

Study of the Medicinal Plant *Flueggea virosa*: Review on Its Uses and Some Phytochemical and Biological Properties for the Last Decade

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Abstract

Many infectious diseases are treated with antibiotics and antivirals. But the emergence of antimicrobial-resistant strains and mutant microorganisms has made antimicrobial resistance a major global health threat, as drugs previously effective against infections are no longer effective. Pathogens have developed resistance to antimicrobial agents, resulting in more infections and deaths. Medicinal plants and microorganisms were the major source of medicines over many centuries. It is well known that plants contain several metabolites. These are active against many diseases. Plants have been found to have a range of beneficial effects, from fighting parasites to treating various diseases. Among them, several *Flueggea* species are used in traditional medicine. *Flueggea virosa* is a deciduous shrub or small tree growing up to 6 metres tall. Its bark is grey-brown and sometimes cracked or rough. Leaves and stems of this plant (*F. virosa*) have long been used for their medicinal properties in traditional medicine in the world. While modern research has yet to catch up with traditional knowledge, preliminary studies support the plant's potential for many therapeutic uses, particularly in the treatment of inflammatory, infectious, and digestive conditions. This study highlights some of the key work carried out (medicinal, chemical and pharmacological properties) on *Flueggea virosa* over the last ten years, with a view to further research and applications.

Keywords

Flueggea virosa, Traditional Medicine, Pharmaceutical Properties

1. Introduction

Plants have long been important in traditional medicine. They are paramount to all civilisations that have used them, either wild or cultivated, to feed, defend and clothe; and then, they serve as the foundation for numerous modern pharmaceuticals [1] [2]. Plants are an endless source of bioactive compounds (alkaloids, saponosides, flavonoids...) that have long been used for medicine and other purposes [3]. Using plants to treat human diseases is very old and has evolved with human history. Until the 20th century, most medicines were plant-based. Two-thirds of today's medicines have a natural origin [4] [5]. Medicinal plants are still a main source of new drugs, as they provide raw materials for new drug molecules [6] [7]. The use of plants as food or medicine has also been important to the development of animal breeding worldwide [8]. The therapeutic potential of plants used in treating diseases must be assessed pharmacologically. It is well known that plants contain several metabolites that are active against many diseases. Many pharmacological activities worldwide involve the *Euphorbiaceae* family (China, Africa, Asia, South America...). It is important to evaluate the therapeutic potential of medicinal plants. The genus *Flueggea* is widespread in Asia, South America, Oceania and Europe with sixteen species. The plant genus *Flueggea* was named in honor of the botanist Johannes Flügge (1775-1816), who was a native of Hamburg (Germany) and the author of the famous monograph on *Paspalum* plants (*Graminum Monographiae* published in 1810). *Flueggea* shrubs or small trees are dioecious or monoecious. *Flueggea* is a small genus of subfam. Their leaves are alternate with entire or blunt margins and short petioles. The inflorescence is an axillary raceme; male flowers are numerous and in clusters, female flowers solitary or in clusters. Some, e.g. *Flueggea suffruticosa* and *Flueggea virosa*, have long been traditional medicines in Southeast Asia and Africa for their medicinal effects [9].

F. virosa is also an important medicinal plant in tropical Africa, used alone or in combination with other plants, for a variety of purposes, including liver, kidney, urinary and venereal diseases, bile deficiency, testicular inflammation, frigidity, sterility, heavy menstruation, rheumatism and arthritis. The plant has been around for a long time [10]-[12]. There is evidence of the use of a digging stick of *F. virosa* dated to ~39,000 years before present by the Stone Age inhabitants in South Africa [10] [13]. Modern research has shown that the main chemical constituents of the genus *Flueggea* are alkaloids, terpenoids, flavonoids and phenols [11]. The general objective of this study was to review the last decade's (2014-2024) the literature published in scientific journals, books, reported from theses, conference papers and other grey materials.

2. Method

This work has investigated the medicinal uses of the plant *F. virosa*, including its role in an ethnobotanical, ethnomedical and biological use during the last decade.

Its focus is identification, and it can help researchers conduct further studies. Literature was searched using Google, thesis, ResearchGate, Google Scholar, Pub-

med and open access peer-reviewed journals. The review was conducted until February 2024. The search query used was *Flueggea virosa*: ethnobotanical and ethno-medicinal study, and then pharmacological activity. In addition, a manual search was carried out using the bibliographic references of the selected articles, particularly those published between 2014 and 2024.

3. General Information [14]

Each plant is a species with a scientific name, but known by several names depending on the language, country or continent where it is found. The same applies to the role it plays in society. A plant can be used in many fields: wood, medicine, crafts, etc. *Flueggea virosa* is a deciduous shrub or small tree. It grows up to 4 metres, but sometimes 7 metres. Its branches emerge from the base and spiral up (Figure 1). The plant can be deciduous in seasonal climates, but evergreen where there is a more regular supply of moisture. This versatile plant has many medicinal and other uses. It is one of the most important wild medicinal plants in the Sahel. This plant has many uses and is cultivated in many places for its attractive appearance. The plant is often spared during land clearance or weed control. *Flugella virosa* is widely distributed, has a large population and is not threatened.

