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Review Article

Ethnobotanical, phytochemical and pharmacological properties of *Galinsoga parviflora* (Asteraceae): A review

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Abstract

Galinsoga parviflora belongs to the family Astraceae. It is distributed in Central and South America, Europe, West Indies, Mexico, Australia, Africa and Asia. The plant is used in traditional preparations for wound healing as well as for the treatment of blood coagulation problems, cold, flu, toothache, and dermatological and eye diseases. The healing properties of Galinsoga parviflora are due to the presence of diverse secondary metabolites. The plant is non-toxic, and is used as fodder for cattle. Humans also use it as a vegetable for preparing soups and salad. Crude extracts and pure compounds isolated from the plant possess potent pharmacological activities such as antibacterial, antifungal, antioxidant, anti-inflammatory and nematicidal effects. They exhibit urease and α-glucosidase activities, and have been shown to exert cytotoxic, hepatoprotective and hypoglycemic effects. Over thirty-eight compounds from Galinsoga parviflora have been isolated and characterized.

The present review focuses on the ethno-medicinal uses, isolated natural products and biological activities of Galinsoga parviflora.

Keywords: *Galinsoga parviflora (Astraceae), Ethnomedicinal, Hepatoprotective, Hypoglycemic, Wound healing, Blood coagulation*

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INTRODUCTION

The genus *Galinsoga* belongs to the family Astraceae, and is widely distributed in South and North America [1]. The Spanish botanist and physicist Mariano Martinez de Galinsoga gave the plant its name [2]. *Parviflora* is a latin word which means small flower (*parvo* = small, and *flor* = flower), a reference to the small size of its flowers [3]. The plant is abundant in Central America, South America, Europe, West Indies, Mexico, Australia, Africa and Asia. In Pakistan, it can be found in Balochistan, Hunza, Dir, Swat, Gilgit, Murree and Kashmir [4].

G. parviflora is an abundant plant in agricultural areas of most regions of the world, and it grows readily on sunny or shady fertile soil, uncultivated areas, wastelands and roadsides [3,5,6]. It is a herbaceous plant with an erect and multi-branched stem, and normally grows to a height of about 0.6m. It produces small-headed flowers

comprising yellow disk florets centrally bounded by red or pink-tipped ray florets [3,7]. The fruits of *G. parviflora* are sparse hairy achenes, and the leaves produce a pleasant smell when crushed. The flowering period of the plant is from May to September. The juice of the whole plant is used as a healing agent for treating wounds and body injuries, while the roots provide effective remedy against beetle bites [6].

Generally, the aerial portions of *Galinsoga* species are used in anti-inflammatory drug preparations in traditional medicine for the treatment of dermatological problems such as eczema and lichens [8]. Indeed, *G. parviflora* features very prominently in the folk medicine history of America, Asia, Africa and Europe. This plant has been used as an anti-scurvy agent due to its high level of vitamin C [5]. It is also used to stop bleeding [9,10], and for treating cold sores [11], common cold and flu [12]. The flowers possess analgesic properties, and are applied in making preparations for relief of toothache [13]. It has been reported that aqueous extracts of aerial parts of the plant exert protective effects against damages caused by UV irradiation and it is also used for wounds and eye diseases [14,15]. Appreciable levels of calcium, magnesium and proteins are present in *G. parviflora* [16]. In Zimbabwe, South Africa and Tanzania, the tender leaves and shoots of *G. parviflora* are consumed as vegetable [16-18]. Similarly, fresh leaves of *G. parviflora* are used for making salad, and the dried whole plant is employed in making soups in Latin and North America [3, 19]. In addition, *G. parviflora* is used as fodder for cattle [8]. The use of *G. parviflora* as food by humans and lower animals shows that the plant is non-toxic [20].

This review was carried out to present in-depth information on extant literature concerning the ethno-botanical uses, isolated compounds and biological properties of *G. parviflora*.

COMPOUNDS ISOLATED FROM *G. parviflora*

Thirty eight compounds (**1**-**38**) have so far been isolated from *G. parviflora*. These can be classified into seven categories: flavonoids, aromatic esters, diterpenoids, caffeic acid derivatives, steroids, phenolic acid derivatives and miscellaneous compounds. List of compounds has been incorporated in Table 1.

Flavonoids

Flavonoids can be aglycones, glycosides or methylated derivatives. This diverse group is major class of compounds isolated from *G. parviflora*. They are known to possess numerous biological activities [21]. In 1977, two flavonoids, apigenin 7-β-D-glucoside (**1**) and luteolin 7-β-D-glucopyranoside (**4**) were isolated from dried leaves of *G. parviflora* [22]. The plant was extracted with 70% ethanol on a water bath. The compounds were separated on column of polyamide sorbent and identified on the basis of melting points and UV-VIS spectroscopy.Two new flavonoids: galinsoside A (**2**) and galinsoside B (**3**); and two known flavanones: 3,5,7,3′,4′-pentahydroxy flavanone (**7**) and 7,3′,4′-trihydroxy flavonone (**10**) were isolated from methanol extract of whole plant material at room temperature. The ethyl acetate soluble fraction of the methanol extract was subjected to a series of column chromatographic techniques to obtain compounds **2, 3, 7 and 10** and their structures were established by UV, IR, MS and NMR spectroscopy [22]. Surywanshi *et al* isolated two new compounds,3, 5, 7, 8, 4′ - pentahydroxy-3′-methoxyflavone-3-O-α-L-rhamnopyranosyl-7-O-β-D-glucopyranosyl-(1→4)-O-β-D-xylopyranoside (**8**) and 3,5,3′,5′-tetrahydroxy-7,4′-dimethoxy-flavone-3-O-α-L-rhamnopyranosyl-(1→3)-O-α-L-arabino-pyranosyl-3′-O-β-D-galactopyranoside (**11**), and two known flavonoids, kaempferol (**5**) and quercetin (**9**) from air-dried and powdered stems of the plant [8]. The compounds **5**, **8**, **9** and **11** were purified using TLC and column chromatography from acetone soluble fraction and the structures assigned using melting points, FTIR, NMR and FABMS spectroscopic data [8]. In 2014, Afza *et al* isolated and characterized a new flavonoid glucoside, parviside A (**6**) from *n*-butanol fraction and determined its structure on the basis of spectral data from 1D and 2D NMR techniques [24]. The structures of compounds (**1**-**11**) are given in Figure 1.

