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Linking phytochemistry to traditional uses and pharmacology of an underexplored genus – *Psydrax*: a review

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Abstract The genus *Psydrax* is one of the ethnomedicinally important genera of the Rubiaceae family which has only received a limited scientific attention, despite coming from a pharmacologically and phytochemically important plant family. The genus has found applications in ethnomedical management of diabetes, stomach disorders, inflammations, cardiovascular diseases, epilepsy, wounds, malaria and fever. To unveil knowledge gaps, stimulate research interest and unravel opportunities for drug discovery from the genus *Psydrax*, we have carried out an extensive review on its traditional applications, phytochemistry and pharmacology for the first time. Literature on these topics was obtained from Google Scholar, Pubmed and ScienceDirect journal articles published from 1788 to September, 2021. Only articles written in English were reviewed. While several species of *Pysdrax* used in traditional medicine have not been chemically explored for drug discovery, over a hundred secondary metabolites have so far been identified in few species of the genus, and majority of these chemotaxonomic markers are iridoids. Bioactive extracts and some isolated constituents of *Psydrax* species have shown various in vitro and in vivo pharmacological properties including anti-hyperglycemia, anti-inflammatory, anticonvulsant and antimicrobial, and thus, support some of the ethnomedical uses of the plants. For an evidence-informed application of the genus, *Psydrax*, in traditional medicine, more ethnobotanical surveys, elaborate in vivo pharmacological assays, in-depth toxicity and holistic phytochemical studies are required to fully exploit more species of the genus prior to future clinical studies. Following documented traditional uses of *Psydrax* species, the deliberate cultivation of medicinal plants under this genus is recommended for sustainability in medicinal plant utilization.

Keywords Psydrax · Phytochemistry · Ethnopharmacology · Traditional medicine · Pharmacology

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Introduction

The Rubiaceae plant family has served as an important source of bioactive compounds and "leads" for drug discovery and development (Buathong et al. 2019; Koehbach et al. 2013; Maldonado et al. 2017; Wijnsma and Verpoorte 1986). While other genera within the Rubiaceae family have received considerable research attention as well as reviews on their species (Fan et al. 2020; Gibbons 2020; Heitzman et al. 2005; Kala 2015; Taher et al. 2020) which has stimulated further research, *Psydrax* genus has been underexplored scientifically; the genus has not been previously reviewed to reveal knowledge gaps and provide opportunities for further studies.

The genus name, *Psydrax* Gaertn., originally introduced, in 1788, by Joseph Gaertner in his book (Gaertner 1788) was abandoned until A. Richard included it in one of his papers in 1830, and was later reinstated by Bridson in 1985 (Bridson 1985). It belongs to the Vanguerieae tribe of the Rubiaceae family and is subdivided into two subgenera, the palaeotropical subgenus *Psydrax*, which exists as trees, shrubs or sometimes as scandent, and the African subgenus *Phallaria*, which exists as lianas or scandent shrubs (Bridson 1986, 1985). In this review, the common name *Psydrax,* would be adopted for the two subgenera, *Phallaria* and *Psydrax.* The full lineage of the genus, according to the *NCBI taxonomy* database, is shown in Table 1.

While *Psydrax* is known to be monophyletic (Bremer 2009; Lantz and Bremer 2004), with defined morphological characters, it still shares most of its characters with *Keetia* (Bridson 1985; Lantz et al. 2002; Lantz and Bremer 2004), which is a closely related genus also transferred from *Canthium*) and its circumscription is somehow problematic, with species more readily added to it (Davis et al. 2007). However, the Southern African *Canthium* s. str. (the remaining part of *Canthium* after the reinstatement of *Psydrax* and *Keetia*) and *Psydrax* can be distinguished distinctively by the anatomical features of their leaves and young stems (Tilney et al. 1990, 1988), while *Keetia* can be distinguished morphologically from *Psydrax* by its pyrene, anther and carlyx-limb (Bridson 1986; Lantz et al. 2002). *Psydrax* species go with varying synonyms which are adopted by different authors, and their number keeps increasing as new species, which are yet to be included in *The Plant List* database, are being discovered (Arriola and Alejandro 2013; Arriola et al. 2017; Mahyuni et al. 2019). In 2020, a new species, *P. gialaiensis*, was discovered in Gia Lai Province, Southern Vietnam (Quang et al. 2020) and has been uploaded on the website of the *World Checklist of Selected Plant Families(WCSP)* alongside another new species, *Psydrax lanceolatus.*

As the largest and widest geographically distributed genus of Vanguerieae tribe (Lantz et al. 2002; Lantz and Bremer 2004), *Psydrax* is reportedly found in three continents, Africa, Asia and Oceania. According to the *WCSP* (wcsp.science.kew.org), accessed on 22 September, 2021, 130 species are included in the genus, as listed with their continental distributions in Table 2. However, two species, *P. horizontale* and *P. hullensis,* were missing in *WCSP* database, but were included in *Tropicos* and *The Plant List* databases, and eight names out of the 130 species' names in the *WCSP* database were unaccepted. Bridson and other group of researchers (Bridson 1985; Lantz et al. 2002) reported that more than thirty species of the genus are

Table 1 Taxonomic Ranking of *Psydrax*

Rank	Name
No Rank	Cellular Organisms
Superkingdom	Eukaryota
Kingdom	Viridiplantae
Phylum	Streptophyta
Subphylum	Streptophytina
Clade	Embryophyta
Clade	Tracheophyta
Clade	Euphyllophyta
Clade	Spermatophyte
Class	Magnoliopsida
Clade	Mesangiospermae
Clade	Eudicotyledons
Clade	Gunneridae
Clade	Pentapetalae
Clade	Asterids
Clade	Lamiids
Order	Gentianales
Family	Rubiaceae
Subfamily	Ixoroideae
Tribe	Vanguerieae
Genus	*Psydrax*

Table 2 A list of species in *Psydrax* genus compiled from *World Checklist of Selected Plant Families* (WCSP) and *The Plant List* databases

S/N	Species	Author	Date of discovery	Continental distribution
1	***Psydrax acutiflora***	(Hiern) Bridson	1985	Africa
2	***Psydrax ammophilus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
3	***Psydrax amplifolius***	(Elmer) A.P. Davis	2008	Asia
4	***Psydrax angustifolius***	A. Rich. ex DC	1830	
5	***Psydrax ankotekonensis***	(Cavaco) A.P. Davis & Bridson	2007	Africa
6	*Psydrax approximates*	(Korth.) Mahyuni & K.M. Wong	2018	Asia
7	***Psydrax arnoldianus***	(De Wild. & T. Durand) Bridson	1985	Africa
8	***Psydrax attenuatus***	(R. Br. ex Benth.) S.T. Reynolds & R.J.F. Hend	2004	Oceania
9	*Psydrax attenuatus var. attenuatus*			Oceania
10	*Psydrax attenuatus fo. megalanthus*	S.T. Reynolds & R.J.F. Hend	2004	Oceania
11	***Psydrax attenuatus fo. myrmecophilus***	S.T. Reynolds & R.J.F. Hend	2004	
12	***Psydrax attenuatus var. myrmecophilus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
13	*Psydrax attenuata var. tenellus*	S.T. Reynolds & R.J.F. Hend	2004	Oceania
14	***Psydrax austro-orientalis***	(Cavaco) A.P. Davis & Bridson	2007	Africa
15	***Psydrax banksii***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
16	***Psydrax bathieanus***	(Cavaco) A.P. Davis & Bridson	2007	Africa
17	***Psydrax bridsonianus***	Cheek & Sonké	2004	Africa
18	***Psydrax calcicola***	(Craib) A.P. Davis	2008	Asia
19	*Psydrax capensis*	J.C. Manning & Golblatt		Africa
20	***Psydrax connatus***	De Wild. & T. Durand	1900	
21	***Psydrax cymiger***	(Valeton) S.T. Reynolds & R.J.F. Hend	2004	Oceania
22	***Psydrax dicoccos***	Gaertn	1788	Asia
23	***Psydrax dicoccos var. dicoccos***			Asia
24	***Psydrax dicoccos var. lanceolatus***	(Arn.) Ridsdale	1996	Asia
25	***Psydrax dicoccos var. obovatifolius***	(G.A.Fu) Lantz	2011	Asia
26	***Psydrax dunlapii***	(Hutch. & Dalziel) Bridson	1985	Africa
27	***Psydrax esirensis***	(Cavaco) A.P. Davis & Bridson	2007	Africa
28	***Psydrax fasciculatus***	(Blume) A.P. Davis	2008	Asia
29	***Psydrax faulknerae***	Bridson	1985	Africa
30	***Psydrax ficiformis***	(Hook. f.) Bridson	1993	Asia
31	***Psydrax forsteri***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
32	***Psydrax fragrantissimus***	(K.Schum) Bridson	1985	Africa
33	*Psydrax gialaiensis*	B.H. Quang, T.B. Tran &V.S. Dang	2020	Asia
34	***Psydrax gilletii***	(De Wild.) Bridson	1985	Africa
35	*Psydrax glaber*	(Blume) Deb & M. Gangop	2012	
36	***Psydrax graciliflorus***	(Merr. & L.M. Perry) S.T. Reynolds & R.J.F. Hend	2004	Oceania
37	***Psydrax grandifolius***	(Thwaites) Ridsdale	1996	Asia
38	***Psydrax graniticola***	(Chiov.) Bridson	1985	Africa
39	*Psydrax gynochthodes*	(Baill.) Arriola, Axel H., Alejandro & Yayen	2014	Asia
40	***Psydrax horizontalis***	(Schumach.) Bridson	1985	Africa

Table 2 continued

S/N	Species	Author	Date of discovery	Continental distribution
41	***Psydrax johnsonii***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
42	***Psydrax kaessneri***	(S. Moore) Bridson	1985	Africa
43	***Psydrax kibuwae***	Bridson	1985	Africa
44	***Psydrax kingii***	(Hook. f.) Bridson & Springate	1996	Asia
45	***Psydrax kraussioides***	(Hiern) Bridson	1985	Africa
46	***Psydrax lamprophyllus***	(F. Muell.) Bridson	1985	Oceania
47	***Psydrax lamprophyllus fo. lamprophyllus***			Oceania
48	*Psydrax lamprophyllus fo. Latissimus*	S.T. Reynolds & R.J.F. Hend	2004	Oceania
49	*Psydrax lanceolatus*	(Arn.) R.Kr. Singh & Arigela	2020	Asia
50	***Psydrax latifolius***	(F. Muell. ex Benth.) S.T. Reynolds & R.J.F. Hend	2004	Oceania
51	***Psydrax laxiflorens***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
52	***Psydrax lepidus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
53	***Psydrax lividus***	(Hiern) Bridson	1985	Africa
54	***Psydrax locuples***	Bridson	1985	Africa
55	***Psydrax longipes***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
56	***Psydrax longistylus***	(Merr.) A.P. Davis	2008	Asia
57	*Psydrax lucidulus*	(Miq.) Mahyuni & K.M. Wong	2018	Asia
58	***Psydrax lynesii***	Bridson	1985	Africa
59	***Psydrax maingayi***	(Hook. f.) Bridson	1985	Asia
60	***Psydrax majus***	A. Rich	1830	
61	***Psydrax manambyana***	(Cavaco) A.P. Davis & Bridson	2007	Africa
62	***Psydrax manensis***	(Aubrév. & Pellegr.) Bridson	1985	Africa
63	***Psydrax martini***	(Dunkley) Bridson	1985	Africa
64	***Psydrax medius***	A. Rich. ex DC	1830	
65	***Psydrax micans***	(Bullock) Bridson	1985	Africa
66	***Psydrax moandensis***	Bridson	1985	Africa
67	***Psydrax moggii***	Bridson	1985	Africa
68	***Psydrax montanus***	(Thwaites) Ridsdale	1996	Asia
69	***Psydrax montigenus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
70	*Psydrax multiflorus*	Arriola, Axel H. & Alejandro	2017	Asia
71	***Psydrax mutimushii***	Bridson	1985	Africa
72	***Psydrax mutimushii subsp. mutimushii***			Africa
73	*Psydrax mutimushii subsp. wagemansii*	Bridson	1985	Africa
74	***Psydrax nitidus***	(Craib) K.M. Wong	1989	Asia
75	***Psydrax obovatus***	(Klotzsch ex Eckl. & Zeyh.) Bridson	1985	Africa
76	*Psydrax obovatus subsp. ellipticus*	Bridson	1985	Africa
77	***Psydrax obovatus subsp. obovatus***			Africa
78	***Psydrax occidentalis***	(Cavaco) A.P. Davis & Bridson	2007	Africa
79	***Psydrax odoratus***	(G. Forst.) A.C. Sm. & S.P. Darwin	1988	Oceania
80	*Psydrax odorata subsp. arnhemicus*	S.T. Reynolds & R.J.F. Hend	2004	Oceania
81	***Psydrax odoratus fo. Australianus***	S.T. Reynolds & R.J.F. Hend	2004	
82	***Psydrax odoratus subsp. australianus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania

