Bulletin of Faculty of Pharmacy, Cairo University xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Bulletin of Faculty of Pharmacy, Cairo University

journal homepage: www.elsevier.com/locate/bfopcu

Review Paper

Notes on the genus *Paramignya*: Phytochemistry and biological activity

Ninh The Son

Department of Bioactive Products, Institute of Natural Products Chemistry, Vietnam Academy of Science and Technology (VAST), 18 Hoang Quoc Viet, Caugiay, Hanoi, Viet Nam

ARTICLE INFO

Keywords:
Paramignya
Coumarins
Tirucallanes
Acridone alkaloids
Bioactive

ABSTRACT

Genus *Paramignya* belongs to Rutaceae family, with interesting secondary metabolites, comprising main classes of compounds coumarin and coumarin glycosides, acridone alkaloids, tirucallane and tirucallane glycosides, phenols, and flavonoids, as well as several compounds limonoid, lignin glycoside and sterol. *Paramignya* species has been employing as folk medicines against hepatitis, diabetes, cancer, nose infections. Many bioactive reported such as cytotoxic assay, antioxidant, antiinflammatory, antiumor cancer, α-glucosidase inhibitory activities indicated either *Paramignya* extracts, fractions, or isolated compounds to become valuable resources for natural new drug developments. However, no evidences are reported for general view about this genus. In current paper, we exhibit overview almost of isolated components and biological evaluations from this genus. These findings are important to improve the values of these medicinal plants for the health benefit, drug discovery and guideline for future researches.

1. Introduction

The genus *Paramignya*, was a member of Rutaceae family and was widely distributed in the tropical Southern Vietnam, Southern Philippines, Thailan, Malaysia, Java-Indonesia, Australia, dry and wet zones of Sri Lanka, including twenty 28 species [1–4]. *Paramignya* species established the values as traditional medicine of each country. The roots of *P. trimera* species, becoming as a folk Vietnamese medicine to treat hepatitis and diabetes [2,5], or Thai used the stems of *P. grithii* for the treatment of nose infections [6]. Chemical investigations have been reporting the existence of predominant coumarins, triterpenes, alkaloids, and their glycoside derivatives [1,2,4,6–13]. Significantly, apart from the easily available information on phytochemistry and bioassay for *P. trimera*, this species had also been concentrated on studied qualitative and quantitative experiments [14–18]. Although natural products from this genus has been increasingly playing important role in drug discovery programs, however, there is no supportive evidence to give general insight into phytochemical and biological activities of extracts, fractions, and isolated compounds. Subsequently, this current paper is an overview of almost naturally occurring compounds (total 67 compounds), including twenty-two coumarin and coumarin glycosides **1–22**, fifteen tirucallane and tirucallane saponins **23–37**, seven acridone alkaloids **38–44**, six flavanones, flavones and flavanone glycoside **45–50**, nine phenols **51–59**, two chromenes **60–61**, two megastigmane glycosides **62–63** and four others **64–67** from genus *Paramignya*, along with an extensive coverage their biological evaluation.

2. Botany

2.1. Nomenclature

According to database of the plant list (www.theplantlist.org, 2017), the following acceptable names, only two *Paramignya* species, which were *P. confertifolia* Swingle and *P. rectispinosa* W.G.Craib were listed at a level of medium confidence, whereas *P. brassii* C.T.White has been reported as a synonym of *Triphasia brassii* (C.T.White) Swingle species, with status of low confidence. Significantly, only five species were studied on phytochemistry and biology, including *P. trimera* (Oliv.) Burkill, *P. scandens* Craib, *P. griffithii* Hook.f., *P. monophylla* Wight, and *P. lobata* Burkill, along with twenty-two species *P. andamanica* Tanaka, *P. angulata* Kurz, *P. armata* Oliv., *P. beddomei* Tanaka, *P. blumei* Hassk., *P. citrifolia* Hook.f., *P. citrifolia* Oliv., *P. cuspidata* (Ridl.) Burkill, *P. dubia* Koord. & Valeton ex J.Moll & Janssonius, *P. glabra* Tanaka, *P. grandiflora* Oliv., *P. hainanensis* Swingle, *P. hispida* (Pierre ex Guillaumin) Pierre ex Guillaumin, *P. littoralis* Miq., *P. longipedunculata* Merr., *P. longispina* Hook.f., *P. micrantha* Kurz, *P. mindanaensis* Merr., *P. missionis* (Oliv.) Burkill, *P. petelotii* Guillaumin, *P. ridleyi* Burkill, and *P. surasiana* Craib were assigned as a status of unresolved and low confidence level [19].

