



Review Article

Traditional Uses, Phytochemistry, and Pharmacological Activities of *Fraxinus xanthoxyloides* (G. Don) DC. (Oleaceae): A Review

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Abstract | *Fraxinus xanthoxyloides* is a plant with several pharmacological and biological properties. It is commonly termed “Afghan ash”. It is distributed in Afghanistan, Morocco, Algeria, India, the Hindu Kush, and the Himalayan mountains of Pakistan. Building on earlier *Fraxinus*-genus reviews, the present review is the first to integrate multi-organ ethnobotanical use with a comparative phytochemical and pharmacological profile specific to *F. xanthoxyloides*, and to identify concrete gaps- dose standardization, mechanism of action, and field-scale validation- that have not been consolidated elsewhere. Different parts of *F. xanthoxyloides* are used to treat different ailments such as root bark (malaria, pneumonia and jaundice), stem bark (labor pain, internal injuries, typhoid fever, trauma, premature birth, expulsion of infant and pneumonia), stem (bone fractures and wounds in cattle), wood (bone fractures, tool handles, walking sticks, fuel, furniture), foliage (fodder), and leaves (malaria, pneumonia, jaundice, anti-inflammatory and analgesic effects). We summarize a total of 30 different compounds (coumarins, cichoriin, fraxin, pyranocoumarins, furanocoumarins, chromones, dimeric coumarins, isofraxisecoside, fraxisecoside, rutin, quercetin, gallic acid, caffeic acid, kaempferol, catechins, myricetin, nummularic acid, cisplatin, ligstroside, oleuropein, esculetin, nicotiflorin, 2-(3, 4-dihydroxy)phenylethyl-O-β-D-glucopyranoside, salidroside, osmanthuside, calceolarioside B, coniferin, syringin, 8-hydroxypinoresinol-4'-O-β-D-glucoside and 8-acetoxypinoresinol-4-O-β-D-glucoside). The proximate and elemental composition of *F. xanthoxyloides* has been reported to include organic matter, moisture, ash, crude protein, crude fiber, crude fats, and nitrogen-free extract, while elements such as phosphorus, potassium, calcium, magnesium, iron, manganese, cadmium, and zinc are also major constituents of this plant. Different studies have also reported the presence of different biological activities (anti-leishmanial, insecticidal, and cytotoxic). However, most pharmacological evidence to date is limited to in vitro and short-term *in vivo* assays, and standardized dose-response data are still lacking; these gaps are addressed explicitly in the roadmap presented here.

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Introduction

The Oleaceae family comprises dicotyledonous flowering plants widely distributed in tropical and temperate regions. Globally, it includes approximately 25 genera and nearly 688 species (Huang *et al.*, 2019). In Pakistan, eight genera and roughly 30 species are recorded, of which around 22 are cultivated (Grohmann, 1974). The distribution of this family extends to Afghanistan, India, Morocco, Algeria, and throughout the Hindu Kush and Himalayan ranges. Within Pakistan, Oleaceae representatives are commonly observed in areas such as Takht-i-Suleiman, the Toba Kakkar Range, Zhob (formerly Fort Sandeman), the western boundary of Waziristan, Safed Koh, Chitral, Malakand, Swat, Punjab, and Baluchistan, usually inhabiting temperate valleys between 1000 and 2500 meters in elevation (Ali and Nasir, 1989-1992; Ali *et al.*, 2001; Ali and Qaiser, 1993-2007 (Ijaz *et al.*, 2020), Outside South Asia, species of Oleaceae are also distributed in northeast Asia, China, North America, and parts of France (Sarfraz *et al.*, 2017).

Fraxinus is a prominent genus within the subtribe Fraxinae and shares a close evolutionary relationship with the subtribe Oleinae of the tribe Oleae (Ijaz *et al.*, 2020). The genus was initially classified by Linnaeus in 1753, who described over 450 taxa, many of which are now considered synonyms. According to the most extensive monograph available, 64 species are currently recognized as valid, although additional species have been reported (Wallander, 2008). Within the Oleaceae family, *Fraxinus* is regarded as monophyletic and is characterized by relatively large imparipinnate leaves and one-seeded samaras.

