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(Mini review)

Phytochemical and biological diversity of genus Ludwigia: A comprehensive review

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ABSTRACT

Onagraceae is common as willowherb or evening primrose family which is divided into two subfamilies; Ludwigioideae (mainly *Ludwigia* genus) and Onagroideae. Genus *Ludwigia* belonging to the family Onagraceae is an important aquatic plant-including genus and characterized by its myriad traditional uses as treatment of hormonal imbalances, urinary complaints, promoting prostate health, and antimicrobial potential. This review focuses on the secondary metabolites and biological significance of various *Ludwigia* species. Different databases were searched to collect data about such important genus such as PubMed, Web of Science, and Google Scholar. *Ludwigia* species were reported to contain a large variety of phytochemicals such as flavonoids, tannins, phenolic acids, triterpenoids, saponins, and volatile/fixed oils. Several health benefits and biological activities were reported for *Ludwigia* plants including anti-inflammatory, antioxidant, cytotoxic, antidiabetic, and antimicrobial. Genus *Ludwigia* is an extremely important genus with various phytochemical compositions related to its pharmacological importance and hence its commercial and economic value.

Keywords: Onagraceae; *Ludwigia*; conventional medicinal uses; secondary metabolites; biological activities.

1. Introduction

Plants are considered the major essence of the production of important secondary metabolites with different chemical classes according to their chemical structure such as triterpenes, and steroids. saponins, phenolic compounds, etc [1]. Herbal phytochemicals were reported to

have different biological activities being antioxidant, antimicrobial, anti-inflammatory, cytotoxicity, antidiabetic, hepatoprotective, and lipid-lowering activities [2]. The Evening Primrose family consists of two major subdivisions, two subfamilies called Onagroideae and Ludwigioideae, and seven tribes [3]. *Ludwigia* genus belonging to the Ludwigioideae subfamily is a pantropic genus comprising about 82 species of aquatic plants, widely distributed in South and North America [4]. Genus *Ludwigia* includes species that were reported for their biological values such as *Ludwigia leptocarpa* reported as antioxidant, *Ludwigia octovalvis* as antidiabetic, *Ludwigia hyssopifolia* aerial parts as anti-inflammatory, *Ludwigia peploides* leaves as cytotoxic along with other activities as an analgesic, antimicrobial, antidiarrheal and hypolipidemic activity. Two species of genus *Ludwigia* L. are common in Egypt including *L. stolonifera* and *L. erecta* (L.) Hara [5]. Moreover, *Ludwigia* genus is well-known for its conventional medicinal uses in the treatment of several ailments being anthelmintic, antidiarrheal, carminative, and anti-inflammatory. Additionally, *L. stolonifera* is known for its economic importance as used for water bioremediation helping to improve the quality of drinking water [4]. The traditional importance of genus *Ludwigia* is summarized in **Table 1** [6].

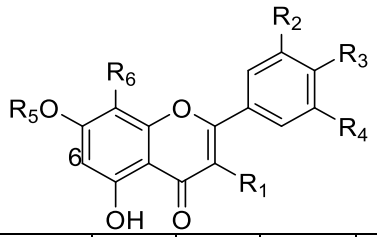
Table (1) Traditional uses previously reported for genus *Ludwigia*

Plants	Traditional uses	References
L. peploides	Treatment of acne vulgaris	[7]
L. octovalvis	Remedy for nephritis, diarrhea, and headache	[8, 9]
L. adscendens	Recovery of skin ulcers, astringent, anthelmintic, and anti-tussive	[10, 11]
L. hyssopifolia	Used as carminative, purgative, astringent, anti-dysentery, anthelmintic, anti-diarrhea, and anti-flatulence	[12-14]
L. leptocarpa	For treatment of diarrhea and rheumatism	[15]

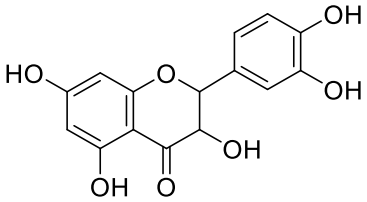
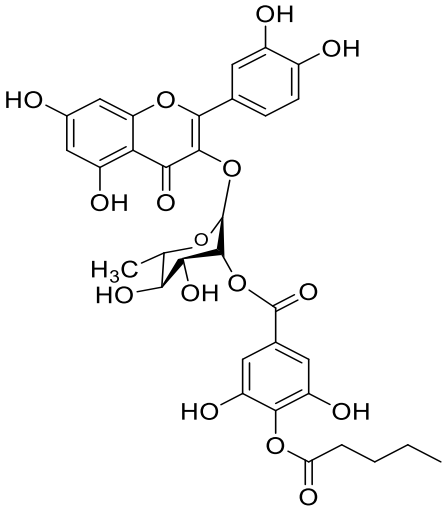
2. Phytochemical composition of genus Ludwigia

Genus *Ludwigia* has several secondary metabolites which are distributed in different species *viz*, flavonoids, triterpenoids, fixed/volatile oils, and steroidal compounds. In this review, phytochemical investigations are focused on flavonoids and phenolic compounds in **Table 2**, steroids and triterpenoids in **Table 3, a**nd finally, miscellaneous compounds also are summarized in **Table 4**. The relative percentage of each identified phytochemical class in genus *Ludwigia* was illustrated in **Figure 1**. Additionally, 85 volatile metabolites were identified in *L. stolonifera* aerial parts and roots n-hexane extracts using GC−MS and classified to, aliphatic, aromatic, and oxygenated hydrocarbons, monoterpenes, diterpenes, alcohols, acids/esters, and sterols [4].

