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Woodfordia fruticosa Kurz.: A Review on its Botany, Chemistry and Biological activities

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Abstract

Woodfordia fruticosa Kurz is a widely used medicinal herb in different South East Asian countries since long back and plays a potential role in curing/treating various ailments/disorders like leprosy, toothache, leucorrhoea, fever, dysentery, bowel disease. This review is intended to provide the currently available information on traditional usage, chemical constituents, various biological activities and its marketed preparations. The scientists or researchers working on this plant will be definitely benefitted from the information summarized in this article.

Keywords: *Woodfordia fruticosa*, Review, Chemistry, Biological activities.

1. Introduction

Traditional medicines have been used by the majority of the world population for thousands of years. The World Health Organization (WHO) reported that an estimated 80 % of the population in developing countries depend on traditionally used medicinal plants for their primary health care. The use of plants and their products in curing diseases is known as herbal medicine, which is considered part of folk or traditional medicine. For many centuries, treatment with medicinal plants was the only resource available for numerous ethnic groups, and nowadays, plants are still used in traditional medicine to treat, alleviate or prevent many diseases [1-2].

Among the numerous species used in folk medicine, *Woodfordia fruticosa* Kurz syn. *Woodfordia floribunda* Salisb. [Lythraceae] has been widely used by practitioners of traditional medicines in different South East Asian countries since long back. Though the entire plant parts exhibits therapeutic properties, but particularly, its flowers have been in great demand in domestic and international markets specialized in the preparation of herbal medicines [3].

This review has been compiled to provide the detailed information on the traditional and local use, chemical constituents present in different parts, macroscopical and microscopical characters, various therapeutic activities and marketed preparations of *Woodfordia fruticosa*.

W. fruticosa is also known as fire flame bush (English); Dhaaya/ Dhaay ke phool, Dhataki, Dhatri, Dhaura, Dhawai, Dhawala (Hindi); Dhai, Dawai, Dhai phul (Bengali); Sireenji (Telegu); Dhatar Jargi (Tamil); Dhavdi, Dhavadina (Gujarati); Dhalas (Marathi); Dhavi (Punjabi); Dhaava (Farsi); Dhangera (Nepali); Tamrapushpi (Kannada); Tatiripuspi (Malayalam); Dhobo, Jaliko, Harwari (Oriya). In Sanskrit, the synonyms are Dhatupushpi (having blood colored flowers), Vahnijwala (flowers red in color, resembling flame), Tamrapushpi (coppery red flowers), Madakara (causes initiation of fermentation), Madyavasini (used in alcoholic preparations), Dadimipatra (leaves resemble pomegranate leaves), Subhiksha, Kunjara, Ratispruha etc. Its taxonomical description is mentioned in Table 1. [4, 5]

Distribution

The plant is widely distributed throughout India, ascending up to an altitude of about 1500 m, and also in a majority of the countries of South East and far East Asia like Sri Lanka, China, Malaysia, Indonesia, Japan and Pakistan as well as Tropical Africa. In North-eastern India, its occurrence is in Tenga and Salari to Nafra areas of East Kameng district, Kawkuth areas in Mizoram and limited northern part of West Bengal adjacent to South Sikkim district of Sikkim. It is also found in Gangetic plains [4-6].

Table 1: Taxonomical description of *W. fruticosa*

Kingdom	:	Plantae
Division	:	Magnoliophyta
Class	:	Magnoliopsida
Order	:	Myrtales
Family	:	Lythraceae
Genus	:	<i>Woodfordia</i>
Species	:	<i>fruticosa</i>

Botanical Description

Macroscopical Characters

The full-grown leafy shrub is about 3.5m high, having spreading and long branches with fluted stems. The bark is cinnamon-brown coloured and smooth, peels off in fibres and the young shoots are terete, mostly clothed with fine white pubescence. The leaves are opposite or sub-opposite in nature. Flowers are brilliant red, innumerable, arranged in dense axillary paniculate-cymose clusters, with short glandular pubescent Pedicels (Figure 1). The calyx is long, striated, covered with glandular dots, with a small campanulate base and a slightly curved long bright red tube that contracts above the included capsule. The petals are slightly longer than the calyx-teeth, narrowly linear, extended at the apex to a long fine point. The fruits are small capsules, ellipsoid and membranous, usually splitting the calyx near the base, and are irregularly dehiscent. The seeds are brown, very minute, numerous, shining, smooth angular and obovate [7].

