



Phytochemical and Pharmacological Potential of Genus *Stellaria*: A Review

Anupam Sharma* and Disha Arora

University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, 160 014, India

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ABSTRACT

The review includes 68 references on the genus *Stellaria*, and comprises ethnopharmacology, morphology, phytoconstituents, pharmacological reports and toxicology of the prominent species of *Stellaria*. Flavonoids, triterpenoid glycosides and phenolic acids constitute major classes of phytoconstituents of the genus. A few species of this genus have medicinal value. Among these, *S. media* Linn. (Caryophyllaceae) has been traditionally used in the treatment of inflammations of the digestive, renal, respiratory and reproductive tracts. The plant is employed in plasters used for broken bones and swellings. Despite a long tradition of use of some species, the genus has not been explored properly. In the concluding part, the future scope of *Stellaria* species, has been emphasized with a view to establish their multifarious biological activities and mode of action.

Key words: Flavonoids, Phenolic acids, *Stellaria media*, Triterpenoid glycosides.

INTRODUCTION

This review emphasizes the traditional, pharmacologic, phytochemical and clinical potential of *Stellaria* species. The potential species of *Stellaria* need to be investigated systematically so as to be exploited as therapeutic agents.

The Genus *Stellaria*

Stellaria is a genus of about 120 species of flowering plants of the family Caryophyllaceae [1]. Its species are annuals or perennials, distributed in the cold and temperate regions. About 23 species occur in India [2]. The most widely used species is *Stellaria media* Linn.

Morphology

S. alsine Grimm. is an annual herb, glabrous. Stems tufted, slightly diffuse, ascending, 15–25 cm tall, much branched; leaves sessile, lanceolate, 0.5–2 cm × 2–4 mm, both surfaces slightly pinkish green, apex acuminate; flowers 3–5 in cymes or solitary, terminal or axillary; pedicel 0.5–2 cm, slender, glabrous, sepals 5, lanceolate, 2–4 × 1 mm, glabrous, apex acuminate; petals 5, shorter than or subequaling sepals, 2-cleft nearly to base; lobes linear, apex obtuse; stamens 5; ovary ovoid; styles 3, sometimes 2, linear, short; fruit ovoid-orbicular capsule, 6 valved; seeds numerous, brown, reniform, slightly compressed [3].

S. aquatica Linn. (Giant chickweed/Water chickweed) is a perennial herb, often found trailing over bushes [2].

S. delavayi Franch. is a perennial herb. Stems 1 m tall, basally branched, apically densely pubescent; leaves sessile or shortly petiolate; leaf blade oblong-lanceolate or lanceolate, 3–10 × 2–4 cm, abaxially densely pubescent, adaxially sparsely pubescent, base rounded, apex acuminate; flowers in cymes, densely glandular pubescent; bracts narrowly lanceolate, densely pubescent, apex acute; pedicel 0.5–1.2 cm, slender, densely glandular pubescent; sepals 5, lanceolate, 5 mm, outside glandular pubescent, apex

acute; petals 5, 2 cleft; stamens 5; styles 3; fruit 6 valved capsule; seeds 2 or 3 [3].

S. dichotoma Linn. is a perennial herb. Stems tufted, 15–30 cm tall, with numerous dichotomous branches, glandular hairy or pubescent, sometimes with 1 line of hairs; leaves ovate, 0.5–2.5 cm × 1–10 mm, both surfaces glandular hairy or pubescent, base rounded or subcordate, apex acute; flowers numerous, in terminal cymes; pedicel 1–2 cm, slender, pubescent; sepals 5, lanceolate, 4–5 mm, apex acuminate; petals 5, lanceolate, 4 mm, subequaling sepals, 2-cleft; lobes sublinear; stamens 10, ovary ovoid or broadly elliptic-lanceolate; styles 3, linear; fruit broadly ovoid capsule, 3 mm, 6 valved; seeds 1–5, brown-black, ovoid-orbicular, slightly compressed [3].

