



REVIEW ARTICLE

Ethanobotanical, phytochemical and pharmacological properties of *Zizyphus nummularia* (Burm. F.): A Review

Babita Aggarwal^{1*}, Pankaj Sharma¹ and HS Lamba²**Abstract**

Zizyphus nummularia (Burm. F.), Family: Rhamnaceae, is widely distributed in dry regions of India. It is a bushy weed used as folk medicine. The plant is valued for its nutritional edible fruits. Traditionally, it is used in mental retardation, fever, diarrhea, dysentery. The plant has been evaluated for various pharmacological activities such as anti-inflammatory, anthelmintic, antibacterial, antifertility activity. Present review discusses phytochemistry and pharmacological aspects of the drug.

Keywords: Chhoti ber; Cyclopeptide alkaloids; Nummularine; *Zizyphus nummularia*

Introduction

Zizyphus nummularia (Burm. F.), a member of family Rhamnaceae, locally known as chhoti ber, is a small, thorny bush distributed in North Western India, majorly grows in dry and arid regions [1,2]. Plant may attain a height of 1-2 m and valued for nutritious edible fruits and as folk medicine. It is thorny shrub with pale purplish and velvety stem and branches. Fruits are reddish brown-black round berries, locally known as “Jhar Beri”[3].

Ethnomedicinme

It posses good astringent action and valued in the treatment of bilious sickness, scabies and boils. Fruit is cooling, astringent, tonic, digestible, laxative, aphrodisiac, anti-emetic, remove biliousness, thirst and burning sensation[1]. The fruit is used in abdominal pain during pregnancy, as an antidote in aconite poisoning and externally applied for wounds[4].

In Baster region, traditionally dried leaves and powdered bark are used to dress wounds, in the treatment of eye disease and tuberculosis[5].

The leaves are used in scabies and other skin diseases. Smoke from dried leaves is inhaled for the treatment of cold & cough. Bark decoction is used as a hip bath for joint pains and as gargle for sore throat and bleeding gums. Root is considered to be cooling and bitter, cures biliousness, cough and headache[2]. The bark and root extract are good remedies against asthma, bronchitis and fever. The leaves are also used for sexual diseases[6]. Bark is good for the treatment of diarrhea, dysentery and colic. Inner bark infusion is used as purgative to relieve constipation[4].

Z. nummularia has been recognized as an underutilized plant worthy of further research. It provides a good source of nutrition and other purposes[7].

Pharmacognosy

Z. nummularia, a thorny shrub, grows well in warm and dry climate on sandy soil and reaches up to a height of 2 meters and valued for edible nutritious fruits and as folk medicine. It is a much branched shrub with spines in unequal pairs. Leaves are dark

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green 1-8cm × 8-10 mm in size; orbicular or ovate-orbicular to elliptical in shape; apex is obtuse and base is round to cordate; entire or serrate margin, densely pubescent above, densely woolly beneath, pedicel 2-4 mm long. Flowers are axillary, sessile pubescent cymes; 3-4 mm in diameter. Calyx pubescent outside, cleft about halfway down; lobes 1 mm, ovate lanceolate. Petals cuneate longer than stamens c. 1.25 mm long, rounded or truncate at apex. Drupe globose, 5-10 mm long, reddish brown-black when ripe, 2 celled, 2 seeded[8]. Due to hard seed coat, germination takes longer duration and in nature conditions the seeds are able to germinate by aging and weathering in soil during months to one year[9].

Reported Phytoconstituents

Zizyphus mainly contain cyclopeptide alkaloids. The cyclopeptide alkaloids are polyamide plant bases composed of amino acid residues in common and highly modified form. All cyclopeptide alkaloids contain 13, 14 and 15 membered ring system except Lasiocarpine-A. These alkaloids are particularly common in plants of family Rhamnaceae and occasionally are found in plants of Sterculiaceae, Fondaceae, Urticaceae, Rubiaceae and Hymenocardiaceae[10].

