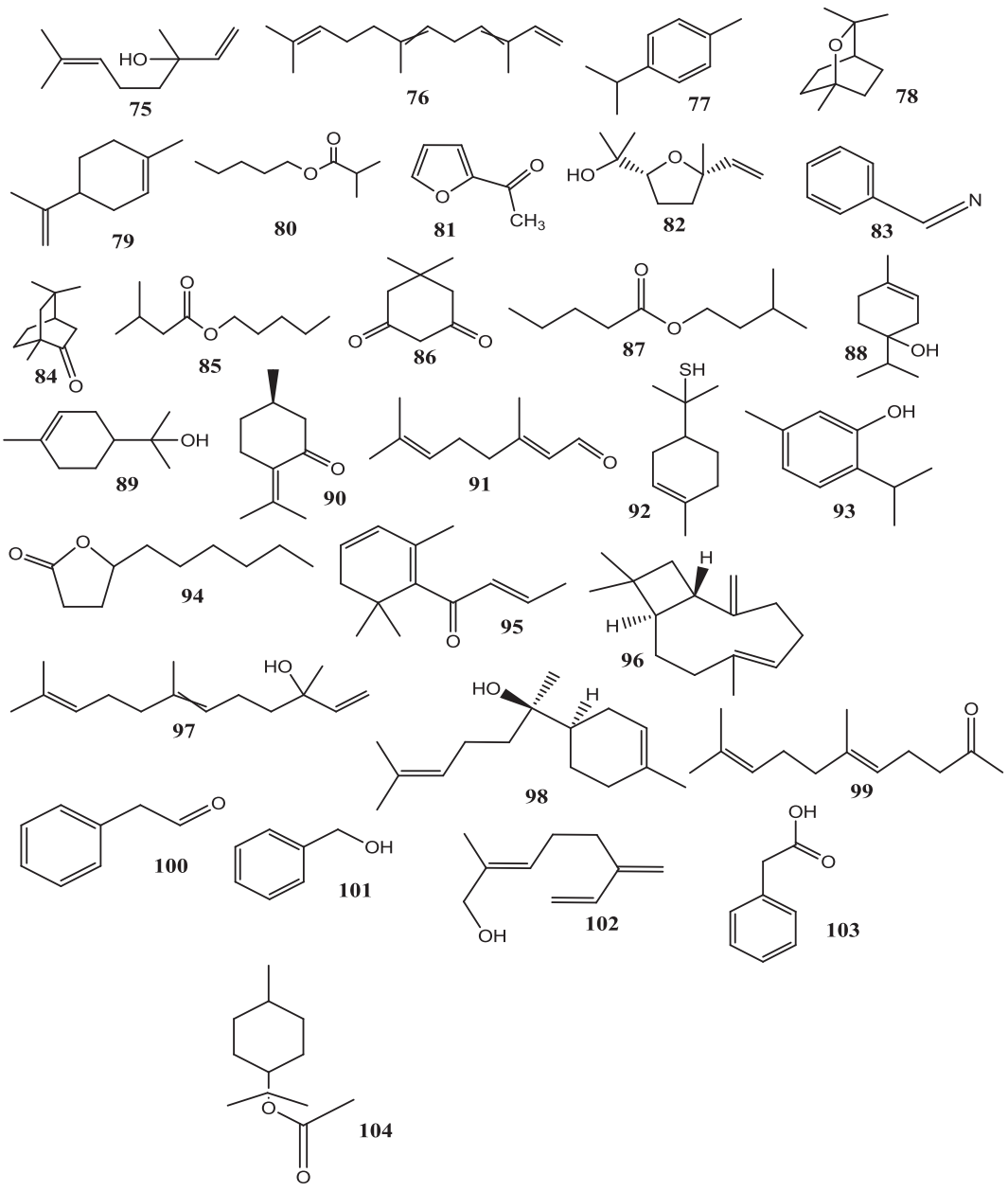

Fig. 4. Some of the major volatile constituents in *Landolphia* species.

mg/ml) of ethanolic leaves extract were assessed on clinical isolates of *Staphylococcus* sp., *Proteus* sp. and *E. coli* using Decosahexanoic acid assay (DHA). At low concentrations, the extracts significantly inhibited the pathogenic isolates with prominent inhibitory activities of *E. coli* (1800 mg/ml), *Proteus* sp. (1000 mg/ml) and *Staphylococcus* sp. (700 mg/ml) (Nwaogu et al., 2007).

