



Taxonomy, phytochemistry, pharmacology and traditional uses of *Flueggea virosa* (Roxb. ex Willd.) Royle: A Review

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Manuscript details:

Received : 21.03.2018
Accepted : 23.04.2018
Published : 26.04.2018

Editor: Dr. Arvind Chavhan

Cite this article as:

Renu, Satya Narain, Archana Rawat, Jaswinder Kaur, Santosh Kumar and Nahid Fatima (2018) Taxonomy, phytochemistry, pharmacology and traditional uses of *Flueggea virosa* (Roxb. ex Willd.) Royle: A Review, *Int. J. of Life Sciences*, Volume 6(2): 579-585.

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Available online on
<http://www.ijlsci.in>
ISSN: 2320-964X (Online)
ISSN: 2320-7817 (Print)

ABSTRACT

Flueggea virosa (Roxb. ex Willd.) Royle. of family Euphorbiaceae is commonly grown medicinal plant. The plant contains large number of phytochemicals such as alkaloids, triterpenoids, resins, steroids, cardiac glycosides, bergenin, menisdaurin and anthraquinones. The study revealed the plant to be a potential source of nutrition, mineral and drugs. This review aims to provide an up to date overview of the phytochemistry, pharmacological data as well as traditional uses of the plant in view of discussing its medicinal value and potential application in complementary and alternative medicine.

Keywords : *Flueggea virosa*, Euphorbiaceae, Phytochemistry, Traditional uses.

INTRODUCTION

India is enriched with a variety of different species of medicinal plants which are used in daily life to treat common ailment to life threatening diseases. *Flueggea virosa*, is a multipurpose plant with a wide range of medicinal, ethnomedicinal and horticultural uses, described as “cure all”(Magaji *et al.*, 2015). People from the folklore have been using to treat variety of ailments since many years ago. Recently, an increasing attention has been drawn to this plant because of the identification of multiple bioactive phytoconstituents and numerous biological and pharmacological activities. The focus of this short review is to elaborate and update the total phytochemical constituents and pharmacological activities reported over the last few years.

Taxonomic Description

Flueggea virosa (Roxb. ex Willd.) Royle, Ill. Bot. Himal. Mts., 9: 328. 1836; Webster in Allertonia 3: 287. 1984; *Phyllanthus virosus* Roxb. ex Willd., Sp. Pl. 4: 578. 1805. *Flueggea microcarpa* Bl., Bijdr. Fl. Ned. Ind. 580. 1826; Hook. f. Fl. Brit. India 5: 328. 1887. *Securinega virosa* (Roxb. ex Willd.) Baill. in Adansonia 6: 334. 1866. *S. microcarpa* (Blume) Pax and K. Hoffm. ex Aubrev., Fl., Forest. Sudano – Guin. 190. 1950. *Chirigodi*, Dalme, *Patala*.



Photoplate: *Flueggea virosa* (Roxb. ex Willd.) Royle., Near Windom Fall, Mirzapur.

Shrubs or trees, 1-8 m tall, entirely glabrous. Leaves opposite, elliptic, oblong-elliptic to obovate, 1.5-7 X 1-4 cm, obtuse to acute or apiculate at apex, rounded or cuneate at base, entire, chartaceous to membranous; lateral nerves 5-9 pairs; petioles 2-10 mm long. Inflorescence axillary, the male glomerules 20-40 flowered, the females up to 10-flowered. Male flowers: pedicels 1.5-5 mm long, filiform; sepals 5, ovate-elliptic, 0.8-1.5 X 0.5-1mm; disc glands 5, 0.3 in diam.; stamens 5; filaments 1-2 mm long; anthers ellipsoid to suborbicular, 0.3-0.5 mm long; pistillode 1-1.5 mm long. Female flowers: pedicels 2-3mm long; sepals 5, ovate-triangular or elliptic, 0.5-1 X 0.4-0.8 mm; disc annular, entire, 1 mm across; ovary subglobose or depressed, 0.5 mm in diam.; styles 0.7-1.5 mm long. Fruits subglobose, 2-2.5 X 3-6 mm, whitish, brown when dry, 3-locular, thin-walled; pedicels 3-5 mm long; seeds plano-convex, faintly reticulate, 2-2.5 mm across, brown.

Flowering and Fruiting: February – September.

Distribution: India, Africa, Yemen, Pakistan, Nepal, Bhutan, Bangladesh, Myanmar, Thailand, China, Taiwan, Japan, Malaysia, Philippines, Indonesia, Australia and Polynesia.

