

Woodfordia fruticosa (L.) Kurz: Integrating Phytochemistry, Novel Bioactivities and Sustainable Utilization Strategies

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ABSTRACT

W. fruticosa categorized from family "Lythraceae" and it is also known as "Fire-flame bush" and it grow in tropical and subtropical regions. It occurs in Africa, Middle East and Asia. According to WHO reports that more than 80% of rural areas use medicinal plant to meet their healthcare needs. It plays vital role in ayurvedic medicine because they are used to make herbal medicine like arishta and asava. Researchers found that plant contains many natural phytochemicals such as tannins, terpenes, phenolic acid and flavonoid. The morphology, phytochemistry, novel bioactivities, clinical studies of *W. fruticosa* are deeply reviewed in this article. Google Scholar, Pub Chem, Chem Draw or Research Gate are the scientific research databases has been used for gathering information for this article. Its Phytochemicals are responsible several bioactivities like antimicrobial, antiviral, antioxidants, wound healing, antiulcer, antifertility and antiatherosclerosis activity. Some clinical studies are done to determine its effects on teeth and also determines mouthwashes of *W. fruticosa* leaves to treat chronic periodontitis. This plant is rare and highly popular so its use must be controlled to prevent overexploitation. Tissue culture, genetic research-controlled cultivation and scientific methods used to ensure availability and efficacy. By using these methods, the plant is able to grow more consistently and produces more beneficial ingredients.

Keywords: Anticancer, Antidiabetic, Bioactive Compounds, Clinical Studies, Herbal Preparation, *Woodfordia fruticosa*.

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Received: 21-07-2026;

Revised: 14-09-2026;

Accepted: 03-10-2026.

INTRODUCTION

W. fruticosa (Figure 1) belong to the family of "Lythraceae" (Table 1), commonly known as Dhataki, Dhaava, Pushpa (Table 2), which grow in tropical and subtropical regions.^[1] According to Ayurvedic books, *W. fruticosa* is one of the most important fermentation agents in Arishtas and asavas.^[2] Aristas are prepared from plant decoctions, while Asavas are made from plant juices. Aristas are used as cardio tonics and digestives.^[3] Arishtas act as general health stimulants. As per CCRIMH monograph (1978), 18 arishtas are mentioned. Out of 18 arishtas, 17 formulations of them include *W. fruticosa* extract as a key ingredient.^[4]

It has a wide geographical range, occurring across parts of Africa (Tanzania, Madagascar, Comoros), the Middle East (Oman, Saudi Arabia), and Asia (Bhutan, China-Guangdong, Guangxi, Myanmar, Yunnan-India, Sri Lanka, Indonesia, Nepal, Pakistan,

and Vietnam).^[5-7] In Indonesia and Malaysia, the dried flowers are known as sidowava or sidawayah which are used for improving fertility in women.^[8] The plant blooms abundantly between January and April, during which its leaves shed and new ones sprout in February-March. The flowers are small, bitter in taste, cold in nature.^[9] Plant all parts flowers, roots, leaves, stem bark, creepers, flowers and fruits are considered beneficial. They are used in treatment of bone diseases, fever, diarrhea, piles, ulcers, cough, asthma, antiviral, antipyretic, antifertility, granuloma-inhibitory, antitumor, hepatoprotective, immunomodulatory and antihyperglycemic effects.^[10] In Nepal and India its leaves are traditionally used to treat fever when combined with dried ginger and sugar and it also used in the management of leucorrhoea, piles and sitz baths etc.^[11] The plant is being overharvested which puts it at risk. At the same time, traditional medicinal uses are not being connected to modern techniques like biotechnology and novel formulations. To integrate new and old knowledge. A fresh review is needed to connect traditional information with recent science, highlight weak spots and effective use in medicines.^[12,13]

Morphological Characteristics

Morphology of *W. fruticosa* are summarized in Table 3 including habit, seeds, flowers, bark, leaves, shoots.