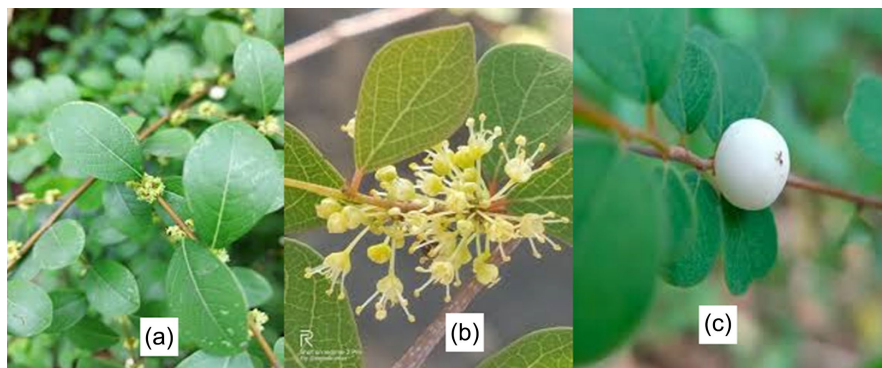


Figure 1. Plant *Flueggea virosa* (Roxb. ex Willd.) Royle, also called *Securinega virosa* (Roxb. ex Willd.) Baill. (a) Leaves and twigs; (b) Leaves and flowers; (c) Leaves, twigs and fruit.

4. Vernacular Names [14] [15] [28]

In our country, several names of plant *F. virosa* (Language) in Benin (Cotonou, Abomey-Calavi) are: Gaagah, tchian tchian, sian sian (Bariba); yéri kalawunfa (Berba); adjaya, gbyihountin, hétré, hounsividjayé, tchaké tchaké (Fon, Goun); koukrinou (Gourmantché); tchamanoudira (Kotokoli); hesré (Watchi); igi agbado, irandjé, wadjidji (Watchi). Vernacular names as recorded in specimen da-ta include: “changa” (Omi); “changaume” (Maputo area); “citanjero” (chi-Tumbu-ka-‘broom’); “kafirapira” (chiChewa); “mafoutagomba”, “mouwana”, “m’palo”, “pomboma” (Tete area); “messossoio” (Inhaminga area); “mparapara” (Mzimba area); “mserecheti” (chiYao); “mu-banda” (Kabompo area); “mulianzovu”; “mun-sosoti”, “musosoti” (chiNdau); “musosia-uria-basimpongo” (chi-

Tonga); “mussos-sote” (Búzi area); “nameresi” (eMakhuwa); “pombuma” (Manica Sofala area); “snowberry” (Lilongwe); “umsosoti” (chiNdao). Chinese Waterberry, Chinese wa-terberry, common bushweed., simpleleaf bushweed, Simpleleaf Bushweed., snow berry., snowberry tree, snowberry-tree, white berry-bush., whiteberry bush, white-berry bush, White-berry bush (En). Balan des savanes. (Fr). mkwamba, Mkwamba, mkwamba maji, mteja., mteja. (Sw). Yuyanmu, Quefanshu, Jinganteng, Baipaoguo, Baihuotan, Baibeizi (China).

5. Ethnobotanical Study

The white berry bush, officially *Flueggea virosa* (Roxb. ex Willd.) Royle is a plant species in the family *Euphorbiaceae*. The ethnobotanical uses of the plant are diverse and include a wide range of medicinal, practical and spiritual uses. *F. virosa* is a medicinal plant distributed throughout tropical areas and traditionally used in Africa, India, China, Bangladesh, Sri Lanka and South-East Asia [9]. The ethnobotanical use of *Flueggea virosa* reflects its importance in folk medicine in countries. This plant is important medically and ecologically [9] [16]. Several *Flueggea* species are used in traditional medicine. Its various parts, such as the leaves, bark, roots, and latex, have been used extensively in traditional medicine for a wide array of therapeutic purposes [9] [17]. This is the case for *F. suffruticosa* (Pall.) Baill., which is commonly used in traditional Chinese medicine for the treatment of inflammatory ailments, such as rheumatism and lumbago [9]. The plant *F. virosa* warrants further investigation, in particular the fruit, which are abundant and edible. The white berries are often consumed by the local population but they are not largely exploited and apparently not commercialized in any form, despite their nutritional and medicinal value. In South Africa, the Mapulana people (an indigenous community of Ehlanzeni district in Mpumalanga province, South Africa) consume the fruit, locally called ditlhalabu or ditlhakawume [18]. The berries are consumed in other African countries (Ethiopia, Tanzania) and also in India, notably in the area of the Warud tahsil village, Amravati district in Maharashtra, for their sweet taste and nutritional value [19]. Whole plant is used to treat eczema, pruritus, rheumatoid arthritis, allergic dermatitis, scald, inflammation and injuries. In Ghana, the pulp of the fruit is used for healing wounds and anti-itching, as well as an extract ointment prepared from the leaves of the plant. The fruit is chewed to treat snake bites. In Tanzania and Burundi, leaf decoctions are given to nursing mothers to treat lactation problems and sick babies at birth. In Tanzania, decoctions of leaves and roots are used to treat abdominal pain [20].