Phytochemistry:

The phytochemical screening of plant revealed the presence of alkaloids (Freiburghaus *et al.*, 1996), triterpenoids (Monkodkaew *et al.* 2009), tannins (Ezeonwumelu *et al.* 2012), flavonoids and saponins (Magaji *et al.*, 2008) resins, steroids (Tanko *et al.*, 2008), cardiac glycosides and anthraquinones (Magaji *et al.*, 2007), 11-*O*-acetyl bergenin, virosecurinine, entphyllanthidine, kaempferol, quercetin, gallic acid, daucosterol and β -sitosterol (Wang *et al.*, 2008). All plant parts of contain indolizidine alkaloids mainly isomers and derivatives of the highly toxic securinene. The alkaloids are grouped in five major groups i. e. Securine type alkaloids (Virosecurinine, viroallosecurinine (root bark) (Saito *et al.*, 1964) and flueggeidine); Neosecurine alkaloids (Virosine A and Virosine B (twigs and leaves); Norsecurinine-type alkaloids (Norsecurinine, dihydronorsecurinine (root bark) (Saito *et al.*, 1964), 14, 15-dihydronorsecurinine (virosine), 14, 15- Epoxynorsecurinine (Root Bark) (Dehmlow *et al.*, 1999), Flueggeainol, flueggeainol ether, Virosaine A, and Virosaine B). Neonorsecurinane alkaloids (Bubbialine and bubbialidine); Norsecurinine-derived oligomeric alkaloids (flueggine A, flueggineB (twig and leaves) (Zhao *et al.* 2011), Norsecurinamines

A and B derived alkaloid dimmers (fruit) (Wang *et al.* 2016), flueggenine A, flueggenine B (root) (Gan *et al.* 2006), flueggenine C, flueggenine D, fluevirosine A, fluevirosine B, fluevirosine C, fluevirosine D, and fluevirosinine A (Knolker, 2015). Flueggethers B and C as dimers and Flueggether D as trimer, three securinega alkaloids isolated from the twigs and leaves (Zhang *et al.*, 2016). Bergenin isolated from the root bark (Magaji *et al.*, 2015) and Friedelin, epifriedelanol, stigmasterol and betulinic acids were isolated from the leaves and twig of the plant (Monkodkaew *et al.*, 2009). Other compounds isolated from the leaves are the isocoumarine bergenin, gallic acid and ellagic acid, and the flavonoids quercetin and rutin flavonoides. The stem bark contains the triterpenes friedelin and friedelinol. Phytochemical screening of aqueous extract of dried root yielded saponins, tannins, cardiac glycosides, and steroids. The twigs contain about 8% tannins and the root bark 0.4 – 0.6% alkaloids and the entire root 0.04% alkaloids (Dickson *et al.*, 2006).

Pharmacological Activities:

Studies showed that the plant has a variety of pharmacological activities including Analgesic, anti-inflammatory, aphrodisiac, sedative, anti-arrhythmic, antidiabetic, antimalarial, anti-HIV, anti-hepatitis C, antidiarrheal, cytotoxic, antimicrobial, antifungal, antioxidant, and laxative.

Analgesic and Anti-inflammatory activity:

The methanolic extract of root bark and leaves has significant Analgesic and Anti-inflammatory activity on animal models (Magaji *et al.*, 2008, Yerima *et al.* 2009). In another study, the aqueous extract of dried root showed acute toxicity, analgesic, anti-inflammatory and anti-pyretic activity in Wistar rats. Acute toxicity tests showed it is generally safe. It showed a significant dose-dependent inhibition of pain in the formalin test (Ezeonwumelu *et al.*, 2012; Ezeonwumelu *et al.*, 2013).

Antidiabetic:

Methanol extract of leaves possess anti-diabetic properties. The extract might be promoting glucose uptake and metabolism or inhibiting hepatic gluconeogenesis (Tanko *et al.*, 2008).

Aphrodisiac:

An aqueous extract of roots is used as an aphrodisiac and in the treatment of impotence, which is one of the manifestations of diabetes mellitus (Moshi *et al.*, 2000; Singh *et al.*, 2010; Singh *et al.*, 2012).

Sedative, Behavioral effects and sleep inducing activity:

Bergenin isolated from root has shown sleep inducing properties and also responsible for the sedative potential of the root (Magaji *et al.*, 2015). The methanol leaf extract shows the presence of alkaloids, tannins, saponins, flavonoids, cardiac glycosides, cyanogenic glycosides, resins, steroids, terpenoids and carbohydrates. The saponins and flavonoids are responsible for sedative activity in mice (Aiyelero *et al.*, 2012).