Exploitation of drug for phytochemical studies reveals the presence of 13-membered *N*-formylcyclopeptide alkaloid, Nummularine T[11], a short side chain 13-membered cyclopeptide alkaloid, Nummularine S[6], Mauritine D, Nummularine-P[12], franguloline, amphibine H, Nummularine K, Nummularine R[13], Jubanine B and Nummularine-O[14], Nummularine B, M and N[15], sitosterol, stigmasterol, betulinic acid, oleanolic acid, sitosterol- β -D-glucoside and stigmasterol- β -D-glucoside[16] in various fractions of stem bark.

Root bark of Zizyphus nummularia is reported to consist of Jubanine- A, B and Mauritine C[17], Nummularine G, H, K, Nummularine D, E, F, nummularine A, B, C[18-20]. A new Dammarane Saponin, Zizyphummin[21] along with n-octacosanol, betulinic acid and quercetin-3-O-galactoside were isolated from leaves[16] of the plant. Benzene extract of whole plant reported to consist of new (25 S)-spirostane which is characterized as nummularogenin, (25 S)-3 α -hydroxy-5 α -spirostane-2,12-dione[22] and a steroidal saponin, manogenin[23] (Table 1).

Pharmacological Uses

Anthelmintic activity

Anthelmintic activity against *Trichostrongylid nematodes* of sheep was investigated by administering increasing dose of crude powder and crude methanolic extract (1.0–3.0g/kg) of *Zizyphus nummularia* (bark) and *Acacia nilotica* (fruit) to nat-

urally infected sheep. Dose and time-dependent anthelmintic effect was observed which is indicated by mortality of worms, and inhibiting egg hatching and larval development. *Acacia nilotica* (LC₅₀ = 512.86 and 194.98 μ g/ml) was found to be more potent than *Zizyphus nummularia* (LC₅₀ = 676.08 and 398.11 μ g/ml) in egg hatch test and larval development assay, respectively[24].

Anti-inflammatory, analgesic and antipyretic activity

The alkaloid fraction obtained from stem bark possesses significant analgesic activity. Ethanolic extract exhibited both antipyretic and anti-inflammatory activities and showed no spermatotoxicity[4].

Ray *et al.* (2015), explored crude ethanolic extract and pure octadecahydro-picene-2,3,14,15-tetranone (IC) in the root bark of *Z. nummularia* for the *in vivo* anti-inflammatory activity. IC was further subjected to suitable *in vitro* and *in silico* studies to find out the mechanism[25].

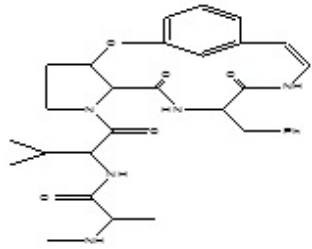
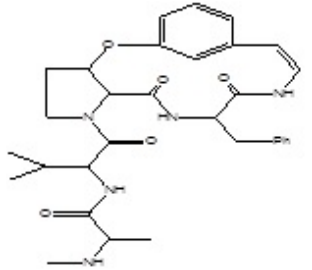
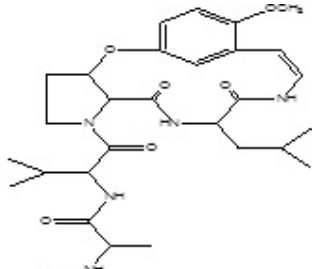
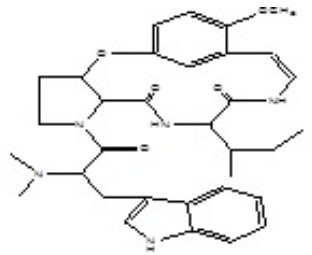
Goyal M. *et al.* (2012) demonstrated that ethanolic extract of *Zizyphus nummularia* leaves is effective at dose 200 and 300 mg Kg⁻¹ in carrageenan and histamine induced inflammation. Authors also investigated the analgesic efficacy against tail flick and acetic acid induced writhing models[26]. In continuation to their work authors further evaluated the cyclopeptide alkaloidal fraction for anti-inflammatory against rat paw oedema, mouse peritonitis and cotton pellet granuloma. They found that cyclopeptide alkaloids at dose 30 mg/kg showed the anti-oedematogenic effect against paw oedema induced by carrageenan, dextran, serotonin and histamine. Authors also confirmed the significant anti-nociceptive effects at doses 20 and 30 mg/kg when analgesia was induced by acetic acid induced writhing, tail flick and hot plate methods[27].