Most *Fraxinus* species are medium-to large-sized trees, but some have adapted to arid environments as shrubs. Their leaves show remarkable variability, including differences in shape, texture, number of leaflets, margin type, petiolule length, hairiness, epidermal papillae, and the presence of rachis wings. Many synonyms in the genus arise from intraspecific variation. The flowers are generally small, with a single pistil and two stamens, consistent with other Oleaceae members. The corolla may be absent or composed of four (occasionally two) free, linear, white petals that are rarely fused. The calyx is usually small, synsepalous, dentate, and occasionally absent. The genus exhibits both insect-pollinated, petaliferous flowers that

grow in large ornamental panicles from terminal buds alongside the leaves and apetalous, wind-pollinated flowers that develop in lateral or terminal inflorescences, usually preceding leaf expansion. The ovary is syncarpous with four ovules (two per locule), although typically only a single ovule develops into a one-seeded samara (Wallander and Albert, 2000), (Wallander, 2008).

F. xanthoxyloides (Figure 1), commonly known as Afghan ash, is a small tree native to dry hills. It is characterized by 5–11 ovate-lanceolate, toothed leaflets with a winged rachis, and flowers that occur in dense clusters. Although the genus *Fraxinus* has been studied globally, *F. xanthoxyloides* remains underexplored despite its ecological resilience in arid regions. This review differs from previous studies by providing the first integrated synthesis of its multi-organ ethnobotany, together with a comparative analysis of its secoiridoid and coumarin profiles.

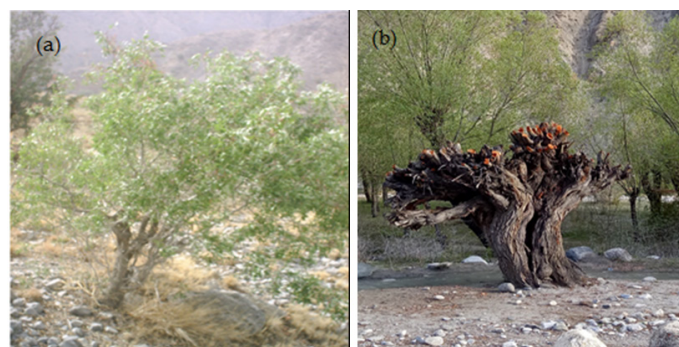


Figure 1: (a) *Fraxinus xanthoxyloides* tree with leaves, (b). Plant due to overcutting of branches for fuel and fodder

Ethnobotany

Scientific literature indicates that *F. xanthoxyloides* has long been valued in traditional and folk medicine for addressing a wide spectrum of health conditions, such as malaria, pneumonia, jaundice, typhoid, bone fractures, traumatic injuries, internal wounds, and complications related to premature delivery. The use of plants as therapeutic agents dates back millennia, and according to the World Health Organization (WHO), nearly four-fifths of the world's population continues to depend on traditional remedies for primary health care needs. Ethnobotanical investigations play a crucial role in recording indigenous medicinal practices (Idu *et al.*, 2008). Research conducted in northern Pakistan shows that the root bark and leaves of *F. xanthoxyloides* are traditionally used to treat malaria, pneumonia, and jaundice, and its leaves also

serve as animal fodder (Younis, 2017; (Khan *et al.*, 2009). Additionally, an infusion prepared from 2-3 g of the stem bark is administered to ease labor pain (Shah and Hussain, 2012). Reports further highlight the use of the stem bark in managing typhoid fever and pneumonia (Khan and Khatoon, 2007), traumatic injuries, and premature infant expulsion (Younis, Rasul, *et al.*, 2018). The wood of the plant is widely used for bone fracture healing, tool handles, and walking sticks (Sarangzai *et al.*, 2013). It is also a major source of fuel (Khan and Khatoon, 2007). Moreover, a bark concoction is used to manage internal injuries (Singh, 2012) and to facilitate the expulsion of a deceased premature infant (Farrukh Hussain *et al.*, 2007). Additionally, a stem decoction is administered for bone fractures and wounds in cattle (Mukerji, 2006), while the foliage serves as animal fodder (Sarangzai *et al.*, 2013). Beyond ethnomedicinal uses, leaves and their fractions have been reported to exhibit significant anti-inflammatory and analgesic properties (Younis *et al.*, 2016).

Table 1: Traditional uses of *Fraxinus xanthoxyloides* (G. Don) DC.