DOI: 10.5530/phrev.20270066

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Phytochemistry

W. fruticosa contains numerous natural compounds. These include tannins, flavonoids and phenolics which are common plant compounds with antioxidant and protective properties (Table 4 and Figure 2). Researchers found that its flowers is extremely rich in meso-inositol, hecogenin, chrysophenol, β -sitosterol, octacosanol, diglucoside, gallic acid, methyl gallate, isoschimalin A, tellimagrandin, heterophyllin A, gemin D, pentagalloylglucose, tetragalloylglucose, kaempferol, caffeic acid, chlorogenic acid, catechin, rutin, butyric acid, furfural, α -terpineol, 4-terpinenol, linalool, farnesol, α -humulene, β -myrcene, pyrazines, saffrole, Methyl nonanoate, Eugenol acetate, Nonanoic acid, 2-Acetylpyrrole, pentadecanoic acid, γ -terpinene, dihydrocarvyl acetate, hexadecenoic acid, ellagic acid, myricetin, Nerol, Epoxylinalol, [Z,E]- α -Farnesene, Junipene, Butanoic acid, Benzenecetaldehyde, Linalool acetate, 5-Methylfurfural, Octanol, 2-Nonenal, 2-Acetylfuran, 2-Ethylhexanol, Tetramethylpyrazine, 2-Methyltetrahydrofuran, sulcatone, 3-Hexenol, pelargonaldehyde, Tetradecane, 2-Pentylfuran, 2-Methylbutanol, 2-Hexenal, 2-Butanone, 3-Methylbutanal, 2-Ethylfuran, 2,3-Butanedione, Pentanal and 4-Terpineol.^[4,5,9,15-17] Leaves are abundant in many compounds such as oleanolic acid, ursolic acid, lupeol, cosmene, γ -curcumene, elemol, β -selinene, germacrene-D, β -caryophyllene, woodfruticosin, glucogallin, quercetin, myricetin-3-O- α -L-arabinopyranoside, cyclopropaneoctanoic acid, palmitic anhydride, dihydrocarvyl acetate, 2H-1-benzopyran-2-one, caryophyllene epoxide and lawsone.^[4,9,18,19] Stem bark contains octacosanol, norbergenin, gum, c-glucosidenorbergenin and identified number of elements using energy spectroscopy such as hydrogen, phosphorus, potassium, calcium, chlorine, iron, carbon, calcium and sulfur were found in leaves while carbon, hydrogen, magnesium, phosphorus, calcium, platinum, sulfur, chlorine, potassium, silicon, and iron.^[4,9,20]

Novel Bioactivities

Anti diabetic activity

Aqueous extract of plant lowers the raised glucose levels in blood to confirm this activity researcher was used alloxan to induce diabetes and extract were given orally. The rat who received the plant extract gained weight over time and displayed lower blood sugar levels than the untreated diabetic rats which indicated improved health. For comparison standard drug glibenclamide was used.^[28] Dexamethasone increases glucose and triglycerides levels in mice while leaves extracts lowering blood sugar and triglycerides similar to pioglitazone.^[29]

Antioxidant activity

Methanolic extract of leaves was evaluated using DPPH free radical technique and strong effect with an IC_{50} value of 1.86 μ g/mL with high potency.^[11] *W. fruticosa* flowers protected rats from

carbon tetrachloride which cause liver and kidney damage. This indicates that the plant has a high potential for antioxidants.^[30,31]

Hepatoprotective activity

Methanolic extract of flowers affects liver cancer caused by N-Nitrosodiethylamine in rats and extract protected liver by increasing antioxidant enzymes and lowering harmful markers in the blood like ALP, bilirubin, LDH, MDA, AFP and prevent or slow liver cancer progression^[32,33] and flowers protected rat liver from diclofenac induced damage.^[34]