S. graminea Linn. (Stitchwort) is a perennial herb, often glabrous. Stems densely tufted, slightly erect, quadrangular, 10–30 cm tall, slender, glabrous or with 2 lines of hairs; leaves sessile, pinkish green, linear to lanceolate, 0.5–4 cm × 1.5–3 mm, base slightly narrow, apex acute; flowers many or sometimes few, in terminal or axillary cymes, 7–11 mm in diam.; bracts lanceolate, 2–5 mm, pedicel 0.5–2.5 cm, slender; sepals 5, green, lanceolate, 4–4.5 mm or longer, shiny, apex acuminate; petals 5, slightly shorter or longer than sepals, 2-cleft nearly to base; stamens 10; filaments filiform, glabrous, 4–4.5 mm; anthers brown, broadly ellipsoid, 0.3 mm; ovary ovoid-oblong; styles 3 or 4, 2 mm; fruit ovoid-cylindric capsule; seeds black-brown, nearly compressed orbicular [3].

S. holostea Linn. (Greater stitchwort) can grow up to 50 cm in height, with leaves that are long, narrow and fresh green. The flowers are white, 20–30 mm across and have five distinctive petals split to about half way down [4].

S. media Linn. (Chickweed) is a winter annual herb with a slender tap root [5], found throughout the Himalayas up to altitudes of 4,300 m [1]. Stems procumbent, 5–40 cm long, characterized by a band of pubescence along one side, much branched, root at the nodes to form mats in lawns; leaves entire, opposite, glabrous; lower leaves ovate to elliptic, petiolate, usually 3–20 mm with acuminate or abrupt apex and subcordate base; upper leaves sessile, up to 25 mm; flowers solitary in the leaf axils and borne in axillary or terminal cymes, white, small, star-shaped, 5 mm in diameter; flower pedicels recurved, 3.5–6 mm long; sepals 5, ovate lanceolate, 3–5 mm, covered with

*Corresponding author.

Dr Anupam Sharma
University Institute of
Pharmaceutical Sciences
Panjab University,
Chandigarh-160 014, India

short glandular hairs outside, apex slightly obtuse; petals 5, oblong, white, deeply bifid, shorter than sepals; stamens 3-10; anthers red-violet; styles 3, linear, 0.5-1 mm long; fruit many seeded, ovoid, capsule 5-7 mm, 6-valved; seeds ovoid to compressed globose, reddish brown, 1-1.3 mm in diameter [3,6-7].

S. pallida Dum. (Lesser chickweed) is an annual or biennial herb. Stems usually decumbent, sometimes ascending, basal branches with 1 line of villous non-glandular hairs; leaves middle and distal sessile, proximal leaves long petiolate; leaf blade suborbicular, small, 5-8 mm, both surfaces glabrous, apex acute; flowers in terminal dichotomous cymes; pedicel slender; sepals lanceolate, 3-4 mm, densely pubescent, apex acute; petals absent or minute; stamens 3-5; anthers grey-violet; styles very short; fruit 3-4 mm capsule; seeds pale red-brown, 0.7-0.8 mm in diameter, margin serrate or smooth [3,8].

S. radians Linn. is a perennial herb. Stems erect or ascending, quadrangular, 40-60 cm tall; leaves oblong-lanceolate, 3-12 × 1.5-2.5 cm, base narrowed into short petiole, apex acuminate; flowers in large terminal, dichotomous cymes; bracts lanceolate; pedicel 1-3 cm; sepals oblong-ovate, 6-8 × 2-2.5 mm; petals 5, broadly obovate, 8-10 mm, 5-7 cleft to middle or below; lobes nearly linear; stamens 10; ovary broadly ellipsoid-ovoid; styles 3, linear; fruit ovoid capsule, 6 valved; seeds 2-5, black-brown, reniform, slightly compressed [3].

S. semivestita Edgew. is a much branched leafy perennial herb found at altitudes of 1,800-2,400 m [2]. *S. uliginosa* Murr. (Bog stitchwort) is a small, erect or prostrate, leafy herb. Leaves lanceolate, 5-20 × 2-4 mm; flowers 3-5, in terminal or axillary cymes; pedicel, 0.5-2 cm, slender, glabrous; fruit ovoid-orbicular capsule, 6-valved; seeds numerous, brown, reniform, slightly compressed [2-3].