6. Ethnomedicinal Uses

Many of the world’s best-selling drugs come from nature, especially plants, microbes and animals. Several traditional medicines involve crushing leaves or bark, producing hundreds of active molecules. It has remained as the most affordable and easily accessible source of treatment in the primary healthcare system of re-

source poor communities [21]. The quality of traditional medicine materials varies greatly between and within source countries and plants. This is due to genetics and other factors. Early studies suggested that *Flueggea virosa* has many potential therapeutic applications, particularly in the treatment of inflammation, infection and digestion, although modern research has not caught up with traditional knowledge [22]. The plant is used in traditional medicine for relieving pain and reducing inflammation, particularly in cases of arthritis, gout, and muscle pain. Extracts from *F. virosa* are applied to reduce swelling and manage chronic inflammatory conditions [23]. *Flueggea virosa* has been used for treating various infections. The plant is reported to have antibacterial, antifungal, and antiviral properties, making it useful for treating wounds, sores, and infections caused by microbes. *F. virosa* is used in treating a wide range of health conditions, often utilizing its bark, leaves, seeds, and roots. Root decoction drunk is used to heal breast and prostate cancers, pneumonia, liver and kidney problems, testicular inflammation, frigidity, sterility, menorrhagia, rheumatism, arthritis, epilepsy, convulsions, mental diseases, uterine and rectal prolapse, infectious diseases including tuberculosis, venereal diseases, urinary tract infections, dysentery, intestinal helminthiasis, malaria, ear aches, HIV related infections, lactation disorders and also is used as a contraceptive during sexual intercourse. Powder from dried roots is used to treat snakebites and promote wound healing. A decoction of the plant's leaves is used to treat a variety of illnesses, including conjunctivitis, headaches, jaundice, fevers, edema, diabetes and dizziness. The fruits treat snake bites, lactation and parturition [10] [11] [22]. In many traditional practices, the plant is used to regulate blood sugar levels. The leaves and other parts of the plant are consumed to help manage diabetes, acting as a natural remedy to lower blood glucose. The plant's extracts have been used to treat cuts, wounds, and ulcers. The bark and leaves are commonly used in poultices or topical applications to aid in wound healing [10] [11] [22]. *F. virosa* has been employed in traditional medicine to treat stomach problems, including indigestion, diarrhea, and dysentery [10] [11]. It is believed to have a soothing effect on the digestive tract. Some traditional uses include the consumption of parts of *F. virosa* to prevent or treat cancer, due to its reported anticancer properties, though this use is not widely validated through scientific studies yet. The plant is sometimes used as a general health tonic, believed to boost vitality, improve stamina, and promote overall well-being. The plant is thought to have strong antioxidant properties, making it valuable in traditional medicine to prevent aging and combat oxidative stress-related diseases. Infusion of its leaves is used to treat Stomach ache, Diarrhea, Hernia, Spleen enlargement [11] [22] [24] [25]. The traditional use of the plant in the medical management of BPH was reported to provide data for the development of a new Improved Traditional Medicine (ITM) based on the stems of *Flueggea virosa* [17]. The entire plant has been used in the treatment of eczema, itching, rheumatoid arthritis, allergic dermatitis, scalding, inflammatory and traumatic conditions [26]-[28]. Moreover, other research showed that the complete plastome sequence of *F.*

virosa would provide a useful resource for the conservation genetics of this species as well as for phylogenetic studies in Phyllanthaceae. Authors explained that its complete plastome is 154,961 bp in length and contains the typical structure and gene content of angiosperm plastome, including two inverted repeat (IR) regions of 27,575 bp. The plastome contains 130 genes, consisting of 80 unique protein-coding genes, 30 unique tRNA gene, 4 unique rRNA genes (5S rRNA, 4.5S rRNA, 23S rRNA and 16S rRNA). The overall A/T content in the plastome of *F. virosa* is 63.10 [29]. Recently, it was reported that with a MIC of 7.0 µg/mL, the ethyl acetate extract of *F. virosa* leaves showed significant inhibitory activity against *Escherichia coli* [30]. The plant has been shown to have various bioactive phytonutrients, with diverse ethnobotanical uses.