Wound healing

W. fruticosa gel was prepared to speed up recovery in mice for this activity three groups were compared and flowers gel enhanced healing by lowering inflammatory cells and encouraging tissue repair.^[7,35]

Antimicrobial activity

W. fruticosa extract was tested against *E. coli*, *Shigella* species show small inhibition zones and *Cryptococcus neoformans*, *Candida albicans* and results confirms that extract preventing fungal adhesion and also disrupting biofilm structures.^[36] In this study various extract is tested but methanol extract of leaves showing inhibition zones of 5-7 mm against *Aspergillus niger*, *Trichoderma harzianum*, *Alternaria burnsii*, *Alternaria solani* and *Fusarium oxysporum* (Fungi) and *E. coli*, *Salmonella typhi*, *Bacillus subtilis* and *Staphylococcus aureus* (bacteria).^[37-40]

Gastrointestinal Effects

Flowers extract decreased dangerous bacteria like *Alistipes*, *Parabacteroides* and *Bacteroides* while increasing good bacteria like *Akkermansia*, *Lactobacillus* and *Bifidobacterium*.^[41,42]

Immunostimulatory activity

Flowers enhances the body nonspecific immunity by stimulating bone marrow cells and release of lysosomal enzymes, nitric oxide, superoxide and myeloperoxidase from macrophages responsible to improves their capacity to engulf and destroy harmful particles.^[43,44]

Antipsoriatic activity

Researcher use mice to treat psoriasis by using combination of formaldehyde and complete freund's adjuvant. Result shows that formulations decreased redness, erythema and scaling.^[45]

Antifertility

Alcoholic extract demonstrated strong antifertility effects in female rats by preventing pregnancy.^[46]

Thrombolytic activity

Its activity was tested using clot lysis technique and result showed that aqueous leaves extract breaking down 41.24% of the clot and

chloroform (38.80%), methanol extract (38.22%) and methanol extract of bark have highest activity at 44.90%.^[47]

Antidiarrheal activity

Leaves and bark extract of leaves were given to mice. Result shows that bark extract reduced diarrheal feces by about 56% and 63% while leaves extract reduced them about 69% and 29%.^[48]

Antilucer activity

Aqueous extract of flower demonstrated strong protective effect than the standard antiulcer drug omeprazole.^[49] *W. fruticosa* contain tannins which is responsible for antiulcer activity in this study diclofenac sodium is used to induced ulcers in rats and demonstrated strong protective properties.^[50,51]

Anti-inflammatory action

Egg protein denaturation method was used to test *W. fruticosa* leaves anti-inflammatory properties which mimics inflammation caused by protein damage. Results showed that *W. fruticosa* extract decreased swelling on the paw and knee and TNF- α levels are also decreased and prevent and reduces inflammatory responses in animals.^[52,53]

Antiatherosclerosis action

Methanolic extracts were examined to determine atherosclerosis caused by triton and high fat diet. Result decrease HDL and increase triglycerides, cholesterol, harmful lipoproteins and decreased tissue damage.^[54]

Antiasthmatic activity

Ethanol extract reversed contractions caused by histamine and acetylcholine by causing total bronchodilation at concentration of 1.6-3.2 mg and protect spasms, airway narrowing and also reducing frequency of cough.^[55]



Figure 1: *Woodfordia fruticosa* (Dhatki) plant belonging to the family lythraceae. shown at column width.

Anti-urolithiasis activity

W. fruticosa extracts demonstrated potent anti urolithiasis properties by preventing kidney damage and stone formation.^[56]

Antidepressant activity

Flower extract was given to animal orally for 14 days and activity were examined using forced swim test and tail suspension test and extract decreased immobility time and shows strong antidepressants activity.^[57]

Antiviral activity

Flower extract demonstrates strong enterovirus 71 with an IC₅₀ of 1.2 μ g/mL with no toxicity up to 100 μ g/mL.^[58]

Alzheimer Disease

Scopolamine was used to induced memory impairments in the mice and used Elevated Plus Maze and Morris Water Maze technique. Result shows that extract enhanced the mice's memory and learning similar to the effect of standard drug piracetam.^[59]

Anticancer activity

Flowers and leaves extract was evaluated on human liver cancer cells (PLC/PRF/5) and determine cytotoxic effect of human breast (MDA-MB-231) and pancreatic (PANC-1) cancer cells.