Aromatic esters

Three new aromatic esters galinosoate A (**12**), galinosoate B (**13**) and galinosoate C (**14**) were successfully isolated form n-hexane soluble fraction of methanol extract of *G. parviflora* through repeated column chromatography. The structures of the compounds were established on the basis of optical rotations, IR, UV, EI-MS, HR-EI-MS, 1D and 2D NMR spectral data [25]. The structures of compounds (**12**-**14**) are given in Figure 2.

Diterpenoids

The presence of ent-15-angeloyoxy-16-kauren-19-oic acid (**15**), ent-15-angeloyoxy-16,17-epoxy-19-kauranoic acid (**16**), ent-kaur-16-en-19-oic acid (**17**) and phytol (**18**) in *G. parviflora* has been discovered by column chromatography

Table 1: Chemical constituents of *Galinsoga parviflora*

S/N	Class	Compound	Plant part used	Ref.
1	Flavonoids	Apigenin 7-β-D-glucoside	Leaves	[22]
2		Galinsoside A	Whole	[23]
3		Galinsoside B	Whole	[23]
4		Luteolin 7-β-D-glucopyranoside	Leaves	[22]
5		Kaempferol	Stem	[8]
6		Parviside A	Whole	[24]
7		3,5,7,3′,4′-pentahydroxyflavanone	Whole	[23]
8		3,5,7,8,4′-pentahydroxy-3′-methoxyflavone-3-O-α-L-rhamnopyranosyl-7-O-β-D-glucopyranosyl-(1→4)-O-β-D-xylopyranoside	Stem	[8]
9		Quercetin	Stem	[8]
10		7,3′,4′- trihydroxyflavanone	Whole	[23]
11		3,5,3′,5′-tetrahydroxy-7,4′-dimethoxyflavone-3-O-α-L-rhamnopyranosyl-(1→3)-O-α-L-arabinopyranosyl-3′-O-β-D-galactopyranoside	Stem	[8]
12	Aromatic esters	Galinosoate A	Whole	[25]
13		Galinosoate B	Whole	[25]
14		Galinosoate C	Whole	[25]
15	Diterpenoids	ent-15-angeloyloxy-16-kauren-19-oic acid	Whole	[26]
16		ent-15-angeloyloxy-16,17-epoxy-19-kauranoic acid	Whole	[26]
17		ent-kaur-16-en19-oic acid	Whole	[26]
18		Phytol	Whole	[28]
19	Caffeic acid	2,3(4,5)- dicaffeoylaltraric acid	Aerial	[20]
20	derivatives	Parviside B	Whole	[24]
21		2,3,4,5-tetracaffeoylglucaric acid	Aerial	[20]
22		2,3,4- or 3,4,5-tricaffeoylaltraric acid	Aerial	[20]
23		2,4,5-tricaffeoylglucaric acid	Aerial	[20]
24	Steroids	7-hydroxy-*β*-sitosterol	Whole	[28]
25		7-hydroxy stigmasterol	Whole	[28]
26		*β*-sitosterol	Whole	[29]
27		*β*-sitosterol-3-*O*-*β*-D-glucopyranoside	Whole	[29]
28		α-spinasterol	Whole	[26]
29		Stigmasterol	Whole	[28]
30	Phenolic acid	3,4- dihydroxy benzoic acid	Whole	[29]
31	derivatives	Gallic acid	Whole	[29]
32		4-Hydroxy benzoic acid	Whole	[29]
33	Miscellaneous	3,4-dimethoxycinnamic acid	Whole	[28]
34	Compounds	Fumaric acid	Whole	[28]
35		Octacosanoic acid	Whole	[29]
36		Triacontanol	Whole	[28]
37		Uracil	Whole	[28]
38		Ursolic Acid	Whole	[29]

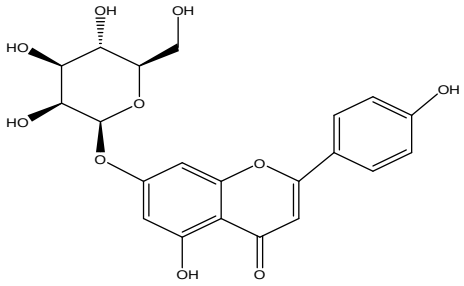
using silica gel and sephadex LH-20 [26]. The structures of these compounds, (**15-18**, Figure 3) were determined by spectral data analysis [26].