7. Chemical Constituents and Biological Activity

Many researchs reported the chemical composition including alkaloids, isocoumarins, steroids and phenolics. Three main categories of phytochemicals have been isolated from *F. virosa*: polyphenols, with bergenin being the most prominent; terpenoids, such as the flueggenoids and related podocarpane-like diterpenoids; and numerous alkaloids derived from securinine and norsecurinine have been cited in the literature [9]-[11]. In several works, it has reported that the aqueous extract of the root of *F. virosa* has been shown to possess potent phytochemicals such as tannic, saponic, terpenic, steroidal, cardiac glycoside, and reducing sugar with certain degree of acute safety and significant analgesic property [31]. Plant *F. virosa* is known to have an extensive range of activities such as cytotoxicity, antimicrobial, antioxidant, antidiabetic, aphrodisiac, laxative, analgesic, anti-inflammatory, antimalarial, anti-HIV, anti-Hepatitis C, antiarrhythmic, antidiarrheal, sedative and trypanocidal activities [12] [22] [32] [33]. We noted that plant extracts have been shown to have anti-parasitic, antimicrobial, anti-epileptic, antidiabetic, anti-cancer and analgesic effects. Reducing sugars, terpenoids, cardiac glycosides, flavonoids, saponins, anthraquinones and alkaloids were found in the qualitative phytochemical analysis of *F. virosa*. It should be noted that significant anthelmintic potential was observed in both leaf and bark extracts. All of the studied extracts showed significant anthelmintic potential which was dose dependent and was compared with piperazine citrate used as reference [10] [11] [34]. As part of research into trypanocidal activity of isolated compounds, El-Hawary *et al.*, (2022) demonstrated that bergenin has been shown to inhibit the growth of the bloodstream form of *Trypanosoma brucei* at an interesting half inhibitory concentration, and it was again responsible for the antitrypanosomal activity of the extracts. This natural compound is a model for the development of semisynthetic compounds with activity against *T. brucei* [35]. This explains why traditional Ugandan healers used a powder of crushed *F. virosa* roots (a spoonful by mouth) to treat sleeping sickness [10] [35]. A moderate antimalarial activity has been confirmed with another chloroquine-resistant strain of *Plasmodium falciparum*, namely the K1 strain (IC₅₀ = 7.6 µg/mL) [36]. Significant antiplasmodic activity

(IC₅₀ = 3 µg/mL) was found for methanol/water leaf extract and root extract. However, the best evidence of activity is from a study using the ethyl acetate fraction of *F. virosa* leaf, where dose-dependent activity was observed in mice infected with *Plasmodium berghei*, with almost total (86%) elimination of parasites and a mean survival time of 17.2 days compared to 10.8 days for controls [10] [33]. The antimalarial property was linked to the polyphenol bergenin. The plant is not a cure-all, though; a similar methanolic extract was inactive against the chloroquine-sensitive *P. falciparum* strain (50 µg/mL). Nevertheless, *F. virosa* is recognised as one of the most important African medicinal plants for the treatment of malaria [37]. Compared to the standard reference product (Fertilo forte Denk) and the control, sperm parameters were significantly improved with the aqueous extract of *F. virosa*. These findings may provide the basis for the use of Traditionally Improved Medicines (TIMs) for the treatment of male infertility [38]. According to Anel-Lopez *et al.* (2015) and Ariyan *et al.* (2020), these beneficial effects on spermatogenesis in *F. virosa*-treated rats could also be related to the antioxidant properties of the alkaloidal and phenolic compounds found in this plant, including flavonoids and total polyphenols [39] [40]. The greatest effect on *F. virosa* erythrocyte inhibition was observed with ethanolic than aqueous extracts, with 95% of ethanolic extracts and 90% of aqueous extracts normalised at a concentration of 10 mg/mL. This activity may result from the presence, alone or in synergy, of other families of compounds contained in the plant [41]. In determining the potential anthelmintic activity of *F. virosa* against *Taenia solium* metacestodes, the investigators found that *F. virosa* showed a 52% dose-dependent response at 50 µg/mL. This study showed an association between *T. solium* metacestodal response to *F. virosa* and praziquantel “drug extracts” (chi-square = 42.28), suggesting an association between metacestodal exposure and the treatment. They recommended further investigation in animal models for activity against the adult tapeworm, showing that both *Vitex doniana* and *F. virosa* herbs have potential anthelmintic activity against *T. solium* metacestodes [42]. In other study, Oghenemaro *et al.* (2021) showed activity of *F. virosa* leaf extracts against *S. aureus* (MRSA) which is methicillin-resistant [43] [44]. This is in agreement with other antimicrobial studies checking by Amenu *et al.*, 2019 [45]. It has been reported that methanolic extract of *F. virosa* exhibited antidiarrheal activity and was potent in the treatment of skin rashes, and then HIV infection [46] [47]. A leaf powder of *F. virosa* can also be used as an insecticidal agent against *Musca domestica* and the transmission of diseases to humans [48]. In other study, Zengin *et al.*, study presented that methanol extracts and infusions of both stem barks and leaves showed a higher antioxidant capacity compared to ethyl acetate extracts. The antioxidant capacity was correlated with the total phenolic content. It showed that *F. virosa* was a rich source of naturally occurring bioactive compounds for new functional products with potential biological benefits [49].