Table 1: List of indigenous names of *W. fruticosa*.^[4-6]

Country	Language/Region	Local Name(s)
India	Hindi	Dhaura, Dhari, Dhatki, Dhatri, Ban-mahendi
	Sanskrit	Agnijwala
	Kannada (Karnataka)	Daathakee, Kusumka, Pushpin, Bela, Taamra Pushpin
	Malayalam (Kerala)	Tatiripushpi, Tamarpushi, Tatire
	Tamil (Tamil Nadu)	Dhattari, Dhathari-jagri
	Telugu (Andhra Pradesh)	Dhaarhupushpika, Dhaathaki
	Urdu	Gul Dhawa
	Oriya (Odisha)	Harwari, Dholoo, Jaliko
	Punjabi (Punjab)	Dhawi
	Jammu and Kashmir	Thwai
	Marathi	Ddhayati, Jaliko, Haiwari
	Bihar	Dawai, Dhaai
Nepal	-	Dhangera, Ras Dhayenro
Sri Lanka	-	Dhataki
Pakistan	-	Dhai, Gul Dhawa

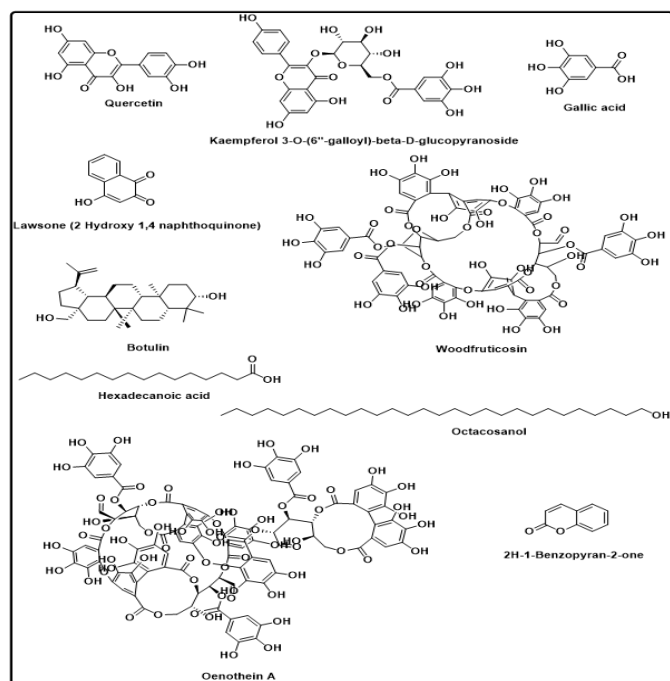


Figure 2: Structures of Phytochemical present in *W. fruticosa*.^[3,4,5,10,15,18,19,21-27]

Result shows it eliminates cancer cells, decreased liver tumours and extracts had an IC_{50} value 230.5 $\mu\text{g/mL}$ for pancreatic cancer cells and 124 $\mu\text{g/mL}$ for breast cancer cells.^[60,61]

Antinutritional Factors

Numerous antinutritional chemicals were found in *W. fruticosa* flowers and study shows that phytate, tannin and oxalate are present whereas saponins are absent. Oxalates can cause kidney stones, phytates can decrease the absorption of minerals including iron, calcium and zinc and tannins also obstruct the digestion of proteins. However, in *W. fruticosa* has mild amounts that are safe.^[62]

