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## *Zizyphus xylopyrus* (Retz.) Willd: a review of its folkloric, phytochemical and pharmacological perspectives

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## PEER REVIEW

## Peer reviewer

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## Comments

This is a good review in which the authors have compiled up-to-date information on folkloric or traditional uses, phytoconstituents present and pharmacological works done on different parts of *Z. xylopyrus*. This helps to study the unexplored area of this potent herb. I recommend this article to be published.

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## ABSTRACT

*Zizyphus xylopyrus* (Retz.) Willd (Rhamnaceae) is an ever-green shrub of tremendous medicinal importance, distributed throughout the North-Western India, Pakistan, and China. Various parts of plant are used in Ayurvedic and other folk medicine for the treatment of different ailments such as obesity, diabetes, snake bite, fever, diarrhoea, insomnia and digestive disorders. The plant also possesses antisteroidogenic, anticonvulsant, antinociceptive, antiinflammatory, antidepressant, antidiarrhoeal and wound healing activity. Research has been carried out using different techniques to support most of these claims. This review is an attempt to compile an up-to-date on its folkloric or traditional uses, phytochemical as well as pharmacological properties of *Zizyphus xylopyrus*.

## KEYWORDS

*Zizyphus xylopyrus*, Cyclopeptide alkaloids, Xylopyrine

### 1. Introduction

India has an ancient heritage of traditional medicine used on the basis of Ayurveda, Siddha and Unani (ASU) system. The materia medica of India provides lots of information on about 2000 drugs of natural origin, including traditional uses and folkloric claims<sup>[1]</sup>. Due to emerging interest the 80% of world's population is adopting traditional medicine, the Government of India has initiated several attempts to explore ethnopharmacology and traditional uses, for the evaluation of their therapeutic potential, as well as help to generate

data to put these botanicals in international market of public healthcare domain<sup>[1,2]</sup>. A considerably small number of marketable drugs or phytochemical entities have entered on evidence based therapeutics, but efforts are still needed to be established for bioactive molecules in herbal drugs<sup>[3]</sup>.

*Zizyphus xylopyrus* (*Z. xylopyrus*) is a large, straggling shrub, 6–10 m tall; young shoots rusty tomentose, spines in pairs on younger branches, one straight, the other curved; nodes swollen at the leaf scars<sup>[4,5]</sup>. It is known by various names in India, e.g. Sanskrit: Ghoti, Gotika; Bengali: Kulphal; English: Jujab and in Hindi: Ghunta, Kakora<sup>[6]</sup>. *Z. xylopyrus* is used

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traditionally in the treatment of variety of diseases such as obesity, urinary troubles, diabetes, skin infections, fever, diarrhoea, insomnia and digestive disorders[7]. Ethnobotanical survey shows that various parts of plant have been used in the treatment of diseases by folk person. *Z. xylopyrus* is one of the chief hosts for the propagation of lac, most satisfactory material for the manufacture of photographic records, a high-grade insulator and used in electrical industry[8]. Dye obtained from the fruits is also used for tanning of leather in industries[9]. People find its place in Ayurvedic Pharmacopoeia of India, but attempts have not made to describe the complete folkloric or traditional uses, phytochemical and pharmacology of this plant. Therefore, an attempt has been made to compile the data of *Z. xylopyrus* which covers its folkloric or traditional uses, phytochemical and pharmacological prospective.

## 2. Taxonomy of plant

Domain: Eukaryota  
 Kingdom: Plantae  
 Subkingdom: Viridaeplantae  
 Phylum: Magnoliophyta  
 Subphylum: Euphylllophytina  
 Infraphylum: Radiatopses  
 Class: Magnoliopsida  
 Subclass: Rosidae  
 Superorder: Rhamnanae  
 Order: Rhamnales  
 Family: Rhamnaceae  
 Genus: *Ziziphus*  
 Species: *xylopyrus*[10]

## 3. Morphology of *Z. xylopyrus*

### 3.1. Fruits

Fruit is a drupaceous berry, globular or round in shape with 1.2 to 1.8 cm in diameter; dark brown in color with astringent taste. Fruit is 3-celled with leathery and hard pericarp while endocarp is stony. Point of detachment of stalk is marked by a rounded concave depression up to 2 mm in diameter. It has about 5–8 mm long seed[5,6,11].