Table 2 continued

S/N	Species	Author	Date of discovery	Continental distribution
83	***Psydrax odoratus fo. Buxifolius***	(Benth.) S.T. Reynolds & R.J.F. Hend	2004	Oceania
84	***Psydrax odoratus subsp. buxifolius***	(Benth.) S.T. Reynolds	2004	Oceania
85	*Psydrax odoratus fo. Foveolatus*	S.T. Reynolds & R.J.F. Hend	2004	Oceania
86	***Psydrax odoratus subsp. odoratus***			Oceania
87	*Psydrax odoratus fo. Parviflorifer*	S.T. Reynolds & R.J.F. Hend	2004	Oceania
88	***Psydrax odoratus fo. Subnitidus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
89	***Psydrax oleifolius***	(Hook.) S.T. Reynolds & R.J.F. Hend	2004	Oceania
90	***Psydrax pallidus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
91	***Psydrax palma***	(K. Schum.) Bridson	1985	Africa
92	***Psydrax paludosus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
93	***Psydrax paradoxus***	(Virot) Mouly	2006	Oceania
94	***Psydrax parviflorus***	(Afzel.) Bridson	1985	Africa
95	*Psydrax parviflorus subsp. chapmanii*	Bridson	1985	Africa
96	***Psydrax parviflorus subsp. melanophengos***	(Bullock) Bridson	1985	Africa
97	***Psydrax parviflorus subsp. parviflorus***			Africa
98	***Psydrax parviflorus subsp. rubrocostatus***	(Robyns) Bridson	1985	Africa
99	***Psydrax pendulinus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
100	***Psydrax pergracilis***	(Bourd.) Ridsdale	1996	Asia
101	***Psydrax polhillii***	Bridson	1985	Africa
102	*Psydrax puberula*	Arriola & Alejandro	2013	Asia
103	***Psydrax recurvifolius***	(Bullock) Bridson	1985	Africa
104	***Psydrax reticulatus***	(C.T. White) S.T. Reynolds & R.J.F. Hend	2004	Oceania
105	***Psydrax richardsiae***	Bridson	1985	Africa
106	***Psydrax rigidulus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
107	***Psydrax robertsoniae***	Bridson	1991	Africa
108	*Psydrax sabahensi*	Mahyuni	2019	Asia
109	***Psydrax salignus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
110	*Psydrax salignus fo. Filiformis*	S.T. Reynolds & R.J.F. Hend	2004	Oceania
111	***Psydrax salignus fo. Salignus***			Oceania
112	***Psydrax sambiranensis***	(Cavaco) A.P. Davis & Bridson	2007	Africa
113	***Psydrax schimperianus***	(A. Rich.) Bridson	1985	Africa and Asia
114	*Psydrax schimperianus subsp. Occidentalis*	Bridson	1985	Africa
115	***Psydrax schimperianus subsp. schimperianus***			Africa and Asia
116	***Psydrax sepikensis***	A.P. Davis	2008	Oceania
117	***Psydrax shuguriensis***	Bridson	1985	Africa
118	***Psydrax splendens***	(K. Schum.) Bridson	1985	Africa
119	***Psydrax suaveolens***	(S. Moore) S.T. Reynolds & R.J.F. Hend	2004	Oceania
120	***Psydrax subcordatus***	(DC.) Bridson	1985	Africa
121	***Psydrax subcordata var. connatus***	(De Wild. & T. Durand) Bridson	1985	Africa
122	***Psydrax subcordatus var. subcordatus***			Africa
123	***Psydrax suborbicularis***	(C.T. White) S.T. Reynolds & R.J.F. Hend	2004	Oceania

Table 2 continued

S/N	Species	Author	Date of discovery	Continental distribution
124	*P. sumatranus*	(Miq.) Mahyuni	2018	Asia
125	***Psydrax tropicus***	S.T. Reynolds & R.J.F. Hend	2004	Oceania
126	***Psydrax umbellatus***	(Wight) Bridson	1993	Asia
127	*Psydrax undulatifolius*	K.M. Wong & Mahyuni	2018	Asia
128	***Psydrax virgatus***	(Hiern) Bridson	1985	Africa
129	***Psydrax whitei***	Bridson	1985	Africa
130	*Psydrax wongii*	Mahyuni	2019	Asia

Names in bold imply presence in both *The Plant List* and *WCSP* databases, while names in plain imply presence only in *WCSP*

native to Africa, and these are not far from the *WCSP's* list of continental distribution of 54 species of the genus in different countries in Africa. Though, *Psydrax* is the largest genus in its tribe, some of its species are rare and at the verge of extinction (Cheek and Sonké 2004; Subashree et al. 2021), and their decreasing population may be ascribed to their traditional uses (Arriola et al. 2017; Tabuti et al. 2009, 2011).

Surprisingly, only about 8% of *Psydrax* species have been reported for their ethnomedicinal uses and pharmacological activities, with *P. subcordata* (DC.) Bridson having the highest coverage. In other words, close to 92% of this genus have not received scientific attention beginning from documentation of local knowledge on the genus via ethnopharmacological surveys, and the ethnomedicinal application of species within this genus in meeting primary healthcare needs. Across Africa, different parts of *P. subcordata* (DC.) Bridson are used in the treatment of varied health issues such as cardiovascular diseases, inflammation, stomach disorder, epilepsy, malaria and fever (Awah et al. 2012; Awantu et al. 2019; Chukwujekwu et al. 2005; Daanaa et al. 2018). *P. dicoccos,* found mostly in Asia, is used in folk medicine for rheumatoid pains and asthma (Kalaichelvi and Dhivya 2016; Neelima et al. 2011). *Psydrax* species have also found applications in ethnoveterinary medicine as wound healing and antiparasitic agents, in the treatment of ectoparasites, and as piscicide in fish farming (Maroyi 2012; Mukandiwa et al. 2012a, b; Nyahangare et al. 2015; Raja et al. 2011).

Phytochemical screening of few of the *Psydrax* species revealed that the major phytochemical class in these plants is the iridoid. Interestingly, iridoids have been reported to possess a number of pharmacological and biological activities, such as antimalarial, antidiabetic, antioxidant, antitumor, antibacterial, antiviral, anti-inflammatory, neuroprotective and cardioprotective effects (Ghisalberti 1998; Tundis et al. 2008). Plants rich in iridoids are also useful antidotes against arthritis, diabetes, tumor, fever, wounds, hypertension and other health conditions (Dinda 2019). Other secondary metabolites have also been identified in *Psydrax* including alkaloids, flavonoids and other terpenoids, and few pharmacological studies have been conducted to link the traditional uses of few species in this genus to the identified phytochemical contents.

This article reviews the ethnopharmacological uses, phytochemistry, and pharmacological properties of *Psydrax* genus from 1788 to September, 2021. The literature search was carried out using Google Scholar, PubMed and ScienceDirect digital repositories following the varied combination of these words: Rubiaceae, Psydrax, Canthium, "Traditional uses", "folkloric medicine", ethnopharmacology, bioactivities, "biological activities", "pharmacological properties", phytochemistry, "phytochemical constituents", phytochemicals. Only peer-reviewed articles written in english language were used by authors with the overall aim to inspire further studies on the genus, Psydrax, particularly its underexplored species.

Table 3 Ethnomedicinal applications of *Psydrax* species in Africa, Asia and Oceania

Species	Part Used	Method of Preparation (Administration)	Uses	Country	References
P. subcordata	SB	Alcoholic extract (NS)	Diabetes	NS	(Achenbach et al. 1981)
	SB	Decoction (NS)	Haemorrhoids, Stomach ulcer	Ghana	(Agyare et al. 2009)
		Paste (Oral)	Body pains		(Appiah et al. 2018)
		Paste (Topical)	Boils		
	NS	NS (NS)	Epilepsy	Cote d'Ivoire	(Daanaa et al. 2018)
	R	Aqueous extract (Oral)	Malaria	Nigeria	(Chukwujekwu et al. 2005)
	SB		Fever		
	R	NS (NS)	Fever		(Awah et al. 2012)
			Malaria, Inflammation, Cardiovascular diseases		
	WP	NS (NS)	Stomach disorders	Cameroon	(Awantu et al. 2019)
	B	Extract (NS)	High blood pressure	NS	(Achenbach 1986)
P. livida	Fr	Raw (Oral)	Food	South Africa	(Magwede et al. 2018)
	L	Paste (Topical)	Wounds in livestock	Zimbabwe South Africa	(Maroyi 2012; Mukandiwa et al. 2012a, b)
			Ecto-parasites in livestock	Zimbabwe	(Nyahangare et al. 2015)
	R	NS (NS)	Fever associated with malaria	Namibia	(du Preez et al. 2020)
P. acutiflora	AP	NS (NS	Malaria	Burkina Faso	(Ilboudo et al. 2013)
P. parviflora	B	NS (NS)	Pains	Guinea-Bissau	(Catarino et al. 2016)
	L				
	RB	Decoction (Oral)	Infectious diseases	Guinea	(Magassouba et al. 2007)
P. horizontalis	L	NS (NS)	Diabetes	Nigeria	(Feenna et al. 2020)
P. schimperiana	SB	Decoction (Oral)	Breast cancer	Kenya	(Ochwang'i et al. 2014, 2018)
		Paste (Topical)			
	L	Cold infusion (Oral)	Stomachache	Ethiopia	(Radol et al. 2016)
		Paste (NS)	Snake bite		(Asfaw et al. 2021)
	Fr	Raw (Oral)	Food		(Gemedo-Dalle et al. 2005)
P. dicoccos	L	Extract and banana (Oral)	Easy delivery	India	(Vaidyanathan et al. 2013)
		NS (NS)	Pain relief		(Chandramouli and Mallikarjuna 2020)
		Decoction (NS)	Fever, cough, asthma and inflammation		(Kalaichelvi and Dhivya 2016)
	F	Raw (Oral)	Food		(Rasingam 2012)
	B	Boil in sesame oil (Topical)	Rheumatoid pains		(Neelima et al. 2011)
	L B and R	NS (NS)	Piscicide		(Dutta et al. 2019; Kalita et al. 2017)
	R	Aqueous decoction/oral	Diarrhoea		(Raja et al. 2011)
P. umbellata	L	NS (NS)	Kidney, bladder diseases		(Vijayashalini et al. 2017)
	WP	NS (NS)	Easy delivery, Uterus related problems		(Pakkala and Patel 2021; Ponnaiah et al. 2018)
P. nitida	L	NS (NS)	Diarrhoea	Malaysia	(Eswani et al. 2010)

Table 3 continued

Species	Part Used	Method of Preparation (Administration)	Uses	Country	References
P. odorata	B and L	NS(NS)	Cephalalgia and as purgative	New Caledonia	(Sévenet and Pusset 1996)

Plant parts used: AP: aerial parts; B: bark; Fr: fruit; L: leaves; R: root; RB: root bark; SB: stem bark; NS: not specified; WP: whole plant

Countries: NS: not specified

Method of preparation (Administration): NS: not specified

Ethnopharmacology

The few reported traditional uses of *Psydrax* species in different parts of Africa, Asia and Oceania and the forms in which they are used are summarized in Table 3. In some of the articles, there was no distinction between stem bark and root bark; the plant part was reported just as bark. Thus, if we take the bark, root bark and stem bark to be different, then the leaf becomes the most explored plant part of the genus in ethnomedicine with about 38% of the reviewed articles reporting leaves as the plant's part used in ethnomedicine preparations, either alone or in combination with other plant parts. The trend in popularity of other plant parts is as follows: bark (approx. 21%), stem bark and root (approx. 17% each), and whole plant and aerial parts (approx. 4% each). The high popularity of the leaf of the genus in ethnomedicine is expected as the leaf is easily accessible and non-destructive of plant biodiversity (du Preez, Shingenge, and Mumbengegwi 2020). In the course of this review, it is observed that the popularity of *Psydrax* in traditional medicine is quite minimal when compared to other genus of the Rubiaceae family (Magassouba et al. 2007), and this could be due to the rarity of the *Psydrax* species. Also observable from some of the reports on the folkoric use of these plants is that the method of preparing and the route of administration of some of the herbal medicines were omitted and only one paper reported the fidelity level for the use of the genus in traditional medicine. These obscurities could impede future scientific investigations to confirm traditional claims for the genus.

Clearly seen in Table 3 is the fact that *P. subcordata* is the most widely used species of the genus in ethnomedicine. In Africa where *P. subcordata* is endemic, it is used in folkloric medicine in four specified and two unspecified African countries and this presents the species as the most popular species in African traditional medicine and Appiah and co-workers recorded a fidelity level of 50% for the use of stem bark preparation of *P. subcordata* in the treatment of boil in Ghana (Appiah et al. 2018). The next most popular species in African traditional medicine is *P. livida*, while in Asia, specifically in India, *P. dicoccos* is the most explored species. In Oceania, *P. odorata* is the only species reported and it is used traditionally as purgative. In the course of this review, it was observed that ethnomedicinal uses of some of these plant species were reported using their synonyms. For instance, *P. subcordata, P. livida, P. acutiflora, P. dicoccos* and *P. odorata* were reported as *Canthium subcordatum, Canthium huillense, Canthium henriquesianum, Canthium dicoccus* and *Plectronia odorata*, respectively.

In four specified African countries – Cameroon, Cote d'Ivoire, Ghana and Nigeria – different parts of *P. subcordata* have found applications in traditional management of some ailments including the management of stomach ulcer, haemorrhoids, body pains and boils using stem bark in Ghana, (Agyare et al. 2009; Appiah et al. 2018); the use of an unspecified part of the plant in the management of epilepsy in Cote d'Ivoire (Daanaa et al. 2018); the use of root and stem bark preparation in the treatment of fever and malaria in Nigeria (Chukwujekwu et al. 2005); the use of the root in the treatment malaria, fever, inflammation and cardiovascular diseases in Cameroon (Awah et al. 2012); the use of the whole plant in the management of stomach disorders in an unspecified African country

(Awantu et al. 2019); and the use of the bark in the management of high-blood pressure (Achenbach 1986). It is always exciting to know that a plant species has medicinal values. However, if the activities of a plant are numerous and unrelated, it becomes a concern and requires conduction of thorough scientific investigations, including cytotoxicity assay and clinical trials, to ascertain the mechanism of action of that plant indicated for those disease conditions (Gertsch 2009). We therefore suggest that *P. subcordata* should be extensively investigated for its phytochemistry and pharmacological properties to confirm its multiple applications in folkloric medicine.

The less popular species in African traditional medicine are *P. horizontalis* whose leaves are used in the management of diabetes in Nigeria (Feenna et al. 2020); in Kenya, stem bark and leaves of *P. schimperiana* are used for the management of breast cancer and stomachache associated with HIV infection, respectively (Ochwang'i et al. 2014, 2018; Radol et al. 2016), while in Ethiopia, the fruit is consumed by humans as one of the edible wild fruits and the roots used for management of diarrhoea (Gemedo-Dalle et al. 2005); in Guinea-Bissau, barks and leaves of *P. parviflora* are used in treating pains (Catarino et al. 2016), while in Guinea the root bark decoction is used for infectious diseases (Magassouba et al. 2007); fruits of *P. livida* are consumed as edible fruits in South Africa (Magwede et al. 2018), while in Zimbabwe the leaf paste is popularly used for treating wounds (Maroyi 2012; Mukandiwa et al. 2012a, b) and ectoparasites in livestock (Nyahangare et al. 2015).

