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Stellaria media Linn.: A comprehensive review highlights the nutritional, phytochemistry, and pharmacological activities

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ABSTRACT

Stellaria media Linn., a member of the family Caryophyllaceae, is generally known by the name of Chickweed. This plant is extensively cultivated globally and is inherent to Africa, Asia, China, Europe, and North America. It is a well-known medicinal plant with immense therapeutic uses. Nutritional studies have revealed the presence of protein, especially 16 amino acids, vitamins, and minerals such as calcium, iron, phosphorus, and zinc. Phytochemicals, mainly flavonoids, isoflavonoids, saponins, tannins, alkaloids, phenolic acids, triterpenoids, phenolic compounds, and anthraquinone are present in chickweed. It has multiple therapeutic potentials like anti-obesity, anti-diabetic, anti-fungal, anti-bacterial, anti-inflammatory, anti-leishmanial, anti-anxiety, and toxicity profiles. The crude extracts and their metabolites did not show any toxicity in the experimental animal. This review summarizes the nutritional, phytochemical, pharmacological, and toxicity studies on this plant concerning its future use in pharmacological drugs.

Implication for health policy/practice/research/medical education:
This review is aimed to provide the nutritional, phytochemistry, and pharmacological activities of *Stellaria media* Linn. The findings revealed the presence of protein, vitamins, minerals, and secondary metabolites such as flavonoids, phenolic compounds, saponins, alkaloids, pentasaccharides, phlobatannins, and sitosterol. Extract and compounds displayed various pharmacological activities such as anti-inflammatory, anti-fungal, anti-bacterial, anti-obesity, anti-diabetic, anti-oxidant, anti-anxiety, anti-leishmanial, and anti-hepatitis.

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Introduction

Before the invention of chemical drugs, people were dependent on medicinal plants in developing and developed countries. Due to their conventional beliefs, people always utilized plants for food, clothing, housing, and health care practices (1). According to World Health Organization (WHO), around 80% of the world's population relied on medicinal plants for primary health care requirements. In developing countries, around 3.3 billion people depend on medicinal plants for daily needs (2). That is why researchers go through the previous works of literature published on various species of medicinal plants to update the current awareness of the community. One such nutrient-dense medicinal plant is *Stellaria media* Linn. (Chickweed).

Stellaria media Linn., also known by the name of Chickweed, belongs to the family of Caryophyllaceae and contains 2630 species and 85 genera (3,4). It is also known to be Buch-bucha in Hindi, Chickweed, Mouse-ear, and Starweed in English (5). It is a perennial or annual herb that grows mainly in the cool season and moderate regions of Asia, Europe, and Northern America (6). In India, it grows in the Himalayas at a height of about 4300 m (7). Chickweed is widespread in open fields and areas of the world that require no cultivation (8). Chickweed is largely cultivated due to its immense pharmacological potential (9). Different parts of the chickweed are used for asthma (10), measles, gastrointestinal disorders, diarrhea, digestive, renal, respiratory, and reproductive tract inflammation (11,12). Various biological metabolites

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present in different parts of the chickweed are alkaloids, saponins, fatty acids, cardiac glycosides, terpenoids, and tannins (13,14). Chickweed leaves possess antipyretic (15), antioxidant (16), anti-cancer, anti-bacterial, anti-fungal, anti-viral, anti-hepatitis, anti-inflammatory (17-20), and anti-obesity properties (21,22). Leaves of the chickweed have a great immune response to the mumps virus vaccine (23). Several studies have reported that chickweed leaves exhibit hypoglycemia, hypolipidemia, and hepatoprotective effects (24- 26). This article aims to review the nutritional, phytochemical, pharmacological, and toxicological studies of chickweed. Furthermore, it emphasizes the current knowledge and scientific advancement regarding chickweed.

Ethnobotanical study

Chickweed germinates in the autumn season and blooms in May and October. The stem is willowy weak, having oval-shaped leaves, and white flowers with deep lobed petals (Figure 1). Chickweed grows up to 40 cm in nitrogen-rich fertile soil, especially in dumping sites, lawns, and meadows. It is widespread in Africa, Asia, Europe, and North America, with fine peculiar hairs in the stem (27). The taxonomy hierarchy of *S. media* Linn. is as follows (28):
Kingdom: Plantae
Subkingdom: Viridiplantae
Division: Tracheophyta
Subdivision: Spermatophytina
Class: Magnoliopsida
Superorder: Caryophyllanae
Order: Caryophyllales
Family: Caryophyllaceae
Genus: *Stellaria* L.
Species: *Stellaria media* (L.)