Caffeic acid derivatives

Caffeic acid (3,4-dihydroxycinnamic), a polyphenolic secondary metabolite which occurs in many plants and beverages, possesses numerous biological activities [27]. In 2016, Dudek, *et al* successfully isolated four new caffeic acid derivatives, 2,3(4,5)-dicaffeoylaltraric acid (**19**), 2,3,4,5-tetracaffeoylglucaric acid (**21**), 2,3,4- or 3,4,5-tricaffeoylaltraric acid (**22**) and 2,4,5-tricaffeoylglucaric acid (**23**) from the hydrophilic extract of aerial parts of *G. parviflora* using preparative HPLC [20]. The structures of the compounds were established by Mass and NMR spectroscopic techniques [20]. Parviside (**20**), another new caffeic acid derivative, was isolated from n-butanol fraction of methanolic extract, and its structure was determined using 1D and 2D NMR techniques [24]. The structures of compounds **19**-**23** are given in Figure 4.

Steroids

Steroids constitute a distinct class of the compounds in *G. parviflora.* In 2013, Mostafa *et al* isolated 7-hydroxy-β-sitosterol (**24**), 7-hydroxy stigmasterol (**25**), stigmasterol (**29)**, β-sitosterol (**26**) and β-sitosterol-3-O-β-D-glucopyranoside (**27**) from light petroleum extract of *G. parviflora* [28]. These compounds were purified using silica



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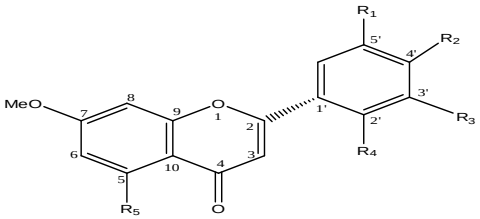
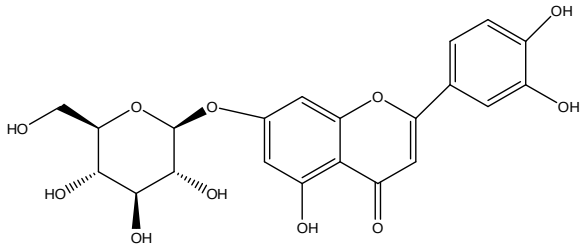


2 R_1 = OH, R_2, R_3, R_5 = H, R_4 = -*O*-*β*-D-glucose
3 R_1, R_2 = H, R_2, R_3 = OH, R_5 = -O-*β*-D-glucose



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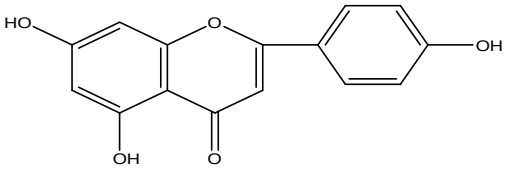

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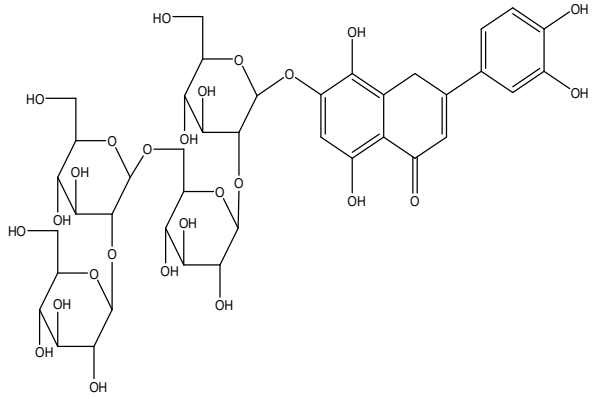

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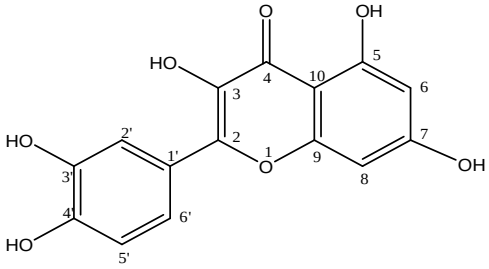

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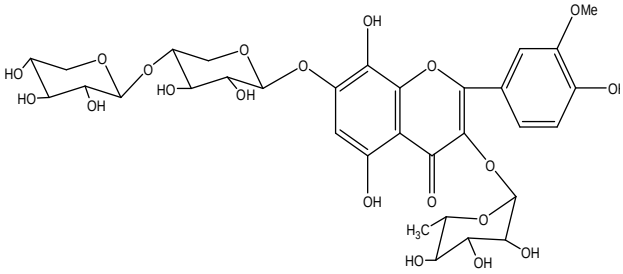

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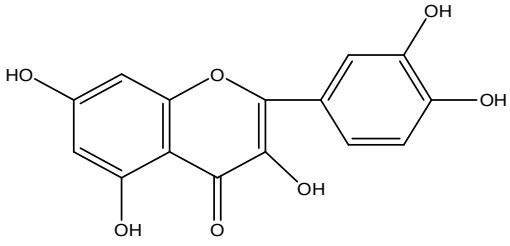

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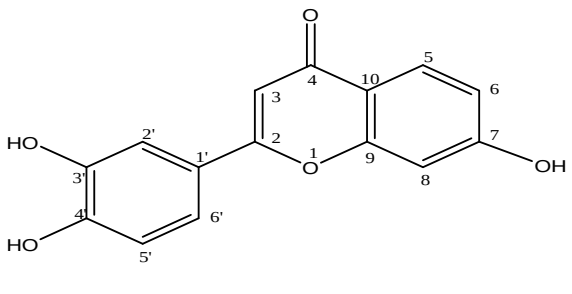

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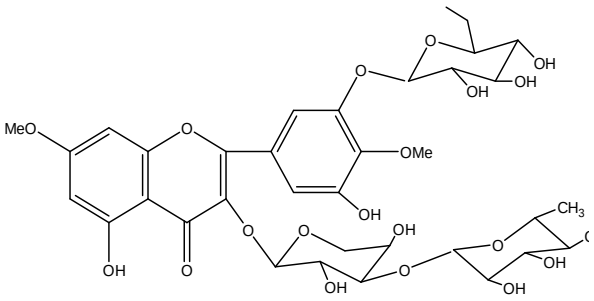