In Asia, different parts of *P. dicoccos* are widely used in Indian ethnomedicine for the treatment of a variety of ailment: the leaf preparations are used for general pain relief (Chandramouli and Mallikarjuna 2020), to ease delivery (Vaidyanathan et al. 2013), and to treat fever, cough, asthma and inflammation (Kalaichelvi and Dhivya 2016); the fruit is edible (Rasingam 2012); the bark powder preparation is used topically to treat rheumatic pains (Neelima et al. 2011); root decoction is used for the treatment of diarrhoea (Raja et al. 2011); the juice obtained from crushing together the leaf and bark is used to treat high blood pressure (Sen and Behera 2016); and in ethnoveterinary medicine, the leaves, bark and root of *P. dicoccos* are used as piscicides for controlling predatory fish species (Dutta et al. 2019; Kalita et al. 2017). The leaf extract of *P. umbellata*, is used for the treatment of urinary tract diseases (Dhivya and Kalaichelvi 2016; Vijayashalini et al. 2017). In Malaysia, an unspecified part of *P. livida* is used in the management of diarrhoea.

In Oceania, New Caledonia to be precise, a mixture of the bark and leaves of *P. odorata* is used for cephalalgia, and as a purgative in combination with other plants and sea water (Sévenet and Pusset 1996).

Phytochemistry

The few *Psydrax* species which have been screened for phytochemicals contain various chemical constituents such as saponins, terpenes, tannins, coumarins, glycosides and flavonoids (Akoto et al. 2019). Out of the over 100 species of the genus, only eight of the species including *P. subcordata*, *P. acutiflora, P. montigena, P. livida, P. odorata*, *P. dicoccos, P. puberula and P. schimperiana* have been explored for phytochemicals, and approximately 131 compounds were identified using different chromatographic and spectroscopic techniques. However, only the structures of fifty-five compounds **(1–55)** isolated from this genus and characterized using NMR and/or LC–MS techniques are given in this review. Their names are also listed in Table 4. About half of the 55 isolated compounds of this genus are iridoids **(1–27)**, while the remaining 50% are other terpenes **(28–35)**, cyanogenic glycosides **(36–39)**, alkaloids **(40–42)** and others we called miscellaneous compounds **(43–55)** because they were too small to be grouped into classes. Twenty-one of the iridoids **(1–21)** were isolated from different parts (stem bark, fruit and leaf) of the moderately studied species of the genus, *P. subcordata*, with shanziside methyl ester **(21)** appearing in both the stem bark and the fruit extracts of the species. The other six iridoids **(22–27)** were obtained from *P. montigena* **(22)** and the leaf and bark of *P. odorata* **(23–27)**. Since iridoid is the most commonly encountered non-volatile chemical constituent of the genus, we adjudge it as the chemotaxonomic marker of the genus and would focus our discussion of the phytochemical importance of *Psydrax* on iridoid.

The rest of the phytoconstituents of the genus listed in **Table 4** are volatile compounds **(56–131)** which were identified by GC–MS analysis. They made up more than half (about 58%) of the 131 phytochemicals of *Psydrax*. Forty-six of them **(56–101)** were identified

Table 4 Chemical constituents of psydrax

Compounds characterized by NMR analysis				
No	Compound name	Plant species	Plant part	References
1	Cerbinal	*P. subcordata*	SB	(Awantu et al. 2019)
2	Cerberinic acid			
3	Subcordatanol I	*P. subcordata*	L and B	(Zhou et al. 2019)
4	Subcordatanol II			
5	Subcordatanol III			
6	Subcordatanol IV			
7	Subcordatanol V			
8	1-*O*- methylcrescentin I			
9	10-Deoxyeucommiol			
10	6*β*-Hydroxy-2-oxabicyclo[4.3.0]$\Delta^{8,9}$-nonen-1-one			
11	Shanzhigenin methyl ester	*P. subcordata*	Fr	(Joubouhi et al. 2015, 2017)
12	1-Epishanzhigenin methyl ester			
13	Linearin			
14	1-Epilinearin			
15	Mussaenoside			
16	Canthiumosides (1)			
17	Canthiumosides (2)			
18	Canthiumosides (3)			
19	Canthiumosides (4)			
20	Canthiumosides (5)			
21	Shanziside methyl ester	*P. subcordata*	SB and Fr	(Achenbach et al. 1981; Achenbach 1986; Joubouhi et al. 2015, 2017)
22	Arborside E*	*P. montigena*	NS	(Yang et al. 2016)
23	6-*O*-benzoylshanzhiside methyl ester	*P. odorata*	B and L	(Coulerie and Poullain 2016; Sévenet and Pusset 1996)
24	8-*O*-benzoylshanzhiside methyl ester			
25	6-*O*-benzoyl-6'-*O*-acetylshanzhiside methyl ester			
26	6,6'-di-*O*-dibenzoylshanzhiside methyl ester			
27	Shanzhisin methyl ester gentiobioside			
28	β-sitosterol	*P. subcordata*	SB and L	(Awantu et al. 2019; Castro et al. 2016)
29	Ursolic acid	*P. subcordata*	SB	(Awantu et al. 2019)
30	Quinovic acid			
31	Oleanolic acid	*P. subcordata*	Fr	(Joubouhi et al. 2015, 2017)
32	Betulinic acid			
33	Glucoside roseoside	*P. subcordata*	SB	(Achenbach 1986; Achenbach et al. 1981)
34	3-*O*-β-D-glucopyranosylquinovic acid	*P. subcordata*	SB	(Awantu et al. 2019)
35	3-*O*-β-D-glucopyranosyloleanolic acid			
36	Prunasin	*P. livida*	L	(Rockenbach et al. 1992)
37	Oxyanthin	*P. livida*	Fr, L and S	(Rockenbach and Nahrstedt 1990; Rockenbach et al. 1992)

Table 4 continued

Compounds characterized by NMR analysis				
No	Compound name	Plant species	Plant part	References
38	Oxyanthin 5''-O-benzoate	*P. livida*	L and S	
39	2*R*-[(2-Methoxybenzoylgenoposidyl)-5-*O*-*β*-D-apiofuranosyl-(1 → 6)-*β*-glucopyranosyloxy]-2-phenyl acetonitrile	*P. schimperiana*	Fr	(Schwarz et al. 1996)
40	Plectrodorine	*P. odorata*	B and L	(Coulerie and Poullain 2016; Sévenet and Pusset 1996)
41	Iso-plectrodorine			
42	N-Desmethylmyrianthine			
43	3',4',7-trihydroxyflavone	*P. subcordata*	Fr	(Joubouhi et al. 2015, 2017)
44	Rutin			
45	7-*O*-(6-*O*-benzoyl-*β*-D-glucosyl)-rutin	*P. dicoccos*	L	(Gunasegaran et al. 2001)
46	D-mannitol	*P. subcordata*	SB	(Achenbach 1986; Achenbach et al. 1981)
47	Orcinol rnonomethyl ether			
48	Scopoletin			
49	Indole			
50	Chromone	*P. acutiflora*	L and Tw	(Ilboudo et al. 2013)
51	Clemahexapetoside B	*P. subcordata*	SB	(Awantu et al. 2019)
52	Psydrin	*P. livida*	L	(Nahrstedt et al. 1995)
53	Psydroside			
54	3,5-dicaffeoylquinic acid	*P. schimperiana*	Fr	(Schwarz et al. 1996)
55	3,4-dicaffeoylquinic acid			
Compounds identified by GC–MS analysis				
56	(E)-2-Hexenal	*P. subcordata*	Fr-E-O	(Essien et al. 2015)
57	α-Pinene			
58	Benzaldehyde			
59	1-Octen-3-ol			
60	3-Octanol			
61	*p*-Cymene			
62	1,8-Cineole			
63	Linalool			
64	Nonanol			
65	Methyl salicylate			
66	β-Cyclocitral			
67	Thymol methyl ether			
68	Geraniol			
69	α-Cubebene			
70	β-Bourbonene			
71	β-Cubebene			
72	β-Elemene			
73	Cyperene			
74	α-Gurjunene			
75	β-Caryophyllene			
76	Calarene			

Table 4 continued

Compounds identified by GC–MS analysis				
77	α-Bergamotene			
78	α-Guaiene			
79	α-Humulene			
80	Nerylacetone			
81	(E)-β-Farnesene			
82	Drima-7,9(11)-diene			
83	γ-Muurolene			
84	Germacrene D			
85	β-Selinene			
86	Valencene			
87	α-Muurolene			
88	(E,E)-α-Farnesene			
89	δ-Cadinene			
90	α-Calacorene			
91	(E)-Nerolidol			
92	(Z)-3-Hexenyl benzoate			
93	(E)-2-Hexenyl benzoate			
94	Caryophyllene oxide			
95	Longiborneol			
96	1-*epi*-Cubenol			
97	Cubenol			
98	Torreyol (= α-Murrolol)			
99	α-Cadinol			
100	Benzyl benzoate			
101	α-Copaene			
102	Furfural	*P. dicoccos*	L	(Raja et al. 2011)
103	Styrene			
104	2,3-Dihydrobenzofuran			
105	Lactose			
106	*m*-Mentha-4,8-diene			
107	2-Furancarboxaldehyde			
108	4-Ethyl-2-methoxyphenol			
109	(-)-Spathulenol			
110	Caryophllene oxide			
111	N-(3,4-Dichlorophenyl)-N-methoxy-N-methyl urea			
112	Cedren-13-ol			
113	2-Pentanethiol			
114	Ledene oxide(II)			
115	Tetracyclo[6.3.2.0(2,5).0(1,8)] tridecan-9-ol, 4–4- dimethyl			
116	2,7-Dioxa-tricyclo[4.4.0.0(3,8)] deca-4,9-diene			
117	Formaldehyde, methyl (2-propynyl) hydrazine			
118	4-cyclopropylnorcarane			
119	2-Methyl benzaldehyde			

Table 4 continued

Compounds identified by GC–MS analysis				
120	1,5-heptadiene-3-yne			
121	14α, 18α-[4-methyl-3-oxo-(1-oxa-4-azabutane-1.4-diyl),(5β)-Pregnane-3,20-β-diol	*P. puberula*	L	(Castro et al. 2016)
122	Digitoxin			
123	Ethyl isoallocholate			
124	Methyl palmitate			
125	Palmitic acid			
126	2-[2-(2-(-pentylcyclopropyl)methylcyclopropyl)methyl] cyclopropyl Cyclopropanebutanoate			
127	Oleic acid			
128	Methyl-6-cis,9-cis.11-trans-octadecatrienoate			
129	β -monoolein			
130	Botulin			
131	(2-(3-acetoxy-4,4,14-trimethylandrost-8-en-17-yl)-propanoic acid			

Plant parts used: *B* bark; *Fr*: fruit; *Fr-E-O* fruit essential oil, *L* leaves, *NS* not specified, *R* root, *S* stem, *SB* stem bark, *Tw* twig

*Compound characterized by electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry (ESI-FTICR-MS)

in the fruit essential oil of *P. subcordata,* nineteen compounds **(102–120)** in the leaf extract of *P. dicoccos* and eleven compounds **(121–131)** plus **(1)** in the hexane fraction of *P. puberula* leaf. One major drawback of characterizing compounds with GC–MS is the ability to match accurately the compounds in a mixture with exact spectra in GC–MS spectra database. GC–MS analysis of a complex mixture is not always 100% accurate; there is a huge possibility of assigning a wrong spectra to a wrong compound. Besides, GC–MS analysis is a destructive analytical method which could cause the breakdown of compounds and ultimately lead to identification of degradation products instead of the original constituents. Thus, in this review, we discovered that some of the compounds identified by GC–MS method are not natural products (for example, **(111, 116 and 117)**). For instance, **(111)** – a herbicide – might have accrued from the use of herbicides on the field where the plant material was harvested or it might be a product of a decomposed secondary metabolite. The expertise of the researcher in interpreting GC–MS spectra is also very important to avoid assigning wrong molecular formulae to compounds. One of the articles reviewed in this paper mistakenly gave a compound two synonymous names (furfural **(102)** and 2-Furancarboxaldehyde **(107)**) and assigned them two different molecular formulae. In summary, we will limit our phytochemistry review of the genus to isolated compounds whose structures were elucidated with other techniques (NMR, LC–MS andESI-FTICR-MS) apart from GC–MS.

Iridoids

Iridoids are a group of monoterpenoids recognized by their basic structure in which a pyran is fused to a cyclopentane, and are usually grouped into glycosidic, non-glycosidic, seco- and bis-iridoids (Ludwiczuk et al. 2017). Their activities could be likened to those of adaptogens and immunomodulators, and they are considered as prodrugs that get easily converted to active pyridine monoterpene alkaloids (Ghisalberti 1998). Chemical structures of iridoids are quite diverse and might be confusing if not well looked at because they often look alike. They play a role in ants' defence mechanism and are commonly found in plants infested with ants. Some patents have been filed for some natural iridoids in a recent review article for many biological activities (Hussain et al. 2019). However, many of them were in vitro investigation with most activities recorded at very high concentrations of iridoids which might be considered scientifically insignificant. For instance, in one of the patents

recorded in Hussain et al. (2019) review article, an IC_{50} value of 104.1 μM was presented for one of the phytoconstituents of *Psydrax* **(21)** as bioactive anti-SARS agent. But all hope is not lost since iridoids are projected as pro-drugs whose activities could be greatly enhanced in vivo. It is worthy of note that some iridoids have shown good activities including cardiovascular, antihepatotoxic, hypoglycemic, hypolipidemic, anti-inflammatory, antispasmodic, antitumor, antiviral, and purgative activities (Ghisalberti 1998; Hussain et al. 2019; Tundis et al. 2008) at low concentrations. They are found naturally in varied forms in different plant species, and a good number has been documented for *Pysdrax* species. The structures of this class of compounds are captured in Fig. 1.