In flowering stage, the bush appears twiggy and formless but entirely swathed in red (Figure 2). This is because the small flowers grow singly or in groups all the way along the branches and side twigs, and it is at this time that the falling of leaves takes place. Each flower, borne on a tiny stem, is a slender tube, slightly curved, the greenish base of which is the sepal. Swelling slightly, the tube divides into narrow, pointed lobes and from within emerges a bunch of long stamens. The whole length, including the stamens, is not more than 2cm. The fruit is a small, covered by the withered sepals and oblong capsule. The narrow, pointed leaves grow straight from the branches, either in whorls of three or opposite. They are dull and harsh, dark green in colour, but paler underneath. Sometimes, they are dotted beneath with small, black glands. From the flowers, rich in tannin, a red dye is obtained which is used to dye silks. The fresh and dried flowers of *W. fruticosa* are shown in Figure 3 [8].

Microscopical Characters [9]

A transverse section of the pedicel flower shows a single layered epidermis, with a fairly thick cuticle. From this layer, numerous unicellular trichomes arise. The epidermis is followed by 7-8 layered cortex, differentiated into collenchymas and parenchyma with plenty of air spaces. The primary xylem is represented by uni- or bi-seriate groups of 3 or 4 tracheids arranged in a ring with phloem on either side of the xylem. The rosette and cluster crystals of calcium oxalate are found in the cortex.

A transverse section of the calyx tube is circular in outline. The cells of the upper epidermis showed scattered trichomes. The calyx tube consists of several layers of ground tissue containing cluster of calcium oxalate crystals and rosettes and bounded on either side by upper and lower epidermis respectively. Anomocytic, actinocytic and anisocytic stomata are present. Vascular bundles are small, collateral and surrounded by bundle sheath. In sepals, the cells of the lower epidermis in surface view are found to be slightly irregular, broad and thin walled in the upper region but thick walled in

the basal region of the calyx. The tissue is differentiated into an abaxial spongy parenchyma in the upper $\frac{3}{4}$ of the calyx tube and into an adaxial palisade.

The anther lobes are tetra sporangiate and the walls separating the locule get disorganized. A transaction of a lobe showed an epidermis formed of large colorless cells followed by a fibrous layer, which appears to be crinkled. Pollen grains are 3-zonocolporate, oblate spheroid shape and its surface is pistillate. The ovary is bicarpellary and laterally flattened and as such appears elongated in transaction.

Tradional Uses of *W. Fruticosa*

W. fruticosa is of the great importance as it contains the ingredients in ayurvedic preparations like Asavas and Aristhas. According to the Indian Ministry of Health and Family Welfare, total 18 aristhas are mentioned in which 17 contains *W. fruticosa* as Aristhas is found to be general health tonic in nature, stimulating properties and also treats one or more systemic disorders. For example, Balaristha containing *W. fruticosa* flowers as constituent of Asava and Aristha which help in treating burning sensations in the stomach. [6] According to the Indian System of Medicine, the flowers of this plant are pungent, acrid, uterine sedative, cooling and useful in leprosy, toothache, leucorrhoea, fever, dysentery and blood disease. Hence, it is known as Kapha (mucilage type body secretion) and Pitta (energy dependent metabolic activity) suppressants in ayurvedic medicine. It is given with jaiphal and qand for treating stomach disorders and with honey for pediatric diarrhea [10].

In Indonesia and Malaysia, crude drug as Sidowava or Sidawayah containing the dried flowers of *Woodfordia* which is used in treating sprue, bowel disease and as an astringent. It is also incorporated into a preparation which is used to make barren women fertile [11-12]. According to Yogaratnakara, the flowers of *W. Fruticosa* has been used as a substituent for *Glycyrrhiza glabra* which is one of the most renowned treatises on Indian Medicine and local traditional knowledge [13].