The alkaloid and saponins assessed in ethanolic and aqueous bark, leaves and root extracts of *L. dulcis* demonstrated noticeable inhibitory activities at 20 mg/ml (Akharaiyi and Boboye, 2009). The first antibacterial appraisal of *L. owariensis* seed was done by Nwokonkwo, (2014). In this study, aqueous extracts significantly inhibited bacterial isolates with MIC of *C. albicans* (16.5 mg/ml), *P. Aeruginosa* (25 mg/ml), *S. faecal* (50 mg/ml) and *E. coli* (100 mg/ml); equally, the MIC observed is between 16 mm and 30 mm. Ethanolic root and leaves extracts of *L. owariensis* demonstrated strong inhibitory activities at 150–2500 μg/ml and 20–2000 μg/ml assessed via DHA. The root extracts showed strong IC_{50} of *Staphylococcus* sp. (340 μg/ml), *Proteus* sp. (320 μg/ml), *E. coli* (1560 μg/ml) while leaves extracts activities include *Staphylococcus* sp. (20 μg/ml), *Proteus* sp. (200 μg/ml) and *E. coli* (550 μg/ml) (Nwaogu et al., 2008).

5.3. Antiulcer and gastric antisecretory effects

Few studies have assessed the antiulcer and antisecretory effects of *Landolphia* species in experimental animals. Till date, only the *in vivo* antiulcer activities of extracts, fractions or isolated compounds from this genus have been reported. The global laboratory initiative and passive laboratory initiative models assessed the gastric acid secretion and ulceration in HC1/ethanol- induced gastric and gastric lesions induced male albino rats using cimetidine as control. The induced rats were treated by oral administration of 100 mg/kg and 200 mg/kg aqueous extract of *L. owarensis* leaves for 14 days. The aqueous extracts significantly reduced gastric acid secretion (43.8–55.27 %) in the two body weights, while chloroform extract reduced the secretion from 14.77 to 23.07 %. The reduction observed in gastric acid secretion intensifies production of gastric mucus. The extracts significantly reduced the

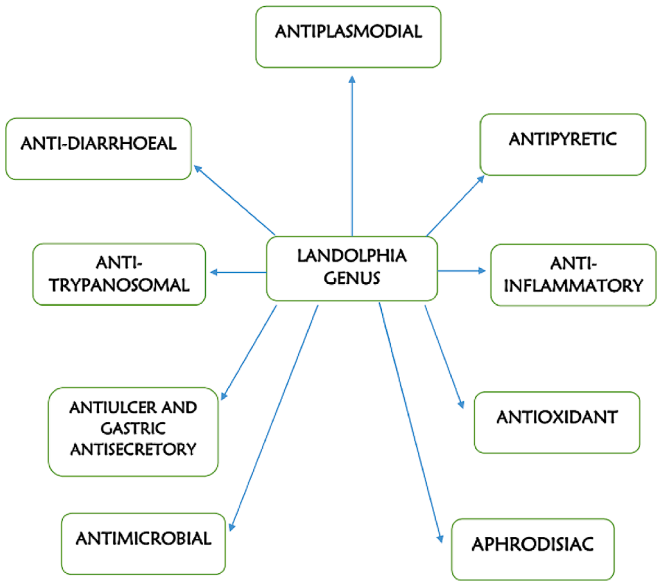

Fig. 5. Pharmacological effects exhibited by the genus *Landolphia.*

induced PLI gastric in the pylorus ligated rats; however, cimetidine reduction was significantly lower to activity exhibited by the extracts (Olaleye et al., 2008).

5.4. Anti-trypanosomal activity

Despite the diverse therapeutic applications of *Landolphia*, the anti-trypanosomal activities have not been fully documented. Anti-trypanosomal appraisals of bark, root and leaves of *L. uniflora* were investigated *in vitro* and *in vivo* in albino rats. The methanolic extracts exhibited pronounced *in vitro* inhibitory activity against *Trypanosoma brucei* at MIC of 1 mg/ml, however, inhibition shown by chloroform bark and leaf extracts were observed at MIC of 2 and 4 mg/ml. Likewise, methanolic leaf extract exhibited strong *in vivo* parasitaemia eradication after 10 days treatment. This prolong the survival time of the rats at 200 and 300 mg/kg body weight (Atawodi and Alafiatayo, 2007).