Nature provides compounds (bioactive metabolites) that help develop new drugs, and scientists are exploring them, particularly from plants, as most have

yet to be chemically and biologically investigated. The following tables list some of the metabolites that have been identified and isolated, some with properties that have been studied in the literature over the last decade.

In total, we noted more than 97 alkaloids present in the *F. virosa* plant. Alkaloids are known for their broad spectrum of activity and are produced in nature to combat herbivores and fungi (**Table 1**). They have great medical, botanical, veterinary and toxicological potential. Research into these substances and their properties is developing intensively.

Table 1. Some alkaloids isolated from *Flueggea virosa* during the last decade.

No.	Compound name	References	No.	Compound name	References
1	(-)-securinine	[28]-[30] [50] [51]	50	2-methyltetrahydro- β -carboline	[57] [58]
2	4-epiphyllanthine	[50] [51]	51	<i>N</i> -methyl-1, 2, 3, 4-tetrahydro- β -carboline	[27]
3	Securitinine	[50]	52	<i>Nb</i> -methyltetrahydroharman	[27]
4	Phyllanthine	[53]	53	1-hydromethyl-2-methyl-tetrahydro- β -carboline	[27]
5	4 α -hydroxy-N-hydrogenallosecurinine chloride	[50]	54	Strychnocarpine	[27] [57]
6	Virosecurinine	[53]	55	1-hydroxymethyl- β -carboline	[27]
7	Viroallosecurinine	[51] [53]	56	1-acetyl- β -carboline	[27]
8	Fluivirosaone A	[54]	57	Flueindoline A	[27]
9	15 β -methoxy-14,15-dihydrosecurinine	[50] [53] [55]	58	Flueindoline B	[27]
10	Fluevirine B	[50] [55]	59	Donaxanine	[27] [57]
11	Dihydroallosecurinine	[53]	60	Hordenin	[57]
12	Margaritarine	[53]	61	Flueggidine	[57] [65]
13	Fludenine A	[57]	62	Flueggine B	[53] [57] [59]
14	Virosinine A	[57]-[63]	63	Flueggine G	[57] [59]
15	Fluevirine F	[26] [53]	64	Fluevirine A	[53] [56] [57]
16	Fluivirosaone B	[54] [57]	65	Flueggine A	[26] [53] [57] [58]
17	Bubbialine	[53] [57] [59]	66	Flueggine C	[55] [57] [66]
18	Niruroidine	[46] [53] [55]	67	Flueggine D	[26] [53] [57] [58] [66]
19	Bubbialidine	[56]-[58]	68	Flueggine H	[52] [59]
20	Virosaine A	[28]-[30] [57] [60]	69	Flueggine I	[57] [59]
21	Virosaine B	[28]-[30] [57] [60]	70	Flueggine B	[26] [53] [57] [58]
22	(-)-norsecurinine	[53] [55] [57]	71	Fluphenylamine A	[57]

Continued

23	14,15-epoxynorsecurinine	[44] [53] [57]	72	Flueggine A	[57]-[59]
24	norsecurinic acid	[57]	73	Flueggether A	[57]-[59]
25	(+)-norsecurinine	[53]	74	Flueggether C	[57] [58]
26	Flueindoline C	[27] [57]	75	Flueggether B	[57] [67]
27	14,15-dihydronorsecurinine	[57]	76	Fluggeaine ether	[53]
28	Fluggeainol	[53] [57]	77	Norsecurinamine A	[53] [57] [58]
29	14 α -methoxy-13,14-dihydronorsecurinine	[50]	78	Norsecurinamine B	[57] [58]
30	14 β -methoxy-13,14-dihydronorsecurinine	[62]	79	Fluevirosine A	[53] [57] [58] [68]
31	Fluevirine C	[53] [56] [57]	80	Fluevirosine B	[57] [58] [68]
32	Fluevirine D	[53] [56] [57]	81	Fluevirosine C	[57] [58] [68]
33	15 α -butoxy-14,15-dihydronorsecurinine	[58]	82	Fluevirosine D	[57] [58] [68]
34	15 β -butoxy-14,15-dihydronorsecurinine	[58]	83	Fluevirosine E	[57] [58] [68]
35	Flueggine E	[55] [57]	84	Fluevirosine F	[57] [58] [68]
36	(+)-securinol A	[50] [53] [59] [63]	85	Fluevirosine G	[57] [58] [68]
37	Securinol B/virosine	[53] [62]	86	Fluevirosine H	[57] [58] [68]
38	(-)-virosine B	[57] [62]	87	Flueggether D	[57] [58]
39	(+)-virosine B	[53] [57] [62]	88	Fluevirosinine A	[53] [57] [59] [66]
40	(+)-2-episecurinol	[57]	89	Fluevirosinine B	[53] [57] [59]
41	(-)-securinol A	[57]	90	Fluevirosinine C	[57] [59]
42	Flueggine F	[55] [57] [59]	91	Fluevirosinine D	[57] [59]
43	(+)-phyllanthidine/ent-phyllanthidine	[50] [55] [56]	92	Fluevirosinine E	[57] [59]
44	Phyllanthidine	[51] [56] [58] [64]	93	Fluevirosinine F	[57] [59]
45	Seculactine A	[57]	94	Fluevirosinine G	[57] [59]
46	Methyltryptamine	[27] [57]	95	Fluevirosinine H	[57] [59]
47	<i>N,N</i> -dimethyltryptamine	[27] [57]	96	Fluevirosinine I	[57] [59]
48	Fluevirine E	[27] [53]	97	Fluevirosinine J	[57] [59]
49	Ethyl dioxindole-3-acetate	[57]			