Botanical name	Part used	Traditional uses	References
<i>Fraxinus xanthoxyloides</i> (G. Don) DC.	Root bark	Malaria, Pneumonia and Jaundice	(K. Khan <i>et al.</i> , 2009)
	Stem bark	Labor pain, Internal injuries, typhoid fever, traumas, premature birth expulsion of infant and pneumonia	(S. M. Shah & Hussain, 2012); (Singh, 2012); (S. W. Khan & Khatoon, 2007); (Younis, KHAN, <i>et al.</i> , 2018)
	Stem	Bone fractures and wounds in cattle	(Mukerji, 2006)
	Wood	Bone fracture, tool handles, walking sticks, fuel, furniture	(Afzal <i>et al.</i> , 2009); (Sarangzai <i>et al.</i> , 2013); (S. W. Khan & Khatoon, 2007)
	Foliage	Fodder	(Afzal <i>et al.</i> , 2009); (Sarangzai <i>et al.</i> , 2013)
	Leaves	Malaria, Pneumonia, Jaundice, Anti-inflammatory and analgesic effects	(Younis <i>et al.</i> , 2016); (K. Khan <i>et al.</i> , 2009)

Traditional practitioners in the Hindu Kush region use various plant organs with high specificity. Nonetheless, the ethnobotanical record for this

species is almost entirely descriptive: reported uses are rarely accompanied by a stated dose, preparation ratio, or duration of treatment, and no two sources employ a consistent unit of measurement. Although several reports describe its use for malaria and pneumonia, there is a lack of clinical validation for dose standardization in folk medicine (Table 1). In our view, this absence of standardized dosing is the single greatest obstacle to translating the ethnobotanical record into a testable pharmacological hypothesis.

Phytochemistry

One of the notable characteristics of plant physiology and phytochemistry is the determination of plant metabolites using sophisticated analytical methods. The initial step in establishing a comprehensive database that will be used to ensure quality evaluation and validation of herbal medicaments is phytochemical screening. It can also be used to predict potential biological effects and identify appropriate marker compounds (Jaina *et al.*, 2013).

Over the last five years, the genus *Fraxinus* has received increased attention from researchers worldwide. One such species is *F. xanthoxyloides*, which is widely distributed and abundant in nature and has attracted significant phytochemical interest. According to the findings of these studies, the plant contains numerous bioactive compounds, including coumarins and secoiridoids (Huang *et al.*, 2019), as well as rutin, quercetin, gallic acid, caffeic acid, kaempferol, catechins, and myricetin (Younis *et al.*, 2020).

The presence of coumarins (such as cichoriin and fraxin) and secoiridoids (such as isofraxisecoside) is considered a characteristic feature of *F. xanthoxyloides*. These secoiridoids occur either as glucosides or as phenyl hydroxyphenylethylglycosesesters. In addition, lignans, flavonoids, and simple phenolic compounds are present, although their levels appear to be quite low (Kostova and Iossifova, 2007). A summary of all reported compounds is presented in Table 2.

Coumarins

Coumarins have been observed in *F. xanthoxyloides* in both glucosidic and free forms. Several species of this genus are known to be valuable natural sources of coumarins for commercial production. Several analytical techniques have been designed to study coumarin concentrations in plant extracts and fractions,

both quantitatively in a quantitative and qualitative manner to facilitate this research (Hegnauer, 1969; Murray *et al.*, 1982; Younis *et al.*, 2016). Younis *et al.* (2016) stated that the plant itself contains simple coumarins, furanocoumarins, pyranocoumarins, chromones, and even dimeric coumarins. Moreover, isoferraxin was successfully extracted from the stem bark of *F. xanthoxyloides* (G. Don) Wall. ex (Hadroug *et al.*, 2019). Previous phytochemical studies have also validated the existence of coumarins, secoiridoid glucosides (oleoside type), phenylethanoid glycosides, and other phenolic compounds in the bark of this plant (Iossifova *et al.*, 2002).

Secoiridoids

Secoiridoid glucosides are among the most

common phytochemical classes (Jin *et al.*, 2020). These are monoterpene derivatives (cyclopentane) biosynthesized by the cleavage of cyclomethene oxime structures at the C-7 and C-8 positions. These metabolites are notorious for their highly diverse pharmacological activities, such as anti-diabetic, anti-inflammatory, immunosuppressive, neuroprotective, anti-cancer, and anti-obesity effects. A new secoiridoid, iso-fraxitelesesecoside, was extracted from the stem bark of *F. xanthoxyloides* (Huang *et al.*, 2019).