Chemical Constituents

The compounds identified in *W. fruticosa* are predominantly phenolics, particularly hydrolysable tannins and flavonoids. Desai *et al* (1971) first demonstrated the presence of octacosanol and β -sitosterol in the stems [14]. These were subsequently reported from the flowers also [15], with β -sitosterol encountered even in the leaves [16]. The other non-phenolic constituents reported include the steroids hecogenin (1) and meso-inositol from the flowers [17] along with triterpenoids lupeol (2a), betulin (2b), betulinic acid (2c), oleanolic acid (3a) and ursolic acid (3b) from the leaves [16]. Besides the flavonoids or tannins, the phenolic constituents found in the plant include gallic acid in leaves and stems [18, 19]; ellagic acid (4) in leaves and flowers; bergenin (a C-glycoside of gallic acid, 5a) and the new constituent norbergenin (5b) in stems [18]; chrysophanol-8-O- β -d-glucopyranoside (6) in flowers [17], and the naphthaquinone pigment lawsone (7) in leaves [20].

The flavonoid constituents characterized by various groups include six quercetin glycosides [3-rhamnoside from flowers [16], 3- β -l-arabinoside (polystachoside) from flowers and leaves [21], and 3-O- α -l-arabinopyranoside, 3-O- β -d-xylopyranoside, 3-O-(6''-galloyl)- β -d-glucopyranoside, and 3-O-(6''-galloyl)- β -d-galactopyranoside (8) from leaves [19], three myricetin glycosides [3-O- β -d-galactoside in flowers and leaves [21], and 3-O- α -l-arabinopyranoside (9), 3-O-(6''-

galloyl)- β -d-galactopyranoside in leaves ^[19], as also naringenin 7-glucoside (**10**) and kaempferol 3-*O*-glucoside (**11**) in flowers ^[16]. Examination of the flowers by Nair *et al.* (1976) for the orange-red pigment led to the identification of pelargonidin 3,5-diglucoside ^[21] (**12a**), followed by the anthocyanidin pigment cyanidin 3,5-diglucoside (**12b**) ^[22].

Various hydrolysable tannins isolated from the flowers by Yoshida's group include 1,2,3,6-tetra-*O*-galloyl- β -d-glucose; 1,2,4,6-tetra-*O*-galloyl- β -d-glucose; 1,2,3,4,6-penta-*O*-galloyl- β -d-glucose; tellimagrandin; gemin D; heterophyllin A and oenotherin B, woodfordins A-D, oenotherin A; isoschimawalin A and woodfordins E-I ^[23-27]. The structures of phytoconstituents isolated from *W. fruticosa* have been shown in Figure 4.

Biological Activities

Antimicrobial activity

Against fourteen human pathogens, different extracts of dried flowers of *W. fruticosa* evaluated for their significant antibacterial activity. Five different solvents were used for extracting dried flowers like ethanol, methanol, petroleum ether, chloroform and water. Out of these five extracts tested, petroleum ether extract showed significant activity when compared to Gentamicin used as a standard drug ^[28]. The in vitro antibacterial activity of the crude methanolic extract of *W. fruticosa* flower has been reported on comparing it with the standard drug ciprofloxacin using the agar well diffusion method. The methanolic extract has been reported to be most active against *Pseudomonas pseudoalcaligenes*. The methanolic extract was more effective against gram negative bacteria as compared to gram positive bacteria ^[29]. The diethyl ether, chloroform, petroleum ether and acetone extracts of *W. fruticosa* leaves were evaluated against four bacterial species strains by using disc diffusion method. The extracts of petroleum ether, chloroform, acetone and diethyl ether were found to be effective against all the strains ^[30].

Hepatoprotective activity

Hepatoprotective activity of petroleum ether, ethyl alcohol, chloroform and aqueous extract of the flower of *W. fruticosa* has been reported against phenytoin induced liver damage in rats ^[31] and carbon tetrachloride induced hepatotoxicity ^[32]. The methanolic extract of the flowers of *W. fruticosa* has been reported for hepatoprotective activity against acetaminophen induced hepatic injury in rats ^[46] and diclofenac sodium induced hepatic damage in rats ^[33].