Macroscopic description

A macroscopic description of the chickweed has been labelled in (Table 1). This helps the local people easily identify the chickweed plant by its physical appearance.

Traditional medicinal uses

Since ancient times, people have utilized chickweed

Figure 1. Plant of *Stellaria media* Linn.

and used it in folk medicines for curing illnesses like inflammation (31), rheumatism, and viral infections in China (32). In North America and Europe, leaves are used for the treatment of itching, burns, and cuts on external skin (33,34). The whole plant of chickweed has been used as a plaster for broken bones and acts as a cooling agent (35,36). It is used to reduce pain, heal wounds, stop bleeding (37), and also for the treatment of cancer (38), kidney diseases (39), neurological disorders, and inflammation (40). Chickweed leaves and juice have various medicinal benefits, especially in liver diseases, lung infections, thyrotoxicosis, hemorrhoids and joint pain (41). Fresh leaves and shoots salad are used for kidney (42), liver, lung, and heart diseases (43). It is also used as demulcent, expectorant (44), carminative, astringent, depurative, emmenagogue, and galactagogue (45). The leaves, flowers, stems, and roots of the chickweed have the renowned potential for psychological disorders, inflammation in the respiratory, and reproductive system (46,47).

Nutritional profile

Chickweed leaves are rich in protein, fat, fiber, carbohydrates, and various dietary minerals (48). Chickweed is one of the nutrient-dense plants that contains 16 essential amino acids of the total free amino acids (27.27%) and total bound amino acids (48.05%) in their aerial parts. The protein requirement from the chickweed is complete as compared to other green leafy vegetables (49). The leaves are also appraised to contain minerals such as calcium, iron, copper, zinc, magnesium, potassium, phosphorus, and sodium (50). The leaves are rich in vitamins A, B_1, B_2, B_3, C, E, and rutin (51). Chickweed leaves also contain chlorophylls

Table 1. Macroscopic description of *Stellaria media* Linn. (29,30)

Plant parts	Description
Leaves	Leaves are simple, opposite, with smooth surface, oval in shape, and greenish-yellow in color. Lower leaves are 3-20 mm long, having stalks, whereas upper leaves are 20 mm long without stalks.
Flowers	Flowers are white in color, a quarter of an inch in diameter, have clusters with a central stem, solitary occurs in axils, bisexual, petals are shorter than sepals, and anthers are violet-reddish in color.
Roots	Roots are fibrous with a dense network, fragile, weak, and shallow with a tap root system.
Stems	The stem is weak, long, trails on the ground, and 5-40 cm in length.
Fruits	Fruits are capsule-shaped and have a number of tiny seeds.
Seeds	Seeds are reddish-brown in color.

and carotenoids in fresh, frozen, and dried forms (52). The composition of amino acids is listed in Table 2 and important dietary minerals are mentioned in Table 3. The richness of various important nutrients in chickweed helps mankind with nutritional balance as well as for curing various diseases. Also, chickweed is displayed to possess amino acids and minerals; hence has the potential to be used in drugs for numerous diseases associated with the deficiency of nutrients.

Phytochemistry

The whole plant of the chickweed is rich in lipids (55), triterpenoid (56), C-glycosyl flavones (57), flavonoids and phenolic compounds (58), saponins (59), phlobatannins, sitosterol, alkaloids, and pentasaccharide (60-62). Bioactive metabolites isolated from the aerial parts of the chickweed are 2-amino-adipic acid, 5-acetoxydotetracont-3-en-1-ol, 6,7-dimethylheptacosane, oxalic acid, saccharopine, and saponarin (63). Another phytochemical study identified active biological metabolites from different parts of the chickweed and its extracts. The flavonoids are mainly 7-O-β-D-glucoside isovitexin (saponarin), apigenin 6-C-glucoside (isovitexin), isovitexin 7,2-di-O-glucoside, apigenin 6-C-β-D-galactosyl-8-C-α-L-arabinoside, isovitexin 7-O-galactosyl-2-O-glucoside, apigenin 6-C-α-L-arabinosyl-8-C-β-D-galactoside, apigenin 6-C-β-D-galactosyl-8-C-β-L-arabinoside, apigenin 6,8-di-C-α-L-arabinoside, apigenin 6-C-β-D-glycosyl-8-C-β-D-galactoside, quercetin 3-O-rutinoside (rutin), coumarins, and vitamin C (64-67). Phenolic compounds that are present in chickweed leaves extracts are luteolin, quercetin, kaempferol, sinapic acid, rutin, vanillic acid, protocatechuic acid, catechin hydrate, and α-resorcylic acid (68). Miscellaneous compounds that are isolated from the aerial part of the chickweed are 6- methylheptyl-3′-hydroxy-2′-methylpropanoate, 2, 4, 5, 7-tetramethyloctane, and 2, 2, 4-trimethyloctan-3-one. These important metabolites help in weight loss, and anti-inflammatory activities (69). Furthermore, a list of the various phytochemicals found in different parts of the chickweed plant is mentioned in (Table 4).