Rutin

Rutin is a flavone derivative and a naturally occurring product that was first extracted from buckwheat in the 19th century. This low-molecular-weight polyphenolic compound is very common in fruits and vegetables, and

Table 2: Different compounds found in *Fraxinus xanthoxyloides* (G. Don) DC.

Plant Source	Compound name	References
<i>Fraxinus xanthoxyloides</i> (G. Don) DC.	1. Coumarins	(Kostova & Iossifova, 2007); (Younis <i>et al.</i> , 2016)
	2. Cichoriin	
	3. Fraxin	
	4. Pyranocoumarins	(Younis <i>et al.</i> , 2016)
	5. Furanocoumarins	
	6. Chromones	
	7. Dimeric coumarins	
	8. Isofraxisecoside	(Hadroug <i>et al.</i> , 2019); (Y.L. Huang <i>et al.</i> , 2019)
	9. Fraxisecoside	Hadroug, 2018
	10. Rutin	(Younis <i>et al.</i> , 2020)
	11. Quercetin	
	12. Gallic acid	
	13. Caffeic acid	
	14. Kaempferol	
	15. Catechins	
	16. Myricetin	
	17. Nummularic acid	(Younis, Khan, <i>et al.</i> , 2018)
	18. Cisplatin	(Ijaz <i>et al.</i> , 2020)
	19. Ligstroside	Hadroug, (2018)
	20. Oleuropein	
	21. Esculetin	
	22. Nicotiflorin	
	23. 2-(3, 4-dihydroxy)phenylethyl-O-β-D-glucopyranoside	
	24. Salidroside	
	25. Osmanthuside	
	26. Calceolarioside B	
	27. Coniferin	
	28. Syringin	
	29. 8-Hydroxypinoresinol-4'-O-β-D-glucoside	
	30. 8-Acetoxypinoresinol-4-O-β-D-glucoside	

buckwheat is one of the major dietary sources of this compound. Rutin, a flavonoid glycoside also known as Vitamin P, has various biological effects, such as anti-platelet, antiviral, and antihypertensive effects and it can reinforce capillary walls. These effects are mainly due to its strong antioxidant and radical-scavenging characteristics (Guo *et al.*, 2007). Besides, rutin has been linked with several pharmacological properties, including anti-inflammatory, anti-allergic, anti-bacterial, antiprotozoal, vasoprotective, antitumor, hypolipidemic, cytoprotective, antispasmodic and anticarcinogenic effects (Yang *et al.*, 2008). It has been confirmed in extracts of *F. xanthoxyloides* by high-performance liquid chromatography (HPLC) analysis (Younis *et al.*, 2020).

Quercetin

The most common plant flavonoid is quercetin, which can be found in tea and onions and is well known as a powerful antioxidant. The name quercetin name derives from the Latin quercetum (oak). It has a variety of pharmacological effects, such as anti-allergic, anti-inflammatory, anticancer, cardioprotective, antitumor, antiviral, anti-diabetic, immunomodulatory, antihypertensive, and gastroprotective activities. Besides its medicinal significance, quercetin is essential in plant physiology, including seed germination, pollen development, antioxidant defense mechanisms, and photosynthesis, which contribute to overall plant growth and development. It is also a powerful antioxidant that increases plant resistance to various biotic and abiotic stress factors (Derosa *et al.*, 2021). Quercetin has been recognized and confirmed in *F. xanthoxyloides* by HPLC profiling (Younis *et al.*, 2020).

Gallic acid

Gallic acid, or 3,4,5-trihydroxybenzoic acid is a trihydroxybenzoic acid commonly found in plants worldwide. It has documented antioxidant properties and potential applications as an anticancer agent. Notably, gallic acid has been shown to induce cytotoxicity in specific types of cancerous cells without harming normal, healthy cells (Zhao and Hu, 2013). In the same context, Younis *et al.*, (2020) used HPLC to determine the gallic acid content of *F. xanthoxyloides*.

Caffeic acid

Caffeic acid, chemically known as 3,4-dihydroxycinnamic acid, is a phenylpropanoid. It

is one of the main derivatives of cinnamic acid and is found in plants (Riaz *et al.*, 2019). Multiple studies have demonstrated its wide range of biological activities, such as antioxidant, antiviral, anticancer, and anti-inflammatory effects (Lin and Yan, 2012). Similarly, Younis *et al.* (2020) reported the presence of caffeic acid through *F. xanthoxyloides* HPLC analysis.