In a recent study, involving the stem bark of *P. subcordata*, two non-gylcosidic iridoids **(1** and **2)** were isolated, alongside other constituents (Awantu et al. 2019). Another set of non-glycosidic iridoids **(3–8)**, which were novel and two known ones **(9** and **10)** were isolated from leaf and bark extracts of *P. subcordata* (Zhou et al. 2019). The largest number of iridoids **(11–21)** was isolated from iso-butanol fraction

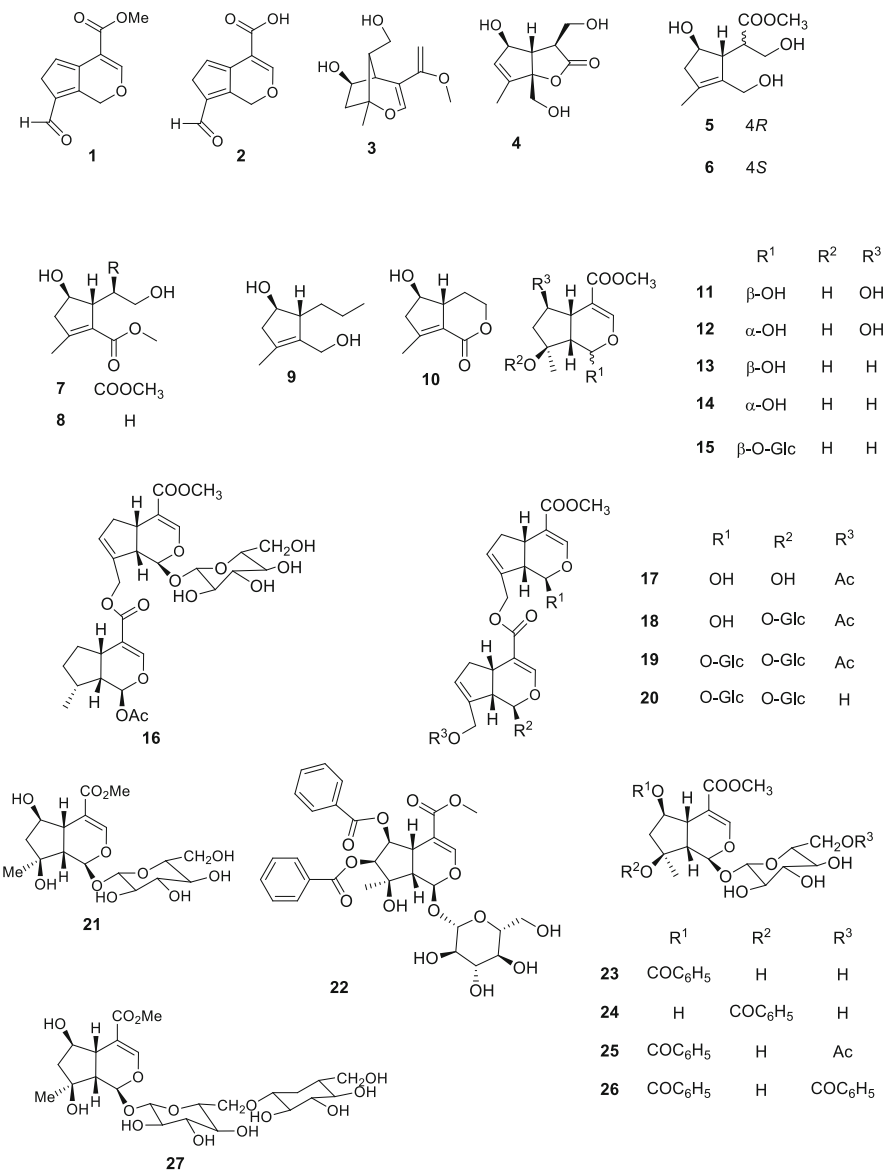


Fig. 1 Iridoids and their glycosides

of methanol extract of *P. subcordata* dried fruits, and out of the eleven iridoids, five (**16–20)** were novel compounds (Joubouhi et al. 2015). Compound **(22)** was characterized in an extract of *P. montigena* using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry (ESI-FTICR-MS) (Yang et al. 2016), while (**21** and **27)** were obtained from the methanol extract of the stem bark of *P. subcordata* (Achenbach 1986; Achenbach et al. 1981), after an initial isolation of only **(27)** from the same extract (Achenbach et al. 1980). Out of the 22 iridoids so far isolated from *P. subcordata,* **(21)** is observed to be the most common and widely distributed iridoid of the species; it was isolated as the major component of the methanol extract of dry fruits and stem bark of *P. subcordata*. Another species that yielded iridoids is *P. odorata*; its leaf and bark produced four glycosidic iridoids **(23–26)**, in company with other non-iridoid constituents (Coulerie and Poullain 2016; Sévenet and Pusset 1996). These data on iridoids suggest that the genus accumulates high amounts of this class of metabolites which may be of taxonomic relevance in plant systematics if further investigation is carried out.

Other terpenes and terpenoids

Terpenes are a class of compounds often found abundantly in essential oils because of their high volatility, and they are usually characterized using GC–MS technique. However, in this review, eight terpenes were isolated from three species of the genus and their structures and names are given in Fig. 2 and Table 4 respectively.

A non-glycosidic terpenoid **(28)** was isolated and characterized with NMR technique from the stem bark of the methanol extract of *P. subcordata* (Awantu et al. 2019) as well as in a GC–MS analysis of the n-hexane fraction of the leaves of *P. puberula* (Castro et al. 2016). The presence of **(28)** in two different species of the genus indicates possible similarities in the biosynthetic gene clusters of *Psydrax* species. In other studies, four non-glycosidic terpenoids **(29–32)** and three non-glycosidic terpenoids **(33–35)** were obtained from methanol extract of the stem bark and fruit of *P. subcordata* (Achenbach et al. 1981; Awantu et al. 2019; Joubouhi et al. 2015).

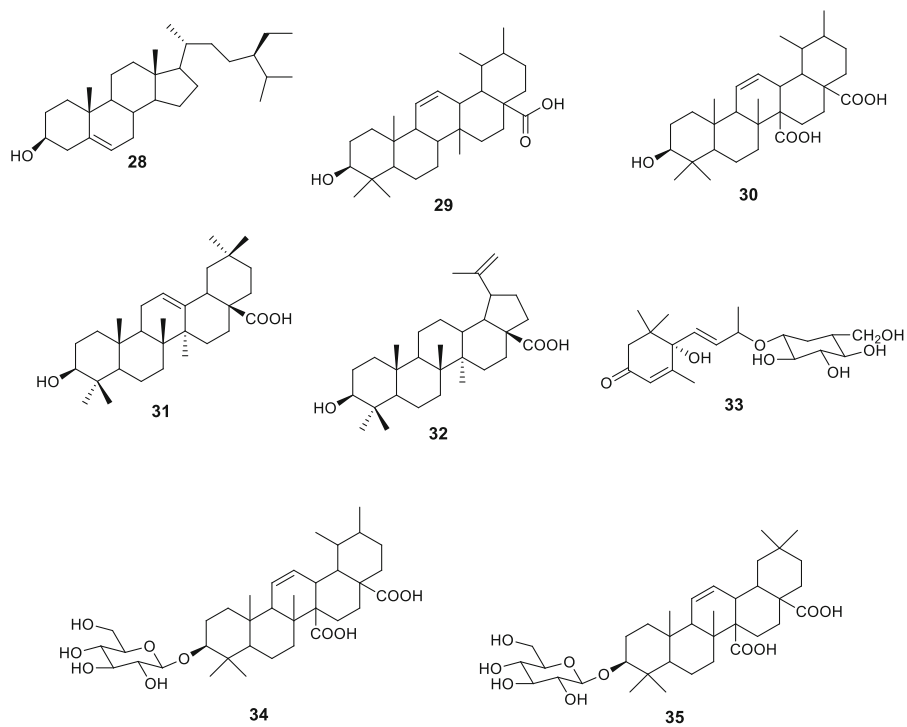


Fig. 2 Terpenes and their glycosides

Cyanogenic glycosides

Cyanogenic glycosides are often considered toxic due to the ease of transformation of their aglycones to hydrogen cyanides a poisonous chemical (Yulvianti and Zidorn 2021), and could be seen as unimportant therapeutic agents. However, a bioactivity of this class of compound was reported by Tan et al (2012) in their study of the neuroprotective effects of prunasin gallates against H_2O_2 induced oxidative damage of NG108-15 cells. They reported in vitro neuroprotective property of highly glycosylated trigallates and tetragallate of prunasin **(36)**, one of the compounds isolated from *Psydrax*, at a concentration of 100 µM of the test samples and a positive control, catechin (Tan et al. 2012). It is obvious that this report was marred by the high concentration of test samples and the reference drug used. Also the bioavailability of these compounds are not guaranteed in vivo due to the high polarity of the glycosylated compounds and a possible loss of the sugar moiety in vivo. Apart from **(36)**, two other cyanogenic glycosides (**37** and **38**) were isolated from methanol extracts of the leaf, stem and root of *P. livida* (Rockenbach et al. 1992) and the fourth cynogenic glycoside **(40)** was from a methanol extract of ripe fruits of *P. schimperiana* (Schwarz et al. 1996). The chemical structures of these compounds are shown in Fig. 3.

Alkaloids

It is observed in the course of this review that alkaloid is not a common constituent of this genus and there are some conflicting claims as to whether they are present or absent in the genus. Some researchers discovered zero alkaloid when they chemically profiled the leaf, stem and root barks of *P. subcordata, P. peruviana,* and *P. acutiflora* (Denise P Ilboudo et al. 2013; Goh et al. 1997; Achenbach 1986; Achenbach et al. 1981; Daanaa et al. 2018; Akoto et al. 2019). On the contrary, some other research groups identified alkaloids in a different part of *P. subcordata, P. horizontalis, P. schimperiana* and *P. dicoccos*, but they reported the alkaloid content of *P. schimperiana* and *P. dicoccos* to be small (Anokwah et al. 2016; Feenna et al. 2020; Ochwang'i et al. 2016; Umaiyambigai et al. 2016). To confirm the presence of alkaloids in *Psydrax*, three alkaloids: two monoterpene alkaloids **(40 and 41)** and a peptide alkaloid **(42)** were isolated from *P. odorata* bark and leaf (Coulerie and Poullain 2016) and their structures are given in **Fig. 4**. The observed variations in alkaloid content of *Psydrax* species could be attributed to different factors, such as geographical differences, different harvesting seasons and analytical techniques and methods adopted by different authors and/or differences in the genetic make-up of different species of the genus. This inconsistency in the alkaloid contents of the genus calls for further extensive phytochemical studies of the genus across different geographical locations where

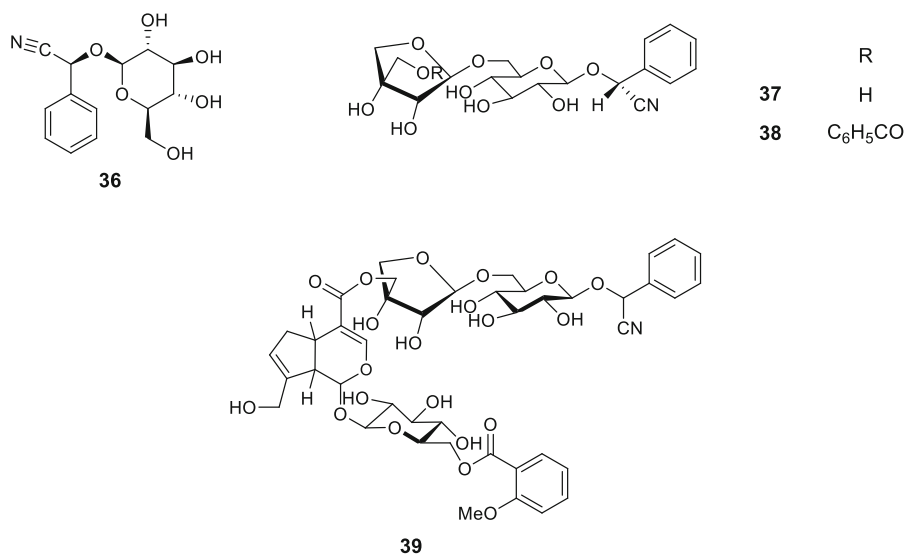


Fig. 3 Cyanogenic glycosides

the species are endemic and adoption of a standard analytical technique and method that will provide a clearer perspective on the types of alkaloids and the alkaloidal content of the genus.

Flavonoids

Flavonoids are relatively rare in *Psydrax*, out of the 55 compounds isolated from the genus, only three were flavonoids: a flavone **(43)** isolated from the fruit of *P. subcordata* (Joubouhi et al. 2015, 2017), and a flavonol **(44)** and its glycoside **(45)** from *P. dicoccos* leaves (Gunasegaran et al. 2001). The structures of the flavonoids are given in Fig. 5.

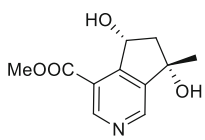
Miscellaneous compounds

The remaining ten compounds are grouped under miscellaneous because of their less popularity in *Psydrax* and their structures are given in Fig. 6. They include, an aliphatic alcohol **(46)**, an aromatic alcohol **(47)**, a hydroxy coumarin **(48)**, indole **(49)** which were obtained from the stem bark of *P. subcordata* (Achenbach 1986; Achenbach et al. 1981); chromone **(50)** obtained from the leaf and twig of *P. acutiflora* (Ilboudo et al. 2013); a cyclic glycoside **(51)** from stem bark of *P. subcordata* (Awantu et al. 2019); a glycosidic furanone **(52)** and aromatic ester **(53)** obtained from the leaf of *P. livida* (Nahrstedt et al. 1995); and two dicaffeoylquinic acids **(54** and **55)** isolated from the fruit of *P. schimperiana* (Schwarz et al. 1996).