2.2. Phylogeny

The Rutaceae were large and complex family, with commonly known as rue or citrus family of flowering plants, comprises of about

Peer review under responsibility of Faculty of Pharmacy, Cairo University.
E-mail address: theson_1988@yahoo.com.vn.

https://doi.org/10.1016/j.bfopcu.2017.12.001
Received 8 May 2017; Received in revised form 4 December 2017; Accepted 6 December 2017

158 genera and approximately 1900 species [20]. According to report of Epifano et al. [20], the Rutaceae were closest related to the Meliaceae and Simaroubaceae [20]. Almost species in the Rutaceae family that are trees or shrubs, a few are herbs, flowers had four or five petals and sepals, sometimes three, mostly separate, eight to ten stamen. Significantly, aromatic oils could be found in many species of this family, especially in terms of genus *Citrus* such as the orange (*C. sinensis*), lemon (*C. limon*), or grapefruit (*C. paradisi*). [21].

Paramignya belongs to Rutaceae family, commonly distributed in South East Asia [1–3], for instance, seven species named *P. armata* Oliv. var. *andamanica* King, *P. griffithii* Hook. F, *P. hispida* Pierre ex Guillaum, *P. monophylla* Wight, *P. petelotii* Guillaum, *P. scandens* (Griff.) Craib, and *P. trimera* (Oliv.) Guillaum, which were found in Vietnam [1,22]. Up to present, studies on phylogeny, morphological characterization, distribution, or pharmaceutical researches of this genus are quite limited. According to research paper of Mabberley (1998), the plants *Luvunga monophylla* (DC.) Mabb., *Atalantia* (?) *recurva* Benth., *Triphasia monophylla* DC, *Atalantia trimera* Oliver, could be considered as *P. trimera* (Oliver) Burkill [3]. Of note, general appearance showed that within the Rutaceae, *Paramignya* species is possibly congeneric with *Luvunga* species [23]. Additionally, morphological characterization of the genus *Luvunga* has been occurred with small different from *Paramignya* in its 3–5 petals, 6–10 stamens and 2–4 locules in the ovary, the simple leaves characteristic of *Paramignya,* including *P. trimera*, sometimes occur in *Luvunga*: petioles shorter than those of the usual trifoliolate leaves, so that *P. trimera* is more logically placed in *Luvunga* species [3].

3. Phytochemistry

Up to present, phytochemical investigations have been focused on various parts (roots, stems, barks, stem barks, leaves, twigs, and fruits) of four species *P. trimera*, *P. scandens*, *P. griffithii*, *P. monophylla*, especially in terms of roots and stems of *P. trimera*. With regards to total 67 compounds, chemical constituents of genus *Paramignya* were classified into a wide range of compounds, including coumarin and coumarin glycosides **1–22** [1,2,7,10–12,24], tirucallane and tirucallane saponins **23–37** [4,6,8,9,13], acridone alkaloids **38–44** [2,12], flavanones, flavones, and flavanone glycoside **45–50** [6,13,25], phenols **51–59** [2,25,26], chromenes **60–61** [2,6,7], and megastigmanes **62–63** [25] (Table 1 and Figs. 1a, 2a, 3a, and 4, 5). Beside, minor components **64–67** were also detected [11,25] (table 1 and Fig. 6). Among the total 67 different phytoconstituents, 24 new compounds were detected which belongs to the groups of coumarin and comarin glycosides **4**, **6–9**, **19–22**, tirucallane and tirucallane saponins **25–28**, and **31–37**, acridone alkaloids **43–44**, and flavanones **46–47**.Fig. 3b.

3.1. Coumarin and coumarin glycosides

Coumarin derivative compounds **1–22** were obtained as dominant components from *P. trimera* and *P. monophylla* species (Fig. 1a and Table 1). Article in phytochemistry of these species revealed most of naturally occurring coumarins **1–5** and **8–22** as free [1,2,7,10–12,24], whereas only two dimeric monoterpene-linked coumarin glycosides compounds **6–7** were reported [1]. Significantly, the most striking features for both major free compounds and their glycosides were that chemical isolated compounds have been found in the 6,7-disubstituted pattern in general molecular formula (Fig. 1a). Comprehensive analysis of free compounds, side chains were built from some typical characteristics such as methoxy, hydroxyl, geranyl, or with pyranyl moieties, meanwhile, glycosyl parts of coumarin glycosides paratrimerins A-B (**6–7**), which spectroscopic data elucidated their detail chemical structures as β-D-glucopyranosyl and β-D-apiofuranosyl (1 → 6)-β-D-glucopyranosyl moieties [1]. In addition, biscourmarin glycosides, with typical monoterpene bridge, which were found in other genus of rutaceous family, such as bisparasin from *Citrus paradise* or thamnosin from *Thamnosma montana* [27]. Consequently, they could be seen as a

Table 1
Chemical structures from *Paramygnia* species sources.