5.5. Anti-diarrhoeal activity

The anti-diarrhoeal activity of mature leaves of *L. owariensis* was assessed on *Salmonella typhi, Shigella dysentriae* and *E. coli* at concentrations of 125–2000 μg/ml. At 2000 μg/ml, the isolated compounds exhibited noteworthy ZOI against *S. typhi* (32 mm), *E. coli* (25 mm) and *S. dysentriae* (20 mm). The isolated compound was identified as *cis*-9-octadecenoic acid which demonstrated dose-dependent inhibitory activities. However, no activity was observed against the isolates at 125 μg/ml (Tannaz et al., 2010; Garba and Garba, 2017).

5.6. Antiplasmodial activity

Few studies have appraised the *in vitro* and *in vivo* antiplasmodial potencies of different *Landolphia* species in experimental animals. Till date, few studies have appraised the antimalarial potential of different parts of *L. dulcis, L. owariensis* and *L. heudelotii.* The early, established and residual parasitaemia infections were assessed in *P. Berghei* infected albino rats using different dose concentrations of ethanolic extract (LOEE), ethyl acetate (LOEF), methanolic (LOMF) and n-hexane (LOHF) (200, 400, 800 mg/kg) fractions of *L. owariensis.* After treatment for 14 days, the fractions considerably suppressed the parasitaemia infections, with activities (suppressive) of 29–86 % (early), 18–95 % (established) and 75–96 % (r+/esidual). The 50 % effective dose for suppressive activities is 514.93 mg/kg (LOHF), 392.95 mg/kg (LOEF), 266.56 mg/kg (LOE) and 165.70 mg/kg (LOMF). The post 30- days' survival index of the treated rats appraised is 50–83.3 % (LOMF), 16.7–66.7 % (LOEF), 16.7–50 % (LOE) and 16.7 % (LOHF). The extract considerably improved the weight and decreased the mortality rate of administered rats (Ezike et al., 2016).

The antiplasmodial assessment of *L. heudelotii* leaves was analysed in human blood infected by chloroquine sensitive-(NF54) and chloroquine resistant (K1) plasmodium strains. Assessments of aqueous extract at trophozoïtes stage exhibited strong IC_{50} activities against NF54 (7 ± 0.14 μg/ml) and K1 (8.11 ± 0.65 μg/ml). However, ethanolic extracts considerably inhibited the plasmodium strain with IC_{50} activities of NF54 (5 ± 1.77 μg/ml) and K1 (18 ± 0.51 μg/ml) (Kipré et al., 2018).

5.7. Antipyretic activities

Fever suppressing potential of stem-bark of *L. buchananii* collected from Mbeere, Kenya was assessed in Swiss albino mice (SAM) using pyrexia inducing agent (20 % turpentine solution) and aspirin. In this study, SAM was grouped into reference, normal, negative and experimental each containing five test organisms. After treatment, bark extract significantly reduced elevated rectal temperature from 0.32 to 2.52 % compared to 1.70 to 2.32 % reduced by aspirin (Nthiga et al., 2016).

5.8. Anti-inflammatory activities

In folk medicine, *Landolphia* species have been well documented for the inhibitory activity to body reactions in detrimental stimuli such as irradiation or metabolic disorder (Son, 2017b). However, few studies have reported the anti-inflammatory potential of the genus in suppressing reactive oxygen species and production of nitrous oxide in animals (Ninh, 2019). The scavenging effects of methanolic, chloroform and aqueous extracts of *L. owariensis* leaves were appraised in paw edema carrageenan and nociception induced rats. The rats were infested by Tail immersion. At $p < 0.05$, methanolic extract significantly reduced paw edema carrageenan in rats, however, nociception in rats was reduced by methanolic and chloroform extracts (Owoyele et al., 2001).