Previous work has shown a variety of interesting biological effects. They have repercussions on the nervous system: stimulant, excitant, hallucinogenic, analgesic, paralyzing, etc. effects on the cardiovascular system: blood pressure regulator, anti-arrhythmic [10] [11] [16] [22] [26] [53] [57] [63] etc. Alkaloids show potential for new uses in preventing and treating inflammation, as well as for inhibiting AChE and treating NDDs. They are used as is or in derivatives that are

better tolerated or have different effects [71]. Synthetic products have grown, but alkaloids still play an important role in medicinal products. Derivatives of these are used for different effects [69] [70]. It appears that this plant is fairly rich in compounds which have an enormous physiological impact on the body.

Plant terpenoids are aromatic and key in herbal therapy. Many terpenoids are pharmacotherapeutically active, and are of great interest to the scientific community. Studies have shown the presence of several terpenoids (63) (Table 2) with significant antimicrobial properties, making them effective against various bacteria, fungi and even certain viruses. These compounds protect cells against oxidative stress, playing a crucial role in the prevention of chronic diseases such as cancer and neurodegenerative diseases [61] [63] [71] [73]-[78].

Table 2. Few terpenoids isolated from the *Flueggea virova* and studied this last decade

No.	Compound name	References	No.	Compound name	References
1	ent-3 β ,12 α -dihydroxypimara-8(14),15-diene	[72]	33	4-hydroxy-12-methoxy-13-methyl-3,4-seco-ent-podocarpa-6,8,11,13-tetraen-3-oic acid	[74]
2	spruceanol	[72]	34	methyl-4,12-dihydroxy-13-methyl-3,4-seco-ent-podocarpa-8,11,13-trien-3-oate	[74]
3	3 α ,20-epoxy-3 β ,12-dihydroxy-13-methyl-ent-cleistantha-8,11,13,15-tetraene	[73]	35	methyl-4,18-dihydroxy-12-methoxy-13-methyl-3,4-seco-ent-podocarpa-8,11,13-trien-3-oate	[74]
4	3 α -hydroxy-12-methoxy-13-methyl-ent-podocarpa-8,11,13-triene	[73]	36	flueggenoid A	[28]
5	6 β ,12-dihydroxy-13-methyl-ent-podocarp-8,11,13-trien-3-one	[72]	37	flueggenoid B	[28]
6	6 β -hydroxy-12-methoxy-13-methyl-ent-podocarpa-8,11,13-trien-3,7-dione	[73]	38	10 α ,12-dihydroxy-13-methyl-9(10 \rightarrow 20)-abeo-ent-podocarpa-6,8,11,13-tetraen-3-one	[73]
7	3 β ,12-dihydroxy-13-methylpodocarpa-8,11,13-triene	[72]	39	10 α -hydroxy-12-methoxy-13-methyl-9(10 \rightarrow 20)-abeo-ent-podocarpa-6,8,11,13-tetraen-3-one	[73]
8	flueggenoid C	[28]	40	3 β ,10 α -dihydroxy-12-methoxy-13-methyl-9(10 \rightarrow 20)-abeo-ent-podocarpa-6,8,11,13-tetraene	[74]
9	3 β ,12-dihydroxy-13-methylpodocarpa-6,8,11,13-tetraene	[72]	41	3 β ,10 α ,12-trihydroxy-13-methyl-9(10 \rightarrow 20)-abeo-ent-podocarpa-6,8,11,13-tetraene	[73]
10	3 α ,20-dihydroxy-12-methoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraene	[73]	42	3 α ,10 α -dihydroxy-12-methoxy-13-methyl-9(10 \rightarrow 20)-abeo-ent-podocarpa-8,11,13-triene	[73]