### 3.2. Leaves

Leaves are green in color with slight aromatic odor and pungent taste. They are alternate, entire in arrangement, glabrous surface with oblique, rounded symmetrical base and obtuse at apex. They have pinnate venation, serrulate margin and about 2–7 cm long[12].

### 3.3. Flowers

Flowers are small, yellowish or yellowish white in color,

4–6 cm across; buds ovoids, densely pubescent; pedicels 3–4 mm long. Calyx lobes 2.0–2.5 mm long, keeled up to the middle, glabrous inside pubescent outside. Five petals, 1.5–2.0 mm long, obovate while sepals are five, united (2.5–3.0)×1.5 mm diameter. Stamens five, disc 10–60 lobed, rarely 5-lobed and glabrous[6,13].

## 4. Phytoconstituents of *Z. xylopyrus*

A large number of cyclopeptide alkaloid has been isolated from *Z. xylopyrus* which are particularly common in plant of Rhamnaceae family. Eighty one different cyclopeptide alkaloids have been reported from various *Ziziphus* species and these include 35 13-membered, 39 14-membered and 7 15-membered ring cyclopeptides[14]. Phytochemical screening results shows that apart from cyclopeptide alkaloid; it contains a number of different phytoconstituents such as flavonoids, tannins, sterols, triterpenoids, saponins and fatty acids[15]. Various phytoconstituent present in different parts of plants are given in Table 1 and Figure 1.

## 5. Folkloric or traditional uses

The use of different parts of *Z. xylopyrus* in traditional system of medicine is given in Table 2.

## 6. Pharmacological properties of *Z. xylopyrus*

### 6.1. Antidepressant activity

Ethyl acetate and precipitated fraction prepared from ethanolic extract of defatted *Z. xylopyrus* leaves were screened for antidepressant activity by employing force swimming test and tail suspension test using Imipramine HCl as a positive control. In both models, precipitated fraction (10 mg/kg, *p.o.*) significantly ( $P < 0.01$ ) reduced more immobility time than ethanolic extract (50 mg/kg, *p.o.*) and ethyl acetate fraction (10 mg/kg, *p.o.*) as compared to positive control. An antidepressant activity might be found due to flavonoids glycosides, which reached the brain tissues through the metabolization process, protecting brain function from central nervous system disturbance, and consequently, exerting an antidepressant effect[16].

### 6.2. Antinociceptive, anticonvulsant and antiinflammatory activity

Ethanolic extract of *Z. xylopyrus* barks (200 mg/kg, *p.o.*) has been evaluated for antinociceptive, anticonvulsant and antiinflammatory activities. Antinociceptive activity was measured by tail flick model using morphine (10 mg/kg, *i.p.*) as standard. Pretreatment with extract remarkably increase the latent period of tail flick time ( $P < 0.01$ ) as

**Table 1**Phytoconstituents present in different parts of *Z. xylopyrus*.

Plant parts	Phytoconstituents
Leaves	Quercetin and quercitrin[4]
Flowers	E-4-hydroxy cinnamic acid, E-4-hydroxy-3-methoxy cinnamic acid, p-coumaric acid, ferulic acid, 5,7,3',4'-tetra hydroxy-3-O-a-L-rhamnosyl favone: quercitrin, 5,7,3',4'-tetrahydroxy 3-O-P-D-galactosyl, hyperoside, kaempferol, 3-O-rutinoside and Rutin[16]
Fruit	3,3,4-tri-O-methyl-ellagic acid, l-leucocyanidin, vitamin C, carotene, citric acid, Oleanolic acid, sucrose and reducing sugars[6,12]
Seed	Unsaponifiable matter: sterol; insoluble mixed fatty acids: myristic, linoleic and oleic acid[17]
Stem bark	Tannins, d-7,3',4'-trihydroxyfavan-3,4-diol, oleanolic acid, Cyclopeptide alkaloids: Amphibine H, Nummularine- K[10,16,18]
Root bark	Kempferol-4'-methylether and Kempferol, Cyclopeptoidal alkaloid; XylopyrineA, B, C, D, E, F, G and H, nummularine-p and sativanine-H[19-24]
Stem wood	Triterpenoids, lupeol, betulinic acid and isoceanothic acid[25]