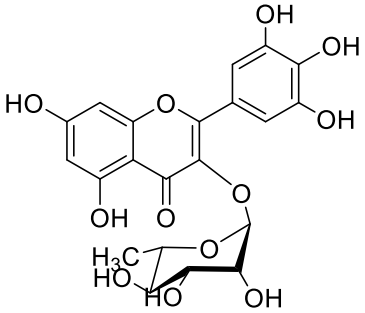
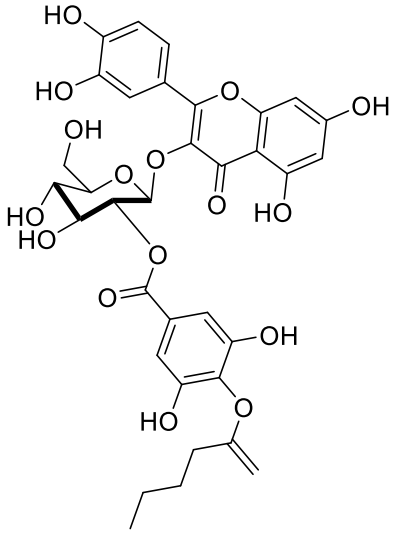
Table (2) Phenolic compounds reported in genus *Ludwigia*

Compound(s)	**Structure(s)**						**Plant(s)**	**References**
Flavonol derivatives								
								
	R_1	**R_2**	**R_3**	**R_4**	**R_5**	**R_6**		
1- Quercetin	OH	OH	OH	H	H	H	*Ludwigia stolonifera*	[16]
2- Quercetin-3-*O*-*α*-*L* Rhamnoside	*O*-*α*-Rha	OH	OH	H	H	H	*Ludwigia stolonifera*	[17]
3- Quercetin-3-*O*-*α*-L-arabinose	O-*α*-L-Arab	OH	OH	H	H	H	*Ludwigia stolonifera Ludwigia perennis*	[16, 17]
4- Quercetin-3-*O*-*β*-D-glycoside	*O*-*β*-Glu	OH	OH	H	H	H	*Ludwigia perennis* *Ludwigia adscendens* *Ludwigia stolonifera*	[10, 17, 18]
5- Quercetin-3-*O*-*β*-D-xyloside	O-*β*-xyl	OH	OH	H	H	H	*Ludwigia stolonifera*	[10]
6- Rutin	*O*-*β*-Glu- α-Rha	OH	OH	H	H	H	*Ludwigia stolonifera*	[10]
7- Quercetin-3-*O*-*β*-D-galactoside	O-*β*-Galac	OH	OH	H	H	H	*Ludwigia stolonifera*	[10]

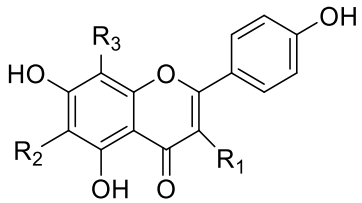
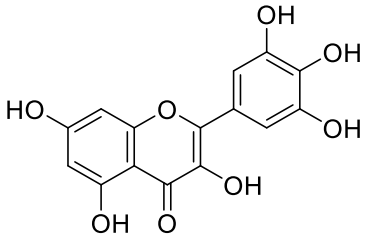
Cont'd Table (2)

Compound(s)	**Structure(s)**	**Plant(s)**	**References**
8- Dihydroquercetin		*L. adscendens*	[11]
9- Quercetin 3-O-α-L-rhamnoside-2"-(4"' O-n-pentanoyl)-gallate		*L. stolonifera*	[18]

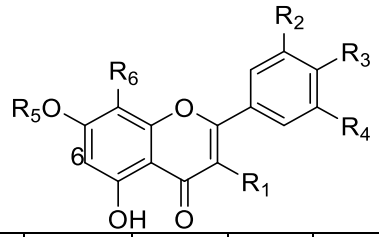
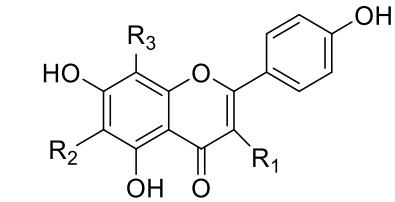
Cont'd Table (2)

Compound(s)	**Structure(s)**	**Plant(s)**	**References**
10- Myricetin-3-*O*-*α*-*L*-rhamnopyranoside		*L. stolonifera*	[18]
11- Avicularine 2´´-(4´´´-*O*-*n*-Pentanoyl)-gallate		*L. stolonifera*	[10]

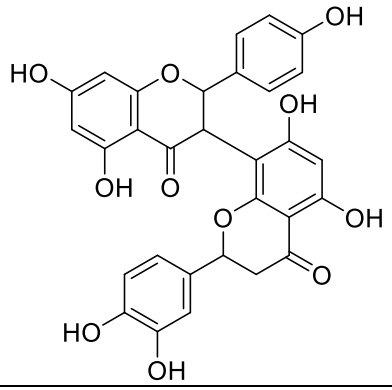
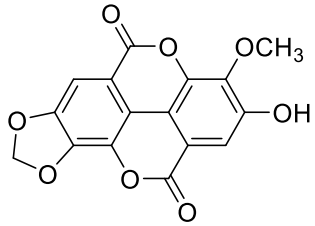
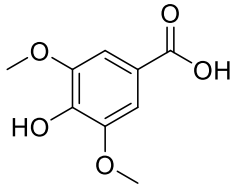
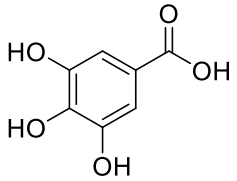
Cont'd Table (2)

Compound(s)	**Structure(s)**			**Plant(s)**	**References**
					
	R_1	**R_2**	**R_3**		
12- Kaempferol	OH	H	H	*L. stolonifera*	[10]
13- Kaempferol-3-*O*-*β*-D- glycoside	*O*-*β*-Glu	H	H	*L. adscendens*	[10, 19]
14- Kaempferol-3-*O*-*β*-D- galactoside	*O*-*β*-Galac	H	H	*L. stolonifera*	[10]
15- Myricetin				*L. adscendens*	[11]