Continued

11	3 β -hydroxy-12-methoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraene	[73]	43	3 β ,10 α -dihydroxy-12-methoxy-13-methyl-9(10 \rightarrow 20)-abeo-ent-podocarpa-8,11,13-triene	[73]
12	3 α ,12-dimethoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraene	[73]	44	10 α -hydroxy-12-methoxy-13-methyl-9(10 \rightarrow 20)-abeo-ent-podocarpa-8,11,13-trien-3-one	[73]
13	3 α -hydroxy-12-methoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraene	[28]	45	10 α ,12-dihydroxy-13-methyl-9(10 \rightarrow 20)-abeo-ent-podocarpa-8,11,13-trien-3-one	[61]
14	3 α ,12-dihydroxy-13-methyl-ent-podocarpa-6,8,11,13-tetraene	[28]	46	methyl-4,7 α -epoxy-12-methoxy-13-methyl-3,4-seco-ent-podocarpa-8,11,13-trien-3-oate	[74]
15	12-hydroxy-13-methyl-ent-podocarpa-6,8,11,13-tetraen-3-one	[72]	47	methyl-4,7 α -epoxy-12-hydroxy-13-methyl-3,4-seco-ent-podocarpa-8,11,13-trien-3-oate	[74]
16	12-methoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraen-3-one	[72]	48	methyl-4,20-epoxy-12-methoxy-13-methyl-3,4-seco-ent-podocarpa-6,8,11,13-tetraen-3-oate	[74]
17	3 α -hydroxy-13-hydroxymethyl-12-methoxy-ent-podocarpa-6,8,11,13-tetraene	[71]	49	methyl-4,20-epoxy-12-methoxy-13-methyl-3,4-seco-ent-podocarpa-8,11,13-trien-3-oate	[74]
18	3 β -hydroxy-13-hydroxymethyl-12-methoxy-ent-podocarpa-6,8,11,13-tetraene	[71]	50	12-hydroxy-20(10 \rightarrow 5)-abeo-4,5-seco-podocarpa-5(10),6,8,11,13-pentaen-3-one	[74]
19	7 α ,20-epoxy-3 α -hydroxy-12-methoxy-13-methyl-ent-podocarpa-8,11,13-triene	[72]	51	12-methoxy-20(10 \rightarrow 5)-abeo-4,5-seco-podocarpa-5(10),6,8,11,13-pentaen-3-one	[74]
20	12-hydroxy-13-methyl-ent-podocarpa-8,11,13-trieno-20,3 α -lactone	[72]	52	heudelotinone	[61]
21	flueggenoid D	[28]	53	3 β ,12-dihydroxy-13-methyl-podocarpane-8,10,13-trene	[61]
22	6,12-dihydroxy-13-methyl-7-oxo-ent-podocarpa-5,8,11,13-tetraeno-20,3 α -lactone	[73]	54	flueggrene A	[75]
23	12-methoxy-13-methyl-ent-podocarpa-6,8,11,13-tetraeno-20,3 α -lactone	[73]	55	flueggrene B	[75]
24	12-hydroxy-13-methyl-ent-podocarpa-6,8,11,13-tetraeno-20,3 α -lactone	[73]	56	lupeol	[76]
25	3 α ,20-epoxy-3 β ,12-dihydroxy-13-methyl-ent-podocarpa-8,11,13-triene	[73]	57	lupeol acetate	[76]

Continued

26	3 α ,20-epoxy-3 β -hydroxy-12-methoxy-13-methyl-ent-podocarpa-8,11,13-triene	[72]	58	glochidone	[61]
27	methyl-12-hydroxy-13-methyl-3,4-seco-ent-podocarpa-4(18),6,8,11,13-pentaen-3-oate	[74]	59	betulinic acid 3 β -calfeate	[77]
28	methyl-12-methoxy-13-methyl-3,4-seco-ent-podocarpa-4(18),6,8,11,13-pentaen-3-oate	[74]	60	glut-5-en-ol	[61]
29	12-methoxy-13-methyl-3,4-seco-ent-podocarpa-4(18),6,8,11,13-pentaen-3-oic acid	[74]	61	maslinic acid	[61]
30	flueggenoid E	[28]	62	methyl maslinate	[61]
31	methyl-4-hydroxy-12-methoxy-13-methyl-3,4-seco-ent-podocarpa-6,8,11,13-tetraen-3-oate	[74]	63	(2R,4S)-2,4-epoxy-4,23,29-trihydroxy-3,4-seco-30-nor-friedel-19-en-3-oic acid methyl ester	[73]
32	methyl-4,12-dihydroxy-13-methyl-3,4-seco-ent-podocarpa-6,8,11,13-tetraen-3-oate	[74]			

Table 3. Some molecules isolated recently from the *Flueggea virosa*.