Important active constituents that are responsible for antioxidant activity are hydroxycinnamic acids, catechins (74), saponosides, vitamin C, polyphenols, mucilage, carotene, and silicon (75). As mentioned earlier, chickweed contains a good amount of phlobatannins, flavonoids, alkaloids, phenolic acid, ascorbic acid, and α-tocopherol that play an excellent role in antioxidant activity (76,77).

Table 2. Amino acids composition of *Stellaria media* Linn. (53)

Amino acids	Free amino acids (FAA) mg/kg dry weight	Bound amino acids (BAA) mg/kg dry weight
Alanine	446.00	1096.80
Aspartic acid	744.01	1805.65
Threonine	71.20	769.23
Glutamic acid	785.60	2202.21
Serine	44.00	656.31
Glycine	55.05	863.86
Valine	287.02	998.78
Methionine	57.90	180.61
Proline	128.71	779.31
Leucine	203.03	1512.32
Isoleucine	126.08	854.59
Lysine	52.67	783.31
Arginine	14.70	834.55
Phenylalanine	10.83	1028.97
Tyrosine	63.40	588.88
Histidine	26.60	432.03
Total amino acids	3116.80	15387.41

Table 3. Mineral composition of *Stellaria media* Linn. (54)

Minerals	mg/100 g
Phosphorus	440
Potassium	2250
Magnesium	220
Calcium	1780
Iron	11.2
Manganese	1.7
Zinc	2.4

Pharmacological properties

Effect on wound healing

Wound healing is a major concern in medicine, especially in the case of diabetic patients. A few studies appraised the wound healing potential of the chickweed. A *in vitro* study on normal human dermal fibroblasts (NHDF) by using the scratch method in a different concentration of chickweed extract has been carried out. Chickweed extract concentration ranging from 12.5 µg/mL to 200 µg/mL was used to assess the cell viability of NHDF. Chickweed extract with 100 µg/mL in 24 hours showed the fastest and strongest wound healing due to the presence of apigenin, vicenin-2, ferulic acid, caffeic acid, and vitamin C (78).

Anti-inflammatory activity

Methanolic leaf extract (MLE) of chickweed was screened for *in vitro* anti-inflammatory effects in rats. Five rats in three groups were used for the study. MLE of chickweed with 100 mg/kg, 300 mg/kg, and 500 mg/kg body weight was used in test rats. The positive control group was treated with Indomethacin (5 mg/kg body weight) and the control group with distilled water (10 ml/kg body weight). MLE with 300 mg/kg body weight was effective for the albumen-induced paw edema and formalin-induced paw lick compared with the control group and the rats treated with Indomethacin (79). The methanolic and aqueous extracts of chickweed were reported to have

Table 4. Phytochemicals in different parts of *Stellaria media* Linn. (28,70-73)

Various parts	Chemical composition
Whole plant	Anthraquinone, alkaloids, acidic components, carbohydrates, cardiac glycosides, cyanogenic glycosides, flavonoids, glycosides, saponins, reducing sugar, resins, steroids, terpenoids, and tannins.
Leaves	Flavonoids: apigenin-7-glucoside, rutin, apigenin, flavone, luteolin-7-glucoside, naringenin-7-glucoside, luteolin, kaempferol, naringenin, scopoletin, and quercetin. Isoflavonoids: formononetin, daidzin, genistin, genistein, glycitein, ononin, isoformononetin, sissotrin, sophoricoside, and tectoridin.
Aerial part	6-methylheptyl-3′-hydroxy-2′-methylpropanoate, 2, 4, 5, 7-tetramethyloctane, and 2, 2, 4-trimethyloctan-3-one.
Roots	Anthocyanidins, carbohydrates, proteins, glycosides, flavonoids, alkaloids, saponins, triterpenoids, and steroids.