5.9. Antioxidant activities

The scavenging potential of *Landolphia* species have been assessed using 2,2-diphenyl-1-picrylhydrazyl (DPPH), Total antioxidant capacity (TAC), 2,2′ –azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) and ferrulic reducing antioxidant potential. The anti-hypertension potential of aqueous and hexane extracts of *L. owariensis* leaves was appraised using DPPH and ABTS. The extracts reduce the production of nitrous oxide with pronounced activities observed at 0.25 to 4.0 mg/ml (87.7 % inhibition), however, at 4.0 mg/ml, captopril significantly displayed 90.07 %. The inhibitory activities demonstrated by the extracts could be linked to total phenolic content (TPC) appraised in aqueous (154.02 mg.GAE/g) and hexane (13.05 mg.GAE/g) extracts (Nwaji et al., 2016). TAC and DPPH free radical scavenging in methanolic extract of *L. heudelotti* root displayed IC_{50} of 108.8 ± 14.52 mg/g and 6.956 ± 0.8121 μg/ml. The activity displayed by the extract could be due to TPC (98.14 ± 14.70 mg/g) appraised (Mireku et al., 2017).

6. Toxicological profile

Medicinal plants and plant-derived drugs or products have long been documented as the bedrock for a diversity of treatments in humans. Since time immemorial, herbs or herbal drugs has been used for the treatment of several critical or life threatening diseases and pharmacological studies have verified its function in the inhibition of innumerable pathogenesis (Sain et al., 2022). The cytotoxicolgical studies of medicinal plants validate its authenticity and safety profile. The cytotoxicity of methanolic extract of *L. owariensis* leaves (250 mg/kg) was assessed on liver, serum and kidney of albino rats. After 12 days, no significant

Table 4
Pharmacological activities of *Landolphia* genus.

S/n	Plant	Parts used	Country	Ethnomedicinal use	Solvent used	Pharmacological activity	Model used	Phytochemicals	References
1	*L. dulcis*	leaves, bark and roots	Nigeria		Aqueous and ethanol	Antibacterial	Pathogenic bacteria isolates	Saponins and alkaloids	Akharaiyi and Boboye, 2009
2	*L. owerrience*	bark	Nigeria	Nutraceutical for the management of neurodegeneration	Ethanol	Antioxidant	Adult male Wistar rats		Oyinbo et al., 2016
3	*L. heudelotii*	leaves	Côte d'Ivoire	To treat malaria and fever	Ethanolic and aqueous	Antiplasmodial	NF54 and K1 *Plasmodium falciparum* strain	Polyterpenes and sterols, Polyphenols, Flavonoids and Alkaloids	Kipré et al., 2017
4	*L. dulcis*	Roots	Nigeria	For sex enhancement naturalRemedies	Ethanol	Aphrodisiac	male albino rats	Alkaloid, Saponin,	Ilodigwe et al., 2012
5	*L. heudelotti*	roots	Ghana	For the treatment of enteritis, gastric ulcers and stomach cramps	Methanol and chloroform	antioxidant		Lignan, neolignans, sesquilignans, a coumarin and an aromadendranesesquiterpene	Mireku et al., 2016
6	*L. owerrience*	roots, root-barks and root-woods	Nigeria	Treatment of diseases of known bacterial aetiology	Ethanol and aqueous	Antibacterial	Bacterial strains	Steroidal cardiac and cynagenetic glycosides	Okeke et al., 2001
7	*L. owerrience*	Seeds	Nigeria	Cure for malaria and gonorrhoea	Ethanol	Antimicrobial	Clinical isolates	Glycosides, saponins and phenols	Nwokonkwo et al., 2014
8	*L. owerrience*	Leaf	Nigeria	Vermifuge and enema for intestinal worms	Aqueous, methanol and chloroform	Anti-inflammatory and analgesic	Adult male and female Swiss miceand albino rats	Alkaloids and some polyphenolic compounds	Owoyele et al., 2001
9.	*L. owerrience*	Leaf	Nigeria	Purgative and to cure malaria	Aqueous, methanol and chloroform	Antiulcer and gastric antisecretory	Gastric lesion induced and Pylorus ligation-induced Wistarrats-		Olaleye et al., 2008
10.	*L. owerrience*	Leaf and root	Nigeria	Purgative and to cure malaria	Ethanol	Antimicrobial	Bacterial strains	Tannins, cyanogenic glycosides	Nwaogu et al., 2008
11.	*L. buchananii*	stem bark	Kenya	Relieve backaches and joint pains	Methanol	Antipyretic	Wistar albino rats, Rattusnorvegicus	Steroids, saponins, cardiac glycosides, terpernoids	Nthiga et al., 2016
12.	*L. owariensis*	Leaf	Nigeria	Treat gonorrhoea infection	Ethanol	Antimicrobial	Bacterial isolates	Alkaloids, flavonoids, tannins and saponins	Nwaogu et al., 2007
13.	*L. uniflora*	Leaves, stem and root bark	Nigeria	Treat piles and fever and snake bite	Petroleum ether, chloroform, methanol and aqueous	Antitrypanosomal	Mice	Steroids and triterpenes, resins, tannins, saponins and flavonosides	Atawodi and Alafiatayo, 2007
14.	*L. owariensis*	fruit	Nigeria	Vermifuge, venereal Infections	Methanol, ethyl acetate, chloroform, hexane	Antimicrobial	Fungi and bacteria isolates	Cyanogenic glycosides, alkaloids,saponins, steroids and triterpenes	Siombor and Anyam, 2015
15.	*L. owariensis*	fruit	Nigeria	Treatment of veneral diseases and tooth cleaning	Ether, ethylacetate and nbutanol	Antimicrobial	Fungi and bacteria isolates	Steroids, saponins, tannins and saponins	Ebi and Ofoefule, 1997
16.	*L. lanceolata*	Fruit	Nigeria		Ethanol	Antioxidant		Flavonoids, saponins, alkaloids, terpenoids, tannins, triterpenoids	Chibuzo et al., 2018
17.	*L. owariensis*	Leaf	Nigeria	Treat malaria and as a purgative	Hexane, ethyl acetate and methanol	Antiplasmodial	*Plasmodium berghei*-infected mice	Alkaloids, flavonoids, saponins and tannins	Ezike et al., 2016
18.	*L. owariensis*	Leaf	Nigeria	For the treatment of hypertension	Ethanol, methanol, water, hexane and acetone	Antioxidant and angiotensin		Gallic acid, p-coumaric acid, quercetin and apiginine	Nwaji et al., 2016
19.	*L. owariensis*	Leaf	Nigeria	Treatment of diarrhoeal	Ethyl acetate	Anti-diarrhoeal	Bacterial isolates	Cis-9-octadecenoic acid	Garba and Garba, 2017