Pharmacological properties

A few numbers of biological assays have been carried out on extracts and constituents of *Psydrax* species to support the acclaimed applications of these plants in the traditional management of a wide range of ailments. Unfortunately, only eight (*P. subcordata, P. palma*, *P. acutiflora, P. montigena*, *P. schimperiana, P. livida, P. horizontalis* and *P. dicoccos*) out of a hundred and thirty species of this genus, as well as *P. peruviana* which is not yet included in the *WCSP* database, have been pharmacologically tested for activities. Of the bioassays conducted for these species, majority are in vitro assays, three are in vivo studies and one is an ex vivo study. These conducted bioassays for the genus are summarized in Table 5 for record purposes, nothwithstanding the concentrations and methods used by different authors. However, only assays conducted with concentrations moderate enough to have any scientific importance are enumerated in the body of this text. It was observed by the current authors that for most in vitro assays conducted for this genus, only few of the studies performed cytotoxicity assay and determined selectivity index (SI) for their bioactive samples to verify the safety of the samples and predict their therapeutic margin. Among the species investigated for bioactivity, *P.*

Fig. 4 Alkaloids



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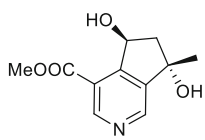

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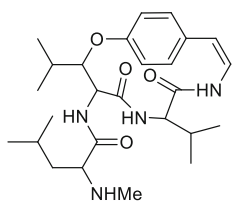
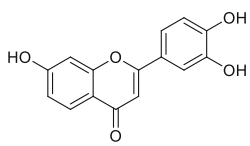
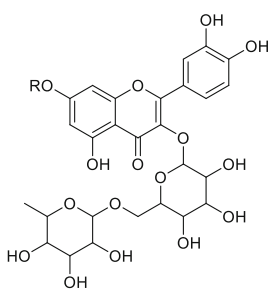


42

Fig. 5 Flavonoids and their glycosides



43



	R
44	H
45	(6-O-benzoyl)-β-D-glucopyranosyl

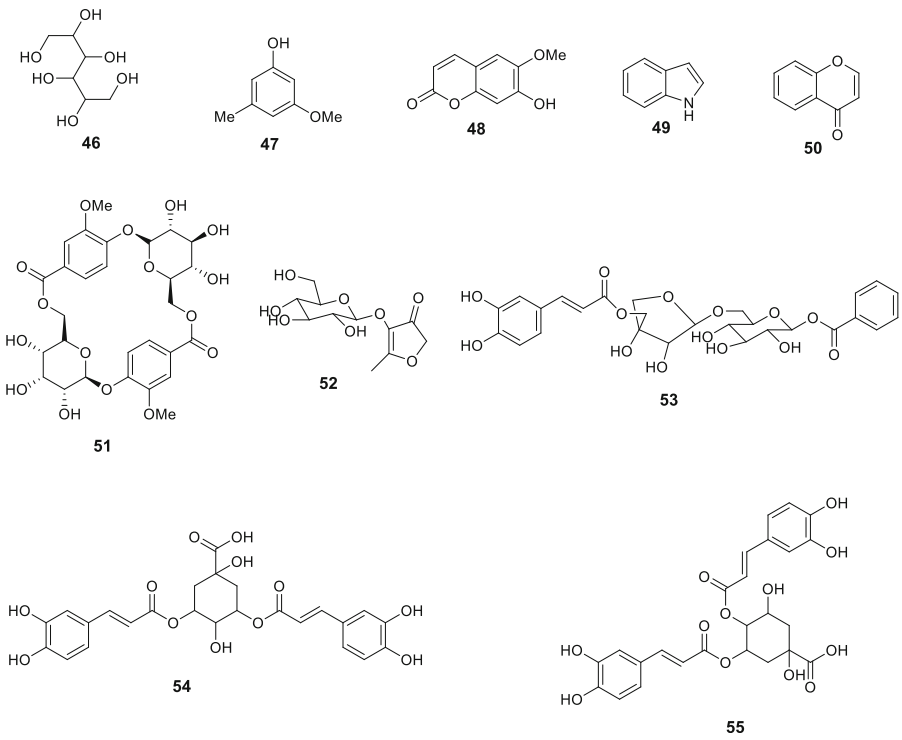


Fig. 6 Miscellaneous Compounds

subcordata is the most explored pharmacologically, while the leaf is the most investigated plant part. *P. palma* was referred to as *Cathium oddonnii*, its synonym, in two articles that reported its bioactivity.

Some of the compounds identified in *Psydrax* have previously been isolated from other medicinal plants and have shown varying pharmacological properties. For instance, β-sitosterol **(28)** was previously isolated from the stem bark of *Solanum surattense* and *Pterospermum acerifolium,* and these plants are used in the herbal treatment of a range of diseases including diabetes (Gupta et al. 2011; Muhit et al. 2010). In an attempt to support the traditional use of *Solanum surattense* in the herbal management of diabetes, Gupta et al. (2011) conducted a 21 day in vivo multiple dose (10, 15 or 20 mg/kg) antidiabetic assay of **(28)** as against 0.3 mg/kg of a reference drug, glibenclamide and also conducted acute toxicity assay of **(28)** in rats to determine the lethal dose (LD50: 120 mg/kg) of the compound **(28)**. They reported antidiabetic activity of **(28)** at all doses in comparison to the positive control (0.3 mg/kg), with 20 mg/kg having the best activity among the test doses. Though the activity of **(28)** was adjudged good, the comparison was done at a very high concentration (20 mg/kg) of the test compound as against glibenclamide (0.3 mg/kg). In another in vivo multiple dose (15 and 30 mg/kg for 30 days) antidiabetic study of an ethyl acetate subfraction of an ethanol extract of the bark of *Pterospermum acerifolium* from which **(28)** was isolated, the authors reported good activity at 30 mg/kg of the fraction as against 0.6 mg/kg of STD drug used in the study (Rathinavelusamy et al. 2014). It was not clear to us what the STD drug was in the article. Rathinavelusamy et al. 2014 after isolating **(28)** from the most active fraction of *Pterospermum acerifolium* conducted an in silico antidiabetic study to determine the inhibitory activity of **(28)** against the human pancreatic α-amylase (HPA). They revealed free binding energy and inhibition constant (K_i) of − 8.39 kcal/mol and 0.269 µmol for **(28)**, and -6.07 kcal/mol and 28.52 µmol for the reference drug, acarbose, and they presented **(28)** as a potential HPA inhibitor when compared to acarbrose (Rathinavelusamy et al. 2014). These reports are proof-of-concept of the potential antidiabetic property of **(28)** which is one of the phytoconstituents of the stem bark and leaf of a *Psydrax* species, *P. subcordata* (Awantu et al. 2019; Castro et al. 2016).

Table 5 In vitro and in vivo assays of extracts and chemical constituents of *Psydrax* species

Species	Part of plant used	Extract	Compound	Assay method	Assay type	References
P. subcordata	R	PE, D, E, aM	–	In vitro	Antibacterial, anti-inflammatory	(Awah et al. 2012; Chukwujekwu et al. 2005)
	SB	M	**(1–10, 28–30, 34, 35, 51)**	In vitro	Antiplasmodial, antibacterial, antifungal, antioxidant, antidiabetic	(Anokwah et al. 2016; Awantu et al. 2019; Zhou et al. 2019)
	L	aE	**(3–10)**	In vivo In vitro	Anticonvulsant Antidiabetic	(Daanaa et al. 2018; Zhou et al. 2019)
	Fr	E-O, EA, iBu, M	**(11, 13, 15–19, 21)**	In vitro	Antioxidant, antibacterial, antifungal, toxicity	(Essien et al. 2015; Joubouhi et al. 2017)
P. palma	SB	M	–	In vitro	Antiplasmodial, antitrypanosomal	(Memvanga et al. 2015; Mesia et al. 2008)
P. acutiflora	L/T	H, dP, D, EA, aM, W	–	In vitro	Anti-inflammatory, antiplasmodial	(Ilboudo et al. 2013)
P. montigena	UsP	M	**(22)**	In vitro	Antiplasmodial	(Yang et al. 2016)
P. schimperiana	SB	D-M, W	–	In vitro	Cytotoxicity	(Ochwang'i et al. 2018)
	Fr	M	**(39, 51, 52)**	In vitro	Insecticidal	(Schwarz et al. 1996)
P. livida	L	A	–	In vitro	Antibacterial	(Mukandiwa et al. 2012a)
P. horizontalis	L	M	–	In vivo	antidiabetic	(Feenna et al. 2020)
P. dicoccos	L	PE, C, EA, M	–	In vitro	Antibacterial, antifungal	(Umaiyambigai et al. 2016)
P. peruviana	SB	H, M	–	In vitro	Antibacterial, antifungal	(Akoto et al. 2019)

Plant parts used: *Fr* fruit, *L* leaves, *R* root, *SB* stem bark, *T* twig, *NS* not specified

Extracts used: *A* acetone; *aE* aqueous ethanol, *aM* aqueous methanol, *C* chloroform, *D* dichloromethane, *D-M* dichloromethane-methanol mixture, *dP* di-iso-propyl, *E-O* essential oil, *E* ethanol, *EA* ethyl acetate, *H* hexane, *iBu* iso-butanol, *M* methanol, *PE* petroleum ether, *W* water

Antimicrobial activity

European Committee on Antimicrobial Susceptibility Testing (EUCAST), and Clininal and Laboratory Standards Institute (CLSI) provide standard methods called antimicrobial susceptibility testing (AST) for conventional antimicrobials for rational comparison among antimicrobial assay results generated by researchers (Bubonja-Šonje et al. 2020). Unfortunately, there are no such established methods for assessing the antimicrobial properties of plant materials due to the complexity of plant samples and this leads many researchers to adopting varied modified AST to achieve their desired goals (Bubonja-Šonje et al. 2020). The result of these of these incoherent test methods is the generation of incomparable, difficult-to-interpret and often times misinterpreted research outcomes (Bubonja-Šonje et al. 2020; Cos et al. 2006; Eloff 2019; Gertsch 2009). This is what was observed in the course of this review, different researchers adopted varying test methods; different concentrations of plant samples were used; test organisms and media were not similar in many cases; and endpoint parameters (MIC, IC_{50}) assessed were dissimilar (Cos et al. 2006).

Some of the articles reviewed reported sample concentrations far above the recommended MIC value for plant extracts and pure compounds ((0.1 mg/mL (100 µg/mL) for extracts/fractions or less than 25 µM for pure compounds), and acceptable maximum in-test concentration of 1 mg/mL for plant mixtures and 0.1 mg/mL for pure plant constituents (Ríos and Recio 2005); many articles reported activity as minimum inhibitory concentration (MIC) values instead of

concentration at 50% inhibition (IC_{50}), which is adjudged to be scientifically significant at a value less than 0.1 mg/mL (100 µg/mL) for extracts/fractions or less than 25 µM for pure compounds; some authors used concentration of microbial inoculum greater than the acceptable standard of 10^5 CFU/mL for bacteria and 10^3 or 10^4 CFU/mL for fungi (Cos et al. 2006). Another crucial observation made in this review is that, some authors adopted agar diffusion method which is not a generally acceptable standard method for determining the MICs of plant extracts/fractions because of the low polarity of most plant's antimicrobial constituents which often hinders their diffusion through the polar agar medium used for the tests and ultimately leads to false negative result (Eloff 2019). Eloff also pointed out that an MIC value less than 0.1 mg/mL is scientifically relevant for further antimicrobial studies, that anything above this benchmark should not be pursued for further investigation (Eloff 2019). Being guided by these recommendations, we hereby enumerate only the in vitro antimicrobial assay results of extracts and pure compounds of the genus whose IC_{50}/MIC value is less than 100 µg/mL for plant extract/fraction and less than 25 µM or < 10 µg/mL for pure compounds, as well as those that used microbial inoculum concentration of 10^5 CFU/mL for bacteria and 10^3 or 10^4 CFU/mL for fungi. To the best of our knowledge, no antimicrobial in vivo assay nor clinical trial has been reported for either the extracts nor phytoconstituents of this genus.

Antimicrobial assay conducted by Awantu et al. (2019) for eight compounds **(1, 2, 28, 29, 30, 34, 35 and 51)** they isolated from the stem bark of *P. subcordata,* against three Gram positive bacteria (*Staphylococcus aureus, Staphylococcus saprophiticus, Streptococcus faecalis*), three Gram negative bacteria (*Klebsiella pneumonia, Pseudomonas aeruginosa*) and two fungi species (*Candida albicans* and *Candida krusei*) using broth dilution method showed only **(1, 2 and 30)** to be effective. They reported the following results for the three active compounds using gentamicin (IC_{50} 2.4 µg/mL) and nystatin (IC_{50} 4.8 µg/mL) as positive control for bacteria and fungi, respectively: **(1)** was active against only *C. albicans* (IC_{50} 9.7 µg/mL); **(2)** was active against *C. albicans* (IC_{50} 4.8 µg/mL), *C. krusei* (IC_{50} 9.7 µg/mL) and *S. aureus* (IC_{50} 9.7 µg/mL); **(30)** was active against *C. albicans* (IC_{50} 9.7 µg/mL), *K. pneumonia* (IC_{50} 9.7 µg/mL) and *P. aeruginosa* (IC_{50} 4.8 µg/mL) (Awantu et al. 2019). In another study conducted by Joubouhi et al.(2017) for the fourteen compounds **(11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 31, 32 and 43)** they isolated from the fruit extract of *P. subcordata* using micro dilution method, only **(13)** displayed antibacterial activity against a Gram-positive bacterium, *S. aureus,* with an MIC value of 8 µg/mL; they used two reference drugs – ampicillin (MIC 8 µg/mL) and ciprofloxacin (MIC 2 µg/mL). None of the compounds was active against any of the Gram-negative bacteria strains (four strains of *Vibrio cholerae,* and *Shigella flexneri*) used by the authors (Joubouhi et al. 2017).

In a preliminary study to support the use of *P. livida* leaves in the traditional treatment of wound myiasis in animals, a group of researchers Mukandiwa et al. (2012b) carried out an in vitro antibacterial assay of four extracts (hexane, dichloromethane, acetone and methanol) of *P. livida* leaves against two Gram-positive bacteria (*Staphylococcus aureus* and *Enterococcus faecalis*) and two Gram-negative bacteria (*Pseudomonas aeruginosa* and *Escherichia coli*), which are implicated in the pathogenesis of wound myiasis, by adopting microdilution assay method. They discovered that the dichloromethane extract was the most active among the extracts. However, the dichloromethane extract was active against only *S. aurus* with MIC values of 78 µg/mL as against the MIC value (0.78 µg/mL) for gentamycin, the reference drug.