Anti-arrhythmic activity:

Berginin showed significant anti-arrhythmic activity in rats and has good potential for treating cardiac arrhythmias (Pu *et al.*, 2002). It also shows an inhibitory effect on the growth of the bloodstream form of *Trypanosoma brucei* with an IC₅₀ (the half maximal inhibitory concentration) value of 1 μ M (Tabuti, 2007).

Antimalarial activity:

Methanol and water extracts of the leaves have shown strong antimalarial activity, significantly inhibiting the growth of *Plasmodium falciparum* in vitro in a dose-dependent manner (Kaou *et al.*, 2007; Muthaura *et al.*, 2007).

Anti-HIV activity:

Flueggether A and Virosinine A were isolated from the root bark and both alkaloids show Anti-HIV activity (Zhang *et al.*, 2015).

Anti-Hepatitis C activity:

The nonalkaloid dinorditerpenoides (9(10-20)-abeo-ent podocarpane) extract from the roots exhibited anti-Hepatitis C Virus activity (Chao *et al.*, 2014; Chao *et al.*, 2016). Two trinorditerpenes, flueggrenes A and B, have been isolated from the roots which show the anti-Hepatitis C virus activity (Chao *et al.* 2013).

Antidiarrheal activity:

Methanolic extracts of leaves, stem bark and root bark of plant on a castor oil-induced diarrheal model showed the leaves and root bark extract to possess pharmacological activity against diarrhea (Magaji *et al.*, 2007).

Cytotoxic activity:

Study of hexane and ethyl acetate fraction of twigs and leaves of *Flueggea virosa* yielded friedelin, epifriedelanol, stigmasterol, heptanolide and betulinic

acids. The betulinic acid of the isolated compounds considered as high potential source of cytotoxic activity. Alcoholic leaf extracts showed significant cytotoxicity in different tumour cell lines *in vitro*. Virosecurinine was primarily responsible for the cytotoxicity; viroallosecurinine was only cytotoxic to one of the cell lines (Tatematsu *et al.*, 1991). The twigs and leaves yielded flueggines A and B, two dimeric indolizidine alkaloids. Flueggine B exhibited growth inhibitory activity against MCF-7 (Michigan Cancer Foundation-7) and MDA-MB-231 (M. D. Anderson and MB stands for Metastasis Breast cancer) human breast cancer cells (Monkodkaew *et al.*, 2009).

Antimicrobial and antifungal activity:

Petroleum spirit, chloroform and ethanol extracts of the root bark were tested for antimicrobial activity against a range of organisms *in vitro* antimicrobial activity (Dickson *et al.*, 2006; Danlam *et al.* 2015). Ethanol and chloroform extracts of the plant have shown significant antimicrobial activities, and moderate antioxidant and free-radical scavenging activities. A methanol extract of the dried fruit pulp and the ethanolic root extract have shown significant antifungal activities against *Trichytum mentagrophytes* and *Candida albicans* (Tabuti, 2007).

Antioxidant activity:

From the leaves of *Flueggea virosa* one new flavonoid glycoside, 3-O-kaempferol 4-O-(galloyl)-beta-D-glucoside, one new bergenin derivative, 11-O-caffeoylbergenin, along with other known flavonoids and phenolic derivatives, were isolated. The isolated compounds showed that they were able to quench DPPH (2, 2-Diphenyl-1-Picrylhydrazyl) radicals and had a direct scavenging activity on superoxide anion. Kaempferol 3-O-(4-galloyl)-beta-D-glucopyranoside, 11-O-caffeoylbergenin, and glucogallin exhibited the highest antioxidant capacity (Sanogo *et al.*, 2009). In a study of South African plants for antioxidative activity using the DPPH radical scavenging assay, acetone extract of plant showed the highest antioxidant activity with IC50 of 30µg/ml closely matching ascorbic acid (Chauke *et al.*, 2012).

Laxative activity:

The leaves are considered laxative (Burkil, 1994).

Traditional uses:

The plant is used as an ornamental hedge because of its attractive foliage, white waxy berries and the bushy nature. All parts of the plant are used (roots, leaves,

wood, juice) but roots are considered most active part. Different parts of this plant, such as leaves, barks, stems and roots, are used in different forms of preparation (infusion, decoction, and maceration). Root decoction used to treat testicular inflammation, frigidity, sterility, heavy menstruation, rheumatism, arthritis. Root powder taken in water is used to treat liver, bile, Kidney, Urinary and venereal diseases, upper respiratory tract infections, ranging from cough to tuberculosis, and to treat abdominal complaints, including stomach-ache, dysentery, intestinal worms and schistosomiasis (Tabuti *et al.*, 2007). Water in which the roots have been boiled is taken for stomachaches, dysmenorrhoea, and is given to nursing mothers whose milk is unsuited for the child, it is also used for treating infestation of intestinal worms and for infected ears (Burkil, 1994). In Tanzania root decoction is used to treat epilepsy, convulsions and rectal and uterine prolapsed, Tharaka people of Kenya used to treat malaria (Kaigongi and Musila, 2015). In Nhema communal area, Zimbabwe and in south-central Zimbabwe extract drunk as pneumonia medicine and drunk before sexual intercourse as a contraceptive; dried root powder used as snake antidote and applied on wounds (Maroyi, 2011; Maroyi, 2013) In Northern Nigeria decoction used for treatment of mental diseases (Magaji *et al.*, 2007). The fruits are edible when mature. Pulped fruits are also rubbed on the skin to treat itch. The fruit is chewed to treat snake bite. In Burundi and Tanzania a leaf decoction is taken to treat lactation disorders and is also given to nursing mothers whose baby is sickly at birth or to women with risk of still-born babies. The decoction of the leaves and roots is used for abdominal pain in Tanzania while the leaf decoction is drunk for fever by the Yorubas of South western Nigeria (Yerima *et al.* 2009). The decoction of the leaf with some other plants is used in northern Nigeria for the treatment of mental illness and painful swelling (Neuwinger, 1996). In Uganda leaf powder is taken for abortion. A decoction of leafy twigs or fresh leaf sap is used as nose drops to cure epilepsy and insanity. Leafy sap is used in conjunctivitis, ear ache and as nose drop to treat headache and migration. Leaves are used in dysentery, worms and roots in venereal diseases in Jaunpur district in Uttar Pradesh (Srivastva *et al.*, 2003). Leaves or leafy twigs in decoction or infusion are commonly taken to treat malaria, fever, jaundice, measles, oedema, vertigo, sickle cell anemia, convulsions, vomiting, stomachache, intestinal worm, dysentery and constipation (Schmelzer *et al.*, 2008). The leaves are used in the treatment of stomachache, rheumatism, diarrhea, epilepsy, diabetes, body pain and

fever (Danlami *et al.*, 2013; Kaigongi and Musila, 2015). Leaves possess anti-diabetic properties (Tanko *et al.*, 2008). Young leaves and roots are used by Chuka community (Kenya) for coughs and malaria (Odongo, 2013). The bark is astringent. It is used in children's medicine.

Some other uses are: Bark-tannin has been recorded as 8.9% and is used for tanning in India. A black dye is also obtained from the bark in India used for dyeing matting (Burkil, 1994). The reddish-yellow wood is fine-textured, close-grained, hard, strong, elastic and is said to be durable, valued for use in houses and rafters, and tool handles (Ruffo *et al.*, 2002). The tough virgate stems are commonly used to make beds, fishing-stakes, wicker-traps, for part of roof-structures of huts, to reinforce granaries, etc. They are woven into shelves and also split for use in basketry. Twigs are cut and used as toothbrushes. A gum is obtained from the stem which has been used for sealing envelopes (Tabuti *et al.*, 2007). A red dye is obtained by pounding the fruit in a little hot water. The dye can be used as red ink. The wood is a good fuel and is also used to make charcoal (Maydell, 1990).

CONCLUSION

Whole plant can be considered as an effective source of useful drugs for the treatment of various ailments as indicated by the presence of alkaloids, steroids, saponins, cardiac glycosides, flavonoides and many others secondary metabolites. The phytochemicals in medicinal plants have been reported to be the active principles responsible for the pharmacological potentials of plants. Most of the compounds isolated from the roots and leaves belonging to alkaloids, glycosides and terpenoides category which have a wide range of biological compound. The compounds Flueggeather A and Virosinin A, Viroseurinine, Flueggine B (alkaloids), Betulinic acid (Triterpene), Berginin (C-Glycosides), Flueggrenes A and B (Trinorditerpens), possessing Anti-HIV, anti-proliferative, cytotoxic, anti-arrhythmic and Anti-Hepatitis C activity which are very important in medicinal field. The presence of these chemicals in the plant justifies the local uses of the plant for the treatment of various ailments and suggests that traditional medicines still play an important role in meeting basic health care of local communities. There are many other unrevealed applications of this plant, which remain un-investigated and serve as the basis for

further studies. This review will definitely help the researchers to know its different properties and provide insights for future research aimed at both ethnopharmacological validation of the popular use of plant and its exploration as a new source of bioactive molecules for herbal drugs and for potential application in complementary and alternative medicine.

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