Review Article

Traditional Uses, Phytochemistry and Pharmacological Activities of *Woodfordia fruticosa* (L) Kurz: A Comprehensive Review

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Giri *et al.*: An Update Review on *Woodfordia fruticosa* (L.) kurz

***Woodfordia fruticosa* (L.) kurz belongs to the family 'Lythraceae' has been utilized in traditional medicine for treating common ailments since ancient periods. It is conventionally employed against numerous diseases, including cold, toothache, blood infection, leprosy, dysentery, wounds, rheumatic pain, fever, urinary disorders, inflammation, antifertility and menstrual problem. The enormous potential and effects are extensively validated through *in vitro* and *in vivo* models. The recent updates on the plant *Woodfordia fruticosa* are absolutely essential to identify the bioactive components responsible for its therapeutic effect. Phytochemical investigations prove the presence of 61 compounds belonging to the class of glycosides, terpenes, flavonoids, tannins, sterols, phenolics and essential oils isolated from the different parts of the plant. Pharmacological studies of the plant showed that it poses a wide range of pharmacological properties, including antihyperglycemic, antioxidant, anti-inflammatory, analgesic, hepatoprotective, antibacterial, gastroprotective and wound healing properties. The pharmacological activities of crude extracts from this plant mostly have been reported. A very limited number of studies have reported the activities of isolated compounds of this plant. Hence, this review will help to explore many distinguished pharmacognostic characteristics of the plant as well as the therapeutic efficacy of the plant against several diseases and will recommend further requirements of additional investigations to explore its possible practical applications.**

Key words: *Woodfordia fruticosa*, phytochemistry, antioxidants, hepatoprotective activity, anticancer activity

Herbal medicines are obtained from different parts (leaves, stem, root, flower, etc.) of plants, which have been used extensively everywhere since ancient times for the treatment and cure of different diseases. Even 80 % population of developing countries rely on herbal medicine for their basic health needs because it is easily available in the market at a lower price, considered to have low toxicity as well as ease of preparation and use[1]. The efficiency of herbal medicine mostly depends on the method of preparation, part of the plant used and the form in which the patient should take it. Mainly herbal medicines are often used to persistently maintain the well-being of health because people think being a natural product is always safer. Still, it was found that it might have a tremendous adverse effect or may interact with other drugs if taken simultaneously due to self-medication or when given by over the counter. Hence full knowledge about herbal plants is also necessary for their safe use[2].

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Woodfordia fruticosa (L.) kurz (*W. fruticosa*) is a herbal plant from the family Lythraceae, which is commonly known as Fire flame bush and Shiranjitea worldwide[3]. This plant is available mostly in Asian countries in the southern part of high altitudes and a few parts of gulf countries and Africa. It is used globally as a traditional system of medicine for treating diseases like acute diarrhea, hemorrhages, ulcerations, erysipelas and wounds[4]. It is noticed that the most effective part of this plant is the flower which has a high demand in the national as well as the international market of the southeastern part of Asian countries[5]. This review will focus on the

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future aspect of this plant used for the development of potential lead compound by analyzing the phytochemistry of the plant as well as by scrutinizing the data provided by the different journals on the use of this plant as ethnomedicinal or pharmacological uses in different system of medicines, where the activities will be noticed based on different forms of extraction of plant and phytoconstituents responsible to treat a particular disease.

BOTANY

W. fruticosa is a mature shrub or small tree that is 3.6 m in height (approximately). The branches are generally long and spread with grooved stems. The leaf arrangements are the opposite or subopposite. Flowers are splendid red, numerous, cymose structured with additional panicle, glandulous pedicle and generally blossom in May and June. The petals are marginally more than the calyx teeth, barely straight, stretched out at the apex. The calyx is campanulated in base, stripped and has glandular dots over it. Seeds are numerous shining small brown colored with smooth surface and obovate shape. The bark is distinctively smooth cinnamon-earthy brown colored shaded with fibres coated and the youthful shoots are terete and white pubescent. The fruits are dehiscent, ovate and membraneous, small capsules which split the end of the calyx[3,6-8].

DISTRIBUTION

It is widely distributed in the southern Asian countries and in some parts of countries like Bhutan, China (Yunnan, Guangdong, Guangxi), Japan, India, Myanmar (Burma), Nepal, Vietnam, Malaysia, Pakistan, Sri Lanka and Gulf nation like South Arabia (SW-Saudi Arabia: Asir) and Oman (Dhofar). Furthermore, it is available in Java, Sumatra, Madagascar, Tanzania and Comores[3,9].

TRADITIONAL USES

In the Ayurveda system of medicine, the flowers of this plant are used in the preparation of Aristha and Asava for medicinal purposes as well as for fermentation with some drugs[10]. Flower juice was given twice a day for sunstroke and bark juice was used for the treatment of cold, which was made by decoction[11]. In the region of western Ghat of India, the plant was used for healing wounds[12]. The tribal group (Kondha) of Orissa was found to use this plant for leucoderma disease[13]. According to the ayurvedic pharmacopoeia of India flower of *W. fruticosa* is used against ulcers, defined as "Vrana" and used in the ointment on pimples of smallpox[14]. Tribal people of the Theni district, southern India, use leaf juice to get relief from rheumatic pain[15]. The flowers of this plant are considered to be caustic, pungent, give a cooling effect, act as uterine narcotic and hence useful for toothache, blood infection, leprosy, dysentery and fever. So, in the Ayurvedic system of medicine, it is used as Kapha and pitta for suppressive effect. It is given with honey for the diarrhoea of pediatric patients[16]. In Nepal, the flower and leaf of this plant are used to treat different disorders like fever, urinary disorder, swelling, menstrual problems, etc[9].

PHYTOCHEMISTRY

The phytochemicals present in the plant consist of both organic and inorganic chemicals, which are secondary metabolites of the plant. These chemicals have various activities which indirectly lead to the pharmacological response of the plant. The plant contains various tannins, flavonoids, alkaloids, glycosides, sterols and triterpenoids[17]. The leaves of the *W. fruticosa* were observed to have polyphenolic groups such as lawsone, glucogallin, ellagic acid, gallic acid, quercetin 3-O-(6-β-galloyl)-β-d-galactopyranoside, quercetin 3-O-α-L-arabinopyranoside, methyl 3-O-methylgallate, myricetin 3-O-α-L arabinopyranoside, etc and essential oil containing α-pinene, β-selinene, γ-curcumene, germacrene-D, β-caryophyllene, etc[18-21].

The flower of this plant mostly contains flavonoids (kaempferol, quercetin) and a few non-phenolic compounds like hecogenin[22,23], while the leaves contain terpenoids such as isocarveol, geraniol, citral, thymol, eugenol, geranyl acetate, linalool, thiogeraniol, lupeol, betulin, betulinic acid, oleanolic acid and ursolic acid[20,24]. The stem of this plant contains compounds like β-sitosterol and octacosanol[25]. From the flower, some known and new hydrolyzable tannin constituent is isolated and the structure of that group has been identified by Yoshida *et al.*[26], which contain compounds like 1,2,3,6-tetra-O-galloyl-β-d-glucose, 1,2,3,4,6-penta-O-galloyl-β-d-glucose, tellimagrandin, gemin D, heterophylliin A, woodfordins A, B, C and oenothein B. In 1992 new constituents were introduced by Yoshida *et al.*[27], such as woodfordins E-I and isoschimawalin A. Therefore, *W. fruticosa* contains numerous chemicals in it, which are phenolic, non-phenolic, flavonoids, essential oil, etc., as listed in Table 1[19-33]. Structure of some main chemical constituents of *W. fruticosa* represented in fig. 1.