Clinical Studies

In this study *W. fruticosa* powder mixed with honey to an infant's gums during teething was investigated. 35 out of 40 finish the clinical trial. For half a year parents used this drug three times a day along with regular checkups. common teething symptoms like vomiting, fever, coughing and diarrhea were reduced by drug also help in maintaining normal weight gain. It is safe, efficient and reduces problem related to teeth.^[63] In this study herbal mouthwashes made from leaves of *W. fruticosa* and peels of *Punica granatum* could benefit with chronic periodontitis. Ethanolic extracts are used to prepare mouthwashes. Total 100 patient are divided into two groups in which one group used *Woodfordia* leaves mouthwash and other used *Punica* peel mouthwash. Then researchers evaluated gum health and salivary amylase levels and both groups clearly reduced especially after 1 hr of using the mouthwash and shows potent anti-inflammatory effects.^[64]

Table 2: Taxonomical categorization of *W. fruticosa*.^[4-6]

Taxonomical Hierarchy	Taxon
Kingdom	Plantae
Class	Magnoliopsida
Subclass	Rosidae
Division	Magnoliophyta
Phylum	Streptophyta
Family	Lythraceae
Odour	Myrtales
Genus	<i>Woodfordia</i> , Salisb
Species	<i>Woodfordia fruticosa</i>
Habit	The plant grows in sunny, open places and is also found on mountains and old agricultural land.

Herbal Formulations

Tablet

W. fruticosa tablet formulation were created by researchers and tablets cleared all parameters such as friability, weight variation, hardness and disintegration time then tablets were tested *in vitro* for therapeutic properties and they demonstrated good antimicrobial, anti-inflammatory and antiulcer activity.^[65]

Hand sanitizer

Study focused on preparation of non-alcoholic hand sanitizer from flowers of *W. fruticosa* known as Dhathaki Arka. Alcohol based sanitizers that dry out the skin, this ayurvedic preparation effectively fights with germs and safe for skin. Result reported good sanitization and have antimicrobial activity.^[66]

Vanishing cream

Study focused on creating vanishing herbal cream from *W. fruticosa* leaves. Numerous characteristics of cream are tested such as spread ability, pH, viscosity, compatibility and washability. Result demonstrate that the cream was smooth and uniform had pH of 5.9 and cream was yellowish green with pleasant smell. It was stable and simple to apply leaving no residue and forming a non-greasy layer with viscosity of 27,025 cps. Test verified that it was an oil in water emulsion which is typically more comfortable to apply topically.^[67]

Sustainable Utilization Strategies

The goal of study was to create a technique for micropropagation of *W. fruticosa* which is at risk of going extinct because of its extensive use in ayurvedic medicine. Plant growth regulators such as auxins and cytokinins were cultivated in different concentration on MS media for shoot tip explants either separately and in combination. For direct shoot regeneration combined effects of these hormones were examined. MS media shows best result contain BAP at 2.0

μM which give 52 shoots per explant. The highest number of roots were produced in half strength MS medium supplemented with 5.0 μM IBA and 3% sucrose for root growth. After two weeks, the regenerated plantlets had a survival rate of roughly 70% and have been hardened and successfully transferred to the greenhouse.^[2] Using *Agrobacterium tumefaciens* researchers created a genetic transformation technique for *W. fruticosa*. Transformed tissue were selected by treating leaves segment with bacterium that carried marker and reporter genes then growth on nutritional media supplemented with antibiotics and plant hormones. Hygromycin resistant shoots were generated then successfully rooted and demonstrated a transformation efficiency

of 44.5% with two to three transgenic shoots per explant. The marker gene had incorporated into plant genome confirmed through PCR, RT-PCR, southern blot analysis and GUS staining. By strengthening its therapeutic properties this protocol offers a means of improving the plant.^[68] Seed are tiny and easily self sow easily in open, well-drained soil but germination is more difficult in nursery conditions. since regular seedbeds frequently fail to generate seedlings, planting seed on broken bricks is most effective artificial approach. Light, well-drained soil and sunny location are essential for growing in nursery beds. It is best to spread seeds on ground, push them gently into the soil without covering them and water them sparingly so avoid wash them

Table 3: Morphological characteristics of *W. fruticosa* including habit, fruits, leaves, bark, shoots, seeds, flowers.