Antimicrobial assay conducted by Castro et al. (2016) for crude extract and three fractions (hexane, chloroform and butanol) of *P. puberula* leaf against *S. aureus, P. aeruginosa* and *E. coli*, using microdilution method, showed varying antimicrobial activity. The crude extract and three fractions were all active against only *S. aureus* with MIC values ranging from 31.25 – 62 µg/mL as against the MIC value of about 3.91 µg/mL of ciprofloxacin, the positive control (Castro et al. 2016). An antifungal assay of *P. subcordata* mature fruits' essential oil against *A. niger* showed activity with an MIC value of 39 µg/mL in comparison to a positive control, amphotericin B (MIC value of 0.61 µg/mL) (Essien et al. 2015); the essesntial oil showed no significant activity against any of the bacteria species (*Bacillus cereus*, *S. aureus*, *E. coli* and *P. aeruginosa*) tested. From these enumerated antimicrobial properties, *Psydrax* could hold a promise in the discovery of antibacterial and

antifungal agents with broad spectrum of activity. However, more research works, especially in vivo study of the active samples and cytotoxic assays, is needed to substantiate this knowledge-informed hypothesis. These few promising antimicrobial properties observed for the extracts and constituents of the genus support some of its traditional applications in the treatment of diarrhoea and wound myiasis.

Anti-inflammatory activity

It is recommended that every biological assay should be conducted by adopting a standardized procedure for the assay, using as small an amount of plant sample as possible and a standard positive control (Cos et al. 2006). Whenever a too low or too high concentration is used, a false negative or positive result will prevail. For anti-inflammatory assays, Chukwujekwu et al. (2005) rightly observed that recording a relatively good in vitro prostaglandin synthesis inhibition for a non-polar extract as against more polar extracts does not corroborate the traditional use of the aqueous extracts in the traditional management of inflammation (Chukwujekwu et al. 2005). The possibility of aqueous herbal extracts to elicit anti-inflammatory effect in folkloric medicine could be linked to the high phenolic content of aqueous extracts which are mainly antioxidants and could give anti-inflammatory effect by improving the immune system of the patient (Eloff 2019). For the *Psydrax* genus, different in vitro and in vivo anti-inflammatory assays have been carried out for different extracts of *P. subcordata* and *P. acutiflora*, but we will only report results that used maximum in-test concentration of 1 mg/mL of plant extracts/fractions or 0.1 mg/mL of pure plant constituents in in vitro assays, and in vivo oral concentration of not more than 100 mg/kg for extracts.

Unfortunately, only the in vivo study done by Anokwah et al.(2016) fell within our chosen concentration range. In an in vivo per oral (p.o.) anti-inflammatory assay they conducted for the methanol stem bark extract of *P. subcordata* using carrageenan-induced footpad oedema in seven-day-old chicks, the authors reported dose-dependent percentage oedema inhibitions of 61.21, 53.00 and 49.34% at 300, 100 and 30 mg/kg body weight p.o. doses, respectively, of the extract using two positive controls, dexamethasone (0.3, 1 and 3.0 mg/kg) and diclofenac (10, 30, and 100 mg/kg) given intraperitoneally (Anokwah et al. 2016). Though they recorded anti-inflammatory activity for the plant extract, the concentrations used for the extract were higher than those of the positive control coupled with different routes of administration used for the test sample and the controls.

Antiparasitic activity

Antiparasitic assay like other anti-infection assays should follow some recommended standards previously mentioned to guarantee the authenticity of its results. *Psydrax* species have found applications in traditional management of malaria and fever, and in attempts to support this ethnomedicinal claim, some researchers conducted in vitro antiplasmodial assay of different extracts and constituents of the genus and they came up with varied antiplasmodial activities for the genus. However, it was observed that majority of these in vitro studies investigated either susceptible or resistant strains of *Plasmodium falciparium* and not both strains as deemed appropriate for a primary in vitro antiplasmodial assay (Cos et al. 2006). For studies that determined the IC_{50} of test samples (extracts), the IC_{50} values they obtained were within the acceptable range of below 100 µg/mL for crude extracts, but toxicity assays were not conducted for these active extracts to confirm that the activities reported were not due to non-specific activity and potential toxicity of the extracts (Cos et al. 2006).

In a study involving stem bark methanol extract of *P. subcordata* against a chloroquine resistant *P. falciparum* W2, there was an inhibition against the parasite with an IC_{50} of 3.044 µg/mL, however, fractions and constituents **(1, 2, 28, 29, 30, 34, 35** and **51)** from the extract showed no activity against the parasite strain (Awantu et al. 2019). However, the authors did not give the IC_{50} value for the positive control. In another study, 80% methanol extract of *P. palma*, showed parasitic inhibition against a chloroquine-sensitive *P. falciparum* strain (positive control: chloroquine $2H_3PO_4$ – IC_{50} 0.08 µg/mL), *Trypanosoma brucei brucei* (positive control: suramin – IC_{50} 0.08 µg/mL), and *Trypanosoma cruzi* (positive control: suramin – IC_{50} 0.05 µg/mL), with the same $IC_{50} > 64$ µg/mL, using 96-well tissue culture plates method (Mesia et al. 2008). They also conducted cytotoxicity test for the extract against the MRC-5 human cell-line and got the same IC_{50} value, but they reported the extract as inactive at this IC_{50} comparing

its activity with the activities of extracts from other plants having IC_{50} as low as 0.7 µg/mL and did not calculate the selectivity index (SI) for the extract.

In another study involving different extracts (hexane, diisopropyl ether, dichloromethane, ethyl acetate, and methanol–water) of *P. acutiflora* leaf/twig, tested against chloroquine susceptible and resistant strains of *P. falciparum,* using the parasite lactate dehydrogenase assay method, the exracts displayed variable IC_{50} values against the two strains of the parasite. The diisopropyl ether extract showed highest activity against the parasite strain (IC_{50} 8.8 µg/mL and IC_{50} 9.5 µg/mL) against the susceptible and resistant strains respectively, while the ethyl acetate extract was the least active (IC_{50} 61.3 µg/mL) against the sensitive strain and methanol–water extract showed least activity (IC_{50} 64.8 µg/mL) against the resistant strain. Chloroquine used as the positive control for this study had an IC_{50} of 0.20 µg/mL and IC_{50} 0.009 µg/mL against the sensitive and resistant strains respectively (Ilboudo et al. 2013). (Ilboudo et al. 2013) also tested the in vitro antiplasmodial activity of the most abundant constituent **(50)** of the diisopropyl extract and reported less activity (IC_{50} 18.1 µg/mL and IC_{50} 43.4 µg/mL) for **(50)** against the sensitive and resistant strains, respectively, in comparison with the diisopropyl extract. In addition to these antiplasmodial tests, (Ilboudo et al. 2013) also conducted cytotoxicity tests and calculated SI for the aqueous extract of *P. acutiflora* with IC_{50} 80.0 and 46.91 µg/mL against the sensitive and resistant strains of organism, respectively, and obtained a CC_{50} value of 615.4 µg/mL and SI values of 7.7 and 13.1 for the sensitive and resistant strains, respectively.

Anticonvulsant activity

In the quest to support the folkloric use of ethanol extract of *P. subcordata* in the management of epileptic seizures, Daanaa and co-workers used varying animal models in in vivo anticonvulsant assays of 70% ethanol extract of the leaves of *P. subcordata*. They explored the following animal models and reference drugs: pentylenetetrazole-induced seizure (reference drug: diazepam (0.3, 1 or 3 mg/kg, i.p.)); picrotoxin-induced seizure (reference drug: diazepam (0.3, 1 or 3 mg/kg, i.p.)); maximal electroshock (reference drug: carbamazepine (3, 10 or 30 mg/kg, p.o)); strychnine-induced seizure (reference drug: diazepam (1 mg/kg, i.p.)); 4-aminopyridine-induced seizure (reference drug: sodium valproate, (100, 300 or 600 mg/kg, p.o.)); and lithium/pilocarpine-induced status epilepticus (reference drug: diazepam (1 mg/kg, i.p.), and discovered that the extract worked by delaying the onset of seizure and reducing the duration and frequency of induced convulsions in most of the animal models, at study doses of 30, 100 and 300 mg/kg (p.o.). However, in electroshock and strychnine-induced test models, the hydroethanol extract failed to delay the onset of tonic hind limb extensions and the onset of seizure, respectively (Daanaa et al. 2018). Though the doses of the extract used in this study were ten times those of the reference drugs, this report by Daanaa et al. gives a pharmacological insight to the use of ethanol extract of *P. subcordata* leaves in the ethnomedicinal management of epileptic convulsion and presents the plant as a possible source of anticonvulsant agents if further investigated to find out if there could be any synergistic effect of using the extract in a combination therapy, since herbal medicines are often administered as a mixture of many extracts. Another way to ascertain the use of this extract in traditional medicine is by screening and isolating the active constituent(s) of the extract and carrying out extensive assays (in vitro and in vivo) on the isolated compound(s) and ultimately conduct clinical studies to substantiate their activities. This study by Daanaa et al. (2018) is the only anticonvulsant assay so far done for this genus.

Antihyperglycemic/antidiabetic activity

In a bid to support or refute the ethnomedicinal use of *P. subcordata* bark in the management of diabetes, Zhou et al. (2019) carried out an in vitro protein tyrosine phosphatase 1B (PTP1B) inhibitory assay on eight iridoids **(3–10)** isolated from ethanol extracts of *P. subcordata* leaves and bark. Only **(3)**, one of the six novel iridoids **(3–10)** showed relavant enzyme inhibition with an IC_{50} value of 22.2 µM in comparison with the positive control, oleanolic acid (IC_{50} 4.3 µM). Though this is not very fantastic, but chemical modification of the compound could lead to a better activity. To prove this assertion, when the structures of two enantiomers, subcordatanol III **(5)** and subcordatanol IV **(6)** were transformed to subcordatalactons A and B, respectively, their antihyperglycemic property dramatically improved from IC_{50} value of > 80

μM to 8.9 and 9.8 μM for A and B, respectively (Zhou et al. 2019). We recommend in vitro cytotoxicity assay and calculation of SI for **(3)** as well as in vivo assays to determine its bioavailability and mechanism of action.

Antioxidant activity

Since the antioxidant activity recorded for this genus was from in vitro assay, which is not a sufficient prove of a possible in vivo efficacy of the samples as antioxidants, we hereby present the in vitro radical scavenging results as an indication of the phytoconstituents of the species rather than as a bioactivity. Many a time, extracts that exhibit in vivo antioxidant property are usually high in phenolic content, But, the phytochemical analysis of the eight studied species of *Psydrax* gave only three flavonoids as phenolic compounds which might be considered too small to accord the genus antioxidant properties. Surprisingly, some of the extracts and isolated compounds of the genus exhibited in vitro radical scavenging properties. We decided to present in vitro radical scavenging results of extracts with IC_{50} or EC_{50} values less than 10 or 100 μg/mL for compounds or extracts/fractions and to exclude results with very high concentrations of no scientific relevance. In a study conducted by Awah et al. (2012), 80% methanol root extract of *P. subcordata* displayed DPPH radical scavenging property with an EC_{50} value of 23.9 μg/mL in comparison to ascorbic acid of EC_{50} value of 4.9 μg/mL. Akoto et al. (2019) reported that the methanol extract of *P. peruviana* stem bark also displayed DPPH radical and hydrogen peroxide scavenging activities with IC_{50} values of 12.20 and 24.26 μg/ml, respectively. Two iridoids (**13** and **17**) isolated from the fruit extracts of *P. subcordata* reportedly displayed DPPH radical scavenging activity with EC_{50} values of 1.12 μg/mL and 2.03 μg/mL for **(13)** and **(17),** respectively in comparison with EC_{50} of 1.74 μg/mL for vitamin C, the positive control (Joubouhi et al. 2017). **(13)** and **(17)** are not polyphenolic compounds with inherent antioxidant properties, neither are they glycosidic, yet they exhibited radical scavenging properties. Thus, their radical scavenging properties needs further investigation – probably in vivo studies – to confirm the activity and elucidate the mechanism of action of these extracts and compounds.

Toxicity

Toxicity assays are very paramount in discovering new drugs to confirm the safety of any bioactive extract/fraction or compound. It is also a test of activity of a sample against malignant cells. As previously pointed out, only few researchers take the time to carry out in vitro cytotoxicity assay to test the safety of their plant samples. It is observed in the course of this review that most of the in vitro toxicity tests were done without determining the selectivity index of test samples; an important parameter needed to establish the safety of a sample to healthy cells. Daanaa et al. 2018, in their anticonvulsant in vivo assay of the aqueous ethanol extract *P. subcordata* also determined the acute toxicity of the extract in animal model and reported no death in 14 days the test lasted, but observed reduced activity and sedation of the animals at doses between 300 and 3000 mg/kg body weight. In a different study, extracts and isolated constituents (**62–74**) of *P. subcordata* fruits showed no hemolysis against human red blood cells at maximum concentrations of 512 and 256 μg/mL respectively, and are adjudged to be safe to normal cells (Joubouhi et al. 2017). Feenna and co-researchers reported that acute toxicity and lethality assays of methanol leaf extract of *P. horizontalis* in rats, showed no mortality at the maximum lethal dose of 5000 mg/kg of extract (Feenna et al. 2020). However, contrary to the forgoing non-toxic reports about the genus extracts, in a study involving 80% methanol extract of the root of *P. subcordata,* there was toxicity against human peripheral blood mononuclear cells (PBMC), even at extract's concentration of as low as 10 μg/mL compared to a negative control (Awah et al. 2012). No relevant bioactive cytotoxicity of the extracts, fractions or compounds of this genus was encountered by authors in the course of this review. We therefore recommend that more toxicity assays be conducted for extracts and constituents of *Psydrax* species to ascertain their efficacy against abnormal cells and safety to normal cells.