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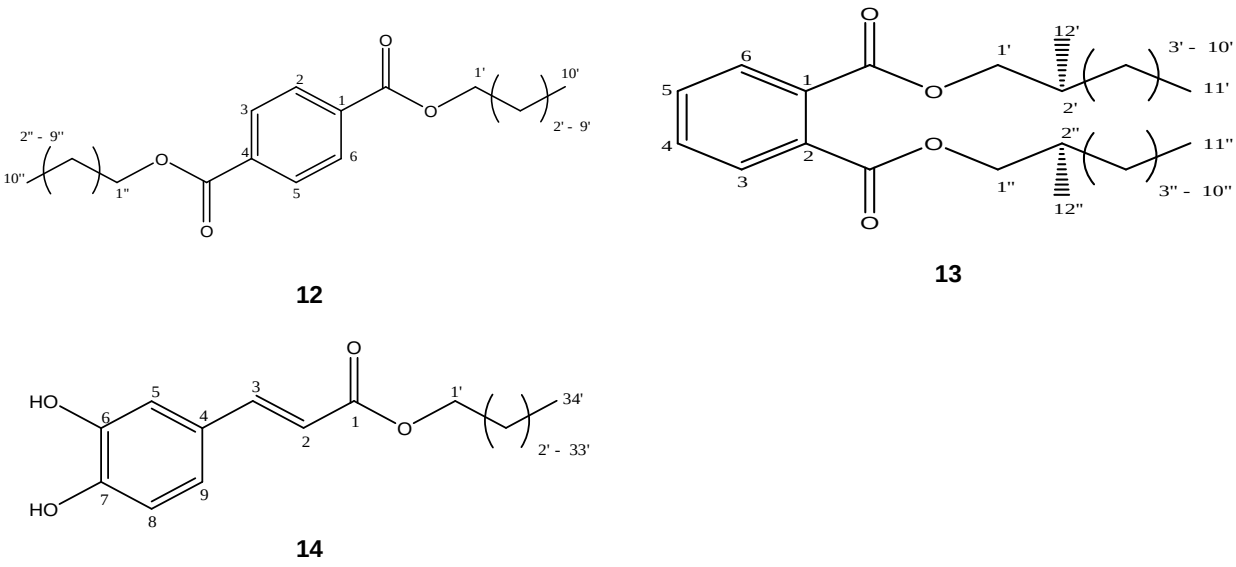
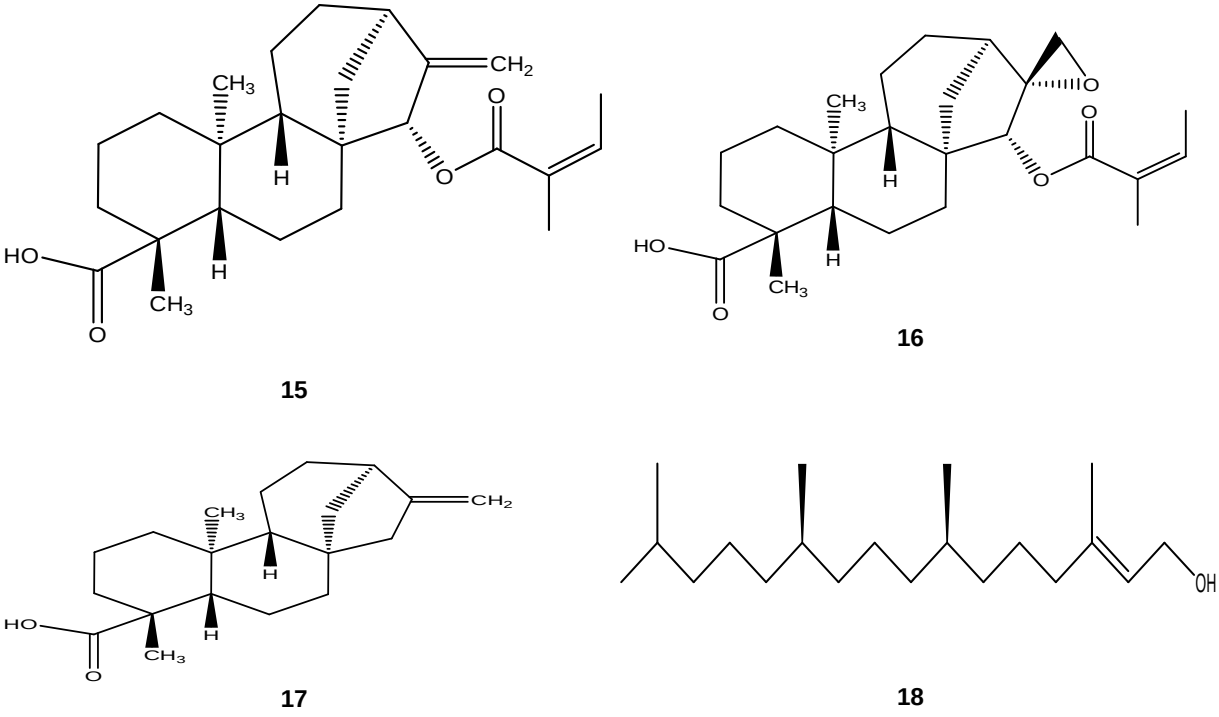
Figure 1: Structures of flavonoids isolated from *Galinsoga parviflora*



12 **13** **14**

Figure 2: Structures of aromatic esters isolated from *Galinsoga parviflora*



15 **16** **17** **18**

Figure 3: Structures of diterpenoid compounds isolated from *Galinsoga parviflora*

gel column chromatography, and their structures were established by melting point determination, IR, UV as well as Mass, ^{1}H and ^{13}C-NMR spectroscopic techniques [28]. In another study, Pan *et al* purified α-spinasterol (**28**) from *G. parviflora* using silica gel column chromatography, and determined its structure by spectral data from analysis [26]. The structures of compounds**19-23** are given in Figure 4 while compounds **24**-**29** are shown in Figure 5.