TABLE 1: LIST OF PHYTOCHEMICALS PRESENT IN DIFFERENT PARTS OF *W. fruticosa*

S No.	Name of Phytochemicals	Part	Molecular Formula	Chemical class	References
1	1,2,3,4,6-penta-O-galloyl-ß-d-glucose	Flower	$C_{41}H_{32}O_{26}$	Tannin	[26]
2	1,2,3,6-tetra-O-galloyl-ß-d-glucose	Flower	$C_{34}H_{28}O_{22}$	Tannin	[26]
3	1,2,4,6-tetra-O-galloyl-ß-d-glucose	Flower	$C_{34}H_{28}O_{22}$	Tannin	[26]
4	2,6 dimethyl 1,3,5,7 octatetraene	Leaves	$C_{10}H_{14}$	Triterpenoid	[19,21]
5	α-pinene	Leaves	$C_{10}H_{16}$	Triterpenoid	[19,21]
6	ß-caryophyllene	Leaves	$C_{15}H_{24}$	Triterpenoid	[19,21]
7	ß-selinene	Leaves	$C_{15}H_{24}$	Triterpenoid	[19,21]
8	ß-sitosterol	Flower	$C_{29}H_{50}O$	Phytosterols	[25]
9	γ- curcumene	Leaves	C15H24	Triterpenoid	[19,21]
10	Astragalin/ kaempferol-3-glucoside	Flower	$C_{21}H_{20}O_{11}$	Glycoside	[28]
11	Benzyl benzoate	Leaves	$C_{14}H_{12}O_2$	Aromatic ester	[24]
12	Betulin	Leaves	$C_{30}H_{50}O_2$	Triterpenoid	[20]
13	Betulinic acid	Leaves	$C_{30}H_{48}O_3$	Triterpenoid	[20]
14	Chrysophanol-8-O-ß-D-glucopyranoside	Flower	$C_{21}H_{20}O_9$	Glycoside	[25]
15	Citral	Leaves	$C_{10}H_{16}O$	Triterpenoid	[24]
16	Diethyl phthalate	Leaves	$C_{12}H_{14}O_4$	Phthalic acid	[24]
17	Elemol	Leaves	$C_{15}H_{26}O$	Triterpenoid	[19,21]
18	Ellagic acid	Leaves and Flowers	$C_{14}H_6O_8$	Phenolic	[23,29]
19	Eugenol	Leaves	$C_{10}H_{12}O_2$	Triterpenoid	[24]
20	Gallic acid	Leaves and Flowers	$C_7H_6O_5$	Phenolic	[20,22]
21	Gemin D	Flower	$C_{27}H_{22}O_{18}$	Tannin	[26]
22	Geraniol	Leaves	$C_{10}H_{18}O$	Triterpenoid	[24]
23	Geranyl acetate	Leaves	$C_{12}H_{20}O_2$	Triterpenoid	[24]
24	Germacrene-D	Leaves	$C_{15}H_{24}$	Triterpenoid	[19,21]
25	Glucogallin	Callus cells	$C_{13}H_{16}O_{10}$	Phenolic	[30]
26	Hecogenin	Flower	$C_{27}H_{42}O_4$	Steroid	[23]
27	Heterophylliin A	Flower	$C_{34}H_{26}O_{22}$	Tannin	[26]
28	Isocarveol	Leaves	$C_{10}H_{16}O$	Triterpenoid	[24]
29	Isoschimawalin A	Flower	$C_{55}H_{34}O_{35}$	Tannin	[27]
30	Juglalin/ Kaempferol 3-O-arabinoside	Flower	$C_{20}H_{18}O_{10}$	Glycoside	[28]
31	Kaempferol	Flower	$C_{15}H_{10}O_6$	Flavonoid	[22]
32	Kaempferol 3-O-(6″-galloyl)-ß-d-glucopyranoside	Flower	$C_{21}H_{20}O_{11}$	Glycoside	[28]
33	Lawsone	Leaves	$C_{10}H_6O_3$	Naphthoquinone	[18]
34	Linalool	Leaves	$C_{10}H_{18}O$	Triterpenoid	[24]
35	Lupeol	Leaves	$C_{30}H_{50}O$	Triterpenoid	[20]
36	Methyl 3-O-methylgallate	Leaves	$C_9H_{10}O_5$	Phenolic	[20]
37	Myricetin 3-O-α-L-arabinopyranoside	Leaves	$C_{37}H_{58}O_{10}$	Glycoside	[20]
38	Myristic acid	Leaves	$C_{14}H_{28}O_2$	Fatty acid	[24]
39	Norbergenin	Stem	$C_{13}H_{14}O_9$	Glycoside	[31]
40	Octacosanol	Flower	$C_{28}H_{58}O$	Fatty alcohol	[25]
41	Oenothein B	Flower	$C_{68}H_{50}O_{44}$	Tannin	[26]

42	Oenothein-C	Flower	$C_{34}H_{24}O_{22}$	Tannin	[22,32]
43	Oleanolic acid	Leaves	$C_{30}H_{48}O_3$	Triterpenoid	[20]
44	Palmitic acid	Leaves	$C_6H_{32}O_2$	Fatty acid	[24]
45	Quercetin	Flower	$C_{15}H_{10}O_7$	Flavonoid	[22]
46	Quercetin 3-O-(6″-galloyl)-β-D-galactopyranoside	Leaves	$C_{28}H_{24}O_{16}$	Glycoside	[20]
47	Quercetin 3-O-α-L-arabinopyranoside	Leaves	$C_{26}H_{28}O_{15}$	Glycoside	[20]
48	Quercetin 3-O-β-D-xylopyranoside	Leaves	$C_{20}H_{18}O_{11}$	Glycoside	[33]
49	Tellimagrandin	Flower	$C_{34}H_{26}O_{22}$	Tannin	[26]
50	Thiogeraniol	Leaves	$C_{10}H_{18}S$	Triterpenoid	[24]
51	Thymol	Leaves	$C_{10}H_{14}O$	Triterpenoid	[24]
52	Ursolic acid	Leaves	$C_{30}H_{48}O_3$	Triterpenoid	[20]
53	Woodfordin A	Flower	$C_{75}H_{56}O_{48}$	Tannin	[26]
54	Woodfordin B	Flower	$C_{75}H_{54}O_{48}$	Tannin	[26]
55	Woodfordin C/Woodfruticosin	Flower and Leaves	$C_{75}H_{52}O_{48}$	Tannin	[26,33]
56	Woodfordin D	Flower	$C_{109}H_{76}O_{70}$	Tannin	[32]
57	Woodfordin E	Flower	$C_{75}H_{56}O_{48}$	Tannin	[27]
58	Woodfordin F	Flower		Tannin	[27]
59	Woodfordin G	Flower		Tannin	[27]
60	Woodfordin H	Flower		Tannin	[27]
61	Woodfordin I	Flower	$C_{75}H_{52}O_{49}$	Tannin	[27]