No	Compounds	Species	Refs.
Coumarins and coumarin glycosides			
1	7-Hydroxycoumarin	*P. trimera*	[12]
2	7-Methoxycoumarin	*P. trimera*	[12]
3	Ostruthin	*P. trimera*	[1,2,7,12,24]
4	Ninhvanin (8-Methoxyostruthin)	*P. trimera*	[1,2,7,12,24]
5	6-(6-Hydroxy-3,7-dimethylocta-2,7-dienyl)-7-hydroxycoumarin	*P. trimera*	[1]
6	Paratrimerin A	*P. trimera*	[1]
7	Paratrimerin B	*P. trimera*	[1]
8	Paratrimerin E (**8a**) 6-(6′,7′-Dihydroxy-3′,7′ -dimethylocta-2′-enyl)-7-hydroxycoumarin (**8b**)	*P. trimera*	[2,7]
9	Paratrimerin F	*P. trimera*	[2]
10	Umbelliferone	*P. trimera*	[2]
11	Scopoletin	*P. trimera*	[2]
12	Xanthyletin	*P. trimeraP. monophylla*	[2,10,24]
13	Pandanusin A	*P. trimera*	[2]
14	8-Geranyl-7-hydroxycoumarin	*P. trimera*	[7]
15	6-(7-Hydroperoxy-3,7-dimethylocta-2,5-dienyl)-7-hydroxycoumarin	*P. trimera*	[7]
16	Luvangetin	*P. trimera*	[7]
17	Poncitrin (dentatin)	*P. monophylla*	[11]
18	Nordentatin	*P. monophylla*	[11]
19	5-Hydroxy-8,8-dimethyl-10-(3′,7′-dimethyocta-1′,6′-dimethylocta-1′,6′-dien-3′-yl) pyranocoumarin	*P. monophylla*	[11]
20	5-Methoxy-8,8-dimethyl-10-(3′,7′-dimethyocta-1′,6′-dimethylocta-3′-dien-3′-yl) pyranocoumarin	*P. monophylla*	[11]
21	5-Methoxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethylocta-1,5-dien-3-yl) pyranocoumarin	*P. monophylla*	[10]
22	5-Hydroxy-8,8-dimethyl-10-(7-hydroxy-3,7-dimethylocta-1,5-dien-3-yl) pyranocoumarin	*P. monophylla*	[10]
Tirucallanes and tirucallane saponins			
23	Flindissone	*P. monophylla*	[4]
24	Deoxyflindissone	*P. monophylla*	[4]
25	Tirucalla-7,24-diene-3β,23-diol	*P. monophylla*	[4]
26	Tirucalla-7,24diene-3β,2123-triol	*P. monophylla*	[4]
27	3-Oxotirucalla-7,24-diene-2123-diol	*P. monophylla*	[4]
28	3-Oxo-tirucalla-7,24-dien-23-ol	*P. monophylla*	[4]
29	2424-Dimethyl-lanosta-25-en-3β-ol	*P. monophylla*	[13]
30	3-Oxo-tirucalla-7,24-diene-21-al	*P. grithii*	[6]
31	Paramignyol A	*P. scandens*	[9]
32	Paramignyol B	*P. scandens*	[9]
33	Paramignyosides A	*P. scandens*	[8]
34	Paramignyosides B	*P. scandens*	[8]
35	Paramignyosides C	*P. scandens*	[8]
36	Paramignyosides D	*P. scandens*	[8]
37	Paramignyosides E	*P. scandens*	[8]
Acridone alkaloids			
38	Citrusinine-I	*P. trimera*	[2,12]
39	Glycocitrine-III	*P. trimera*	[2,12]
40	Oriciacridone E	*P. trimera*	[2]
41	Oriciacridon	*P. trimera*	[12]
42	5-Hydroxynoracronycin	*P. trimera*	[2,12]
43	Paratrimerin C	*P. trimera*	[2]
44	Paratrimerin D	*P. trimera*	[2]
Flavanones, flavones, and flavanone glycoside			
45	Amoradicin	*P. grithii*	[6]
46	3′,4′-Dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-furano-(4″,5″:6,5)-flavanone	*P. grithii*	[6]
47	3′,4′-Dihydroxy-7-methoxy-8-(3-methylbut-2-enyl)-2‴-(1-hydroxy-1-methylethyl)-furano-(4″,5″:6,5)-flavanone	*P. grithii*	[6]
48	Carpachromene	*P. monophylla*	[13]
49	3′-Methoxycarpachromene	*P. monophylla*	[13]
50	Atripliside B	*P. scandens*	[25]
Phenols			

(*continued on next page*)