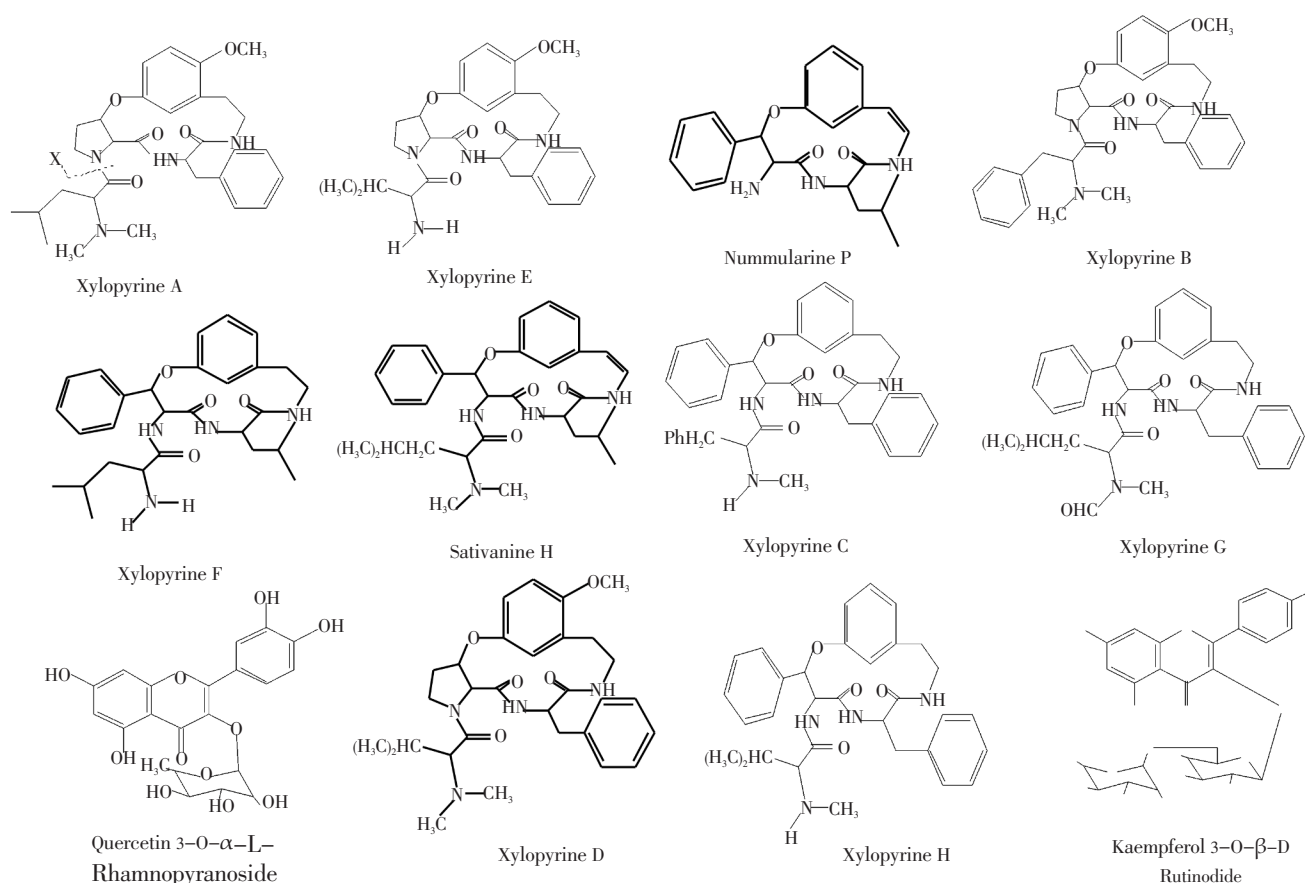
**Table 2**Folkloric/traditional uses of *Z. xylopyrus*.