inhibition effects for collagenase, hyaluronidase, and lipoxidase at doses of 50–500, 10–200, 5–50, and 100–500 µg/mL for 2,2-diphenyl-1-picrylhydrazyl (DPPH), hydrogen peroxide (H_2O_2), oxygen gas (O_2), nitrogen oxide (NO), and peroxynitrite ion ($ONOO^-$). However, all the above extracts were performed by high-performance liquid chromatography (HPLC), high-performance thin-layer chromatography (HPTLC) paired with a diode array detector, and an ion trap mass detector by *in vitro* cell system. The chickweed ethanolic extract showed remarkable scavenging activity at the concentration of 50% (H_2O_2, 132.8 ± 3.9 µg/mL), (NO, 16.5 ± 0.4 µg/mL), and ($ONOO^-$, 11.9 ± 1.1 µg/mL). Also, the aqueous extract showed inhibitory action against superoxide anion (62.7 ± 8.1 µg/mL). The study concluded that apigenin glycoside was the main compound for the anti-inflammatory effects of both extracts (80).

Anti-fungal activity

The *Stellaria media* adenosine monophosphate (SmAMP3), a known peptide isolated from the chickweed leaves, showed anti-fungal activity *in vitro* against various fungi *Aspergillus niger*, *Fusarium solani*, *Bipolaris sorokiniana*, *Alternaria alternata,* and *Botrytis cinerea*. The result showed abnormal growth and spore formation in fungi due to the presence of a chitin-binding site in the SmAMP3 peptide (81). The aqueous extract of chickweed leaf along with *Eclipta prostrata*, *Chenopodium album*, *Oxalis corniculata*, and *Euphorbia pulcherrima* showed anti-fungal activity *in vitro* against *Paecilomyces lilacinus* (82).

Anti-bacterial activity

The whole plant of chickweed showed anti-bacterial activity against both gram-positive, and gram-negative bacteria: *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella Typhi, Pseudomonas aeruginosa,* and *Staphylococcus aureus*. Aqueous and chloroform extracts of chickweed inhibited the growth of bacteria, but the chloroform extract was less effective than the aqueous extract (83). Methanol, ethanol, and water extracts of chickweed had positive anti-bacterial activities against *Escherichia coli*, *Enterobacter cloacae*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Serratia marcescens, Streptococcus pyogenes,* and *Salmonella typhimurium* (84).

Anti-obesity activity

Chickweed has potent anti-obesity activity lowering total cholesterol, low-density lipoprotein (LDL) cholesterol, and total triglyceride. Lyophilized juice (LJ) of chickweed (400-900 mg/kg) was given for 6 weeks to Swiss albino mice. LJ at 900 mg/kg body weight inhibited *α*-amylase, pancreatic lipase, and post-prandial triglyceride level, reduced body and liver weight, and increased high-density lipoprotein (HDL) cholesterol level (85). Additionally, alcoholic and methanolic extracts of chickweed leaves have shown anti-obesity activities in female Wistar rats (following 48 days consumption). The methanolic extract containing flavonoids, saponins, and β-sitosterol was more efficient in weight reduction compared to the alcoholic extract of chickweed (86).

Anti-diabetic activity

Chickweed leaves alcoholic extract has been appraised to lower blood glucose levels in alloxan-induced diabetes in rats by using standard procedures. Results demonstrated a significant reduction in pancreatic β-glucosidase, α-amylase, fasting blood sugar, and hemoglobin A1c (HbA1c) (-48.4%) in comparison with the control group (87). The whole plant extract of chickweed has been used traditionally by Bongaigaon district tribes for the treatment of diabetes (88).

Anti-oxidant activity

An anti-oxidant is a chemical substance that hinders the oxidation of molecules that cause oxidative stress. Free radicals and reactive oxygen species (ROS) are very reactive in nature, competent to damage the deoxyribonucleic acid (DNA), lipids, protein, and carbohydrates that lead to homeostatic imbalance (89). The alcoholic extract of chickweed has shown significant results for oxidative stress in rats. The extract dose of 5 ml/kg showed remarkable anti-oxidant capacity (90). Additionally, the scavenging capacity of the aerial parts of chickweed extract was appraised by 2,2-azinobis(3-

ethylbenzothiazoline-6-sulfonate) (ABTS) radical cation scavenging, metal chelating activity, and DPPH. The extract showed an excellent metal chelating activity as compared to DPPH, and ABTS radical cation scavenging capacity (91). Also, methanolic extract of chickweed seeds has shown significant results for anti-oxidant activity by using DPPH (92).