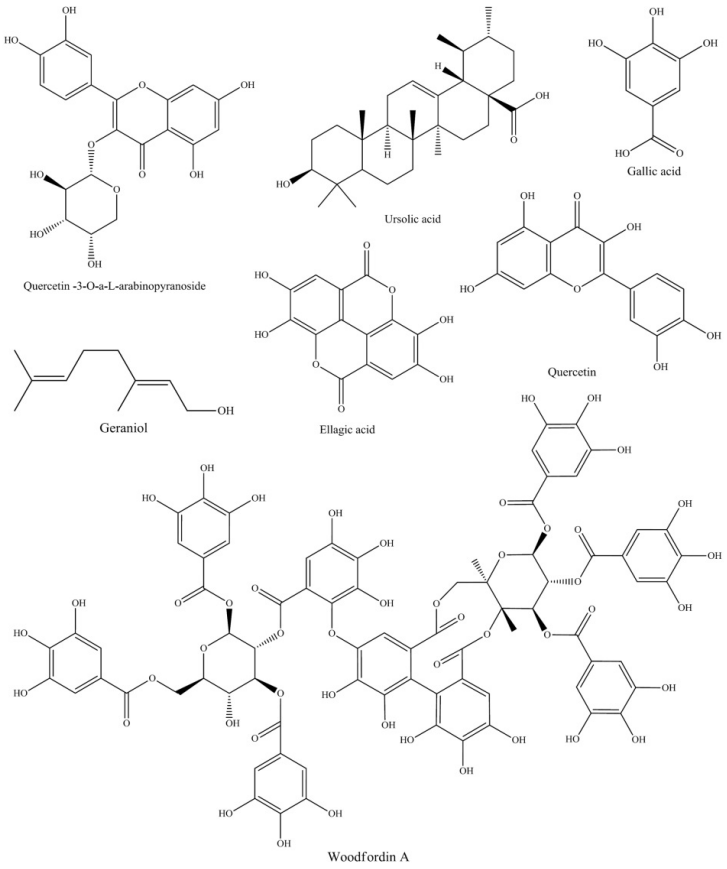

Fig. 1: Chemical structure of some main chemical constituents of *W. fruticosa*

PHARMACOLOGICAL ACTIVITIES

Anti-hyperglycemic activity:

Hyperglycemia is a condition that arises due to a metabolic disorder, in which the glucose level in the blood becomes high due to several reasons like insulin resistance, damage of β cells of the pancreas, etc. Drugs that help bring down the glucose level to the normal range are known as antihyperglycemic drugs[34]. The α-amylase inhibitory activity done by Tayab *et al.*[35] observed that the n-hexane Fraction of the Methanolic Extract of *W. fruticosa* leaves (NHFMEW) showed a significant α-amylase inhibitory effect as compared to acarbose by evaluating their IC_{50} values. The IC_{50} was 156.32±1.32 µg/ml and 103.77±1.02 µg/ml for NHFMEW and Acarbose, respectively. This suggests the extract of the plant contains a bioactive component that is responsible for the antihyperglycemic activity[35]. In another study, diabetes was induced in rats with streptozotocin-nicotinamide which was then treated with methanolic extract of *W. fruticosa* in doses of 100, 200, and 400 mg/kg body weight. It was found that extract help in the recovery of β cell of the pancreas and alters the Glucose Transporter (GLUT) proteins expression of GLUT-2 and GLUT-4, which help regulate normal glucose level in the blood by translocating insulin[36]. In another study, the flower extract of *W. fruticosa* was given orally in different doses with or without glyburide to the alloxan-induced diabetic mice and normal mice. The extract showed the dose-dependent results for the antihyperglycemic effect and also showed synergistic effect with glyburide[37]. Another study showed the antidiabetic effect of ethanolic extract of the *W. fruticosa* leaves against dexamethasone-induced insulin resistance diabetes in mice. The results showed that the extract at doses 100, 200, and 400 mg/kg body weight was significantly ($p<0.01$) effective after 22 d of treatment, thus supporting the traditional claim of the plant in the treatment of diabetes and also it can be a future effective medicine for the treatment of diabetes[38]. Anti-hyperglycemic activity of ethanolic extract of *W. fruticosa* flower was studied against the streptozotocin-induced diabetic rat model. Results depicted that after 21 d of treatment with the extract (250 and 500 mg/kg body weight) significantly decreased fasting blood glucose levels and improved insulin levels. In diabetic rats treated with ethanolic extract, the levels of glycolytic enzymes increased significantly, while the levels of gluconeogenic enzymes decreased significantly. The extract also decreased lipid peroxidation by significantly raising catalase, superoxide dismutase, glutathione reductase and glutathione peroxidase activities. So, it can be concluded that *W. fruticosa* has a potential antihyperglycemic effect by controlling glucose homeostasis and antioxidant efficacy[39].

Anti-depressant activity:

Depression is a mental health disorder characterized by a consistently depressed mood or a loss of interest in activities, resulting in considerable impairment of daily life. A study was performed to evaluate the antidepressant activity of NHFMEW and Ethyl Acetate Fraction of the Methanolic Extract of *W. fruticosa* leaves (EAFMEW) using animal models, namely Tail Suspension Test (TST) and Forced Swimming Test (FST). Results depicted that mice treated with NHFMEWF or EAFMEWF at doses of 100 mg/kg or 200 mg/kg body weight exhibited active behaviours (swimming and struggling) by reducing immobility behaviours in a dose-dependent way in both of the models. At a dose of 200 mg/kg, EAFMEWF had a considerable antidepressant-like effect in both models, which was found to reduce the duration of the depression-like state (immobile behaviour) by more than 50 % (*vs.* control group) and was equivalent to the positive control (fluoxetine-treated) group. So, the results concluded that both fractions were proven to have a substantial influence on depressive-like behaviours in mice at the higher dose[35]. Another study was performed to explore the antidepressant activity of fresh flower extract of *W. fruticosa* using behavioural screening models (FST and TST). The extract was given twice a day for 14 d. Results showed a significant reduction of immobility in both the tests after 1 h of the last oral dose[40].

Anti-inflammatory activity:

Inflammation is the multi-step process that occurs due to the entry of harmful substances from outside, i.e. microbes (bacteria, viruses, etc.) or injuries that cause redness, swelling, heat and pain[41]. The methanolic extract of *W. fruticosa* flowers shows effective anti-inflammatory activity in the model of histamine, carrageenan, dextran, formaldehyde and serotonin-induced rat paw oedema with a dose of 400 mg/kg and 600 mg/kg body weight. The results of the experiment showed significantly ($p<0.05$) decreased volume of paw oedema in all models by methanolic flower extract[42]. Carrageenan and egg albumin induced inflammation were treated with different extracts of *W. fruticosa* flower, and it was found there is a decrement in the rat paw oedema of 32.46 %, 9.38 %, 26.75 %

in carrageenan-induced rat paw oedema and 32.73 %, 29.83 %, 26.75 % in egg albumin-induced rat paw oedema with respect to methanol, ethyl acetate and hydroalcoholic extract of the plant at a dose of 200 mg/kg body weight[43].

Anti-cancer activity:

Ethanolic extract of *W. fruticosa* flowers has been shown to possess anticancer properties in the human liver's PLC/PRF/5 cell line. Serum parameters, liver histopathology and immunohistochemical analysis of vascular endothelial growth factors were used to assess the extract's impact. In this analysis, the MTT assay was used to determine cell viability. According to the analysis, the synergistic effect of the phytomolecules present in the extract may be responsible for the extract's potential chemoprevention property. This research provided a possible base for the use of *W. fruticosa* flowers in the prevention of hepatic cancer[44].