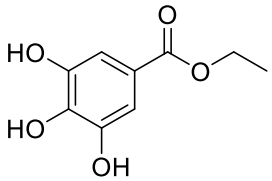
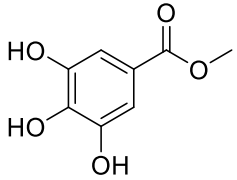
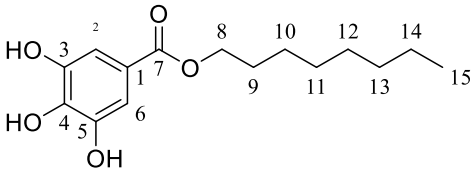
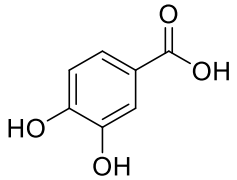
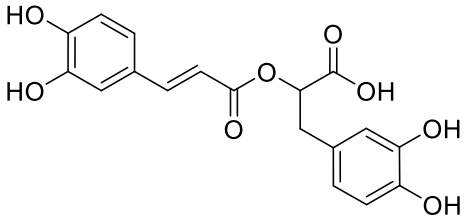
Cont'd Table (2)

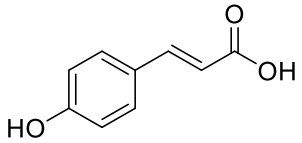
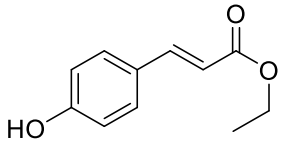
Compound(s)	**Structure(s)**	**Plant(s)**	**References**
Flavone derivatives			
			
	R_1 **R_2** **R_3** **R_4** **R_5** **R_6**		
16- Luteolin-8- C-glycoside	H OH OH H H C-Glu	*L. stenorraphe* *L. leptocarpa*	[17, 20]
17- Luteolin-6- C-glycoside	H OH OH H H H C6-Glu	*L. jussiaeoides*	[21]
			
18- vitexin	H H C-Glu	*L. leptocarpa* *L. hyssopifolia*	[17, 21]
19- Isovitexin	H C-Glu H	*L. brenanii* *L. hyssopifolia*	[17, 21]

Cont'd Table (2)

Compound(s)	**Structure(s)**	**Plant(s)**	**References**
Biflavone			
20- (2R,3S,2´´S)-3´´´,4´,4´´´,5,5´´,7,7´´-heptahydroxy-3,8´´-biflavanone		*L. leptocarpa*	[20]
Phenolic acids and derivatives			
20- Pteleoellagic acid		*L. adscendens*	[11]
21- Syringic acid		*L. hyssopifolia*	[22]
22- Gallic acid		*L. adscendens*	[11]

Cont'd Table (2)

Compound(s)	**Structure(s)**	**Plant(s)**	**References**
23- Ethyl gallate		*L. hyssopifolia*	[14]
24- Methyl gallate		*L. adscendens*	[11]
25- Octyl gallate		*L. stolonifera*	[18]
26- Protocatechuic acid		*L. adscendens*	[11]
27- Rosmarinic acid		*L. adscendens*	[10]

28- *p*-Hydroxy cinnamic acid		*L. hyssopifolia*	[14]
29- *p*-Hydroxy ethyl cinnamate		*L. hyssopifolia*	[19]

Cont'd Table (2)

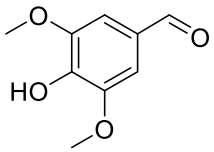
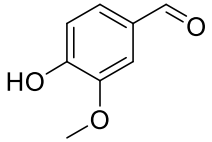
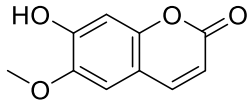
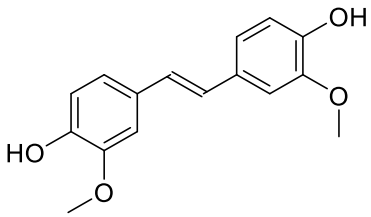
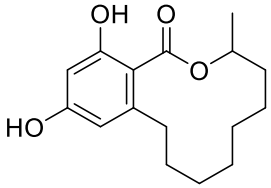
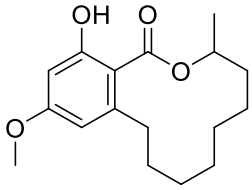
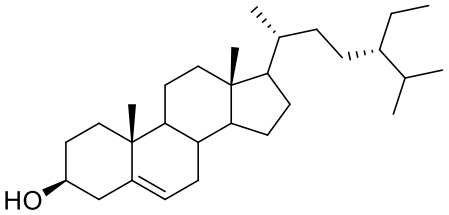
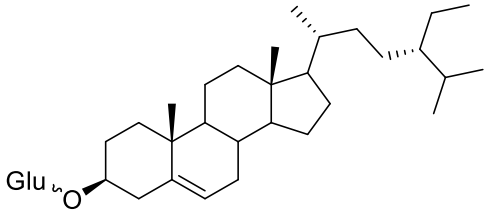
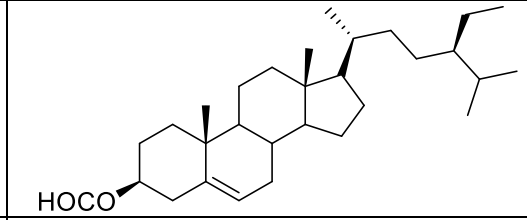
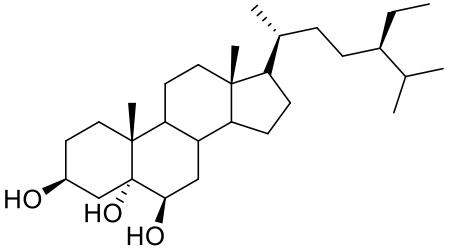
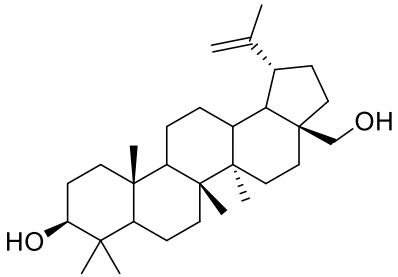
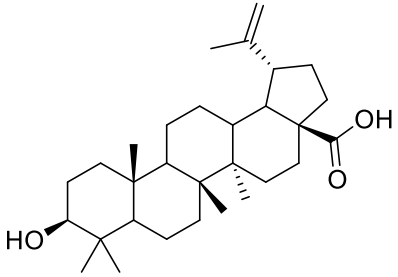
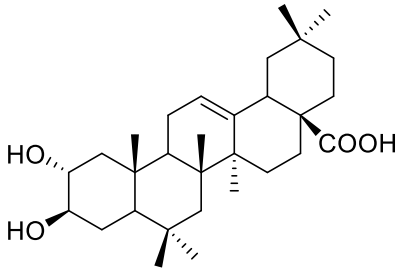
Compound(s)	**Structure(s)**	**Plant(s)**	**References**
Phenolic drivatives			
30- Syringaldehyde		*L. hyssopifolia*	[14]
31- Vanillin		*L. hyssopifolia*	[19]
32- Scopoletin		*L. hyssopifolia*	[19]
33- 3,3'-dimethoxy-,4'-dihydroxy-stilbene		*L. hyssopifolia*	[21]
34- De-*O*-methyllasiodiplodin		*L. hyssopifolia*	[19]
35- Ozoroalide		*L. hyssopifolia*	[19]