S. vestita Kurz. is a perennial, stellate hairy herb. Stems sparsely tufted, diffuse or decumbent, 30-60 cm tall, basally branched; leaves ovate or elliptic to oblong-lanceolate, 1-10 × 0.8-3 cm, apex acute or acuminate; flowers in sparse cymes; peduncles long, densely stellate pubescent; bracts ovate-lanceolate; pedicel 1-3 cm, slender; sepals 5, grey-green, lanceolate, 4-6 mm, outside stellate pubescent, apex acute; petals 5, shorter than sepals, 2-cleft nearly to base; lobes linear; stamens 10; styles 3 or 4; fruit ovoid capsule, 4-5 mm, 6-valved; seeds numerous, reniform, compressed, 1.5 mm [3].

S. yunnanensis Franch. is a perennial herb. Stems erect, 10-30 cm tall, simple or branched; leaves sessile, lanceolate, 3-5 × 0.5-1 cm, abaxially pinkish green, base rounded or slightly narrowed, apex acuminate; flowers in dichotomous cymes, glabrous; bracts lanceolate, apex acuminate; pedicel 1-2 cm, slender; sepals 5, lanceolate, 4-5 mm, apex acuminate; petals 5, slightly shorter than sepals, 2-cleft nearly to base; lobes linear; stamens 10; ovary ovoid; styles 3, linear; fruit ovoid-orbicular capsule, 6 valved; seeds 2-6, brown, reniform, slightly compressed [3].

Ethnopharmacology

A decoction of the leaves of *S. alsine* var. *undulata* is said to be used as a galactagogue. *S. aquatica* is used in China in the treatment of fistulae [2]. *S. dichotoma* var. *lanceolata* is a Chinese traditional medicine for the treatment of inflammation [9].

S. media is said to be very useful in inflammations of the digestive, renal, respiratory and reproductive tracts. The plant has been used as a remedy for haemorrhoids, eye inflammations, blood diseases and eczema; in the

case of first two, internally as well as externally [2]. Seed powder is given to children with milk to cure skin infection and allergy. Leaf paste is applied to heal wounds caused by burning [10], reduces internal inflammation, and external swelling; soothes coughs, colds, sore throats [11], effective against certain respiratory pathogens [12]. The plant is known as cooling, astringent, vulnerary, used in plasters to be employed on broken bones and swellings [13-14]. It is also used in agriculture in livestock diet considered 'refreshing' [15]. The aerial parts of *S. neglecta* Weihe. are also used in agriculture in livestock diet which is considered 'refreshing' [15]. A decoction of *S. vestita* is said to relieve bone ache and rheumatic pains [2].

Phytoconstituents

Eight species of *Stellaria* have been investigated phytochemically. Table 1 summarizes the phytoconstituents of various species of *Stellaria*. Structures of some of the constituents reported from various *Stellaria* species are shown in figure 1.

Pharmacological reports

The available literature reveals that amongst 120 species of *Stellaria*, only seven species, i.e. *S. aquatica*, *S. dichotoma*, *S. delavayi*, *S. holostea*, *S. media*, *S. semivestita*, *S. yunnanensis*, have been evaluated for their pharmacological activities.

Type-1 ribosome inactivating protein (RIP) from *S. aquatica* inhibited protein synthesis in a rabbit reticulocyte lysate with an IC₅₀ of 0.04 nM [51]. The plant has exhibited strong anticancer activity in MTT assays assessing extracts for cytotoxicity against human pulmonary and gastric carcinoma cell lines (Calu-6 and SNU-601, respectively) [53].