Wound healing activity:

The activity of rebuilding the skin and other delicate tissues which are injured is known as a wound healing activity. This activity occurs in a few steps of injury, inflammatory response; cells underneath the dermis start to build collagen, which is followed by regeneration of epithelial tissue[45]. Different wound healing models (incision, dead space, and excision) were evaluated in rats and were treated with ethanolic extract of *W. fruticosa* flower by oral administration of 250 and 500 mg/kg body weight. The result shows dose-dependent decrement of scar area and period of epithelization. Using Enzyme-Linked Immunosorbent Assay (ELISA), the induction of proinflammatory (Interleukin (IL-6) and Tumour Necrosis Factor-α) and anti-inflammatory (IL-10) cytokines were evaluated[46]. The *W. fruticosa* nano-gold particles (WfAuNPs) were prepared biogenically and gel formulation WfAuNPs-Carbopol® 934 was examined in a Wistar albino rat with an excision wound model. Results showed quick accumulation of collagen fibrils, formation of granular tissue, and rejuvenation of epithelial lining leading to fast healing and closures of wounds as compared to the standard drug (5 % Povidone iodine) and control. So, the result concluded that topical application of WfAuNPs-Carbopol® 934 is an effective and easy method to heal wounds and prevents scar formation[47].

Hepatoprotective activity:

The liver plays the typical role of maintaining the metabolic balance of the body, such as the discharge of numerous endogenous and exogenous mixtures, drugs, biotransformation and detoxification. The ability to restore the liver's damage and function is known as the hepatoprotective effect[48]. A study was performed to validate the hepatoprotective activity of *W. fruticosa* flowers against carbon tetrachloride (CCl_4) induced hepatotoxicity in mice. The results showed that the aqueous extract of flowers of this plant was significantly effective in restoring the damaged hepatocyte cell and serum transaminases, lipid peroxidation, glutathione, alkaline phosphatase triglycerides and bilirubin levels. The aqueous extract was found to be safe up to 2 g/kg body weight in mice. So, the results confirmed that the aqueous extract of *W. fruticosa* flowers significantly restores physiological parameters of hepatocytes to normal[49]. In another study, *W. fruticosa* flower extract was used to treat rats' diclofenac sodium, sodium-induced liver toxicity. The result showed that the extract decreases the Alanine Aminotransferase (ALT), Blood Urea Nitrogen (BUN), Alkaline Phosphatase (ALP) and Aspartate Aminotransferase (AST) to the normal level and increased total protein, albumin, etc, ultimately extract help in decreasing the rate of liver toxicity occurred by diclofenac sodium[50]. Another study shows that methanolic extract (400 and 600 mg/kg body weight) of *W. fruticosa* flower can reduce acetaminophen-induced hepatic toxicity in rats by inhibiting liver total protein depletion and restoring levels of serum marker enzymes, biochemical parameters, and reduced Glutathione (GSH)[51]. Nitha *et al.*[52] have performed a study to evaluate the preventive and therapeutic role of methanolic extract of *W. fruticosa* flowers on thioacetamide-induced oxidative stress in rats. According to the results, extract significantly ($p<0.05$) reduced and reversed serum biochemical parameters and liver Malondialdehyde (MDA) levels and increased the other liver antioxidant parameters. The histopathological study also depicted that the extract has potential hepatoprotective activity in a dose-dependent manner. Furthermore, Nitha *et al.*[53] had performed another study to evaluate the effect of methanolic extract of *W. fruticosa* flowers on carbon tetrachloride induced hepatic fibrosis. Biochemical analysis revealed a marked reduction of antioxidant status of serum (ALP, AST, LDH and ALT level), tissue lipid peroxidation, and hydroxyproline level of tissue but enhanced other tissue (GSH, GST, GPx, GR levels) parameters of liver. Histological study shows a substantial decrease in fibrotic septa development in liver tissue, and the immunohistochemical study revealed reduced expression of collagen III[53].

Anti-bacterial activity:

The antibacterial activity of a compound is the ability to destroy or inhibit the growth of bacteria without exhibiting toxicity to the surrounding cells[54]. The antibacterial activity of methanolic extract of *W. fruticosa* flowers was tested against gram-positive bacteria (*Bacillus subtilis* and *Micrococcus flavus*) and gram-negative bacteria (*Pseudomonas pseudoalcaligenes*) at two different doses in the agar well diffusion method, where the standard drugs ciprofloxacin and amoxicillin were used. It was observed that the methanolic extract was more effective against gram-negative bacteria than gram-positive bacteria[55]. Chougale *et al.*[56] performed a study, antibacterial activity was measured by the different fractions of *W. fruticosa*, i.e., petroleum ether, chloroform, diethyl ether and acetone fraction against *Escherichia coli* NCIM 2065, *Bacillus subtilis* NCIM 2921, *Staphylococcus aureus* NCIM 5022 and *Pseudomonas aeruginosa* NCIM 5029. The result showed that acetone extract was most effective against *Bacillus subtilis* NCIM 2921, although all extracts have antibacterial activity as they have a zone of inhibition against the above bacteria. Another study was performed to determine the antimicrobial activity of different fractions of methanolic extract of *W. fruticosa* leaves against multi drug resistant bacteria and host toxicity of the extracts was measured using cultured lymphocytes from human umbilical cord blood. Results showed that n-butanol fraction of methanolic extract of *W. fruticosa* leaves has a better minimum inhibitory concentration (<1.89 mg/ml extract) and minimum bactericidal concentration (9.63 mg/ml extract) against selected bacteria. Results also depicted that the extract has no host toxicity as revealed in human lymphocytes[24].

Antioxidant activity:

The disproportion between the cellular uptakes of Reactive Oxygen Species (ROS) and cellular production leads to oxidative stress, which causes damage to the various cell, DNA, protein or lipid of the human body and causes diseases like diabetes, heart disease and cancer, etc. Antioxidants have the potency to prevent the cells' apoptosis or necrosis from oxidative stress[57]. Extract of the different parts of the *W. fruticosa*, i.e. bark, flowers and leaves, were prepared from ethanol, distilled water and methanol by Chaturvedi *et al.*[58]. It was found that methanolic extract of bark shows effective radical scavenging activity compared to ethanolic and distilled water extract, with the value of radical scavenging for methanol, ethanol and distilled water was 96.52±0.02 %, 57.80±0.2 %, and 86.52±0.03 % respectively[58]. Another study was performed to determine the antioxidant activity of the methanolic extract of *W. fruticosa* leaves and its n-hexane and ethyl acetate fraction by using 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay. Results depicted that the methanolic extract shows the strongest antioxidant activity (IC_{50}=1.86±0.16 µg/ml) in DPPH radical scavenging assay[35].

Anti-enteroviral activity:

Enterovirus 71 (EV71) is a positive, small single-stranded RNA virus from the Enterovirus genus belonging to the Picornaviridae family. In children and infants, it causes severe infection in the hand, mouth and foot[59]. The compounds having activity against enterovirus are known to exhibit anti-enteroviral activity. Choi *et al.*[60] reported that the extract of *W. fruticosa* flowers and isolated gallic acid were evaluated for anti-enteroviral activity. The gallic acid isolated from flower extract is effective anti-EV71 compared to the flower extract of *W. fruticosa*.