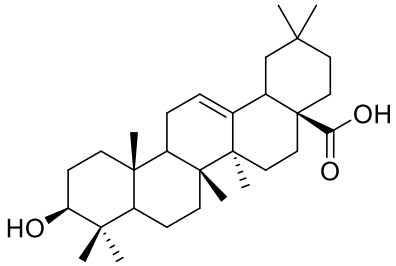
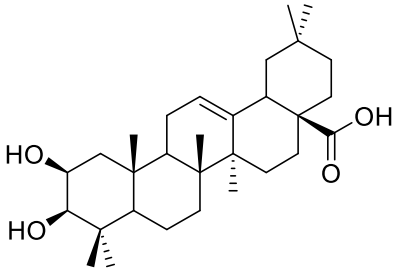
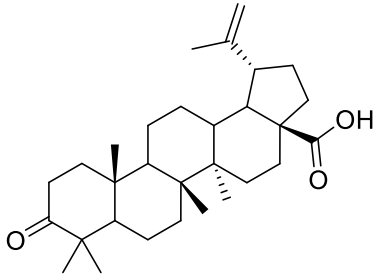
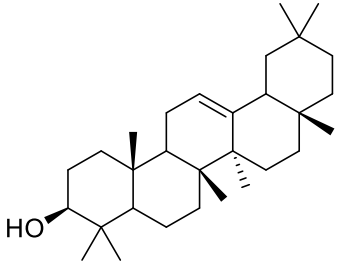
Table (3): Sterols and Saponins reported from genus *Ludwigia*

Compound(s)	Structure(s)	Plant(s)	References
36- *β* -sitosterol		*L. hyssopifolia*	[23]
37- *β*-sitosterol-3-*O*-*β*-D-glycoside		*L. hyssopifolia*	[23]
38-Sitost-5-en-3*β*-ol		*L. abyssinica*	[24]
39-5α,6β-dihydroxy-sitosterol		*L. abyssinica*	[24]

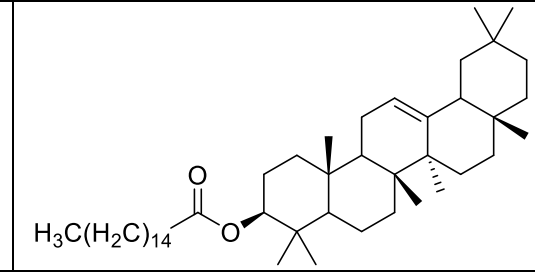
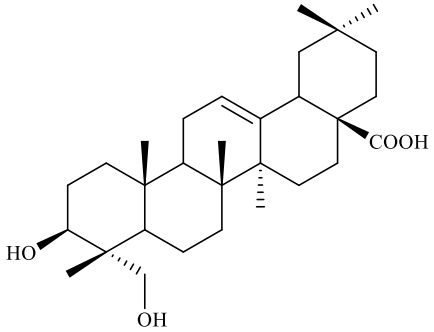
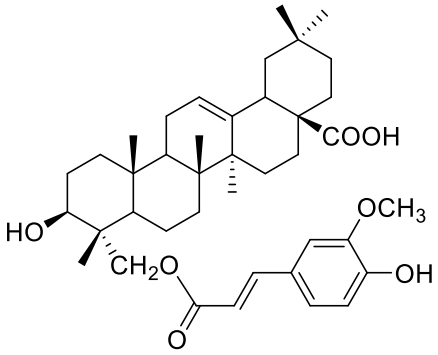
Cont'd Table (3)

Compound	**Structure(s)**	**Plant (s)**	**References**
40- Betulin		*L. adscendens*	[11]
41- Betulinic acid		*L. adscendens*	[11]
42-Maslinic acid		*L. abyssinica*	[24]