Cardioprotective activity

Arjunaristha is an important ayurvedic formulation used for cardiovascular disorders, prepared by fermenting the decoction of specified plant materials using flowers of *W. fruticosa* ^[34]

Antioxidant activity

Antioxidant activity of *W. fruticosa* flowers was confirmed by using ABT and DPPH free radical scavenging models in petroleum ether, chloroform and methanol extracts ^[35].

Antiulcer activity

Both chloroform and methanol extracts of *W. fruticosa* roots showed significant antiulcer activity in ethanol, hydrochloric acid and Diclofenac sodium induced ulcer in stomach of female wistar albino rats ^[36].

Immunomodulatory activity

The *in-vitro* and *in-vivo* immunomodulatory activity of ethanolic extract of the flowers of *Woodfordia fruticosa* has been reported. For this in mice, the effect of non specific immune responses was examined. *In-vitro* immunomodulatory activity of the extract was examined on murine peritoneal macrophage phagocytosis (using nitroblue tetrazoleum dye reduction, lysosomal enzyme activity, myeloperoxidase, nitric oxide) and on proliferation of bone marrow cells by salforhodamine 'B' (SRB) assays. The *in-vivo* activity has shown on bone marrow cells and macrophages by using cyclophosphamide induced myelosuppression and carbon clearance test respectively. The significant increase in the release of myeloperoxidase, lysosomal enzyme, nitric oxide and superoxide from macrophages along with significant increase in phagocytic index in carbon clearance test indicates stimulatory activity of the extract in macrophages. The extract was found to show 60% increased bone marrow cells proliferation and offer protection towards cyclophosphamide induced myelosuppression which represent the stimulation of bone marrow ^[37].

Anti fertility activity

The anti fertility activity of various extract of dried flowers of *W. fruticosa* has been reported in female albino rats. The ethanolic extract of the powder of the dried flowers was prepared by extracting successively with petroleum ether, chloroform, benzene, ethanol and was also extracted individually with 50% aqueous alcohol and water. Anti fertility activity of successive alcoholic, aqueous and hydro alcoholic extracts was studied in female albino rats. The results revealed that the alcoholic extract possessed significant abortifacient activity, whereas aqueous and hydro alcoholic extracts held moderate activity as compared to the control. Thus, the successive alcoholic extract showed promising abortifacient activity at 100kg/mg body weight ^[38].

Anti tumor activity

Woodfordin C, a macro ring hydrolysable tannin dimer isolated from dried flower of *W. fruticosa*, has been reported to exhibit anti tumor activity ^[24].

In Vivo Pharmacological Studies

Analgesic activity

Rose *et al.* (2013) designed to evaluate the analgesic activity of *W. fruticosa* stem bark in albino rats by using chemical and thermal models of acetic acid induced writhing test and nociception hot plate method respectively. The petroleum ether, chloroform, ethanol and aqueous extracts were administered orally to the rats in their respective groups at a dose of 200mg/kg according to their body weight. Analgin was a standard drug administered to the standard group. The results of aqueous extract and alcoholic extract exhibited statistically significant (** $P < 0.01$ & * $P < 0.05$) analgesic activity in albino rats. The aqueous extract found to be the most potent in comparison to petroleum ether and alcoholic. Comparison with standard and test groups, aqueous extract group followed by alcoholic and petroleum ether extract exhibited significant analgesic effect in animal models. Phytoconstituents present in bark are flavonoids, steroids, glycosides and tannin. Analgesic activity of *W. fruticosa* stem bark may be due to presence of steroids, flavonoids or glycosides ^[39].

Antihyperlipidemic activity

Khera *et al.* (2012) investigated the potential role of methanolic flower extract of *W. fruticosa* in lowering lipid parameters in mice fed with a high cholesterol diet. Swiss albino mice were randomly divided into five groups of six and were administered either: 0.5 ml water (negative controls); 30 mg cholesterol (hypercholesterolemic animals); methanolic extract of *W. fruticosa* flowers at 400mg/kg body weight (positive control); or the same doses of both cholesterol and the extract (test animals); Atorvastatin at 10mg/kg body weight (drug control). The effects of extract on the lipid profile were assessed by measuring concentrations of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), and very low-density lipoprotein cholesterol (VLDL-c). Administration of cholesterol showed significant elevation ($p < 0.001$) of TC, LDL-c, VLDL-c, and TG concentrations, and of the TC: HDL-c ratio ($p < 0.05$). Administration of MEWF extract in cholesterol fed mice caused a significant decrease ($p < 0.001$) in the concentrations of serum TC, LDL, VLDL TGs as well as TC: HDL-c ratio when compared with cholesterol fed control mice and results were also comparable to that of drug control group. These results suggest lipid-lowering effects of *W. fruticosa* flowers which serve as a new potential natural product for controlling hyperlipidemia [40].