Dichotomaside D from *S. dichotoma* var. *lanceolata* inhibited the release of β-hexosaminidase (IC₅₀=64 μM) as well as tumour necrosis factor-α and interleukin-4 (IC₅₀=16, 34 μM) in RBL-2H3 cells. These findings suggest that dichotomide D is more effective against the late phase reactions in type-1 allergy than in the immediate phase [29]. Dichotomin A shows cell growth inhibitory activity [55]. The enzymolytic extract of proteins or saccharides of *S. dichotoma* has a good antioxidant effect, and can be used for preventing or treating aging or various diseases caused by oxides generated by active oxygen [55]. Dichotomin D also showed potent cyclooxygenase inhibitory activity [56].

Intraperitoneal administration of the ethanol-precipitated water extract of the root demonstrated anti-pyretic effect in feverish rabbits induced by triple vaccine. The anti-pyretic action of the root was not notable until reaching 2 years of cultivation and became greater with increasing cultivation time. The ether extract of the root also exerted anti-pyretic and anti-inflammatory responses. α-spinasterol contained in the root suppressed the pro-inflammatory actions of prostaglandin E₂, bradykinin, histamine and 5-hydroxytryptamine, reduced leukocyte migration, inhibited plantar edema induced by carrageenin and hot plate, and prevented croton oil-induced granuloma [57]. Furthermore, the vasodilatory cyclic peptides dichotomin J and K have been isolated from *S. dichotoma* and have demonstrated a vasorelaxant effect on rat aorta tissue [29].

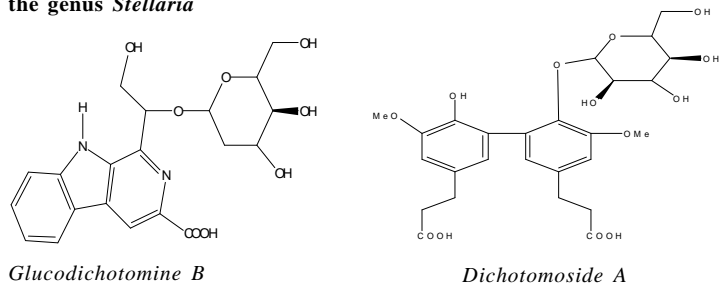
Delavayin-C from the roots of *S. delavayi* exhibited moderate antibacterial and antifungal activity comparable with the standard drug benzyl penicillin and standard antifungal agent fluconazole, respectively [58]. Methanol extract of *S. holostea* showed activity against *Pseudomonas aeruginosa* (MIC=0.1 mg/ml) [59].

Flavones of *S. media* are used in medicine for resisting HIV and herpes virus

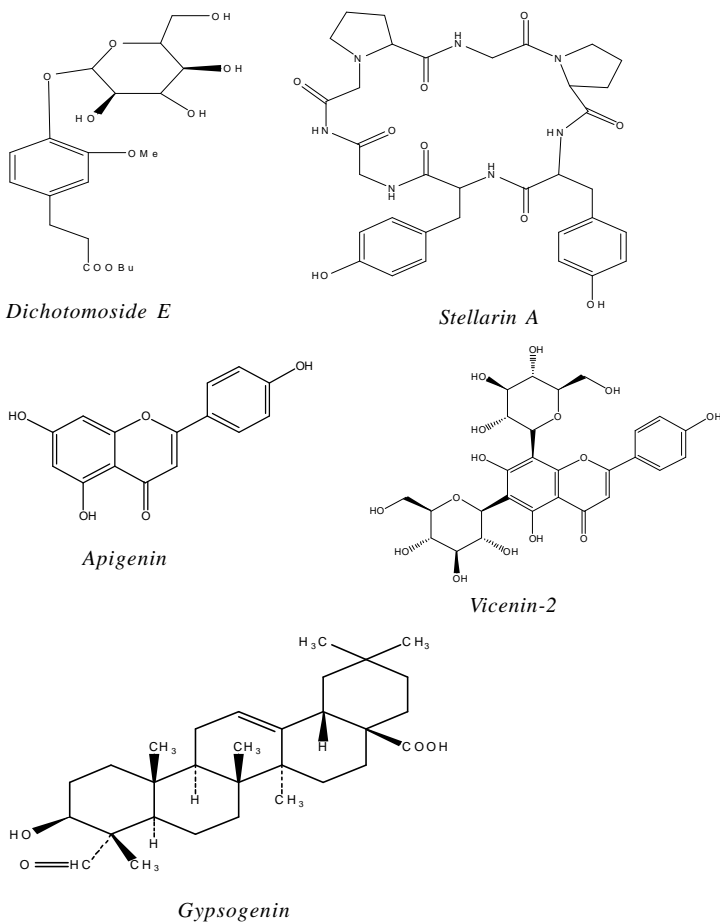
Table 1: Phytoconstituents of various species of *Stellaria*