Plant Part	Morphological Features	Function	Reference
Habit	It has perennial leafy shrub that typically grows up to 3-3.5m tall. It is distinguished by its long, spreading branches with fluted stems that giving robust and ornamental appearance.	Its distinct shrub habit makes it easily recognizable in wild habitats. It is used ornamentally due to bright flowers.	[8]
Fruits	The fruits are small, ellipsoid membranous capsules. They are irregularly dehiscent, capsule is typically enclosed within the persistent calyx tube which protects the developing tubes. The fruit capsules are ovate to elliptic with lengths between 6 to 10 mm and 2.3 to 4.5 mm in widths.	Fruits traits help to distinguish species within Lythraceae.	[8]
Leaves	Leaves are arranged in opposite or sub opposite manners. Leaves are simple in structure, lanceolate leaves forming dense foliage that enhances the shrub's leafy habit. Its leaves vary in size ranging from 8 to 30 mm in width and 18 to 111 mm in length, cymose inflorescences comprising 3 to 16 flowers.	Leaves arrangement is a key taxonomic trait. In traditional medicine it is used in inflammation and fever.	[8]
Bark	Its bark is smooth and cinnamon brown in colour, with characteristic tendency to peel off in fibrous strips.	Bark texture and colour are diagnostic and it is conventionally used in treatment of wound healing and as astringent.	[4]
Shoots	The young shoots are cylindrical (terete) and covered with fine white soft hairs.	Pubescence protects tender shoots and used in identification of juvenile plants.	[14]
Seeds	The seeds are numerous, brown, smooth, shiny, angular and obovate in shapes. A unique feature of this species is its triangular shaped seeds	large number of seeds ensure propagation and seed morphology has taxonomic significance.	[14]
Flowers	The plant produces numerous bright red flowers that are borne in dense axillary paniculate cymose clusters. Each flower has short glandular pubescent pedicels, a striated calyx covered with glandular dots and a small bell-shaped base with a slightly curved red tube. The petals are little longer than the calyx teeth and taper into fine points, which enhances the striking appearance of the blossoms. The plant flower forming a hypanthium that is 9 to 11 mm long and 2 to 5 mm wide. The petals are brick red are 3 to 4.5 mm in length and 0.5 to 0.75 mm in width. The ovary is teardrop shaped are 4 to 6 mm long and 1.25 to 2 mm broad. The reproductive structures are distinct stemens are straight with short filaments and prominent anthers ranging from 3 to 16.5 mm in length.	It is traditionally used in Ayurveda as a fermentation initiator in herbal formulations like asava and arishta.	[4]

Table 4: Phytochemical present in *W. fruticosa* including phenolic acids, fatty alcohols, tannins, flavonoids, naphthoquinones, coumarins, alkaloids.

Sl. No.	Phytochemicals	Plant Parts	Class	Reference
1.	Gallic acid	Flowers	Phenolic acids	[3,4,5,10,15,21-25]
2.	Octacosanol	Flowers	Long chain aliphatic alcohol (fatty alcohol)	[4,5]
3.	Quercetin	Flowers	Phenolic acids	[4,21-24,26]
4.	Oenothien A	Flowers	Tannin	[4,5, 22]
5.	Hexadecanoic acid	Flowers and Leaves	Fatty acid	[18]
6.	Kaempferol 3-O-(6''-galloyl)- β -D-glucopyranoside	Flowers	Flavonoid	[23,24]
7.	Lawsone (2-Hydroxy-1,4-naphthoquinone)	Flower	Naphthoquinone	[4,25]
8.	2H-1-Benzopyran-2-one	Flowers and leaves	Coumarin (benzopyrone class)	[18]
9.	Woodfruticosin	Flowers	Tannin	[27]
10.	Botulin	Leaves	Alkaloid	[19]