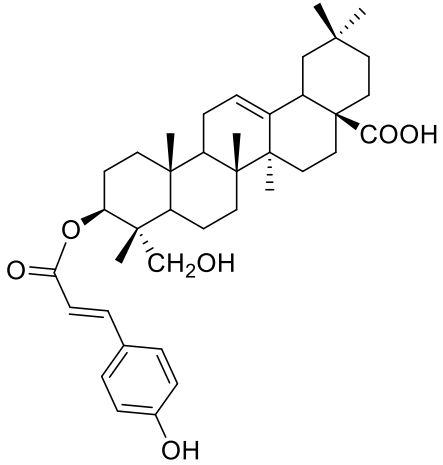
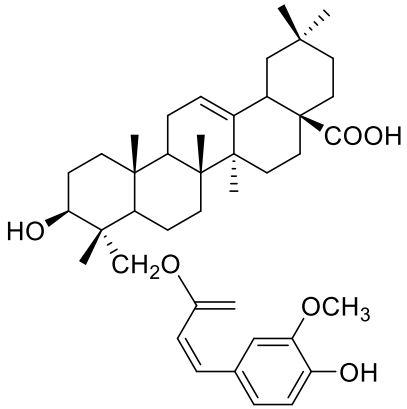
Cont'd Table (3)

Compound	Structure(s)	Plant (s)	References
43- Oleanolic acid		*L. octovalvis* *L. leptocarpa*	[9, 25]
44- 2β-hydroxy oleanolic acid		*L. leptocarpa*	[25]
45- Betulonic acid		*L. adscendens*	[11]
46- β-amyrin		*L. octovalvis*	[25]

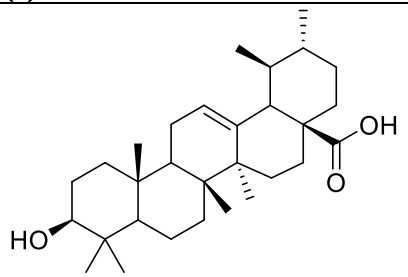
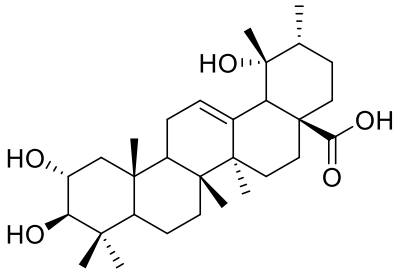
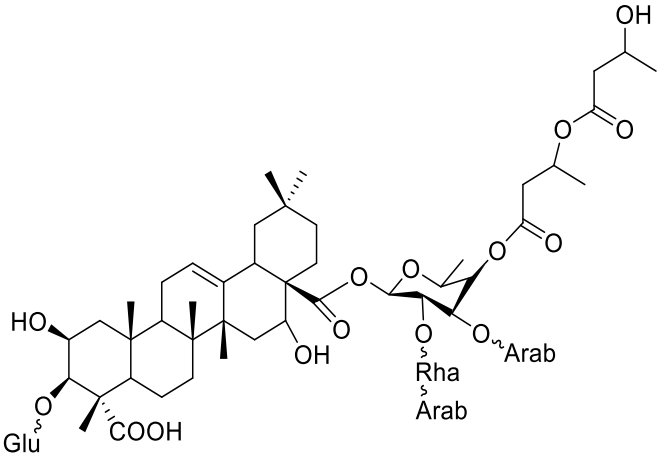
Cont'd Table (3)

Compound	Structure(s)	Plant (s)	References
47- *β*-amyrin palmitate		*L. octovalvis*	[26]
48- Hederagenin		*L. stolonifera*	[18]
49- (23E)-feruloylhederagenin		*L. octovalvis*	[9]

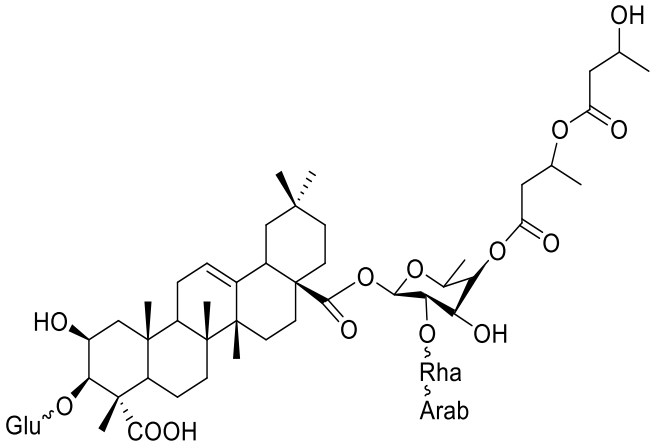
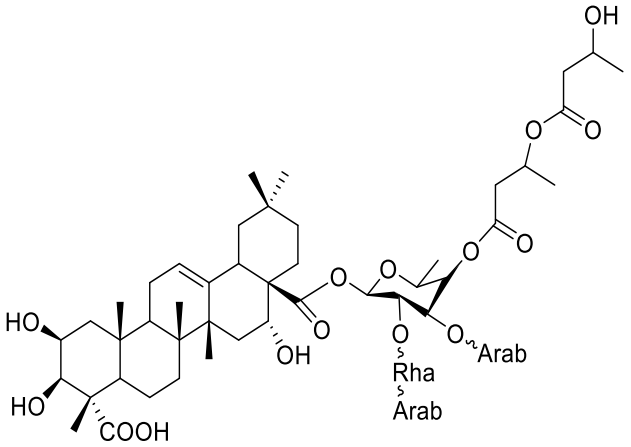
Cont'd Table (3)

Compound	Structure(s)	Plant (s)	References
50- (3Z)-coumaroylhederagenin		*L. octovalvis*	[9]
51- (23Z)-feruloylhederagenin		*L. octovalvis*	[9]

Cont'd Table (3)

Compound	Structure(s)	Plant (s)	References
52- Ursolic acid		*L. octovalvis*	[9]
53- 23-hydroxy tormentic acid		*L. hyssopifolia*	[23]
54- 3-*O*-*β*-D-glucoside-28-*O*-*β*-D-xyloside-(1→4)-*α*-L-rhamnoside-(1→2)-[*α*-L-arabinoside-(→3)] -4-*O*-(3'-hydroxybutanoyloxy-3-hydroxybutanoy-loxy) -*β*-D-fucoside zanhic acid		*L. leptocarpa*	[20]