Kaempferol

Kaempferol is a type of flavonoid belonging to the flavonol subclass, which is rarely found in a wide range of food plants. Due to its powerful antioxidant and anti-inflammatory actions, kaempferol has attracted considerable academic attention, especially regarding its molecular mechanisms and potential in the treatment of inflammatory diseases (Rajendran *et al.*, 2014). Kaempferol has been determined in *F. xanthoxyloides* by HPLC profiling (Younis *et al.*, 2020).

Catechins

Catechins are defined as a category of polyphenolic metabolites belonging to the flavonoid family that often exist in large quantities in a variety of fruits, vegetables, as well as plant-derived beverages. They belong to the flavanol group (Gadkari and Balaraman, 2015). These compounds have been demonstrated to protect against a variety of degenerative diseases and to have antitumor and immune-modulating effects, especially in states of immune dysfunction (Boyer and Liu, 2004). Research also indicates that catechins have a higher ability to act as antibacterial agents against gram-positive bacteria than Gram-negative bacteria (Ikigai *et al.*, 1993). Younis *et al.* (2020) have carried out widespread research on catechins in *F. xanthoxyloides*.

Myricetin

Myricetin is a naturally occurring bioflavonoid that is widely found in plant species. It has been known to possess good anticarcinogenic and antimutagenic effects, but ironically, it has also shown mutagenic effects in Ames test assays (Park *et al.*, 2016) (Ong and Khoo, 1997). Younis *et al.*, (2020) used HPLC to demonstrate the presence of myricetin in *F. xanthoxyloides*.

Nummularic acid (NA)

Nummularic acid (NA), chemically designated as (19S) 3 β -hydroxy-urs-12-en-29 β -oic acid, is a pentacyclic triterpenoid with the molecular formula

$C_{30}H_{48}O_3$. It was first isolated in 2007 from *Evolvulus nummularius* (Dinda *et al.*, 2007); (Younis, Khan, *et al.*, 2018). Subsequent investigations by Younis and colleagues (2018) identified this compound as a key phytochemical constituent of *F. xanthoxyloides*, a species valued in traditional medicine for more than a hundred years. In addition, nummularic acid has been recognized for its notable anticancer potential.

Cisplatin

Cisplatin is a highly effective chemotherapeutic drug, extensively employed in the treatment of testicular tumors. However, its clinical application is limited by a major drawback: the induction of oxidative stress, which leads to alterations in tissue physiology and biochemical composition (Yucel *et al.*, 2019). In this context, Ijaz *et al.* (2020) investigated the therapeutic potential of *F. xanthoxyloides* extract in mitigating cisplatin-induced testicular damage in albino rats.

Fraxisecoside

The molecules consist of a coumarin glucoside and a secoiridoid glucoside, connected through the glucose moiety of the coumarin and the carboxyl group at the C-7 position of the secoiridoid (Hadroug *et al.*, 2019). Earlier phytochemical investigations on the bark of *Fraxinus rhynchophylla* Hance led to the identification of several coumarins, including fraxidin, fraxin, and fraxisecoside (Si *et al.*, 2009). The occurrence of fraxisecoside in *F. xanthoxyloides* was likewise confirmed by Hadroug *et al.* (2019).

Ligstroside

The compound ligstroside was first identified in *Ligustrum obtusifolium* Sieb. et Zucc. (Jensen *et al.*, 2002). Subsequently, two new secoiridoid diglucosides (angustifolioside A and B) were obtained from the methanolic leaf extract of *Fraxinus angustifolia*, along with the previously recognized secoiridoid glucosides ligstroside and oleuropein (Calis *et al.*, 1993). Consistent with these findings, Hadroug (2019) also confirmed the occurrence of ligstroside in *F. xanthoxyloides*.

Oleuropein

The presence of oleuropein in *F. xanthoxyloides* was further verified by (Omar, 2010; Piroddi *et al.*, 2017; Hadroug *et al.*, 2019).