Phenolic acid derivatives

Phenolic acids are important phytochemicals in the heath of plants, and they are present in foods in the form of sterols, alcohols and hydroxy fatty acids [30]. Three well-known benzoic acid derivatives: 3,4-dihydroxy benzoic acid (**30**), gallic acid (**31**) and 4-hydroxy benzoic acid (**32**) have been isolated from *G. parviflora* using column chromatography on silica gel [29]. The structures of these compounds were established through data from melting point, IR, UV as well as Mass spectroscopic and ^{1}H-NMR spectroscopic data [29]. These structures (**30**-**32**) are given in Figure 6.

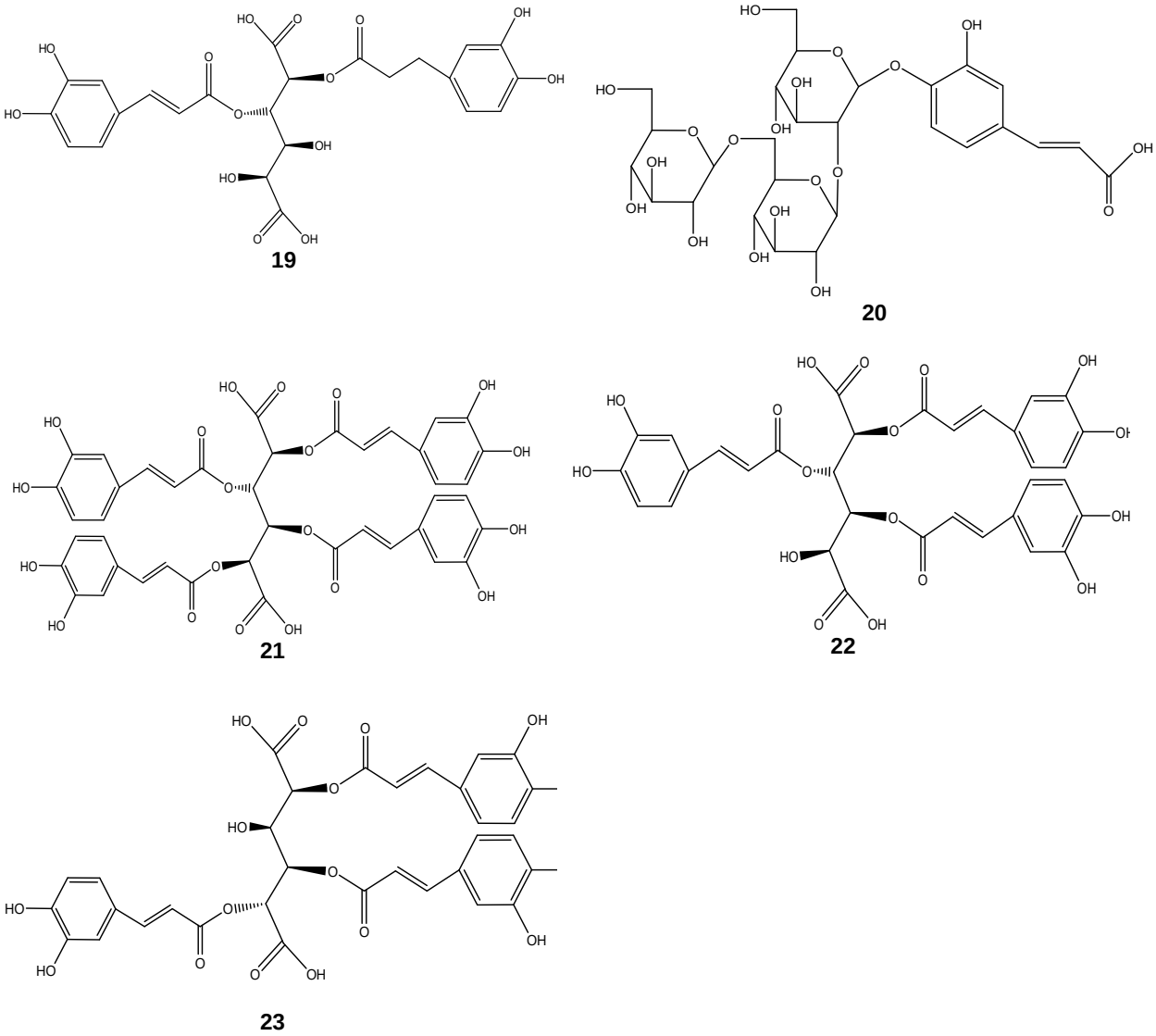


Figure 4: Structures of caffeic acid derivatives isolated from *Galinsoga parviflora*

Miscellaneous compounds

Other compounds have also been isolated and characterised from *G. parviflora*. Studies using silica gel chromatography have revealed the presence of 3,4-dimethoxy cinnamic acid (**33**), fumaric acid (**34**), triacontanol (**36**) and uracil (**37**) in ethyl acetate and light petroleum fractions of the plant using column chromatography on silica gel [28]. The structures of the compounds were established through melting point and spectroscopic data (IR, UV, Mass, ^{1}H and ^{13}C-NMR spectroscopic techniques) [28]. Moreover, Ferheen *et al* isolated octacosanoic acid (**35**) and ursolic acid (**38**) from *G. Parviflora* by column chromatography on silica gel columns [29], and structurally characterised them using IR, UV, Mass and 1H-NMR spectroscopic data, as well as data from melting point determination [29]. The structures of compounds (**33**-**38**) are shown in Figure 7.