Anti-inflammatory activity

Baravalia *et al.* (2012) investigated anti-inflammatory activity of methanol extract of *W. fruticosa* flowers. Two doses (400 and 600 mg/Kg) were evaluated for the anti-inflammatory activity against the carrageenan, histamine, dextran, serotonin and formaldehyde-induced rat paw edema, cotton pellet-induced granuloma and formaldehyde-induced analgesia in rats. The extract produced significant ($p < 0.05$) decrease in paw volume in different models of paw edema. The extract also inhibited the formation of granuloma in cotton pellet-induced granuloma and reduced the frequency of formaldehyde-induced paw licking. These results showed that the methanol extract of *W. fruticosa* flowers have potent anti-inflammatory compounds and justifies the traditional uses for the treatment of inflammatory conditions [41].

Antihyperglycemic activity

Verma *et al.* (2012) investigated the antihyperglycemic activity of *W. fruticosa* (kurz) flowers extract in glucose metabolism and lipid peroxidation in streptozotocin-induced diabetic rats. The ethanolic extract of *W. fruticosa* flowers (250 and 500mg/kg) significantly reduced fasting blood glucose level and increased insulin level after 21 days treatment in streptozotocin diabetic rats. The extract also increased superoxide dismutase, glutathione reductase, catalase, glutathione peroxidase activities significantly and reduced lipid peroxidation. In ethanolic extract treated diabetic rats, glycolytic enzymes showed a significant increase in their levels while a significant decrease was observed in the levels of the gluconeogenic enzymes. The extract also had a favorable effect on the histopathological changes of the pancreatic β -cells in streptozotocin induced diabetic rats. The results suggest that the ethanolic flower extract possess potential antihyperglycemic effect by regulating glucose homeostasis [42].

Anthelmintic activity

Sengupta *et al.* (2013) investigated the anthelmintic activity of methanol and petroleum ether extracts of dried flowers of *W. fruticosa* against the Indian earthworm *Pheritima posthuma* (having anatomical and physiological resemblance with the intestinal roundworm parasites of human beings). Different concentrations of the extract ranging from 50-100 μ g/ml were tested and results were expressed as time required for paralysis and death of the worms. Albendazole (20mg/ml) and piperazine citrate (10mg/ml) were used as a reference standards and negative control was DMSO (1%). Methanolic extract exhibited significant anthelmintic activity as compared to petroleum ether extract [43].

Marketed Preparations

Based on the traditional use of *W. fruticosa* in different diseases and disorders and its reported biological activities, various marketed preparations of this plant, alongwith several other herbs, are widely formulated by reputed pharmaceutical and ayurvedic industries. A list of such marketed preparations has been mentioned in the table 2.

Conclusion and Future Perspective

The data presented in this review highlights the geographical, morphological, microscopical characteristics of *W. fruticosa*. Various marketed preparations containing *W. fruticosa* along with several other medicinal plants are widely prescribed by various traditional medical practitioners. A review of reported biological activities alongwith main phytoconstituents isolated in this plants have also been summarized. Thus, by getting into more detailed study, it may also be possible to formulate the certain dosage forms of this herbal plant without in combination with other herbal plants. There are certain traditional uses of this plants which are not scientifically proved or evaluated. For example, traditional use of the flowers in the preparation of Ayurvedic 'Aristha's or 'Asava's (Elixir of life) needs a relook. The concept of 'value addition' needs to be revisited in the light of modern science of health and diseases. The recent findings of macro cyclic ellagitannins in the management of cancers and inflammations also need to be looked into in details. The scientists or researchers working on this plant will be definitely benefitted from the information summarized in this article.

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