Gastroprotective activity:

Peptic ulcer is a disease that causes damage to the submucosal epithelium due to the breakdown of the mucosal layer. The ulcer is caused mainly due to *Helicobacter pylori* (*H. pylori*) bacteria or the acid of the stomach[61]. An agent which protects the mucosal layer damage as well as inhibits the excess acid secretion is known to have gastroprotective activity. Khan *et al.*[22] investigated that the hydroalcoholic extract of *W. fruticosa* flower was shown to have effective gastroprotective activity by inhibiting the *H. pylori* bacterial infection in a gastric ulcer model at 31.25-62.5 mg/kg body weight. In another study, ulcer was induced in Wistar albino rats with ethanol which was treated with aqueous extract of *W. fruticosa* flower. It showed the dose-dependent reduction of ulcer by the aqueous extract at 100 mg/kg and 200 mg/kg body weight, where 200 mg/kg body weight showed significant lower ulcer index and higher percentage protection and was more effective than the standard drug omeprazole. The presence of ellagic acid in the *W. fruticosa* flower, as confirmed by high-performance liquid chromatography and high-performance thin-layer chromatography was considered to be responsible for this gastroprotective activity[29].

Antifertility activity:

Antifertility compound has the tendency to stop the

fertilization process by preventing implantation, ovulation, zygote formation or causes abortion in females, while in the male, it inhibits testosterone, spermatogenesis or sperm mortality[62]. Antifertility activity of alcoholic, aqueous and hydroalcoholic extract from the flower of *W. fruticosa* was observed in the albino rat. It was found that alcoholic extract exhibited abortifacient activity at a dose of 100 mg/kg body weight rat compared to other extracts, i.e. hydroalcoholic and aqueous[63].

Prebiotic activity:

The effect of *W. fruticosa* extract was evaluated on two lactic acid bacteria *Lacticaseibacillus casei* and *Lacticaseibacillus rhamnosus*, showing prebiotic-like characteristics. Administration of *W. fruticosa* at 0.5 mg/ml and 1 mg/ml stimulated probiotic growth ($p<0.05$), improved adhesion to Caco2 cells ($p<0.05$) while preventing foodborne pathogens *Escherichia coli* and *Staphylococcus aureus* ($p<0.05$). The comprehensive metabolomic studies attributed variation in metabolite pool in response to *W. fruticosa* supplementation. So, *W. fruticosa*, with potential prebiotic properties, can be utilized in the development of novel products focusing on gut microbial regulation to improve health[64].

Analgesic activity:

Certain compounds tend to activate the opioid receptor of the central nervous system by blocking the activity of nociceptors, leading to producing analgesic activity[65]. Analgesic activity of methanol extract of *W. fruticosa* flowers was evaluated against formaldehyde induced paw licking response in rats. Results showed nociceptive reaction of the extract in a dose-dependent manner[42]. The models of nociception were used: Acetic acid induced writhing test and hot plate method for the observation of the analgesic activity of *W. fruticosa* bark extract, which is prepared in petroleum ether, chloroform ethanol and aqueous. It was found that the dose of 200 mg/kg body weight shows analgesic activity by both alcoholic and aqueous extract, but the alcoholic effect was a little stronger[66].

Antipsoriatic activity:

Psoriasis is a chronic inflammatory skin condition caused by the immune system. It is a non-communicable disease that arises due to the hyperplasia of keratinocytes in the skin. Antipsoriatic behavior of ethanolic extract of *W. fruticosa* flowers was studied by using a novel *in vivo* screening model. Psoriasis was induced in Swiss albino mice by applying 0.1 ml of Complete Freund's Adjuvant (CFA) and formaldehyde mixture (1:10) to the dorsum surface of their skin for 7 d. Subsequently, animals were treated with 0.05 % and 0.1 % (w/w) ointments of the extract once daily for 3 w. The severity of psoriatic lesions (redness, erythema, and scales) was reduced ($p<0.05$), and epidermal thickness was decreased in animals treated with the ointment from 7th d to 21st d[67]. Another study showed that gold nanoparticles of ethanolic extract of *W. fruticosa* flower could alleviate psoriasis skin inflammation in mice induced by topical application of imiquimod (IMQ) (5% w/w) for 11 successive d. Treatment with carbopol ointment gel of *W. fruticosa* gold nanoparticle (1 %) radically exerts a positive therapeutic effect on skin inflammation and serum cytokines levels which results in the improvement of psoriatic symptoms and disease activity index score (5.28±0.19) from the 4th d of treatment schedule, which was observed to be consistent till the 12th d (0.63±0.08) [23]. As a result of this research, it was discovered that *W. fruticosa* flowers have antipsoriatic activity and can be used to treat psoriasis.

Immunostimulatory activity:

Ethanolic extract of *W. fruticosa* flowers was evaluated for immunostimulatory activity on both *in vitro* as well as *in vivo* non-specific immune responses in mice. For this study, Shah *et al.*[68] conducted *in vitro* Sulforhodamine B (SRB) assay on isolated murine peritoneal macrophages to know phagocytosis and proliferation of isolated murine bone marrow cells. The *in vitro* study was supported by *in vivo* study to explore the potential of the extract on phagocytic activity of macrophages by carbon clearance test performed on experimental mice and bone marrow cells by cyclophosphamide-induced myelosuppression. By activating macrophages and bone marrow cells, the extract activates non-specific immune responses. So, the ethanol extract of *W. fruticosa* flowers could be used as a complementary therapeutic agent and as a potential immunostimulant against cytotoxic drugs[68].

Anti-asthmatic activity:

Asthma is characterized by chronic inflammation of the airways, causes bronchoconstriction and may increase mucus secretion. Ethyl acetate, acetone, methanol and hydro-alcohol extracts of *W. fruticosa* flowers were tested for anti-asthmatic activity against 2 % acetylcholine and 0.1 % histamine induced bronchospasm in guinea pigs. According to the results, the methanolic extract showed maximum bronchoprotection (48.83 %) and bronchorelaxation (100 %) at the dose of 200 mg/kg

body weight[43]. Similarly, another study was performed by Srivastava *et al.*[69], to determine the anti-asthmatic potential of ethanolic extract of aerial part of *W. fruticosa* against screening models for Cough Variant Asthma (CVA) in albino guinea pigs. The anti-asthmatic effect of the extract was evaluated against *in vivo* citric acid (0.1 g/ml) induced anti-tussive evaluation and *in vivo* aerosol (2 % acetylcholine and 0.1 % histamine) induced CVA. Results confirmed that ethanolic extract has significantly decreased the average cough frequency (4.83±0.30) compared to control. At 200 mg/kg, extract against aerosol-induced CVA was found to have a substantial bronchoprotective effect of 41.75 % and a reduction in the number of coughs (7.16±0.47) compared to control (14.16±0.60). As a result, it can be concluded that ethanolic extract of *W. fruticosa* had bronchoprotective and anti-tussive effects against aerosol-induced CVA at a dose of 200 mg/kg.