PHARMACOLOGICAL ACTIVITIES OF ISOLATED COMPOUNDS AND EXTRACTS

The isolated compounds and various extracts of *G. parviflora* manifest a variety of pharmacological properties such as antibacterial, antifungal, antioxidant, nematicidal, anti-inflammatory, cytotoxic, urease, α-glucosidase, lipoxygenase, hepatoprotective and hypoglycemic activities (Table 2).

Antibacterial activity

Hexane, methanol and water extracts of aerial parts of *G. parviflora* have been evaluated for antibacterial activity against *Bacillus subtilis*, *Micrococcus luteus* and *Staphylococcus aureus*.

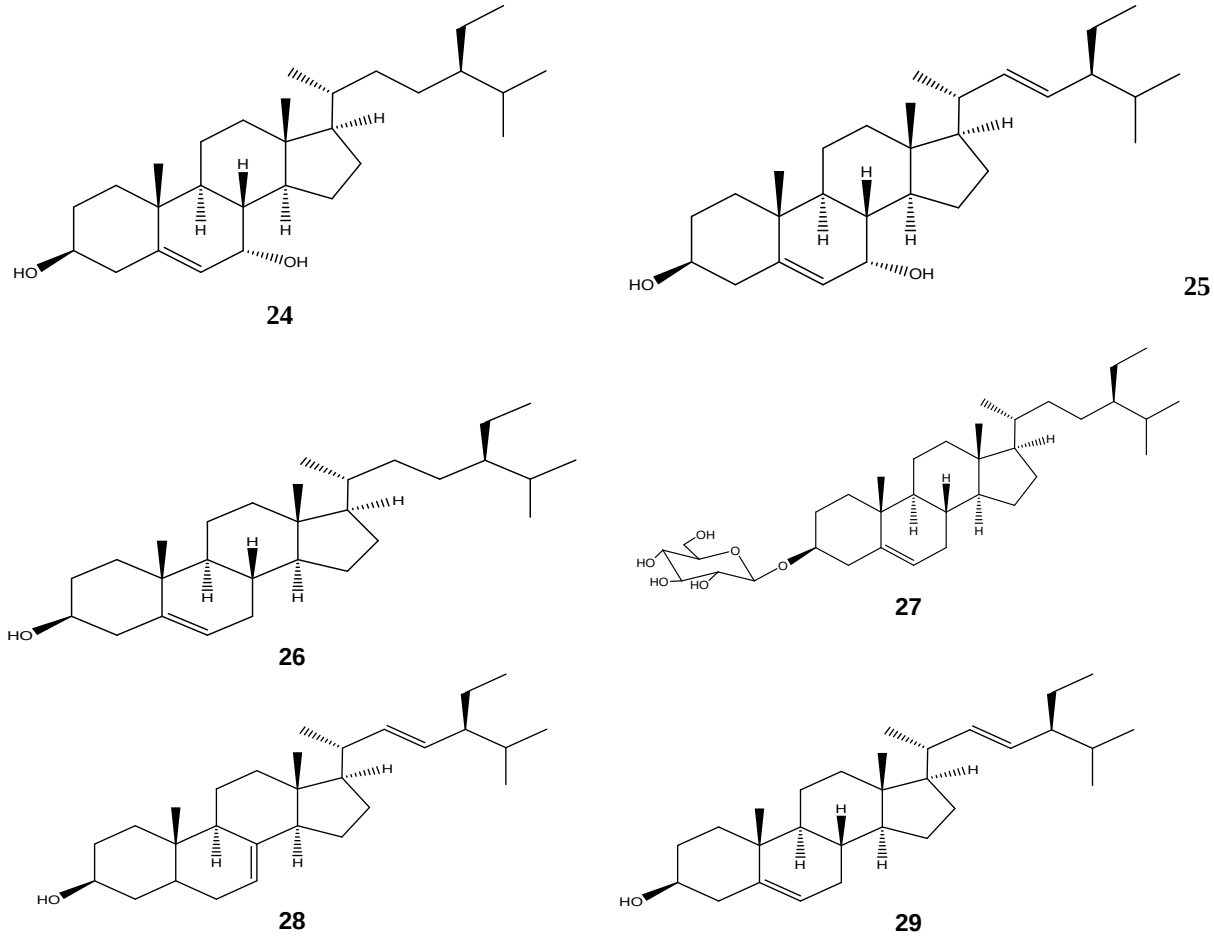


Figure 5: Structures of steroids isolated from *Galinsoga parviflora*

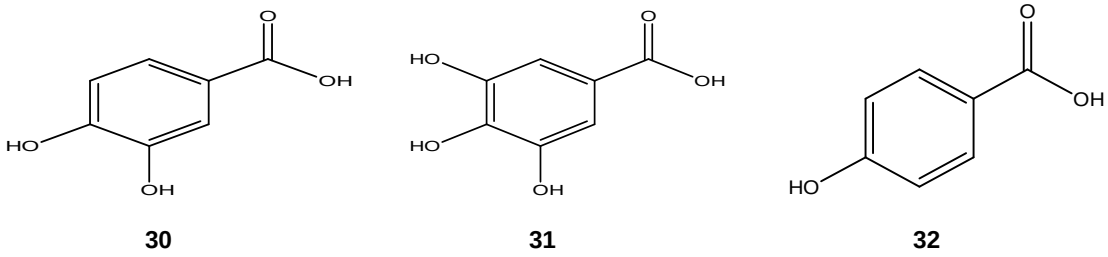


Figure 6: Structures of phenolic acid derivatives isolated from *Galinsoga parviflora*