Cont'd Table (3)

Compound(s)	**Structure(s)**	**Plant(s)**	**References**
55- 3-*O*-*β*-D-glucoside-28-*O*-*β*-D-xyloside-(1→4)-*α*- L-rhamnoside-(1→2)-4-*O*-(3'-hydroxybutanoyloxy-3-hydroxybutanoyloxy)-*β*-D-fucoside medicagenic acid		*L. leptocarpa*	[20]
56- 28-*O*-*β*-D-xyloside-(1→4)-*α*-L-rhamnoside-(1→2)- [*α*-L-arabinoside-(1→3)]-4-*O*-(3'-hydroxybutanoyloxy-3-hydroxybutanoyloxy)-*β*-D-fucoside zanhic acid		*L. leptocarpa*	[20]

Cont'd Table (3)

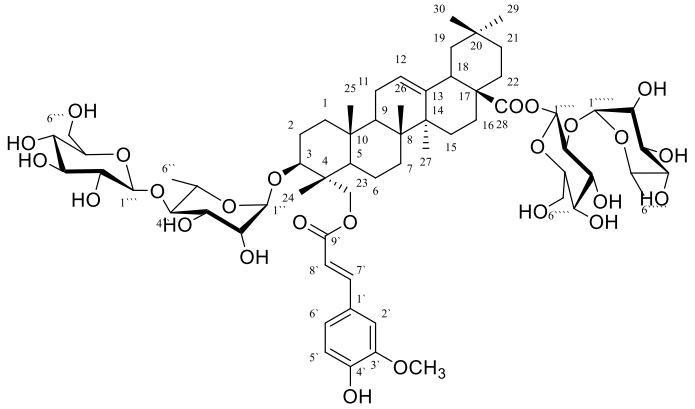
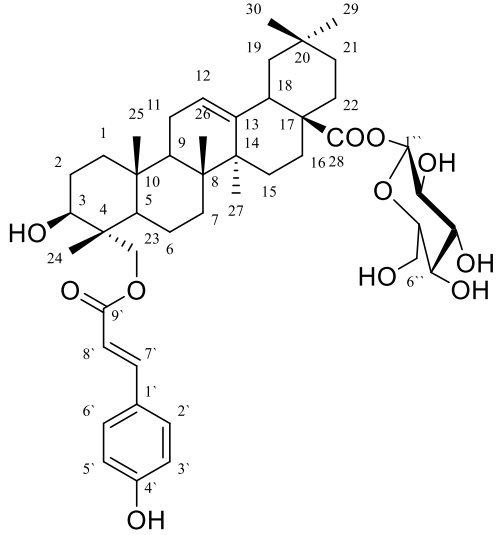
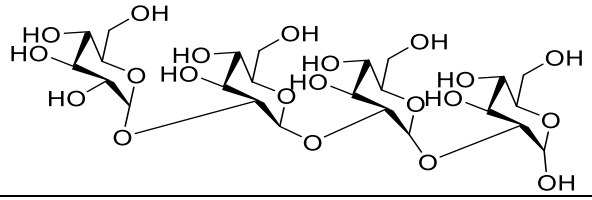
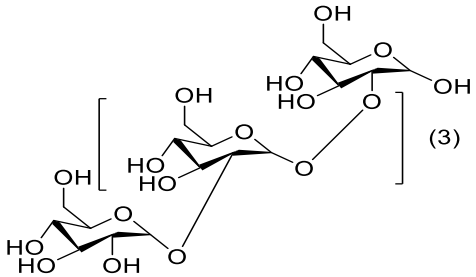
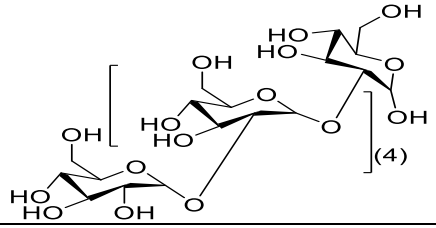
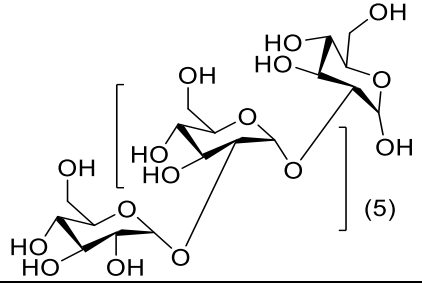
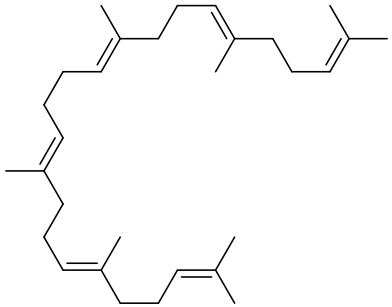
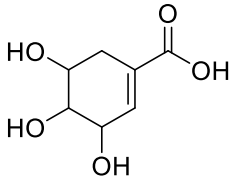
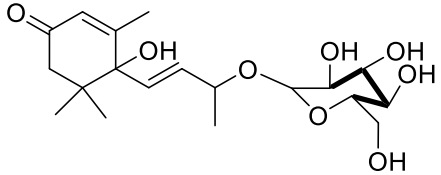
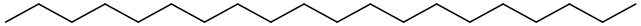
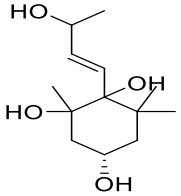
Compound	Structure(s)	plant(s)	References
57- 3- *O*- [*β*-D- glucopyranoside (1→4) *α*-L-rhamnopyranoside] 23- *O*- feruloyl hederagenin 28- *O*- [*α*-L-rhamnopyranoside (1→2) *β*-D-glucopyranoside]		*L. adscendens*	[18]
58- 23-O- Coumaroyl hederagenin 28-O-β-D-glucopyranoside		*L. adscendens*	[18]