Conclusion

We are projecting in this review that the chemotaxonomic marker for *Psydrax* is iridoid. This projection is evidenced in the number of iridoids (twenty-seven)

isolated out of the fifty-five isolated components of the genus. The current review reveals that investigations so far carried out on *Psydrax* are mainly in vitro studies, with very few in vivo studies. No in silico study has been done on the isolated constituents of *Psydrax,* nor any clinical trial so far. The limited in vivo studies of this genus could be one of the reasons why little scientifically significant activities have been recorded for the genus considering the fact that the major constituent of the genus is iridoid, and iridoids are seen as pro-drugs which need to be biotransformed in vivo to elicit activities. Thus, in vivo assays of these plants are strongly recommended by the authors to reveal the hidden treasure of the genus. Many of the documented studies lack depth and thus require further investigation for an evidence-based application of medicinally active species within the genus. Although some documented bioactive phytochemicals reported in a few species of *Psydrax* correlate well with the traditional uses of the plants, many of the studies are more or less preliminary with results of some being low to be given any further scientific attention. Future research study is strongly recommended to be focused on the characterization of bioactive constituents of plant species in the genus and subsequent in vitro and in vivo studies, adopting standard bioassay and analytical methods to ensure consistent and generally acceptable results that could be pursued for potential drug leads. It is also evidenced from this review that the genus is a good source of novel compounds with varying bioactivities, which might qualify as potential leads in drug discovery. Unfortunately, only about six percent of *Psydrax* species have been explored for their ethnobotanical uses, phytochemicals and pharmacological properties; and this represents a lacuna that needs to be filled. There is therefore, a scientific need for further exploration of the genus in order to discover its several other ethnomedicinal applications, phytochemicals and pharmacological properties. In conclusion, authors recommend authentic in vitro, in silico, in vivo assays and even clinical trials of extracts and phytoconstituents of this genus, adopting standard assay methods. They also suggest sustainable utilization of plant resources under this genus via use-informed cultivation and domestication of medicinally important species in order to forestall the loss of species and the decline in plant biodiversity particularly in Africa where many of the species under this genus are endemic.

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Conflict of interest There was no conflict of interest among the authors.

Ethical approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

References

Achenbach H (1986) Investigations on West African medicinal plants. Pure Appl Chem 58(5):653–662. https://doi.org/10.1351/pac198658050653

Achenbach H, Waibel R, Addae-Mensah I (1980) Shanzhisin methyl ester gentiobioside, a New Iridoid - isolation and synthesis. Tetrahedron Lett 21(38):3677–3678. https://doi.org/10.1016/S0040-4039(00)78742-9

Achenbach H, Waibel R, Raffelsberger B, Addae-Mensah I (1981) Iridoid and other constituents of canthium subcordatum. Phytochemistry 20(7):1591–1595. https://doi.org/10.1016/S0031-9422(00)98538-8

Agyare C, Asase A, Lechtenberg M, Niehues M, Deters A, Hensel A (2009) An ethnopharmacological survey and in vitro confirmation of ethnopharmacological use of medicinal plants used for wound healing in bosomtwi-atwima-kwanwoma area, ghana. J Ethnopharmacol 125(3):393–403. https://doi.org/10.1016/j.jep.2009.07.024

Akoto CO, Acheampong A, Boakye YD, Takyi S, Garba R (2019) Phytochemical screening and in vitro antioxidant and antimicrobial activities of the extracts of the stem-bark of psydrax peruviana. Journal of Medicinal Plants Studies 7(5):28–34

Anokwah D, Mensah AY, Amponsah IK, Mireku EA, Mintah DN (2016) Anti-inflammatory, antioxidant and antimicrobial activities of the stem bark of psydrax subcordata. Pharm Lett 8(20):21–28

Appiah K, Oppong C, Mardani H, Omari R, Kpabitey S, Amoatey C, Onwona-Agyeman S, Oikawa Y, Katsura K,

Fujii Y (2018) Medicinal plants used in the ejisu-juaben municipality, southern ghana: an ethnobotanical study. Medicines 6(1):1–27. https://doi.org/10.3390/medicines6010001

Arriola AH, Alejandro GJD (2013) A new species of psydrax (Vanguerieae, Rubiaceae) from Luzon, Philippines including its conservation status. Phytotaxa 149(1):27–30. https://doi.org/10.11646/phytotaxa.149.1.4

Arriola AH, Cobangkiat AB, Alejandro GJD (2017) Psydrax Multiflora Sp. Nov. (Rubiaceae) from Palawan, Philippines. Nord J Bot 35(2):182–184. https://doi.org/10.1111/njb.01255

Asfaw A, Lulekal E, Bekele T, Debella A, Abebe A, Degu S (2021) Ethnobotanical investigation on medicinal plants traditionally used against human ailments in ensaro district, north shewa zone, amhara regional state, ethiopia. Research Square. https://doi.org/10.21203/rs.3.rs-720404/v1

Awah FM, Uzoegwu PN, Ifeonu P, Oyugi JO, Rutherford J, Yao X, Fehrmann F, Fowke KR, Eze MO (2012) Free radical scavenging activity, phenolic contents and cytotoxicity of selected nigerian medicinal plants. Food Chem 131(4):1279–1286. https://doi.org/10.1016/j.foodchem.2011.09.118

Awantu AFFAF, Fotsing FYS, Bankeu KJJ, Lenta NB, Tsouh FPVPV, Boyom FFFFF, Assob NJCJC, Tsamo E, Sewald N (2019) Antiplasmodial and antimicrobial potential of canthium subcordatum extracts and isolates. J Phytopharmacol 8(2):52–56. https://doi.org/10.31254/phyto.2019.8205

Bremer B (2009) A review of molecular phylogenetic studies of rubiaceae. Ann Mo Bot Gard 96(1):4–26. https://doi.org/10.3417/2006197

Bridson DM (1985) The Reinstatement of Psydrax (Rubiaceae, Subfam. Cinchonoideae Tribe Vanguerieae) and a revision of the African species. Kew Bull 40(4):687–725. https://doi.org/10.2307/4109853

Bridson DM (1986) The Reinstatement of the African Genus Keetia (Rubiaceae Subfam. Cinchonoidedeae, Tribe Vanguerieae). Kew Bull 41(4):965–994. https://doi.org/10.2307/4102996

Buathong R, Schindler F, Schinnerl J, Valant-Vetschera K, Bacher M, Potthast A, Rosenau T, Vajrodaya S (2019) Uncommon fatty acids, iridoids and other secondary metabolites from the medicinal plant species ixora cibdela craib (Rubiaceae). Phytochem Lett 33:77–80. https://doi.org/10.1016/j.phytol.2019.07.011

Bubonja-Šonje M, Knežević S, Abram M (2020) Challenges to antimicrobial susceptibility testing of plant-derived polyphenolic compounds. Arch Ind Hyg Toxicol 71(4):300–311. https://doi.org/10.2478/aiht-2020-71-3396

Castro SG, Cid JEV, Ibañez WAS, Alejandro GJD, Tan MA (2016) GC-MS metabolite profiling of the hexane extract and antimicrobial characterization of the Philippine endemic rubiaceae species uncaria cordata var. circa, psychotria luzoniensis, and psydrax puberula. Acta Manilana 64:9–16

Catarino L, Havik PJ, Romeiras MM (2016) Medicinal plants of guinea-bissau: therapeutic applications, ethnic diversity and knowledge transfer. J Ethnopharmacol 183:71–94. https://doi.org/10.1016/j.jep.2016.02.032

Chandramouli B, Mallikarjuna K (2020) Enumeration of various ayurvedic formulations listed in an ancient palm-leaf manuscript of Rayalaseema region in Andhra Pradesh State, India. J Ethnopharmacol 251:112552. https://doi.org/10.1016/j.jep.2020.112552

Cheek M, Sonké B (2004) Psydrax bridsoniana (Rubiaceae), a new species of tree from western cameroon. Kew Bull 59:605–608. https://doi.org/10.2307/4110919

Chukwujekwu JC, van Staden J, Smith P (2005) Antibacterial, anti-inflammatory and antimalarial activities of some nigerian medicinal plants. S Afr J Bot 71(3–4):316–325. https://doi.org/10.1016/S0254-6299(15)30105-8

Cos P, Vlietinck AJ, Berghe DV, Maes L (2006) Anti-infective potential of natural products: how to develop a stronger in vitro 'proof-of-concept.' J Ethnopharmacol 106(3):290–302. https://doi.org/10.1016/j.jep.2006.04.003

Coulerie P, Poullain C (2016) New caledonia: a hot spot for valuable chemodiversity part 3: santalales, caryophyllales, and asterids. Chem Biodivers 13(4):366–379. https://doi.org/10.1002/cbdv.201500101

Daanaa S, Abotsi WKM, Boakye-Gyasi E, Woode E (2018) Anticonvulsant effect of the hydroethanolic leaf extract of psydrax subcordata (DC.) bridson in murine models. J Ethnopharmacol 213:384–394. https://doi.org/10.1016/j.jep.2017.11.028

Davis AP, Govaerts R, Bridson DM (2007) New combinations in madagascan vanguerieae (Rubiaceae) for the Genera psydrax, pyrostria, and rytigynia. Blumea - Biodiversity, Evolution and Biogeography of Plants 52(1):139–145. https://doi.org/10.3767/000651907X612382

Dhivya SM, Kalaichelvi K (2016) Medicinal plants used by irula eribes of nellithurai beat, karamadai range, western ghats, tamil nadu, india: an ethnobotanical survey. Journal of Medicinal Plants Studies 4(4):270–277

Dinda, B. 2019. "Pharmacology of Iridoids." Pp. 145–254 in *Pharmacology and Applications of Naturally Occuring Iridoids*. Cham: Springer International Publishing.

Dutta MP, Singh MK, Borah D (2019) Piscicidal plants of northeast india and its future prospect in aquaculture-a comprehensive review. Indian J Nat Prod Resour 10(3):165–174

Eloff JN (2019) Avoiding pitfalls in determining antimicrobial activity of plant extracts and publishing the results. BMC Complement Altern Med 19(106):1–8. https://doi.org/10.1186/s12906-019-2519-3

Essien E, Newby J, Walker T, Setzer W, Ekundayo O (2015) Characterization and antimicrobial activity of volatile constituents from fresh fruits of alchornea cordifolia and canthium subcordatum. Medicines 3(1):1. https://doi.org/10.3390/medicines3010001

Eswani N, Kudus KA, Nazre M, Awang Noor AG, Ali M (2010) Medicinal plant diversity and vegetation analysis of logged over hill forest of tekai tembeling forest reserve, Jerantut, Pahang. J Agric Sci 2(3):189–210. https://doi.org/10.5539/jas.v2n3p189

Fan Q, Na Z, Ji K, Gongpan P, Zhou L, He W, Huang F, Huabin Hu, Song Q (2020) A novel pentacyclic triterpene from the canes of uncaria sessilifructus (Rubiaceae). Nat Prod Res. https://doi.org/10.1080/14786419.2020.1795856

Feenna OP, Estella OU, Obodike EC (2020) Phytochemical analysis and anti-diabetic activity of leaf extract of psydrax

horizontalis schum and thonn (Rubiaceae). Pharmacognosy Journal 12(1):95–102. https://doi.org/10.5530/pj.2020.12.15

Gaertner, Joseph. 1788. *De Fructibus Et Seminibus Plantarum*. Stutgardiae: Typis Academiae Carolinae

Gemedo-Dalle T, Maass BL, Isselstein J (2005) plant biodiversity and ethnobotany of borana pastoralists in Southern Oromia, Ethiopia. Econ Bot 59(1):43–65

Gertsch J (2009) How scientific is the science in ethnopharmacology? Historical perspectives and epistemological problems. J Ethnopharmacol 122(2):177–183. https://doi.org/10.1016/j.jep.2009.01.010

Ghisalberti ELL (1998) Biological and pharmacological activity of naturally occurring iridoids and secoiridoids. Phytomedicine 5(2):147–163. https://doi.org/10.1016/S0944-7113(98)80012-3

Gibbons KL (2020) Hedyotis, oldenlandia and related genera (Rubiaceae: Spermacoceae) in Australia: New Genera and New Combinations in an Asian-Australian-Pacific Lineage. Taxon 69(3):515–542. https://doi.org/10.1002/tax.12236

Goh SH, Lee KH, Chuah CH, Ong HC, Madani L, Pereira JT (1997) A phytochemical study of borneo: selected plants from sabah lowland forests. J Herbs Spices Med Plants 5(1):29–52. https://doi.org/10.1300/J044v05n01_05

Gunasegaran R, Subramani K, Azantha Parimala P, Ramachandran Nair AG, Rodriguez B, Madhusudanan KP (2001) 7-O-(6-O-Benzoyl-β-d-Glucopyranosyl)-Rutin from leaves of canthium dicoccum. Fitoterapia 72(3):201–205. https://doi.org/10.1016/S0367-326X(00)00302-6

Gupta R, Sharma AK, Dobhal MP, Sharma MC, Gupta RS (2011) Antidiabetic and antioxidant potential of β-Sitosterol in streptozotocin-induced experimental hyperglycemia. J Diabetes 3(1):29–37. https://doi.org/10.1111/j.1753-0407.2010.00107.x

Heitzman ME, Neto CC, Winiarz E, Vaisberg AJ, Hammond GB (2005) Ethnobotany, phytochemistry and pharmacology of Uncaria (Rubiaceae). Phytochemistry 66(1):5–29. https://doi.org/10.1016/j.phytochem.2004.10.022

Hussain H, Green IR, Saleem M, Raza ML, Nazir M (2019) Therapeutic potential of iridoid derivatives: patent review. Inventions 4(2):1–16. https://doi.org/10.3390/inventions4020029

Ilboudo DP, Basilico N, Parapini S, Corbett Y, D'Alessandro S, Dell'Agli M, Coghi P, Karou SD, Sawadogo R, Gnoula C, Simpore J, Nikiema J-B, Monti D, Bosisio E, Taramelli D (2013) Antiplasmodial and anti-inflammatory activities of canthium henriquesianum (K. Schum), a plant used in traditional medicine in burkina faso. J Ethnopharmacol 148(3):763–769. https://doi.org/10.1016/j.jep.2013.04.049

Joubouhi C, Mabou FD, Tebou FPL, Ngnokam D, Harakat D, Voutquenne-Nazabadioko L, Tebou PLF, Ngnokam D, Harakat D, Voutquenne-Nazabadioko L (2015) Five new iridoïd dimers from the fruits of canthium subcordatum DC (Syn. Psydrax Subcordata DC). Phytochem Lett 13:348–354. https://doi.org/10.1016/j.phytol.2015.07.021

Joubouhi C, Tamokou J, Ngnokam D, Voutquenne-Nazabadioko L, Kuiate J (2017) Iridoids from canthium subcordatum iso-butanol fraction with potent biological activities. BMC Complement Altern Med 17(17):1–8. https://doi.org/10.1186/s12906-016-1536-8

Kala SC (2015) Medicinal attributes of family rubiaceae. International Journal Pf Pharmacy and Biological Science 5(2):179–181. https://doi.org/10.4103/0973-7847.95866