Esculetin (6, 7-dihydroxycoumarin)

Esculetin is a naturally occurring compound widely

distributed in medicinal plants such as *Artemisia capillaries* Miq., *Artemisia scoparia* Waldst. & Kitam., *Citrus limonia* Osbeck, and *Ceratostigma willmottianum* Stapf. It has been shown to possess multiple pharmacological properties, particularly anti-proliferative and antioxidant activities (Kok *et al.*, 2009); (Kim *et al.*, 2016). The presence of esculetin in *F. xanthoxyloides* was also confirmed by Hadroug *et al.* (2019).

Nicotiflorin

Nicotiflorin is a naturally occurring flavonol glycoside that has been isolated from multiple plant species (Dehaghani *et al.*, 2017). It is associated with diverse pharmacological properties, including reduction of arterial blood pressure and heart rate, hepatoprotection against CCl_4 -induced liver injury, as well as pronounced antioxidant, anti-inflammatory, antinociceptive, antihypertensive, and antianaphylactic activities. In addition, nicotiflorin has shown neuroprotective potential by mitigating cerebral ischemic damage, memory impairment, and oxidative stress in multi-infarct dementia model rats (Gamal-Eldeen *et al.*, 2004; Wang *et al.*, 2015) (Dehaghani *et al.*, 2017; Huang *et al.*, 2007). Its occurrence in *F. xanthoxyloides* has also been validated by Hadroug *et al.* (2019).

2-(3,4-dihydroxy) phenylethyl-O- β -D-glucopyranoside Hadroug *et al.* (2019) also found the existence of 2-(3,4-dihydroxy) phenylethyl-O- β -D-glucopyranoside in *F. xanthoxyloides*.

Salidroside

Salidroside is a principal bioactive compound in several medicinal plants and is recognized for a broad spectrum of pharmacological effects, including anti-aging, anti-fatigue, antioxidant, antiviral, and anti-inflammatory activities, along with notable neuroprotective and cardioprotective roles (Chen *et al.*, 2009); Tan *et al.*, 2009; (Zhu *et al.*, 2011); (Xu *et al.*, 2013); (Yuan *et al.*, 2013). More recently, salidroside has been shown to inhibit cell proliferation and trigger apoptosis in various cancer cell lines, such as lung, bladder, neuroblastoma, and glioma, although its full anticancer mechanisms remain to be fully elucidated (Zhao *et al.*, 2015). The detection of salidroside in *F. xanthoxyloides* was also confirmed by Hadroug *et al.* (2019).

Osmanthuside H

Osmanthuside has previously been isolated from

plants such as *Tabebuia impetiginosa* (Mart. ex DC.) Standl. (Warashina *et al.*, 2006) and *F. sieboldiana* Blume (Lin *et al.*, 2010), later Hadroug *et al.* (2019) identified this compound in *F. xanthoxyloides*.

Table 3: Proximate and Elemental composition of *Fraxinus xanthoxyloides* (G. Don) DC. (Zaman, 2021).

Botanical name	Proximate composition (%)	References
<i>Fraxinus xanthoxyloides</i> (G. Don) DC.	Organic matter	(Zaman & Badshah, 2021)
	Moisture	
	Ash	
	Crude protein	
	Crude fiber	
	Crude fats	
	Nitrogen free extract	(Zaman & Badshah, 2021)
	Elemental Composition (%)	
	P	
	K	
	Ca	
	Mg	
	Fe	
	Mn	
	Cd	
	Zn	

Calceolarioside B

Calceolarioside B has demonstrated significant antiproliferative activity against a range of tumor cell lines, including prostate cancer, human bladder carcinoma (T-24), human gastric adenocarcinoma, uterine carcinoma, and murine melanoma (Khong and Judeh, 2017). Amorim *et al.* (2017) identified calceolarioside B from *Sinningia hatschbachii* Chautems through spectroscopic techniques, Verdan *et al.* (2015) identified it from *Sinningia aggregate* (Ker Gawl.) Wiehler. Similarly, Hadroug *et al.* (2018) identified calceolarioside B from *F. xanthoxyloides*.