Table 5
The nutrient compositions of Landolphia (Marracuene, 2008; Nwaogu and Igwe, 2010; Bassey, 2012).

Nutrients	*L. membranacea* leaves	*L. owerrience* seed pulp	*L. kirkii* fruit
Moisture content (%)	75.5	–	–
Ash (mg/kg)	5.33	–	2.9 ± 0.0
Protein (mg/kg)	8.74	11.85 ± 0.4	2.1 ± o.20
Fibre (mg/kg)	8.33	3.5 ± 0.30	–
Fat (mg/kg)	13.95	17.40 ± 0.20	0.9 ± 0.1
Carbohydrate (mg/kg)	65.55	52.40 ± 0.4	–
Potassium (mg/kg)	448.00	205.04 ± 0.15	–
Sodium (mg/kg)	100.00	48.02 ± 0.20	–
Magnesium (mg/kg)	240.00	2.91 ± 0.05	–
Calcium (mg/kg)	240.00	110.20 ± 0.10	–
Phosphorus (mg/kg)	250.00	20.08 ± 0.05	–
Iron (mg/kg)	129.00	9.50 ± 0.40	–
Oxalic acid/oxalate (mg/100 g)	580.80	56.01 ± 0.02	–
Phytic acid/phytate (mg/100 g)	43.36	48.15 ± 0.05	–
Tannins (mg/100 g)	2.93	–	–
Cyanogenic glycoside (mg/100 g)	–	33.20 ± 0.01	–

variations was observed in acid and phosphate level of liver, serum and kidney, however, increase in serum enzyme activity was observed (Ilesanmi et al., 2011). Likewise, haematological parameters of experimental rats were unaltered after 14 days treatment with aqueous and ethanolic extract of *L. dulcis* leaves (Akharaiyi and Boboye, 2015). Biochemical effects of methanolic extract of *L. owariensis* leaves on liver function of Wister strain albino rats was evaluated. After 15 days treatment, no variation was observed in albumin, total protein concentration and serum activity of ALT, AST and ALP, however, there were significant decreases in haemoglobin and bilirubin concentrations (Nwogu et al., 2008). Aqueous extract of *L. owariensis* bark showed no biochemical and histological effects on rats, but, extract significantly reduced the biochemical and histological neurodegeneration of cerebellar cortex and NF-IR was induced in Purkinje cells after four days treatment (Oyinbo et al., 2016).