The hexane extract (100 mg/mL) showed antibacterial activity against *B. subtilis*, *M. luteus* and *S.aureus,* whereas the methanol and aqueous extracts did not produce any antibacterial effects [31]. Compounds **8** and **11** have been screened for antibacterial effects against various gram (+ve) and gram (-ve) bacteria [8]. Compound **8** showed very good activity against *E. coli* at the highest concentration used, but it exhibited less activity against *P. aeruginosa,* and *S. aureus* at minimum concentration. In contrast, compound **11** exhibited the highest activity against *S. aureus* at the highest concentration but showed less activity against *E. coli,* and *B. subtilis* at minimum concentration [8].

Light petroleum and ethyl acetate fractions of ethanol extract of *G. parviflora* showed weak antibacterial effect against all tested gram-positive bacteria, except *B. Subtilis.* All the extracts exhibited weak antibacterial effects against the tested gram-negative bacteria, *K. pneumoniae* and *S. typhimurium*, but produced significant activity against *E. coli* and *P. aeruginosa*, relative to the standard drug

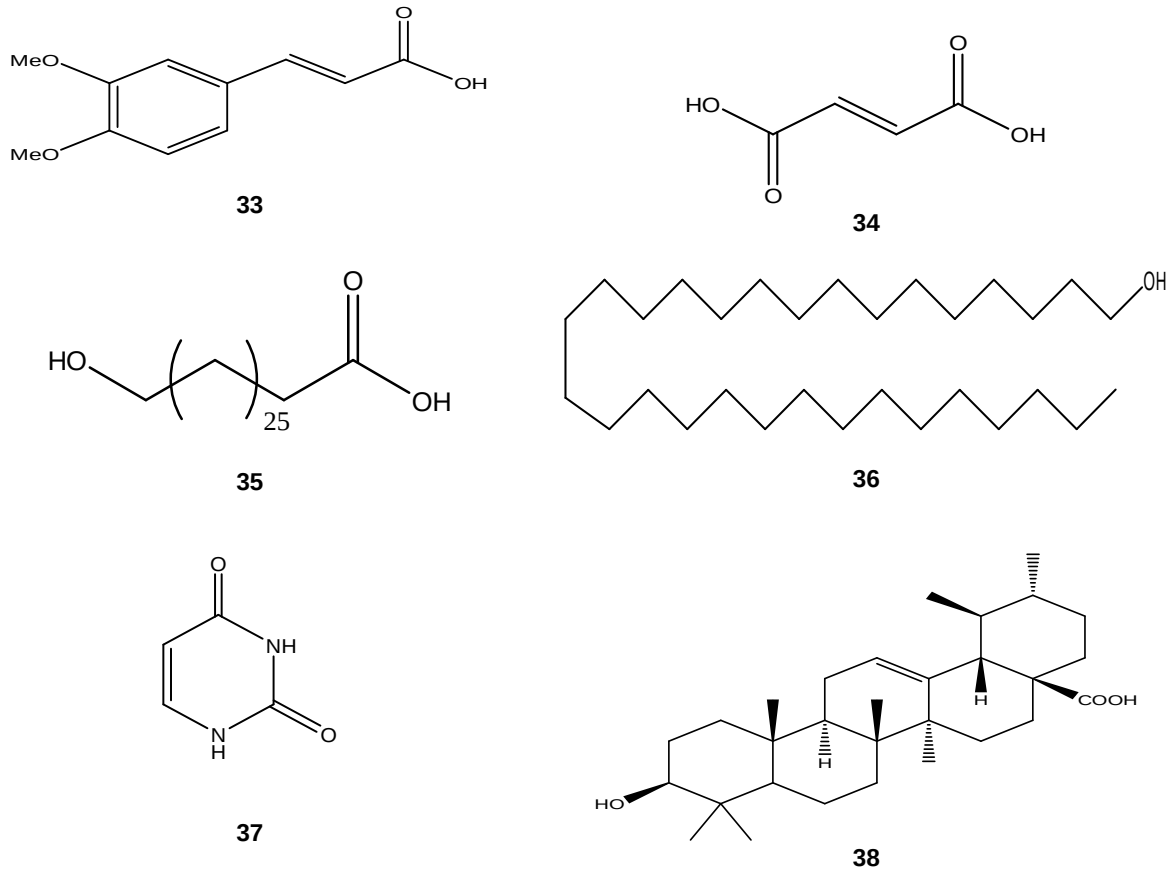


Figure 7: Structures of the miscellaneous compounds from *Galinsoga parviflora*

Table 2: Pharmacological activities of *G. Parviflora*

Activity	Microorganism/Assay/Cell line culture	Extract/Fraction/Compound	Ref.
Antibacterial	*B. subtilis, M. luteus* and *S. aureus*	Hexane, methanol, H_2O fractions	[31]
	E. coli, P. aeruginosa, S. aureus and B. subtilis	Compounds **8** and **11**	[8]
	B. subtilis, E. coli and *P. aeruginosa,*	Ethanol and light petroleum, ethyl acetate fractions	[28]
	S. aureus and *B. cereus*	Leaf oil	[32]
Antifungal	*A. niger* and *C. albicans*	Ethanol and light petroleum, ethyl acetate fractions	[28]
Antioxidant	DPPH radical scavenging,	Ethyl acetate , methanol, H_2O fractions	[5]
	Linoleic acid peroxidation	Compounds **2** and **3**	[23]
	Superoxide scavenging		
Cytotoxic	HL60 (human promyelocytic leukemia cell)	Chloroform, ethyl acetate fractions	[26]
	MCF-7 (human breast cancer cell line)	Ethanol	[28]
Nematicidal	*M. incognita* and *C. litoralis*	Ethyl acetate fraction	
		Compounds **26, 27**, **30**, **31**, **32**, **35** and **38**	[29]
Anti-inflammatory	Cyclooxygenase (COX-1) assay and	Methanol, hexane, H_2O fractions	[31]
	Lipoxygenase (5-LOX)		[33]
Urease	Urea using indophenol method	Compound **2**, **3**	[23]
α-Glucosidase	α-Glucosidase inhibition assay	Compound **3**	[23]
Hepatoprotective	ALT (alanine amino transferase) and total albumin	Ethanol	[28]
Hypoglycemic	Blood glucose reduction	Ethanol	[28]

cefotaxin [28]. Studies have also revealed that the leaf oil of *G. parviflora* exhibited specific antibacterial properties against gram positive *S. aureus* and *B. cereus* [32].

Antifungal activity

It has been reported that light petroleum, ethyl acetate fractions and ethanolic extract of *G. parviflora* exhibited significant antifungal activities against *A. niger* and *C. albicans*, when compared to the standard antifungal drug nystatin [28].

Anti-inflammatory activity

The aerial part extracts of *G. parviflora* have been tested for anti-inflammatory activity using the cyclooxygenase (COX-1) assay. The methanol, hexane and water extracts (500 µg/mL) showed 90.0±1.5, 68.0±4.5 and 54.0±2.5% inhibitions, respectively against cyclooxygenase [31]. Methanolic extract of *G. parviflora* (IC_{50} 30.7 µg/mL) showed high level of anti-inflammatory activity against 5-lipoxygenase (5-LOX) [33].

Antioxidant activity