Coniferin

Coniferin is a glucoside of coniferyl alcohol (Lemmich *et al.*, 1983). Coniferin, a coniferyl alcohol glucoside, has been detected in the cambial sap of many tree species (Tsuyama *et al.*, 2013). Coniferin has also been detected, though not quantified, in various foods including lemons, asparagus, soft-neck garlic, black salsify, and red beetroot. Consequently, it may serve as a potential biomarker for the dietary intake of these foods (Duke, 1994); (Shinbo *et al.*, 2006). Similarly, Hadroug *et al.* (2019) studied coniferin in

F. xanthoxyloides.

Syringin

Syringin is a phenolic glycoside isolated from several medicinal plants, including *Magnolia sieboldii* K. Koch and *Tinospora cordifolia* (Willd.) Hook. f. & Thomson, although its biological activities have been described in only a limited number of studies (Cho *et al.*, 2001; Liu *et al.*, 2025). Syringin was isolated and characterized from *Musa x paradisiaca* L. tepal extract (MPTE) by Krishnan *et al.*, (2014). Another plant from which syringin was extracted is *Ilex rotunda* Thumb (Wang *et al.*, 2008). Similarly Hadroug *et al.* (2018) also analyzed syringin from *F. xanthoxyloides*.

8-Hydroxypinoresinol-4'-O-β-D-glucoside

8-Hydroxypinoresinol-4-O-β-D-glucoside is an active compound reported to possess antiarrhythmic properties in *Valeriana officinalis* L. (Liu *et al.*, 2021) and antioxidant activity in *Valeriana prionophylla* Standl. (Li *et al.*, 2022), Additionally, 8-hydroxypinoresinol-4'-O-β-D-glucoside has been isolated from *F. xanthoxyloides* (Hadroug *et al.* 2018).

8-Acetoxypinoresinol-4-O-β-D-glucoside

8-Acetoxypinoresinol-4-O-β-D-glucoside is a lignan glycoside, a class of aromatic polycyclic compounds in which a lignan moiety is glycosidically linked to a carbohydrate unit (Yannai, 2012). Consistent with our findings, Hadroug *et al.* (2019) also reported the isolation of 8-Acetoxypinoresinol-4-O-β-D-glucoside from *F. xanthoxyloides*.

Proximate and elemental composition

Plants not only provide essential nutrients such as fats, proteins, and carbohydrates, but also contain phytochemicals that play vital medicinal roles (Khan *et al.*, 2020). Proximate analysis involves classifying plant components into categories such as moisture, ash, crude protein, lipids, fiber, and nitrogen-free extract (AOAC, 1990). Living organisms require approximately 40 macro- and microelements to survive, and an element is deemed essential when its deficiency leads to a decline in physiological processes (Zaman and Badshah, 2021). Zaman (2021) studied organic matter, moisture, ash, crude protein, fiber, fats, and nitrogen-free extract, along with eight elements (phosphorus, potassium, calcium, magnesium, iron, manganese, cadmium, and zinc) in *F. xanthoxyloides* from the Terich Valley, Hindukush range (Figure 1 and Table 3). The analysis revealed

significant concentrations of calcium and magnesium, supporting the plant's nutritional and medicinal potential. However, the presence of cadmium, even in trace amounts, suggests that the plant may act as a bio-accumulator. This poses a potential risk for long-term medicinal use, indicating that toxic elemental levels must be monitored in traditional remedies to ensure safety.

Pharmacology

Anti-Leishmanial activity

Leishmaniasis refers to a group of diseases caused by various species of *Leishmania*, each associated with distinct clinical manifestations. It is considered the third most prevalent vector-borne disease worldwide, after malaria and filariasis (Solano-Gallego *et al.*, 2009). In 1960 leishmaniasis was initially reported in Pakistan in the north countries. The disease was once limited to these regions but has since spread across the nation. Both cutaneous and visceral leishmaniasis are health-threatening, and mucocutaneous leishmaniasis is infrequently reported (Bhutto *et al.*, 2016); (Shah *et al.*, 2014). The therapeutic efficacy of plant extracts against these infections can be attributed to their various bioactive substances in them, which include essential oils, phenolic compounds, and aldehydes (Sahreen *et al.*, 2013). Methanolic leaf powder extract of *F. xanthoxyloides* has been investigated for its strong anti-leishmanial activity against *Leishmania tropica* in the promastigote stage (Younis *et al.*, 2016)

The chloroform extract of *F. xanthoxyloides* (FXC) showed significant anti-leishmanial activity, with an LD₅₀ of 15.23 ± 0.9 µg/mL compared with the reference drug glucantime, which had an LD₅₀ of 5.6 ± 0.4 µg/mL (Table 4). These findings suggest that the chloroform fraction of *F. xanthoxyloides* can be regarded as a viable source of anti-leishmanial compounds and further studies are needed to identify and characterize its bioactive components. The mechanism underlying this activity—whether via induction of oxidative stress in the parasite or disruption of the mitochondrial membrane—remains unresolved, and we note that an LD₅₀ roughly three-fold higher than that of glucantime indicates that the extract is markedly less potent than the reference drug, not simply “promising” in absolute terms.