W. fruticosa IN AYURVEDIC FORMULATIONS

Ayurveda is the world's oldest system of medicine, focused on the use of plants (or herbs) for the preparation of medicines. Traditionally flowers of *W. fruticosa* were used in the preparation of ayurvedic formulations 'asavas' and 'arishthas' by fermentation[10]. Manwar *et al.*[70] studied the role of *W. fruticosa* flowers in the preparation of Ayurvedic formulations. They isolated 24 yeast strains from the *W. fruticosa* flower, out of which four have alcohol producing ability in the presence of sugar in jaggery. They also revealed *Saccharomycopsis fibuligera* as the most effective among all yeast strains present in the *W. fruticosa* flower[70]. Ashvagandharishta is a well-known ayurvedic polyherbal formulation widely used as a health tonic, prepared by the fermentation process. A consortium of yeasts derived from *W. fruticosa* flowers produced Ashvagandharishta with satisfactory organoleptic qualities. It also showed effective hepatoprotective activity against CCl_4 induced hepatotoxicity in the rat model. Hepatoprotective activity of Ashvagandharishta was primarily achieved by preventing oxidative damage. The upregulation of the CAT and GPx genes, as well as the downregulation of the proinflammatory IL6 gene, has been identified as a probable mechanism of action[71]. Another ayurvedic formulation, 'Arjunāriṣṭa' contains *Terminalia arjuna* as the major constituent and is prepared by the fermentation process using microorganisms isolated from the *W. fruticosa* flowers[72]. A study confirmed the anti-inflammatory effects of Arjunāriṣṭa by reducing oxidative stress, proinflammatory cytokines and chemokines. It also helped animals with colitis by changing the composition of their gut microbiota[73].

'Kanakasava' is a polyherbal Ayurvedic formulation used to treat pulmonary disorders such as coughing, breathing difficulties and asthma. It contains Datura (*Datura metel*), Vasaca (*Adhatoda vasica*), Dhataki (*W. fruiticosa*) and Grape (*Vitis vinifera*) extracts as main constituents. A study was performed to evaluate the role of Kanakasava against ovalbumin-induced bronchial asthma and related airway inflammation in rats. Results depicted that Kanakasava treatment significantly ($p<0.01$) reduced increased IgE, cytokines, nitrites and eosinophil and neutrophil influx in blood and broncheo-alveolar lavaged fluid. The significant improvement in lung functioning ($p<0.01$) and reduction of mast cell degranulation ($p<0.01$) support these outcomes. So, the results confirm the potential of Kanakasava in airway disorders such as bronchial asthma[74]. Another study was performed to evaluate the wound healing activity of an Ayurvedic polyherbal formulation containing *W. fruticosa* by using excision and incision wound animal models. Results showed ample reduction of wounds (99.82±0.10 %) in experimental animals after treatment with the formulation[75].

CONCLUSION AND FUTURE PERSPECTIVE

Scientists are constantly looking into natural products because the conventional medical system utilizes synthetic compounds with one or more adverse effects. *W. fruticosa* is an effective traditional medicine which has been used since ancient times for the treatment of various types of disorders. The present review reported the data related to traditional uses, phytochemical constituents, and pharmacological activities of *W. fruticosa*. According to the reported data, the majority of the research was done on extracts of different parts of the plant, especially the flowers, which showed a wide range of pharmacological activities. Different pharmacological activities of *W. fruticosa* graphically represented in fig. 2. However, the molecular mechanism needs to be elucidated for their specific pharmacological activities. This article report over 60 substances isolated or identified from various parts of *W. fruticosa*. Phytochemical studies confirmed that most chemical constituents belong to tannins, flavonoids, alkaloids, glycosides, sterols and triterpenoids. Amongst these identified phytochemicals, only a few exhibit significant pharmacological effects. Though a lot of research work has been done on *W. fruticosa* extracts, isolated phytochemicals are still unexplored, which can have a potent role in drug development.

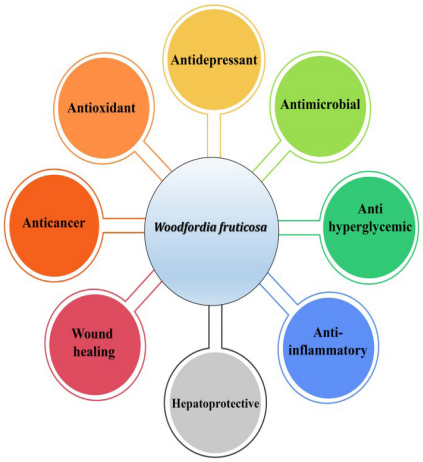

Fig. 2: Graphical representation of pharmacological activities of *W. fruticosa*

Bioassay-guided isolation may be used in the future to discover the key bioactive chemicals responsible for pharmacological effects. Although *W. fruticosa* has a wide range of medicinal and traditional applications, there is still a scarcity of information on the exact mechanisms underlying the pharmacological activities. Therefore, extensive research on different types of phytochemicals obtained from this plant is required to determine their exact target sites, structure-activity relationships, pharmacological activities and mechanism of action for the development of safe and effective herbal drugs for better management of different diseases.

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Conflicts of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Kumar D, Sharma M, Sorout A, Saroha K, Verma S. *Woodfordia fruticosa* Kurz.: A review on its botany, chemistry and biological activities. J pharmacognosy Phytochem 2016;5(3):293-98.
2. Vickers A, Zollman C, Lee R. Herbal medicine. West J Med 2001;175(2):125-8.
3. Baravalia Y, Nagani K, Chanda S. Evaluation of pharmacognostic and physicochemical parameters of *Woodfordia fruticosa* Kurz. flowers. Pharmacogn J 2011;2(18):13-8.
4. Khare CP. Indian medicinal plants: An illustrated dictionary. Springer Science & Business Media; 2008.
5. Oudhia P. Interaction with the herb collectors of Gandai Region, Chhatisgarh, MP, India; 2003.
6. Khare CP. Indian herbal remedies: Rational Western therapy, ayurvedic, and other traditional usage, Botany. Springer science & business media; 2004.
7. Shome U, Mehrotra S, Sharma HP. Pharmacognostic studies on the flower of *Woodfordia fruticosa* Kurz. Proceedings: Plant Sciences 1981;90(4):335-51.
8. Kirtikar KR. Indian Medicinal Plants, Vol. 2. Lalit Mohan Basu, Allahabad, India; 1935:1074-76.
9. Bhattarai S, Bhuju DR. Medicinal usefulness of *Woodfordia fruticosa* (Linn.) Kurz. of Nepal. Ethnomedicinal plants: Revitalization of traditional knowledge of herbs. Science Publishers New York: CRC press; 2011. p. 253-68.
10. Atal CK, Bhatia AK, Singh RP. Role of *Woodfordia fruticosa* Kurz (Dhataki) in the preparation of Asavas and Arishtas. J Res Ayurved Sidd 1982;3:193-9.
11. Murad W, Ahmad A, Gilani SA, Khan MA. Indigenous knowledge and folk use of medicinal plants by the tribal communities of Hazar Nao Forest, Malakand District, North Pakistan. J Med Plant Res 2011;5(7):1072-86.
12. Wayal SR, Gurav SS. Pharmacognostic and phytochemical investigation of potentially important plants of Western Ghats, India. Int J Pharm Sci Res 2019;10(6):3101-8.
13. Mohapatra SP, Sahoo HP. Some lesser known medicinal plants of the Kondha and Gond tribes of Bolangir, Orissa, India. Ethnobotanical leaflets 2008;2008(1):1003-6.
14. The Ayurvedic Pharmacopoeia. Ayurvedic Pharmacopoeia India Part-I. Government of India, 2013.
15. Jeyaprakash K, Ayyanar M, Geetha KN, Sekar T. Traditional uses of medicinal plants among the tribal people in Theni District (Western Ghats), Southern India. Asian Pac J Trop Biomed 2011;1(1):S20-5.
16. Rani S, Rahman K, Younis M, Basar SN. Dhawa (*Woodfordia fruticosa* (L.) Kurz.): A versatile medicinal plant. Int J Pharm Sci Drug Res 2015;7(4):315-20.
17. Bernhoft A. A brief review on bioactive compounds in plants. Bioactive compounds in plants-benefits and risks for man and animals 2010;50:11-7.
18. Saoji AG, Saoji AN, Deshmukh VK. Presence of Lawsone in *Ammania bacciferra* Linn. and *Woodfordia fruticosa* Salisb. Curr Sci 1972;41(5):192.
19. Kaur R, Kaur H. The Antimicrobial activity of essential oil and plant extracts of *Woodfordia fruticosa*. Arch Appl Sci Res 2010;2(1):302-9.
20. Dan S, Dan SS. Chemical examination of the leaves of *Woodfordia fruticosa*. J Ind Chem Soc 1984;61(8):726-7.
21. Joshi M, Kaur S, Verma M, Mishra T. Analysis of antimicrobial activity of *Woodfordia fruticosa*, *Adhatoda vasica* and *Ricinus communis* against multi-drug resistant bacteria. Res J Pharm Tech 2019;12(6):2987-94.
22. Khan IA, Singh A, Mindala DP, Meena S, Vij B, Yadav AK, *et al.* Preclinical development of gastro-protective botanical candidate from *Woodfordia fruticosa* (Linn.) Kurz: Chemical standardization, efficacy, pharmacokinetics and safety pharmacology. J Ethnopharmacol 2019;241:112023.
23. Raghuwanshi N, Yadav TC, Srivastava AK, Raj U, Varadwaj P, Pruthi V. Structure-based drug designing and identification of *Woodfordia fruticosa* inhibitors targeted against heat shock protein (HSP70-1) as suppressor for Imiquimod-induced psoriasis like skin inflammation in mice model. Mater Sci Eng C Mater Biol Appl 2019;95:57-71.
24. Dubey D, Patnaik R, Ghosh G, Padhy RN. *In vitro* antibacterial activity, gas chromatography–mass spectrometry analysis of *Woodfordia fruticosa* Kurz. leaf extract and host toxicity testing with *in vitro* cultured lymphocytes from human umbilical cord blood. Osong Public Health Res Perspect 2014;5(5):298-312.