Plant Part	Disease	Method of administration
Stem bark	Stomachache	Fresh stem bark powder is soaked in water for twelve hours and filtered; filtrate is taken orally in empty stomach for 3 d in single dose[26]
	Cholera	Stem bark paste is made into pills and taken orally[27]
	Bleeding of piles as well as from nose and mouth	Root bark powder of <i>Z. xylopyrus</i> Willd., <i>Anogeissus latifolia</i> (DC), <i>Acacia catechu</i> Wild., and whole plant of <i>Viscum articulatum</i> given orally with water[28]
Root bark	Skin rashes	Bark is boiled with water; water is used to bath for curing skin rashes[29]
	Diabetic	Fruits powder is taken orally with milk for 5 d[30]
Fruit	Stomachache	Fruit powder (3–4 g) along with pinch of ginger powder taken orally thrice in a day[31]
	Urinary spasm	Fresh fruits crushed with water and taken twice a day[32]
	Sterility in women's	The crushed fruit powder is soaked in water and kept overnight (macerate, decoction) and this extract is taken by the women early in the morning for 7 d to check oogenesis[33–35]
	Diarrhoea	Fruits and bark are used in the treatment of diarrhoea[36]
Leaves and Flowers	Urinary problem	Leaves are chewed for 15 d in case of urinary problem[32]
	Pimples and boils	Leaf paste is applied on pimples while leaves are ground along with latex of <i>Ipomea carnea</i> applied on boils [37]
Leaves and stems	Snake bites	Decoction of <i>Muraya koenigii</i> Spreng (stem bark), <i>Terminalia bellerica</i> Roxb (leaves) and <i>Z. xylopyrus</i> Retz. (leaves) were taken internally[38]
	Leucoderma	Paste of <i>Z. xylopyrus</i> leaves and flowers of <i>Datura innoxia</i> was applied on patches at night till relief[39]
Root	Hysteria, antidote for fox, antiseptic, headache	–
	Asthma	<i>Z. xylopyrus</i> roots were crushed along with stem barks of <i>Calotropis gigantea</i> (Linn.), <i>Erythroxylum monogynum</i> Roxb., <i>Pterocarpus marsupium</i> Roxb., and 10–12 dry chillies; administered for 2–3 d with one liter of water once a day[40]
	Pyorrhoea and bristles	Used in pyorrhoea and to check oogenesis[41]
Seed	Pain after cough and cold	The roasted seed powder paste is applied over the chest for relieving the pain after cough and colds[42]
	Diarrhoea	The dried seeds are pounded to make a fine powder and kept in air tight containers. One table spoon full of powder is mixed in a cup of (50 mL) water or boiled milk or even in tea and taken orally in case of diarrhoea. The medicine is administered thrice a day, for 2 d[43]

compared to positive control which is considered as index of antinociception. Anticonvulsant activity has been evaluated by supramaximal electroshock seizure using phenobarbitone (20 mg/kg, *i.p.*) as positive control; hand limb extensor response was measured as a positive test result. Pretreatment with ethanolic extract protect the animal from electroshock induced convulsions up to 50% ( $P < 0.05$ ) as compared to phenobarbitone treated animals ( $P < 0.001$ ). Inflammation was induced by 1% carrageenin; extent of oedema was measured by mercury displacement method using plethysmographically as positive response. Extent of paw oedema was found less in animals pretreated with ethanolic extract ( $P < 0.01$ ), caused overall 49% decrease in oedema induced by carrageenin[44].

### 6.3. Antisteroidogenic activity

Ethanolic extract of *Z. xylopyrus* leaves (250 mg/kg and 500 mg/kg, *p.o.*) were studied on the onset of reproductive maturity and the ovarian steroidogenesis in prepubertal female mice. It caused remarkably a dose-dependent delay in sexual maturation ( $P < 0.01$ ) as evidenced by the age at vaginal opening and appearance of first estrus. Further, statistically a dose-dependent elevation of the ovarian cholesterol, ascorbic acid and protein contents occurred ( $P < 0.05$ ) while significantly decreased ( $P < 0.05$ )  $\Delta 5-3\beta$ -hydroxysteroid dehydrogenase and glucose-6-phosphate dehydrogenase activities, weight of ovary and uterus. Antisteroidogenic effect of treated prepubertal female mice might be due to delay in onset of puberty and



**Figure 1.** Chemical structures of various phytoconstituents present in different parts of *Z. xylopyrus* (Retz.) Willd.

suppressed ovarian steroidogenesis[33].