Anti-anxiety activity

The methanolic extract of the chickweed isolates two bioactive compounds, 2,2,4-trimethyloctan-3-one, and 6-methylheptyl-3′-hydroxy-2′-methylpropanoate with anxiolytic activities. The activity of two bioactive compounds was analyzed using five different tests such as mirrored chamber test, elevated plus-maze model (EPM), light and dark test, open field test, and m-chlorophenylpiperazine (mCPP) induced hypo-locomotion model in mice (93). Furthermore, chloroform, methanol, petroleum ether, and water extracts of chickweed at 50, 100, 200, or 400 mg/kg body weight showed anxiolytic activity in mice by using EPM model. Methanolic extract at 100 mg/kg body weight displayed an anti-anxiety effect due to the presence of fixed oils, fats, flavonoids, proteins, carbohydrates, triterpenoids, and tannins (94).

Anti-leishmanial activity

Aerial part extracts of the chickweed and their fractions exhibited anti-leishmanial activity by using *Leishmania tropica* that has been isolated from the patient in Peshawar (Pakistan). The inhibitory effect was dose-dependent at half-maximal inhibitory concentration (IC_{50}) value of methanol extract, n-hexane fraction, chloroform fraction, ethyl acetate fraction, n-butanol fraction, and water fraction (185.9 µg/mL, 170.4 µg/mL, 155.5 µg/mL, 36.4 µg/mL, 49.5 µg/mL, and 184.8 µg/mL, respectively) (95,96).

Anti-hepatitis activity

Anti-hepatitis B virus (HBV) activity of chickweed is dose-dependent. The crude extract of fresh chickweed leaves at a dose of 30 µg/mL protected against *in vitro* human HBV-transfected liver cell line. After treatment for 6 d, it has shown significant protection rates ranging from 27.92%, and 25.35%. In addition, the potential for anti-viral effect is due to the presence of protein, polysaccharides, flavonoids, and C-glycosides in chickweed leaves (97).

Skin care

Chickweed leaves soaked either in oil or water were used to make herbal skincare products (98). The herbal cosmetic products were free from synthetic chemicals. Additionally, due to the presence of active biological compounds, the extract was used to make lotions, balms, salves, and creams that were helpful to lower skin irritation, redness, and itching (99).

Toxicological profile

Medicinal plants are considered safe and non-toxic; however, not all medicinal plants are safe in high doses. Also, the specific dose of the particular medicinal plant is not well documented or cited (100). Thus, the toxicology study of medicinal plants will be helpful for its authenticity and safety purposes. Studies have reported that the median lethal dose (LD50) of chickweed leaves ethanolic extract in mice by using the up and down method is >5000 mg/kg body weight (80,101). Also, numerous active biological compounds are present in chickweed, such as cardiac glycosides, flavonoids, linalool, mentol, saponins, phenolics, terpenoids, and 1, 8-cineole. These biological compounds at high doses cause various side effects such as cyanosis, dermatitis, dizziness, diarrhea, nausea, and erythema multiforme. Furthermore, due to the presence of nitrates in chickweed, an overdose may cause breathing problems, fatigue, vertigo, headache, staining on lips or fingers, and gestational pain in pregnant women (102).

Conclusion

Chickweed has been substantially used in traditional medicines. Major biologically active compounds such as flavonoids, saponins, flavonoids aglycone, tannins, alkaloids, phenolic compounds, phenolic acids, triterpenoids, and anthraquinone are present in the chickweed. Additionally, chickweed is rich in protein and 16 essential amino acids. Also, it contains minerals such as calcium, iron, potassium, zinc, and vitamins. Various crude extracts, pure compounds, and formulations displayed therapeutic efficacies such as anti-obesity, anti-diabetic, anti-inflammatory, anti-fungal, anti-oxidant, stomach cramps, and skin infection. This work highlights an extensive overview of the phytochemistry, pharmacology, and therapeutic uses of chickweed. Additionally, biologically active compounds isolated from chickweed would lead to the development of therapeutic drugs. Furthermore, toxicity studies are also important to ensure its safe usage in the future.

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Authors' contribution

CM conducted internet and literature search. SR developed the idea, carried out the computation, and wrote the whole manuscript. ES encouraged, supervised, assessed, evaluated the article, and corrected all drafts. All authors have studied, looked thoroughly, read the manuscript, and validated the publication of the article.

Conflict of interests

All authors declare that there is no conflict of interest for this review.

Ethical considerations

All ethical issues including (etiquette and ethics, authorship issues, data fabrication, duplicate publication, falsification, and plagiarism) have been carefully observed by all authors.

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