25. Chauhan JS, Srivastava SK. Phytochemical investigation of the flowers of *Woodfordia fruticosa*. Planta Med 1979;36(06):183-4.
26. Yoshida T, Chou T, Nitta A, Miyamoto K, Koshiura R, Okuda T. Woodfordin C, a macro-ring hydrolyzable tannin dimer with antitumor activity, and accompanying dimers from *Woodfordia fruticosa* flowers. Chem Pharm Bull 1990;38(5):1211-7.
27. Yoshida T, Chou T, Nitta A, Okuda T. Tannins and related polyphenols of Lythraceous plants. III. Hydrolyzable tannin oligomers with macrocyclic structures, and accompanying tannins from *Woodfordia fruticosa* Kurz. Chem Pharm Bull 1992;40(8):2023-30.
28. Lee YE, Kodama T, Win NN, Ki DW, Hoang NN, Wong CP, *et al.* Flavonoids from *Woodfordia fruticosa* as potential SmltD inhibitors in the alternative biosynthetic pathway of peptidoglycan. Bioorg Med Chem Lett 2021;36:127787.
29. Syed YH, Khan M. Chromatographic profiling of ellagic acid in *Woodfordia fruticosa* flowers and their gastroprotective potential in ethanol-induced ulcers in rats. Pharmacogn Res 2016;8(Suppl 1):S5-11.
30. Chalageri G, Dhananjaya SP, Raghavendra P, Kumar LS, Babu UV, Varma SR. Substituting plant vegetative parts with callus cell extracts: Case study with *Woodfordia fruticosa* Kurz.–A potent ingredient in skin care formulations. S Afr J Bot 2019;123:351-60.
31. Kalidhar SB, Parthasarathy MR, Sharma P. Norbergenin, a new c-glycoside from *Woodfordia fruticosa* kurz. Indian J Chem Sect B 1981;20(8):720-1.
32. Yoshida T, Chou T, Matsuda M, Yasuhara T, Yazaki K, Hatano T, *et al.* Woodfordin D and oenothein A, trimeric hydrolyzable tannins of macro-ring structure with anti-tumor activity. Chem Pharm Bull 1991;39(5):1157-62.
33. Kadota S, Takamori Y, Nyein KN, Kikuchi T, Tanaka K, Ekimoto H. Constituents of the leaves of *Woodfordia fruticosa* Kurz. I: Isolation, structure and proton and carbon-13 nuclear magnetic resonance signal assignments of Woodfruticosin (Woodfordin C), an inhibitor of deoxyribonucleic acid topoisomerase II. Chem Pharm Bull 1990;38:2687-97.
34. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet 2017;389(10085):2239-51.
35. Tayab MA, Chowdhury KA, Jabed M, Mohammed Tareq S, Kamal AM, Islam MN, *et al.* Antioxidant-rich *Woodfordia fruticosa* leaf extract alleviates depressive-like behaviors and impede hyperglycemia. Plants 2021;10(2):287.
36. Arya A, Al-Obaidi MM, Karim RB, Taha H, Khan AK, Shahid N, *et al.* Extract of *Woodfordia fruticosa* flowers ameliorates hyperglycemia, oxidative stress and improves β-cell function in streptozotocin–nicotinamide induced diabetic rats. J Ethnopharmacol 2015;175:229-40.
37. Bhatia A, Khera N. Hypoglycaemic activity of orally administered *Woodfordia fruticosa* flower extract in alloxan-induced diabetic mice. Int J Life Sci Biolechnol Pharm Res 2013;2:2250-3137.
38. Bhujbal SS, Providencia CA, Nanda RK, Hadawale SS, Yeola RR. Effect of *Woodfordia fruticosa* on dexamethasone induced insulin resistance in mice. Rev Bras Farmacogn 2012;22:611-6.
39. Verma N, Amresh G, Sahu PK, Rao CV, Singh AP. Antihyperglycemic activity of *Woodfordia fruticosa* (Kurz) flowers extracts in glucose metabolism and lipid peroxidation in streptozotocin-induced diabetic rats. Indian J Exp Biol 2012;50:351-58.
40. Sareetha AV, YP SP. Repeated oral administration of ethanolic extract of *Woodfordia fruticosa* (L.) Kurz. flowers against the animal models of depression. Natl J Physiol Pharm Pharmacol 2021;11(5):490-4.
41. Medzhitov R. Origin and physiological roles of inflammation. Nature 2008;454(7203):428-35.
42. Baravalia Y, Vaghasiya Y, Chanda S. Brine shrimp cytotoxicity, anti-inflammatory and analgesic properties of *Woodfordia fruticosa* Kurz flowers. Iran J Pharm Res 2012;11:851.
43. Hiralal Ghante M, Bhusari KP, Duragkar NJ, Ghiware NB. Pharmacological evaluation for anti-asthmatic and anti-inflammatory potential of *Woodfordia fruticosa* flower extracts. Pharm Biol 2014;52(7):804-13.
44. Nitha A, Prabha SP, Ansil PN, Latha MS. Antiproliferative effect of *Woodfordia fruticosa* Kurz flowers on experimentally induced hepatocellular carcinoma in rats and in human hepatoma cell line. J Pharm Res 2013;6(2):239-48.
45. Garg VK, Paliwal SK. Wound-healing activity of ethanolic and aqueous extracts of *Ficus benghalensis*. J Adv Pharm Technol Res 2011;2(2):110.
46. Verma N, Amresh G, Sahu PK, Mishra N, Rao CV, Singh AP. Wound healing potential of flowers extracts of *Woodfordia fruticosa* Kurz. Indian J Biochem Biophys 2013;50:296-304.
47. Raghuwanshi N, Kumari P, Srivastava AK, Vashisth P, Yadav TC, Prasad R, *et al.* Synergistic effects of *Woodfordia fruticosa* gold nanoparticles in preventing microbial adhesion and accelerating wound healing in Wistar albino rats *in vivo*. Mater Sci Eng C Mater Biol Appl 2017;80:252-62.
48. Lahon K, Das S. Hepatoprotective activity of *Ocimum sanctum* alcoholic leaf extract against paracetamol-induced liver damage in Albino rats. Pharmacogn Res 2011;3(1):13.
49. Chandan BK, Saxena AK, Shukla S, Sharma N, Gupta DK, Singh K, *et al.* Hepatoprotective activity of *Woodfordia fruticosa* Kurz flowers against carbon tetrachloride induced hepatotoxicity. J Ethnopharmacol 2008;119(2):218-24.
50. Baravalia Y, Vaghasiya Y, Chanda S. Hepatoprotective effect of *Woodfordia fruticosa* Kurz flowers on diclofenac sodium induced liver toxicity in rats. Asian Pac J Trop Med 2011;4(5):342-6.
51. Baravalia Y, Chanda S. Protective effect of *Woodfordia fruticosa* flowers against acetaminophen-induced hepatic toxicity in rats. Pharm Biol 2011;49(8):826-32.
52. Nitha A, Ansil PN, Prabha SP, Wills PJ, Latha MS. Preventive and curative effect of *Woodfordia fruticosa* Kurz flowers on thioacetamide induced oxidative stress in rats. Asian Pacific Journal of Tropical Biomedicine 2012;2(2):S757-64.
53. Nitha A, Prabha SP, Ansil PN, Latha MS. Methanolic extract of *Woodfordia fruticosa* Kurz flowers ameliorates carbon tetrachloride-induced chronic hepatic fibrosis in rats. Toxicol Ind Health 2016;32(7):1224-36.
54. Singh K, Mishra A, Sharma D, Singh K. Antiviral and antimicrobial potentiality of nano drugs. In: Applications of targeted nano drugs and delivery systems 2019 p. 343-356.
55. Parekh J, Chanda S. *In vitro* antibacterial activity of the crude methanol extract of *Woodfordia fruticosa* Kurz. flower (Lythraceae). Braz J Microbiol 2007;38:204-7.
56. Chougale AD, Padul MV, Saiful Arfeen M, Kakad SL. Antibacterial activity directed fractionation of *Woodfordia fruticosa* Kurz. leaves. J Med Plant 2009;8(31):75-81.
57. Gilgun-Sherki Y, Rosenbaum Z, Melamed E, Offen D. Antioxidant therapy in acute central nervous system injury: Current state. Pharmacol Rev 2002;54(2):271-84.
58. Chaturvedi PA, Ghatak AA, Desai NS. Evaluation of radical scavenging potential and total phenol content in *Woodfordia fruticosa* from different altitudes. J Plant Biochem Biotechnol 2012;21(1):17-22.
59. Shang L, Xu M, Yin Z. Antiviral drug discovery for the treatment of enterovirus 71 infections. Antiviral Res 2013;97:183-94.