away. If soil start to dry up it is advised to water it once or twice a day. The plant can be cultivated by cutting from hardwood and softwood both of which are regarded as simple methods.^[69] Vegetative propagation by stem cuttings is therefore the most dependable technique. When branch cuttings are planted in moist, shaded soil which root quickly and start to flower within two years making it simple for farmers to cultivate plants. This decreases dependence on wild harvesting and ensures supply for the pharmaceutical and ayurvedic sectors. The authors stress the importance of tissue culture research, organized farming and cultivation of herbal gardens in order to preserve the species satisfy industrial demand and stop habitat loss.^[70] During growing season, a balanced 10-10-10 fertilizer can be applied sparingly but it Favours well-draining loamy soil and does not require extensive treatment. Healthy growth is maintained by replanting in early spring every two to three years. The plant can be multiplied by cutting obtained during growing season or by seeds propagation. After flowering pruning helps the plant maintain its shape, promote new development and remove unhealthy branches.^[71]

CONCLUSION

W. fruticosa are rich in bioactive components which exhibits broad range biological activities such as antiviral, Wound healing, antioxidants, antimicrobial, anticancer, anti-inflammatory, cardioprotective, Alzheimer and antidiabetic effect but most study still remain limited mechanistic and molecular level research and more precise therapeutic pathways are required. Most studies still limited *in vitro* and animal studies to determine safety, effectiveness and dosage toxicity evaluation, clinical trials and active biomarker characterization are still necessary. Future studies may focus on mechanism based pharmacological evaluation, isolation of phytochemical and formulation development. The sustainable use of *W. fruticosa* is equally significant because of its ecological importance and increasing popularity in herbal formulations.

For long term sustainability without losing biodiversity methods including cultivation, conservation agricultural intervention is important.

ACKNOWLEDGEMENT

The authors are grateful to the School of Pharmaceutical Sciences, Bahra University, Solan for the support and assistance in the preparation of this review article.

ABBREVIATIONS

***W. fruticosa*:** *Woodfordia fruticosa*; **ALP:** Alkaline Phosphate; **AFP:** Alpha-Fetoprotein; **BAP:** 6-Benzylaminopurine; **CFA:** Complete Freund's Adjuvant; **DPPH:** 2,2-Diphenyl-1-Picrylhydrazyl; **GC-MS:** gas Chromatography-Mass Spectrometry; **GUS:** Beta-Glucuronidase; **HDL:** high-density lipoprotein; **HPLC:** High-Performance Liquid Chromatography; **HPTLC:** High-Performance Thin-Layer Chromatography; **IBA:** Indole-3-Butyric Acid; **IC₅₀:** Half Maximal Inhibitory Concentration; **LDH:** Lactate Dehydrogenase; **MDA:** Malondialdehyde; **MS:** Murashige and Skoog; **PCR:** Polymerase Chain Reaction; **RT-PCR:** Reverse Transcription PCR; **TNF- α :** Tumour Necrosis Factor-Alpha; **VEGF:** Vascular Endothelial Growth Factor; **WHO:** World Health Organization; **CCRMH:** Central Council for Research in Indian Medicine and Homoeopathy; **HSP70:** Heat Shock Protein 70.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

Manish Kumar: Conceptualization, literature survey and drafting. **Shruti Thakur:** Conceptual guidance, supervision, critical revision and final approval of manuscript. **Vishnu Das,**

Joohee Pradhan, Isha Sharma: Literature survey, editing, and assistance in manuscript preparation.

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Cite this article: Kumar M, Thakur S, Das V, Pradhan J, Sharma I. *Woodfordia fruticosa* (L.) Kurz: Integrating Phytochemistry, Novel Bioactivities and Sustainable Utilization Strategies. *Pharmacog Rev*. 2027;21(41):13-20.