Insecticidal Activity

Plants are potential replacements for traditional insecticides and acaricides, serving as sources of bioactive substances that tend to act on a narrower

range of target arthropods, biodegrade into non-toxic compounds, and are therefore considered greener; their compatibility with integrated pest management further supports sustainable use (Sarwar *et al.*, 2025). The brine shrimp lethality assay was used to test the insecticidal activity of the methanolic leaf extract of *F. xanthoxyloides*. The chloroform fraction (FXC) was the most active, with an LD₅₀ of 28.15 ± 1.8 µg/mL, followed by the *n*-hexane fraction (FXH) at 67.59 ± 2.3 µg/mL; the remaining fractions showed relatively low activity. Correlation analysis indicated no significant relationship (*p* > 0.05) with insecticidal activity (Younis *et al.*, 2016) (Table 4). These LD₅₀ values were not benchmarked against a standard insecticide in the source study, so their practical significance for pest control cannot yet be assessed.

Table 4: Different biological activities of *Fraxinus xanthoxyloides*

Plant Source	Biological assay	Reference
<i>Fraxinus xanthoxyloides</i> (G. Don) DC.	Anti-Leishmanial Activity	(Younis <i>et al.</i> , 2016)
	Insecticidal Activity	
	Cytotoxic Activity	

Cytotoxic activity

Cytotoxicity is the capacity of a substance to cause toxicity in living cells (Riss and Moravec, 2004). The methanolic leaf extract of *F. xanthoxyloides* was evaluated for its anti-cytotoxic potential (Younis *et al.*, 2016). Assessment of the extract/fractions was carried out using the sulforhodamine B (SRB) assay described by You *et al.* (1995). Results from Younis *et al.* (2016) demonstrated that *F. xanthoxyloides* exhibited no cytotoxic effects at a concentration of 20 µg/mL.

Future perspectives and roadmap for research

- **Molecular target discovery:** Investigate the specific pathways (e.g., mitochondrial disruption) through which *F. xanthoxyloides* secoiridoids exert anti-leishmanial effects.
- **Standardization:** Establish HPTLC fingerprints to reconcile the varying doses (2–3g) reported in ethnobotanical surveys into a pharmaceutical standard.
- **Toxicity monitoring:** Given the plant's potential as a bio-accumulator, long-term studies must assess the safety of trace cadmium levels found in traditional preparations.

Conclusions and Recommendations

The current review concluded that *F. xanthoxyloides* has strong evidence of several pharmacological and biological activities. Different parts (root bark, stem bark, stem, wood, foliage, and leaves) of *F. xanthoxyloides* are used to treat different ailments (malaria, pneumonia, jaundice, labor pain, internal injuries, typhoid fever, trauma, premature birth expulsion of infants, bone fractures, and wounds in cattle). In total, 30 different compounds were studied in this plant for proximate and elemental composition, as well as different biological activities (anti-leishmanial, insecticidal, and cytotoxic). Considering its significant economic value and contribution to the germplasm resources of cultivated plants in Pakistan, it is imperative to acknowledge that northern Pakistan is a vital component of the Central Asian Center of Diversity.

Novelty Statement

The present study is a piece of research that synthesizes current work and establishes a new perspective.

Authors Contribution

Muhammad Adnan: Conceptualization, Data Curation, Formal analysis, Investigation.

Muhammad Nauman Khan: Conceptualization, administration and original draft writing, Investigation, Methodology, Resources, Project administration and original draft writing.

Akhtar Zaman: Conceptualization, Data Curation

Hansa Gul: Data Curation, Formal Analysis and Investigation, Software, validation, visualization.

Alevcan Kaplan: Formal Analysis and Investigation, Software, Validation, Visualization.

Sana Wahab: Investigation, Methodology, Resources, Writing review and editing.

Maryam Bibi: Writing review and editing.

Declaration Statements

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Generative AI and AI-assisted technology statement

The authors declare that no generative AI and AI assisted technology was used in the creation of this manuscript.

Competing Interests

The authors declare no conflicts of interest.

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