60. Choi H, Song J, Park K, Baek S. *In vitro* anti-enterovirus 71 activity of gallic acid from *Woodfordia fruticosa* flowers. Lett Appl Microbiol 2010;50:438-40.
61. Lanas A, Chan FK. Peptic ulcer disease. Lancet 2017;390(10094):613-24.
62. Xiao PG, Wang NG. Can ethnopharmacology contribute to the development of anti-fertility drugs? J Ethnopharmacol 1991;32(1-3):167-77.
63. Khushalani H, Tatke P, Singh KK. Antifertility activity of dried flowers of *Woodfordia fruticosa* kurz. Indian J Pharm Sci 2006;68(4):528-9.
64. Shubha JR, Tripathi P, Somashekar BS, Kurrey N, Bhatt P. *Woodfordia fruticosa* extract supplementation stimulates the growth of *L. casei* and *L. rhamnosus* with adapted intracellular and extracellular metabolite pool. J Appl Microbiol 2021;131(6):2994-3007.
65. Calixto JB, Beirith A, Ferreira J, Santos AR, Filho VC, Yunes RA. Naturally occurring antinociceptive substances from plants. Phytother Res 2000;14(6):401-18.
66. Rose BN, Prasad NK. Analgesic activity of extracts of *Woodfordia fruticosa* stems bark in animal models. Indian J Biol Pharm Res 2013;4(4):175-80.
67. Srivastava AK, Nagar HK, Chandel HS, Ranawat MS. Antipsoriatic activity of ethanolic extract of *Woodfordia fruticosa* (L.) Kurz flowers in a novel *in vivo* screening model. Indian J Pharmacol 2016;48(5):531.
68. Shah AS, Juvekar AR. *In vitro* and *in vivo* immunostimulatory activity of *Woodfordia fruticosa* flowers on non-specific immunity. Pharm Biol 2010;48(9):1066-72.
69. Srivastava AK, Siddharth SA, Hemant N, Rajnish S, Gaurav S. Phytopharmacological evaluation of aerial parts of *Woodfordia fruticosa* (L.) Kurz in cough variant asthma. Pharmacogn J 2015;7(5):296-99.
70. Manwar J, Mahadik K, Paradkar A, Sathiyanarayanan L, Vohra M, Patil S. Isolation, biochemical and genetic characterizations of alcohol-producing yeasts from the flowers of *Woodfordia fruticosa*. J Young Pharm 2013;5(4):191-4.
71. Bhondave PD, Devarshi PP, Mahadik KR, Harsulkar AM. 'Ashvagandharishta'prepared using yeast consortium from *Woodfordia fruticosa* flowers exhibit hepatoprotective effect on CCl_4 induced liver damage in Wistar rats. J Ethnopharmacol 2014;151(1):183-90.
72. Randive DS, Sayyad SF, Bhinge SD, Bhutkar MA. Preparation of Arjunāriṣṭa using microbes isolated from *Woodfordia fruticosa* flowers (dhayati). Anc Sci Life 2016;36(1):42.
73. Cota D, Mishra S, Shengule S. Arjunarishta alleviates experimental colitis *via* suppressing proinflammatory cytokine expression, modulating gut microbiota and enhancing antioxidant effect. Mol Biol Rep 2020;47(9):7049-59.
74. Arora P, Ansari SH, Anjum V, Mathur R, Ahmad S. Investigation of anti-asthmatic potential of Kanakasava in ovalbumin-induced bronchial asthma and airway inflammation in rats. J Ethnopharmacol 2017;197:242-9.
75. Wayal SR, Gurav SS. Evaluation of wound healing potential of Bhallatakadi Ghrita–cow ghee based polyherbal formulation: *In vivo* excision and incision wound model. J Complement Integr Med 2021;18(3):507-15.