Table (4): Oligosaccharides and other compounds reported from genus *Ludwigia*

Compound(s)	Structure(s)	Plant(s)	References
59- α-D-Tetraglucoside		*L. adscendens*	[18]
60- α-D-Pentaglucoside		*L. adscendens*	[18]
61- α-D-Hexaglucoside		*L. adscendens*	[18]
62- α-D-Heptaglucoside		*L. adscendens*	[18]

Cont'd Table (4)

Compound	Structure(s)	plant(s)	Reference(s)
63- Squalene		*L. adscendens*	[11]
64- Shikimic acid		*L. alternifolia*	[21]
65- Roseoside		*L. stolonifera*	[26]
66- Octadecane		*L. adscendens*	[27]
67- Pentacosane		*L. adscendens*	[24]
68- Eicosane		*L. adscendens*	[24]
69- Megastigmane		*L. stolonifera*	[28]

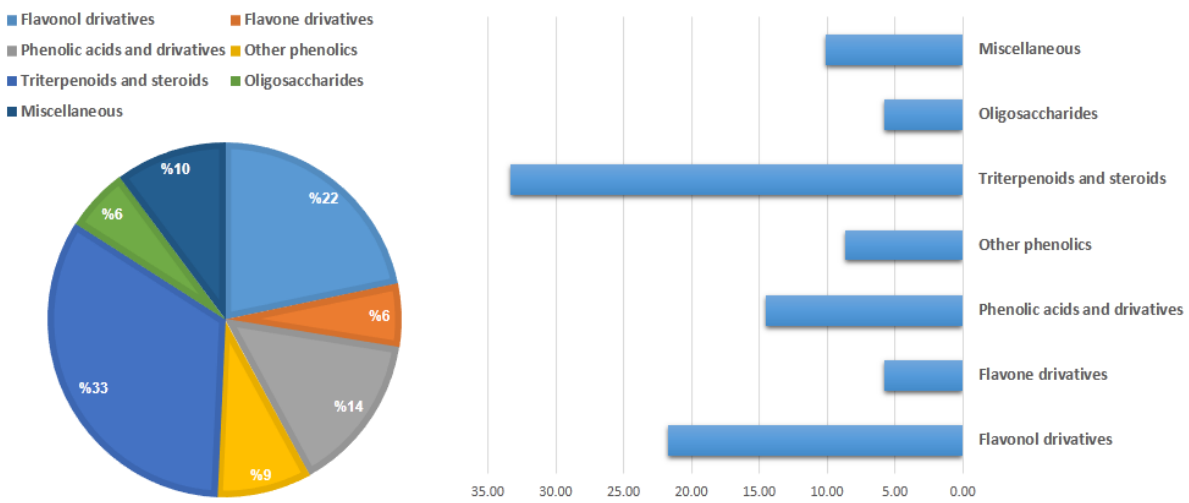


Figure 1. Relative percentage of each identified phytochemical class in genus *Ludwigia*

3. Biological importance of genus *Ludwigia*

Various species of the genus Ludwigia have been documented to possess biological activities, such as anti-inflammatory, antitumor, antioxidant, antidiabetic, antimicrobial, and miscellaneous activities. Pharmacological studies were mentioned in the following subsections, **Table 5**.

Table 5. Biological activities reported in genus *Ludwigia*

Biological Activities	Plant(s)	References
Antioxidant activity	Different extracts of *L. octovalvis*	[29]
	Different fractions of *L. adscendens*	[10]
	Leaf methanolic extract of *L. peploides*	[30]
	Ethylacetate and butanol extracts of *L. leptocarpa*	[25]
	Aerial parts methanolic extract of *L. hyssopifolia*	[31]
	Different extracts of *L. stolonifera*	[4]
Antidiabetic activity	Different extracts of *L. stolonifera*	[16, 18]
	Aqueous ethanolic and methanolic extract of *L. octovalvis*	[32, 33]
Hypolipidemic activity	Aqueous methanolic extract of *L. octovalvis*	[34]
Antimicrobial activity	Different extracts of *L. octovalvis*	[29]
	Ethylacetate extract of *L. hyssopifolia*	[13]
	Leaves ethylacetate and butanol extracts of *L. abyssinica*	[35]
	Leaf methanolic extract of *L. peploides*	[30]
	Leaves ethylacetate and butanol extracts of *L. decurrens*	[35]
	Ethylacetate and butanol extracts of *L. leptocarpa*	[20, 25]
	Ethylacetate and butanol extracts of *L. stolonifera*	[18]
Antitumor activity	Different extracts of *L. stolonifera*	[16, 18]
	Aerial parts ethylacetate and methanolic extracts of *L.hyssopifolia*	[13, 14, 31]
	Leaf methanolic extract of *L. peploides*	[30]
	Ethylacetate and butanol fractions *L. octovalvis*	[9]
Anti-inflammatory activity	Aerial parts ethylacetate of *L. stolonifera*.	[16]
	Aerial parts methanolic of *L. hyssopifolia*	[31]
Antidiarrheal activity	Different extracts of *L.hyssopifolia*	[12]
Miscellaneous activities	Aerial parts ethylacetate extract of *L. stolonifera* (Hepatoprotective)	[16, 18]
	Aqueous leaf extract of *L. hyssopifolia* (Bio herbicide)	[22]
	Aqueous and methanolic extracts of *L. erecta* (Antimalarial)	[36]
	Leaf methanolic extract of *L. peploides* (anti-acne)	[30]
	Aerial parts and root n-hexane extracts of *L. stolonifera* (metal chelation assay)	[4]
	L. octovalvis hydro alcoholic extract revealed antihypertensive activity	[37]