Kalaichelvi K, Dhivya SM (2016) Ethno medicinal knowledge of plants used by irula tribes of nellithurai beat, karamadai range, western ghats and phytochemical screening of selected lamiaceae species. Adv J Pharm Life Sci Res 4(2):54–64

Kalita BC, Tag H, Gogoi BJ, Hui PK (2017) Diversity and traditional uses of some poisonous plants of Arunachal Pradesh. IJARIIE 3(1):755–763

Koehbach J, Attah AF, Berger A, Hellinger R, Kutchan TM, Carpenter EJ, Rolf M, Sonibare MA, Moody JO, Wong G-S, Dessein S, Greger H, Gruber CW (2013) Cyclotide discovery in gentianales revisited-identification and characterization of cyclic cystine-knot peptides and their phylogenetic distribution in rubiaceae plants. Biopolymers 100(5):438–452. https://doi.org/10.1002/bip.22328

Lantz H, Bremer B (2004) Phylogeny inferred from morphology and DNA data: characterizing well-supported groups in vanguerieae (Rubiaceae). Bot J Linn Soc 146(3):257–283. https://doi.org/10.1111/j.1095-8339.2004.00338.x

Lantz H, Andreasen K, Bremer B (2002) Nuclear RDNA ITS sequence data used to construct the first phylogeny of vanguerieae (Rubiaceae). Plant Syst Evol 230:173–187. https://doi.org/10.1007/s006060200003

Ludwiczuk A, Skalicka-Woźniak K, Georgiev MII (2017) Terpenoids. Elsevier

Magassouba FBB, Diallo AKK, Kouyat´e M, Mara F, Mara O, Bangoura O, Camara A, Traor S, Diallo AKK, Zaoro M, Lamah K, Diallo S, Camara G, Traor´e S, Keita A, Camara MKK, Barry R, Keita S, Oulare K, Barry MSS, Donzo M, Camara K, Tote K, VandenBerghe D, Totte J, Pieters L, Vlietinck AJJ, Balde AM, Kouyaté M, Mara F, Mara O, Bangoura O, Camara A, Traoré S, Diallo AKK, Zaoro M, Lamah K, Diallo S, Camara G, Traoré S, Kéita A, Camara MKK, Barry R, Kéita S, Oularé K, Barry MSS, Donzo M, Camara K, Toté K, VandenBerghe D, Totté J, Pieters L, Vlietinck AJJ, Baldé AMM (2007) Ethnobotanical survey and antibacterial activity of some plants used in guinean traditional medicine. J Ethnopharmacol 114(1):44–53. https://doi.org/10.1016/j.jep.2007.07.009

Magwede K, van Wyk BEE, van Wyk AEE (2018) An Inventory of Vhavenda Useful Plants. S Afr J Bot 122:57–89. https://doi.org/10.1016/j.sajb.2017.12.013

Mahyuni R, Chikmawati T, Ariyanti NS (2019) Short communication: two new species and new record of psydrax gaertn. (Rubiaceae: Vanguerieae) in Borneo. Biodiversitas Journal of Biological Diversity 20:2011–2015. https://doi.org/10.13057/biodiv/d200730

Maldonado C, Barnes CJ, Cornett C, Holmfred E, Hansen SH, Persson C, Antonelli A, Rønsted N (2017) Phylogeny predicts the quantity of antimalarial alkaloids within the iconic yellow cinchona bark (Rubiaceae: Cinchona Calisaya). Front Plant Sci 8:1–16. https://doi.org/10.3389/fpls.2017.00391

Maroyi A (2012) Use of traditional veterinary medicine in nhema communal area of the Midlands Province,

Zimbabwe. Afr J Tradit Complement Altern Med 9(3):315–322. https://doi.org/10.4314/ajtcam.v9i3.3

Memvanga PB, Tona GL, Mesia GK, Lusakibanza MM, Cimanga RK (2015) Antimalarial activity of medicinal plants from the democratic republic of congo: a review. J Ethnopharmacol 169:76–98. https://doi.org/10.1016/j.jep.2015.03.075

Mesia GK, Tona GL, Nanga TH, Cimanga RK, Apers S, Cos P, Maes L, Pieters L, Vlietinck AJ (2008) Antiprotozoal and cytotoxic screening of 45 plant extracts from democratic republic of congo. J Ethnopharmacol 115(3):409–415. https://doi.org/10.1016/j.jep.2007.10.028

Muhit MdA, Khanam SS, Islam MdS, Rahman MS, Begum B (2010) Phytochemical and biological investigations of pterospermum acerifolium wild bark. J Pharm Res 3(11):2643–2646

Mukandiwa L, Eloff JN, Naidoo V (2012a) Evaluation of plant species used traditionally to treat myiasis for activity on the survival and development of lucilia cuprina and chrysomya marginalis (Diptera: Calliphoridae). Vet Parasitol 190(3–4):566–572. https://doi.org/10.1016/j.vetpar.2012.06.027

Mukandiwa L, Naidoo V, Eloff JN (2012b) In Vitro antibacterial activity of seven plants used traditionally to treat wound myiasis in animals in Southern Africa. J Med Plants Res 6(27):4379–4388. https://doi.org/10.5897/jmpr11.1130

Nahrstedt A, Rockenbach J, Wray V (1995) Phenylpropanoid glycosides, a furanone glucoside and geniposidic acid from members of the rubiaceae. Phytochemistry 39(2):375–378. https://doi.org/10.1016/0031-9422(94)00906-A

Neelima M, Prasad GP, Sudarsanam G, G. P. enahala Pratap, and B. Jyothi. (2011) Ethnobotanical Studies in rapur forest division of Nellore District in Andhra Pradesh. Life Science Leaflets 11:333–345

Nyahangare ET, Mvumi BM, Mutibvu T (2015) Ethnoveterinary plants and practices used for ecto-parasite control in semi-arid smallholder farming areas of Zimbabwe. J Ethnobiol Ethnomed 11(30):1–16. https://doi.org/10.1186/s13002-015-0006-6

Ochwang'i DO, Kimwele CN, Oduma JA, Gathumbi PK, Kiama SG, Efferth T (2016) Phytochemical screening of medicinal plants of the kakamega country, kenya commonly used against cancer. Med Aromat Plants 05(06):1–7. https://doi.org/10.4172/2167-0412.1000277

Ochwang'i DO, Kimwele CN, Oduma JA, Gathumbi PK, Mbaria JM, Kiama SG (2014) Medicinal plants used in treatment and management of cancer in Kakamega County, Kenya. J Ethnopharmacol 151(3):1040–1055. https://doi.org/10.1016/j.jep.2013.11.051

Ochwang'i DO, Kimwele CN, Oduma JA, Gathumbi PK, Kiama SG, Efferth T (2018) Cytotoxic activity of medicinal plants of the Kakamega County (Kenya) against drug-sensitive and multidrug-resistant cancer cells. J Ethnopharmacol 215:233–240. https://doi.org/10.1016/j.jep.2018.01.004

Pakkala KR, Patel HA (2021) Overview on some indigenous medicinal plants utilized in treatment of gynecological disorders by indian women. Doctrines of Integratedive Medicine, Pharmacy and Science-the International Journal 01(01):54–74

Ponnaiah J, Karthikeyan S, Tagore JK (2018) Medicinal plants used for fertility and menstrual disorders by the women belonging to the nilgiris tribe community of Southern India. International Journal of Scientific Research and Reviews 7(4):601–608

du Preez, Iwanette, Whitney Shingenge, and Davis Ropafadzo Mumbengegwi. 2020. "Namibian Plants Used in the Treatment of Malaria and Associated Symptoms." Pp. 45–66 in *ACS Symposium Series*. Vol. 1361. Washington, DC: American Chemical Society.

Quang BH, Tran TB, Ha TD, Van HD, Thanh HNT, Thu HB, Dang VS (2020) A New Species of Psydrax (Vanguerieae, Rubiaceae) from the Gia Lai Plateau, Southern Vietnam. PhytoKeys 149:99–107. https://doi.org/10.3897/phytokeys.149.51710

Radol AO, Kiptoo M, Makokha AO, Tolo FM (2016) Types of herbal medicine used for HIV conditions in Vihiga County, Kenya. European Journal of Medicinal Plants 13(2):1–23. https://doi.org/10.9734/EJMP/2016/23180

Raja RN, RamaLakshmi S, Muthuchelian K (2011) GC-MS analysis of bioactive components from the ethanolic leaf extract of Canthium Dicoccum (Gaertn.) Teijsm & Binn. J Chem Pharm Res 3(3):792–798

Rasingam L (2012) Ethnobotanical Studies on the wild edible plants of Irula Tribes of Pillur Valley, Coimbatore District, Tamil Nadu, India. Asian Pac J Trop Biomed 2(3):S1493–S1497. https://doi.org/10.1016/S2221-1691(12)60443-2

Rathinavelusamy P, Mazumder PM, Sasmal D, Jayaprakash V (2014) Evaluation of in Silico, in Vitro α-amylase inhibition potential and antidiabetic activity of pterospermum acerifolium bark. Pharm Biol 52(2):199–207. https://doi.org/10.3109/13880209.2013.823551

Ríos JL, Recio MC (2005) Medicinal plants and antimicrobial activity. J Ethnopharmacol 100(1–2):80–84. https://doi.org/10.1016/j.jep.2005.04.025

Rockenbach J, Nahrstedt A (1990) New and known Cyanogenic glycosides from the rubiaceae. Planta Med 56:591–592

Rockenbach J, Nahrstedt A, Wray V (1992) Cyanogenic glycosides from PS psydrax and oxyanthus species. Phytochemistry 31(2):567–570. https://doi.org/10.1016/0031-9422(92)90039-S

Schwarz B, Wray V, Proksch P (1996) A cyanogenic glycoside from canthium schimperianum. Phytochemistry 42(3):633–636. https://doi.org/10.1016/0031-9422(96)00018-0

Sen SK, Behera LM (2016) Some ethnomedicinal plants used against high blood pressure in bargarh district in Western Odisha (India). Tropical Plant Research 3(3):517–521. https://doi.org/10.22271/tpr.2016.v3.i3.068

Sévenet, Thierry, and Jacques Pusset. 1996. "Alkaloids from the Medicinal Plants of New Caledonia." Pp. 1–73 in *Alkaloids: Chemistry and Pharmacology*. Vol. 48.

Subashree K, Dar JA, Karuppusamy S, Sundarapandian S (2021) Plant diversity, structure and regeneration potential in tropical forests of Western Ghats, India. Acta Ecol Sin 41(4):259–284. https://doi.org/10.1016/j.chnaes.2020.02.004

Tabuti JRS, Ticktin T, Arinaitwe MZ, Muwanika VB (2009) Community attitudes and preferences towards woody species: implications for conservation in nawaikoke,

Uganda. Oryx 43(03):393–402. https://doi.org/10.1017/S0030605309001847

Tabuti JRS, Muwanika VB, Arinaitwe MZ, Ticktin T (2011) Conservation of priority woody species on farmlands: a case study from Nawaikoke Sub-County, Uganda. Appl Geogr 31(2):456–462. https://doi.org/10.1016/j.apgeog.2010.10.006

Taher M, Shaari SS, Susanti D, Arbain D, Zakaria ZA (2020) Genus ophiorrhiza: a review of its distribution, traditional uses, phytochemistry, biological activities and propagation. Molecules 25(11):2611. https://doi.org/10.3390/molecules25112611

Tan HP, Wong DZH, Ling SK, Chuah CH, Kadir HA (2012) Neuroprotective activity of galloylated cyanogenic glucosides and hydrolysable tannins isolated from leaves of phyllagathis rotundifolia. Fitoterapia 83(1):223–229. https://doi.org/10.1016/j.fitote.2011.10.019

Tilney PM, van Wyk AE, Kok PDF (1988) The taxonomic significance of anatomical characters of the stem in the Southern African Species of Canthium s.l. (Rubiaceae). S Afr J Bot 54(6):585–595. https://doi.org/10.1016/s0254-6299(16)31258-3

Tilney PM, Kok PDF, van Wyk AE (1990) The taxonomic significance of anatomical characters of the leaf in the Southern African Species of Canthium s.l. (Rubiaceae). S Afr J Bot 56(3):363–382. https://doi.org/10.1016/s0254-6299(16)31066-3

Tundis R, Loizzo M, Menichini F, Statti G, Menichini F (2008) Biological and pharmacological activities of iridoids: recent developments. Mini-Rev Med Chem 8(4):399–420. https://doi.org/10.2174/138955708783955926

Umaiyambigai, D., K. Saravanakumar, and G. A. Raj. 2016. "Phytochemical Profiles, Antibacterial and Antifungal Activity of Leaves from the Psydrax Dicoccos (Gaertn)." *Indo – Asian Journal of Multidisciplinary Research (IAJMR)* 2(1):443–52.

Vaidyanathan D, Salai Senthilkumar MS, Ghouse Basha M (2013) Studies on ethnomedicinal plants used by malayali Tribals in Kolli Hills of Eastern Ghats, Tamilnadu, India. Asian Journal of Plant Science and Research 3(6):29–45

Vijayashalini P, Anjanadevi N, Abirami P, Sharmila M (2017) Ethnomedicinal plants survey in Elanji Hill Village sathyamangalam range of reserve forest, Western Ghats Tamil Nadu India. Int J Biol Res 2(1):22–26

Wijnsma, R., and R. Verpoorte. 1986. "Anthraquinones in the Rubiaceae." Pp. 79–149 in *Progress in the Chemistry of Organic Natural Products*.

Yang B, Feng YJ, Hoan Vu, McCormick B, Rowley J, Pedro L, Crowther GJ, Van Voorhis WC, Forster PI, Quinn RJ (2016) Bioaffinity mass spectrometry screening. J Biomol Screen 21(2):194–200. https://doi.org/10.1177/1087057115622605

Yulvianti M, Zidorn C (2021) Chemical diversity of plant cyanogenic glycosides: an overview of reported natural products. Molecules 26(3):719. https://doi.org/10.3390/molecules26030719

Zhou J, Zhenlong Wu, Oyawaluja BO, Coker HAB, Odukoya OA, Yao G, Che C-T (2019) Protein tyrosine phosphatase 1B inhibitory iridoids from psydrax subcordata. J Nat Prod 82(10):2916–2924. https://doi.org/10.1021/acs.jnatprod.9b00770