Species	Phytoconstituents
<i>S. media</i>	Phenolic acids: vanillic acid, p-hydroxybenzoic acid, ferulic acid, caffeic acid, chlorogenic acid [16]; flavonoids: apigenin, genistein, vicenin-2 [16]; C-glycosyl flavones [17]; triterpenoid saponin: gypsogenin [18]; pentasaccharide: stellariose [19]; lipids: hentriacontane, hexacosanyl palmitate, methyl stearate, pentacosanol, tricontanol, tricontanoic acid, β -sitosterol and its β -D-glucoside, 6,7-dimethyl heptacosane, 3-methyl-6-hydroxy-hexacos-3-enyl acetate and 5-acetoxydotetracont-3-en-1-ol [20]; others: emodin, physcion, questin, 1-hexacosanol, daucosterol, cyclo-(Leu-Ile), cyclo-(Val-Tyr), α -ethyl-D pyrano-galactoside, kaempferol-3,7- β -L-dirhamnoside [21]; amino acids: uracil, thymine, thymidine, guanosine, 2-chloroadenosine, aspartic acid, glutamic acid, alanine, serine, leucine, glycine, threonine, tyrosine, lysine, histidine, proline, γ -aminobutyric acid [22].
<i>S. dichotoma</i> var. <i>lanceolata</i>	Cyclopeptides: <i>stellaria</i> cyclopeptide [23], dichotomins A-E [24], dichotomin H, dichotomin I [25], dichotomins F-G [26], dichotomins J-K [27]; glycosides: glucodichotomine B, dichotomosides A, B, C, D & dichotomoside E [28], dichotomides I, II [29], 1-O-(6-hydroxyeicosanoyl)- β -D-xylopyranose [30]; C-glycosyl-flavonoids: 6, 8-di-C-galactopyranosyl apigenin, 6-C-galactopyranosyl isoscutellarein [31]; essential oil: desacetylsinguidine, dimethyl-phthalate, pentadecanoic acid-14-methyl ester [32]; alkaloids: stellarines A, B [33]; sterols: a-spinasterol glucoside, ergot-7-enol glucoside, stigmast-7-enol glucoside, α -spinasterol, β -sitosterol, stigmasterol, stigmast-7-enol [34]; glycolipids [35]; others: 5-(hydroxymethyl)-2-furfural, 5-pyrrole-2,2-carboxaldehyde, vanillin, vanillic acid, 1-(4-hydroxy-3-methoxyphenyl) ethanone (Apocynin), phenyl propane, dihydroferulic acid, 3, 4-dimethoxy-hydrocinnamic acid, stigma-7-en-3-ol-palmitate, pinocembrin [36].
<i>S. yunnanensis</i>	Cyclopeptides: stellarin A [37], stellarin B, C [38], yunnanins D-F [39], yunnanins A-C [39-40], stellarin D, E [41], stellarins F, G [42], stellarin H [43].
<i>S. delavayi</i>	cyclopeptides: stelladelin D [44], stelladelin A [45], delavayins A-C [46], stelladelins B, C [47].
<i>S. graminea</i>	Alkaloids [48].
<i>S. holostea</i>	C-glycosyl flavones: di-C-glucosyl-6, 8-apigenin, leucenine, di-C-glucosyl-6, 8-chrysoeriol [49].
<i>S. aquatica</i>	Essential oils: 3-hydroxymethylfuran, a-pinene, limonene, camphor, geraniol, n-hexanol, cis-3-hexen-1-ol, 1-octen-3-ol benzyl alcohol, guaiacol, cresol, eugenol, carvacrol [50], stellarin [51].
<i>S. radians</i>	Essential oils: methyl linolenate, n-hexadecanoic acid, n-carotene, (3 β , 5 α)-stigmast-7-en-3-ol, 22, 23-dihydro-stigmasterol [52].