The ethyl acetate fraction showed strong antioxidant activity at a concentration of 150 mg/mL, relative to 0.1 M ascorbic acid [28]. Studies using methanol extracts showed that the 20 % methanol fraction produced the strongest antioxidant activity against DPPH radicals with SC_{50} value 6.78 ± 0.98 µg/mL, while the 50 % methanol fraction produced maximum scavenging capacity against superoxide, with SC_{50} value of 30.6 ± 3.1 µg/mL [5]. However, the H_2O fraction of the methanol extract exhibited the highest activity, with IC_{50} value of 6.86 ± 1.31 µg/mL against linoleic acid peroxidation. Studies by Ferheen *et al* revealed that compound **2** exhibited strong antioxidant activity, while compound **3** showed moderate antioxidant activity [23].

Nematicidal activity

Hexane, chloroform, ethyl acetate and methanol fractions of the crude extract, and seven isolated pure compounds of *G. parviflora* were assessed for nematicidal activity against *Meloidgyne incognita* and *Cephalobus litoralis* for 24 and 48 h [29]. The ethyl acetate fraction exhibited the highest mortality against *Meloidgyne incognita*. While compounds **27** and **38** showed significant activity against *Cephalobus litoralis,* compound **32** was found to be highly active against both species [29].

Cytotoxic activity

Two fractions of *G. parviflora* extract were subjected to cytotoxicity screening on HL60 (human promyelocytic leukemia) cells. The chloroform and ethyl acetate fractions showed anticancer activities, with IC_{50} values of 8.5 and 10.5 µg/mL, respectively [26]. At low concentrations (down to 100 µg/mL), the ethanol extract displayed weak cytotoxic activity against MCF-7 breast cancer cell line [28].

Urease activity

Strong and moderate inhibitory activities on urease have been exhibited by compound **2** and compound **3,** respectively [23].

α-Glucosidase activity

It has been reported that compound **3** showed strong inhibition against α–glucosidase activity [23].

Hepatoprotective activity

The ethanolic extract of *G. parviflora* (400 mg/kg BW) and the standard silymarin (150 mg/kg BW) significantly decreased the levels of serum alanine aminotransferase (ALT) activity comparing with CCl_4 induced cirrhotic rats group [28].

Hypoglycemic activity

It has been demonstrated that ethanol extract of *G. parviflora* (400 mg/kg) exerted hypoglycemic properties nearly equal to those of the standard drug glibenclamide (5 mg/kg BW) [28].

The pharmacological properties of crude extracts, fractions and isolated pure compounds of *G. parviflora* are summarised in Table 2 and Table 3.

CONCLUSION

Galinsoga is an important genus of Asteraceae family, and exhibits a variety of pharmacological properties. *G. parviflora* is an important member of this genus. Various extracts and chemical compounds of the plant have shown antibacterial, antifungal, antioxidant, cytotoxic, anti-inflammatory, urease, α-glucosidase, hepatoprotective, nematicidal and hypoglycaemic activities. Its phytochemical composition indicates the presence of flavonoids, aromatic esters, caffeic acid derivatives, diterpenoids and phenolic acid derivatives. A large number of compounds have been isolated from *G. parviflora*

and shown to possess diverse biological properties. In addition, crude extracts of the plant and their solvent fractions are associated with diverse pharmacological activities. More studies should be carried out on this interesting plant, with a view to achieving more comprehensive and in-depth analysis of its pharmacological and therapeutic potential.

DECLARATIONS

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Conflict of interest

The authors declare that no conflict of interest is associated with this work.

Contributions of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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