No.	Compound name	References	No.	Compound name	References
1	Rutin	[51]	16	4-nitrophenol	[61]
2	Techtochrysin	[76]	17	Ethyl 2,4-dihydroxybenzoate	[61]
3	Diosmetin	[76]	18	α -tocopherol	[51] [61]
4	Gallocatechin	[51] [61]	19	2,2',5,5'-tetrahydroxybiphenyl	[52]
5	<i>Epi</i> -gallocatechin	[51] [61]	20	(+)-pinoresinol	[52]
6	(+)-ampelosin E	[77] [78]	21	(+)-8-hydroxypinoresinol	[52]
7	Norbergenin	[28]	22	2,5-dihydroxybenzoic acid	[52]
8	Bergenin	[51]	23	protocatechuic acid	[78]
9	11-O-caffeoylbergenin	[53]	24	4E-dehydrochebulic acid trimethyl ester	[53]
10	Glucogallin	[51]	25	3 β -hydroxystigmasta-5,22-dien-7-one	[61]
11	Amiroside	[61]	26	(+)-menisdaurilide	[53] [57]
12	<i>p</i> -hydroxybenzoic acid	[61]	27	(+)-aquilegolide	[57]
13	Vanillic acid	[61]	28	Ethyl manopyranoside	[51]
14	4-hydroxybenzoic acid methyl ester	[61]	29	Menisdaurin	[51]
15	2,4-dihydroxybenzaldehyde	[61]			

Polyphenols are plant compounds that scientists are researching for their health benefits [79] [80]. They mainly have biological effects that scavenge or inhibit reactive oxygen and nitrogen species, transfer electrons to free radicals, activate antioxidant enzymes and ameliorate inflammation and oxidative stress [79] [81]. Over the past decade, a number of polyphenolic compounds from the plant *F. virosa* have been investigated (Table 3).

The results show that the plant contains a large number of phytomolecules with pharmacological properties (Table 3). Phenolic compounds and flavonoids can substitute for bioactive agents in pharmaceuticals and medicine [82]. They also show promising effects in the prevention of diseases such as diabetes, obesity, cancer, cardiovascular diseases, osteoporosis, neurodegenerative diseases [80] [83] [84]. Flavonoids are known to carry antioxidant properties and acts as antibiotics by disrupting functions of microorganisms. Majority of the plants used in traditional system of medicine are rich in polyphenols and flavonoids which not only regulate the growth of plants but also are rich source of phytochemicals employed in human and animal health [85]. These phytochemicals seem to possess great potential for their use in animal health and production system and to replace certain synthetic chemicals which are deleterious on account of their residual effects on human and animal health [86]. Flavonoids are now considered as an indispensable component in a variety of nutraceutical, pharmaceutical, medicinal and cosmetic applications. This is attributed to their anti-oxidative, anti-inflammatory, anti-mutagenic and anticarcinogenic properties coupled with their capacity to modulate key cellular enzyme function [87]. Singh *et al.* showed that bergenin, compound isolated from the plant had an interesting anti-parasitic effect against malaria, inhibiting two parasites, *Falciparum berghei* and *Trypanosoma brucei*, with their half inhibitory concentration IC₅₀ values of 8.07 and 1.00 µM respectively. Furthermore, compound ameliorated systemic host inflammation caused by the parasite [33]. (-)-securinine improved vascular dysfunction and atherosclerosis in mice [88]. Both (-)-securinine and viroallosecurinine showed potential antimalarial activity against *Plasmodium falciparum* and *Leishmania donovani*. The IC₅₀ values were 2.7 and 4.7 µg/mL for (-)-securinine and 2.9 and 19 µg/mL for viroallosecurinine [51]. In 2015, Zhang *et al.*'s study showed that non-cytotoxic flueviroisine B and C suppressed XBP1 (X-box binding protein 1) mRNA cleavage activity in cancer cells by 37% and 35% at 20 µmol/L [68]. Isolated from *F. virosa*, virosecurinine, flueviroisine B and flueggenine D showed moderate anti-HIV activity, especially flueggenine D, which had better safety with a selection index (SI) of 12.6 [46]. Other research presented that (-)-securinine showed certain neuroprotective activity [89].

We have reviewed several articles, thesis, conferences and documents not available online. It is clear that there is a great deal of work being done on the plant. *F. virosa* covers a wide range of ethnobotanical knowledge, phytochemical applications and many pharmaceutical properties. It is a plant with many uses. All its organs are used in pharmacopoeias and modern medicine. Several metabolites

have been identified, isolated and characterized, some of which have interesting biological activities. These various studies carried out on all the organs of *F. virosa*, and the convincing results obtained, largely justify its use by several populations for primitive care, since existing treatments are expensive and not accessible to all sections of the population in developing countries.

8. Conclusion

The final effects of herbal medicines remain complex due to the various components. The effects of natural products from plants and the mechanisms of their action have been the subject of experimental investigation, with the results showing that these products have a complex effect and are useful in the treatment of many infections. This paper has summarised the various uses of the *F. virosa* plant over the last decade. We have noted that various studies have been carried out, highlighting the different constituents identified and isolated from the organs of the plant, as well as a series of activities evaluated on different strains of pathogens. It is clear that we have the presence of different metabolites and their different properties on microbes, bacteria, parasites, etc. This study has enabled us to provide a brief summary of the work that has been done on the plant over the last ten years. We are aware that we have not been able to explore everything, given the broad scope of the research.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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