Fig. 1. Chemical structures of some phytoconstituents reported from the genus *Stellaria*



[60]. It is also used for treating appendicitis [61]. Lipid constituents from *S. media* showed significant inhibition of feeding activity against the insects *Spilosoma oblique* and *Spodoptera litura* [12]. The glycosyl flavones extract can be used as antilipemic agents [62]. The methanol extract of leaves of the plant showed in vitro antioxidant activity and can be used against various inflammatory conditions [63].



An alcoholic extract of *S. semivestita* shows anticancer activity against human epidermoid carcinoma of the nasopharynx in tissue culture [2].

Yunnanins C and D from *S. yunnanensis* showed growth inhibitory activity against mouse P-388 lymphocytic leukemia cells [39,64].

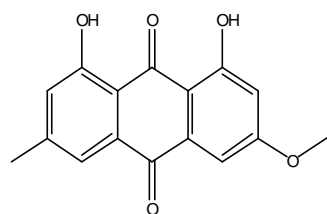
Toxicology

S. media is said to be eaten by cattle, but is fatal to lambs and horses, if eaten in large quantities. In large doses, the plant may temporarily cause a mild form of paralysis in human beings also [2].

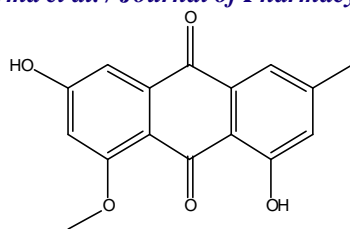
The plant *S. semivestita* is toxic to adult albino mice, the LD50 value being 500 mg/kg body weight [2].

Adverse reactions

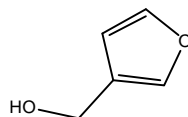
The allergic reactions predominantly contact dermatitis, erythema multiforme and recurrent erythema multiforme with photoaggravation following patch testing to fresh *S. media* leaves has been documented in literature [65,66]. Thin layer chromatography on *S. media* samples revealed the contact allergens borneol, linalool, 1, 8-cineole, menthol and additional terpenes [66]. The plant contains nitrates which have been postulated to produce detrimental effects during human and rodent gestation. The symptoms of nitrate toxicity include headache, vertigo, weakness, difficulty in breathing, cutaneous discoloration that manifests in the fingers or lips [67,68].