3.1. Antioxidant and anti-inflammatory activities

Oxidative stress and the production of reactive oxygen species (ROS) are considered risk factors for many disorders such as atherosclerosis, degenerative diseases, aging, diabetes, and cancer by enhancing the deleterious effects of free radicals in the human body [10]. According to reports, the genus Ludwigia is abundant in phytochemical antioxidants as flavonoids and phenolic compounds [38]. The antioxidant capacity of *Ludwigia octovalvis* leaves aqueous methanol extract was tested by FRAP and DPPH revealing different activities at 1256.88 μM TE/mg and 1080.84 μM TE/mg dry weight, respectively [29]. In another study, the antioxidant activity of leaves methanolic extract of *Ludwigia peploides* was examined by DPPH and (nitroblue tetrazolium) NBT assays revealing IC50 of 58 and 30 μg/ml, respectively, to evaluate the activity of scavenging free radicals [30]. The anti-inflammatory activity of aerial parts ethyl acetate extract of *L. stolonifera* was assayed and revealed inhibitory activity against leukotriene B4 (LTB4) in vitro [10]**.**

3.2. Antitumor activity

One of the most noteworthy traits is the anti-cancer activity of the genus *Ludwigia* **Table 5**. *Ludwigia hyssopifolia* and *Ludwigia peploides* have been reported to have cytotoxic action in their ethyl acetate, aqueous, and methanolic extracts. [9, 30] The cytotoxic activity of leaves crude extract of *Ludwigia peploides* was examined in vitro, with results showing a modest effect on HaCaT cells (Human immortalized keratinocytes) (IC50 > 200 g/ml) and a high effect on B16 cancer cell lines (IC50 = 5.5 g/ml) [30]**.**

3.3. Antidiabetic activity

Diabetes is a metabolic disorder that occurs when the blood glucose level is too high. Patients of type-2 diabetes could be treated by enzymes inhibition as α-glucosidase and α-amylase inhibitors which can be used to prevent the degradation of complex carbohydrates into glucose with fewer side effects and economic reasons [39] In rats with alloxan-induced diabetes, the ethyl acetate extract of *L. stolonifera* aerial portions (50 mg kg^{-1} body wt.) demonstrated a robust hypoglycemic effect [16]. Streptozotocin (STZ) and high-fat diet (HFD)–induced diabetic mice were given an aqueous ethanolic extract of *L. octovalvis* (0.1 g/kg), and the results showed improvement in polyphagia, polydipsia, hyperglycemia, and glucose tolerance, similar to that shown in STZ animals treated with metformin [33]. In HepG2 hepatocellular cells, *L. octovalvis* extract and its active metabolite (*β*-sitosterol) were found to significantly increase AMP-

activated protein kinase phosphorylation, accelerate fluorescent glucose uptake, and decrease glucose synthesis. Additionally, compared to metformin, *L. octovalvis* extract and *β*-sitosterol caused a hypoglycemic effect in streptozotocin (STZ)-induced diabetes and enhanced the memory function of HFD-fed mice [33].

3.4. Anti-microbial effect

The misuse and overuse of antibiotics lead to drug-resistant bacteria. Therefore, it is seen to be crucial to provide safe and effective alternatives to synthetic drug resistance by using antimicrobials derived from plants. *L. octovalvis* roots methanolic extract inhibited *Pseudomonas aeruginosa* at MIC (minimum inhibitory concentration) and MBC (minimum bactericidal concentration) values of 62.5 and 125 g/ml, respectively. *L. octovalvis* leaves methanol extract revealed significant inhibitory activity against E. coli. [29]. And also, *L. hyssopifolia* ethyl acetate extracts had a mild inhibitory impact on gram-positive and gram-negative pathogenic bacteria. [13]. A significant antibacterial effect has been reported for the *L. leptocarpa* aerial, roots, or both sections of the plant in aqueous methanolic, ethanol, ethyl acetate, and butanol extracts. [25]. *Propioni bacterium acnes* was strongly inhibited at 1.9 g/ml of *L. peploides* leaves crude extract when tested for antibacterial activity utilizing disc diffusion and broth micro-dilution against microorganisms that cause acne vulgaris. [30].

4.6. Miscellaneous activities

In addition to the previously mentioned biological activities, *Ludwigia* plants revealed other several activities of different plant extracts. *L. erecta* aqueous and methanol extracts revealed antimalarial activity [36]. *L. stolonifera* showed metal chelation activity as 1mg of *L. stolonifera* aerial parts n-hexane extract equaled 36.36µM EDTA and the percentage of inhibition was 52.78%. Additionally, 1 mg roots n-hexane extract of *Ludwigia stolonifera* equal to 29.67µM EDTA was recorded at 43.62% of inhibition capacity [4]. Recently, *L. octovalvis* hydro alcoholic extract revealed antihypertensive activity owing to its vasodilator effect with EC_{50} of 1.18 mg/ml [37].

Conclusion and future perspectives

Plants are regarded as significant resources of innovative natural compounds of both structural and biological value since they represent a safe, efficient source of natural compounds with health benefits. The phytochemistry and biological diversity of genus *Ludwigia* were introduced herein revealing a collection of major groups of phytochemicals such as flavonoids, tannins,

triterpenoids, volatiles, and saponins. Furthermore, *Ludwigia* species showed a variety of biological properties, including antitumor, antioxidant, anti-diabetic, and anti-inflammatory effects. However, more studies on novel bioactive phytochemicals, biological potential, and pharmaceutical formulations are recommended. Additionally, possible applications of *Ludwigia* species in industrial and food production is important to be further investigated. Moreover, the metal chelation potential of *Ludwigia* plants in water remediation has to be investigated on a large scale to enhance their economic importance in saving water sources.

Conflict of Interest

The authors declare that no conflict of interest.

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