7. Nutritional properties

According to few nutritional studies of the genus *Landolphia*, virtually all parts of *Landolphia* species contain essential nutrients, minerals and antinutrients. The leaves and bark are abundant in minerals such as sodium, calcium, potassium, iron, phosphorus and magnesium (Nwaogu and Igwe, 2010). *Landolphia* contains high amount of antinutrients such as oxalic acid, tannins and phytic acid (Bassey, 2012). Phytochemicals such as flavonoids, tannins, alkaloids, anthraquinones, terpenoids and reducing sugar are present along with *p*-coumaric acid, asteoside, corymesidone, isorhamnetin-diglycoside and caulerpin (Ogbuagu et al., 2012). *Landolphia* has a reasonably low calorific significance and can be dietary supplement in treatment of obesity (Nwaogu and Igwe, 2010). A research evaluated that leaves of *L. membranacea* (Stapf) contain around 75.5 % moisture, 13.95 % crude fat, 5.33 % ash, 8.74 % protein, 8.33 % crude fibre and 65.5 % carbohydrate (Bassey, 2012).

Landolphia has assortment of minerals that are fundamental for growth and development in living organisms. Calcium is an important mineral essential for human proper growth and bone development. It is established that 8 oz of milk can give 300–400 mg, *Landolphia* leaves provide 300–400 mg, *L. membranacea* (Stapf) can provide 240 mg (Bassey, 2012). Most *Landolphia* species can substitute for iron tablets, therefore, can be used for the treatment of malaria, inflammation and anaemia. It is assessed that *L. membranacea* (129.00 mg) and *L. owerrience* (9.50 ± 0.40 mg) contain more iron than Moringa (0.85 mg). The aphrodisiac activity of *Landolphia* could be due to high dietary zinc in the leaves, and could also be responsible for proper growth of sperm cells. High crude fibre in *Landolphia* supports absorption and digestion of food, low fat content enhances storage capacity, high carbohydrate content is responsible for energy supplier or booster. A complete list of nutrients appraised in *Landolphia* species are shown in Table 5.

8. Conclusion and future prospects

Plants and its products are essential in the drug discovery stratagems and could be regarded as scaffold in the development of new drugs or pharmacophores with marked health benefits. One of these plants with considerable biological activities is *Landolphia* species with a number of documented folkloric uses in primary health care systems. From the reviewed literatures, it could be induced that information on the phytochemical and pharmacological activities of the genus *Landolphia* are inadequate. Similarly, the reports on the nutritional assessments of this genus is limited, hence, further investigation the nutritional and proximate analyses of the genus is foreseeable. Several folkloric uses of the genus *Landolphia* have been documented for the treatment of gastric ulcers, dermal infections, malaria, diabetes, cholera, inflammation, gonorrhoea, obesity, enteritis, stomach cramps and sex enhancement remedy, however, scientific authentications of these reported biological activities needs more scrutiny. This could help validate and bridge the gaps between the reported traditional uses and authenticated scientific applications. From the reviewed literatures, leaves, flower, roots, seeds and bark of the genus *Landolphia* have significantly inhibited or suppressed early or established infections; hence, further studies on the isolation of bioactive compounds which could be responsible for these significant therapeutic potencies should be given prompt attention. This genus is indigenous to the tropical Africa and could boost national economy and improve human health and wellbeing if the plants are properly monitored and conserved.

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Oluwole Solomon Oladeji: Conceptualization, Investigation, Methodology, Resources, Software, Writing – original draft, Writing – review & editing. **Abimbola Peter Oluyori:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing. **Adewumi Oluwasogo Dada:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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