Physcion



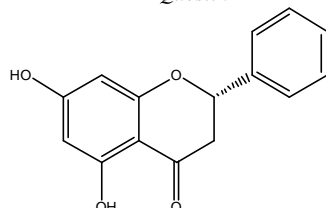
Questin



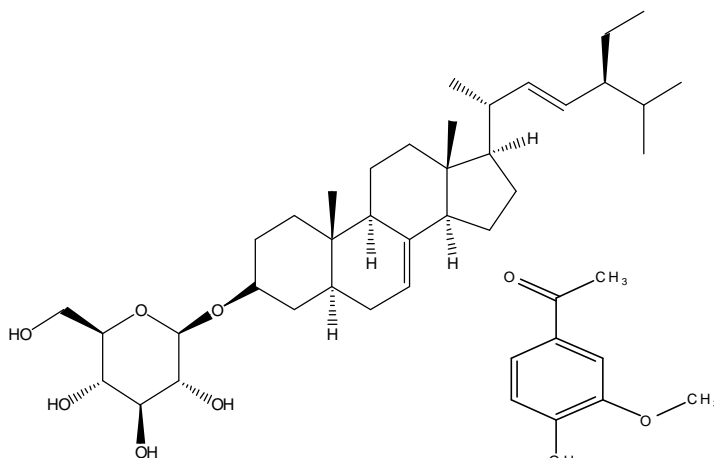
3-hydroxymethyl furan



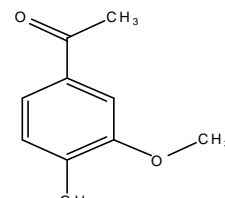
Hentriacontane



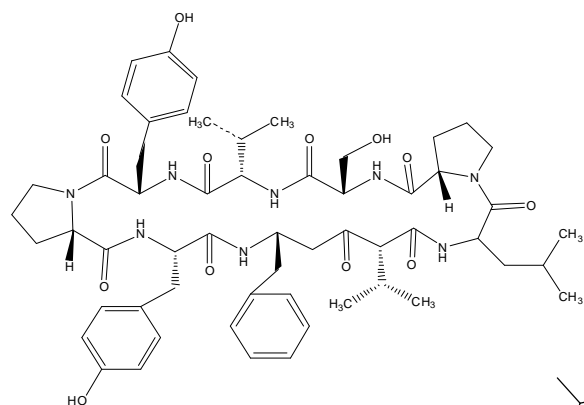
Pinocebrin



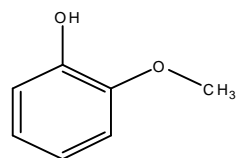
Alpha-spinasterol glucoside



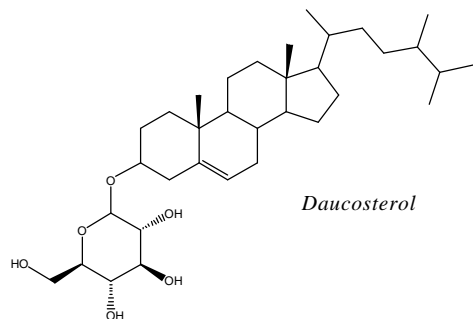
Apocynin



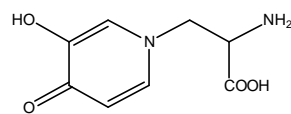
Dichotomin F



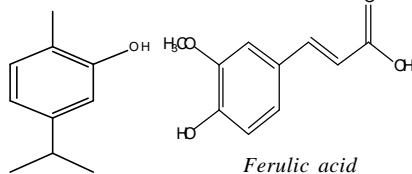
Guaiacol



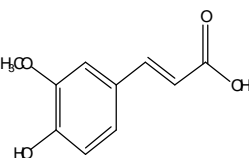
Daucoesterol



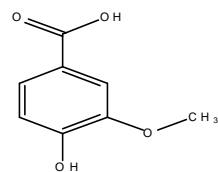
Leucenine



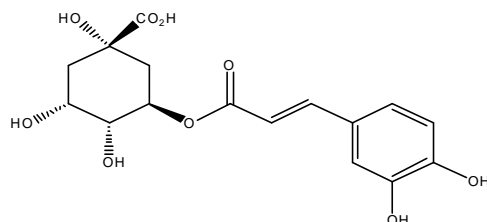
Carvacrol



Ferulic acid



Vanillic acid



Chlorogenic acid

CONCLUSION

About 120 species of the genus *Stellaria* have been reported in various floras. Among these species, most of the ethnopharmacological reports are available on *S. media*, *S. alsine* var. *undulata*, *S. vestita*, *S. aquatica*, *S. dichotoma* var. *lanceolata*. Further, only eight species of *Stellaria* have been partially investigated for their phytoconstituents. A close scrutiny of literature on *Stellaria* reveals that seven species have been investigated pharmacologically. Pharmacological studies infer that *S. media* exhibits antiviral, antilipemic and antitumour properties; *S. yunnanensis* and *S. semivestita* both possess antitumour activity; *S. dichotoma* displays antiallergic, antioxidant and antitumour activities. *S. media* has been included in herbal formulations, which are in clinical use for the treatment of various ailments. Keeping in view the ethnopharmacology, phytochemical and pharmacological reports, low toxicity and frequency of use, *S. media* seems to hold great potential for in depth investigation for various biological activities. Few preliminary pharmacological reports support medicinal potential of some *Stellaria* species. These species need to be investigated systematically with a view to establish their varied pharmacological activities and mode of actions.

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