#### 6.4. Wound healing activity

Wound healing activity of ethanolic extract of *Z. xylopyrus* (10 µg/disc, 50 µg/disc) stem bark was screened *in vivo* using chorioallantoic membrane model in 9-day-old fertilized chick eggs; dose dependent angiogenesis activity was observed in extract treated fertilized chick egg as compared to normal control. Wound healing activity of ointment containing ethanolic extract (5% and 10% w/w) was evaluated using excision and linear incision wound model using 1% framycetin sulphate cream as positive control; significant dose dependent wound contraction ( $P < 0.05$ ) and tensile strength was observed as compared to positive control group[45].

#### 6.5. Antibacterial activity

Aqueous extract of seeds of *Z. xylopyrus* was evaluated for antibacterial activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Escherichia coli* using microtitre-plates, colorimetric and haemocytometric assays. Seeds extract did not show any antibacterial activity[46].

#### 6.6. Biochemical changes in *Z. xylopyrus* by vesicular arbuscular mycorrhizae

The efficacy of six vesicular arbuscular mycorrhizal fungus species *i.e.* *Acaulospora morrowae*, *Gigaspora margarita*,

*Glomus fasciculatum*, *Glomus macrocarpum*, *Scutellospora calospora* and *Sclerocystis rubiformis*, collected from rhizosphere soil of *Z. xylopyrus*, were evaluated for enhancement of nitrate reductase, peroxidase, polyphenol oxidase, glutamine synthetase, protein, phenolic and catechin content in the fruit of tree. Culturing was done under glass house condition and analysis was performed after 180-day inoculation. Among all fungi, *Scutellospora calospora* showed most prominent beneficial effect and caused elevation of assimilating enzymes most efficiently which led to increase biomass and highly proteinous leafy fodder. It will also make the plant more resistant to pathogen as a result of increase peroxidase and polyphenol oxidase[47].

## 7. Conclusion

India can be benefited enormously if we can build a golden triangle among modern science, modern medicine and traditional medicine. Indeed, triangles are a popular concept in complementary medicine, but for the Ayush, the golden triangle represents a golden opportunity to bring these systems together[48]. Numerous drugs have been entered the market throughout the exploration of ethnopharmacological and traditional uses of medicines. Although scientific studies have been carried out by scientist on many Indian botanicals, a considerably small number of marketable drugs or phytochemical entities have entered the evidence based therapeutics. The plants of Rhamnaceae families have a

worldwide distribution, but are more common in subtropical and tropical regions. *Z. xylopyrus* is an indigenous plant with several medicinal properties, attributed by producing secondary metabolites such as flavonoids, cyclopeptides alkaloids and so on. Thus, this review provides excellent accessible sources of folkloric or traditional uses, chemical constituents and pharmacological perspectives of different parts of *Z. xylopyrus*, which help to explore on evidence based therapeutics as well as to establish and validate the safety and practice of this herbal medicine in current scenario.

### Conflict of interest statement

We declare that we have no conflict of interest.

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### Comments

#### Background

*Z. xylopyrus* (Retz.) Willd is a widely distributed herb which is used by folk person or traditionally in the treatment of variety of diseases. This plant also has high industrial value and also found its place in Ayurvedic pharmacopoeia of India.

#### Research frontiers

It is not a research work, but authors have compiled all the updated information available on this plant which helps to identify and explore it more significantly.

#### Related reports

Some earlier works on *Z. xylopyrus* have been studied. Jena *et al.* studied the wound healing potential of *Z. xylopyrus*. Rao *et al.* showed the anticonvulsant and antiinflammatory activities of *Z. xylopyrus*. On the basis of earlier researches, the article has been prepared.

#### Innovations & breakthroughs

Authors have attempted to compile different folkloric or traditional uses, phytoconstituents present and pharmacological works done on distinctive parts. All this information will help researchers to explore further.

#### Applications

It will be significant to know folk uses and

phytoconstituents present in different plant parts to expand unexplored area by scientific evaluation.

### Peer review

This is a good review in which the authors have compiled up-to-date information on folkloric or traditional uses, phytoconstituents present and pharmacological works done on different parts of *Z. xylopyrus*. This helps to study the unexplored area of this potent herb. I recommend this article to be published.

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