Hasan Soliman Yusufoflu (2011), formulated a gel containing 20 and 30% of ethanolic extract of leaves of *Z. nummularia* with the aid of Carbopol and DMSO. Topical application of 0.5 g of gel formulation produced a significant reduction in carrageenan induced paw oedema and increase in rate of wounding healing as compared to the marketed formulation (Betadine)[28].

Antimicrobial activity

S Gautam *et al.* (2011), investigated the aqueous and alcoholic extract of *Zizyphus nummularia* leaves for antibacterial efficacy using agar disc diffusion method and revealed no activity against *B. subtilis* and significant activity against *S. aureus* and *P. aeruginosa*. Antifungal activity was determined against *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans* and *Trichophyton rubrum* using Dry weight method. In fungi maximum efficacy was recorded in alcoholic extract against *C. albicans* (67.25%) and *T. rubrum* (52.75%) while minimum

Table 1: Summary of isolated phytoconstituents from different parts of *Z. nummularia*

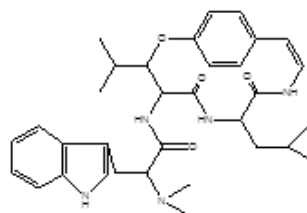
Plant part	Phytoconstituent	Structure	Reference
Stem Bark	Nummularine T		[11]
	Nummularine S		[6]
	Nummularine P		[12]
	Mauritine D		[12]

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Table 1 continued

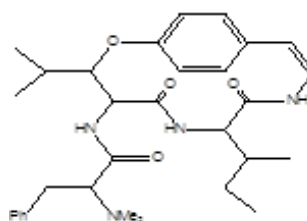
Nummularine K

[13]



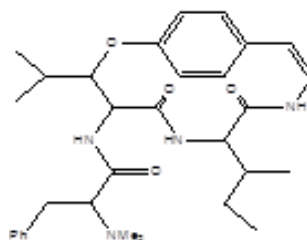
Frangufoline

[13]



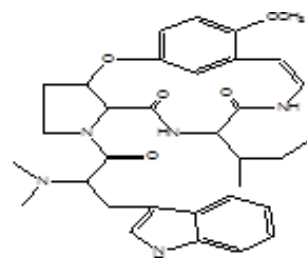
Amphibine H

[13]



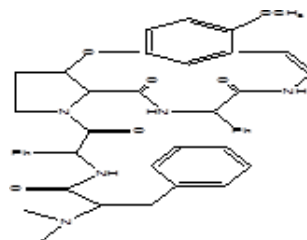
Nummularine R

[13]



Jubanine B

[14]

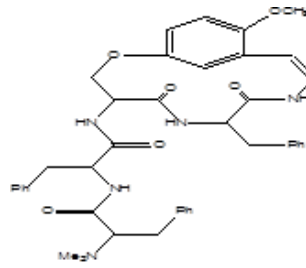


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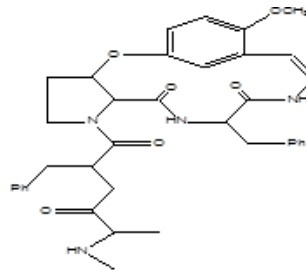
Nummularine O

[14]



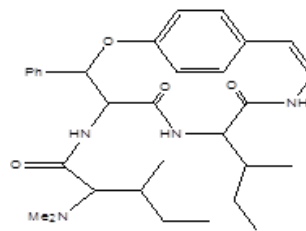
Nummularine B

[15]



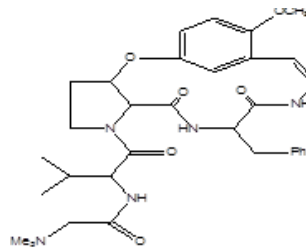
Nummularine M

[15]



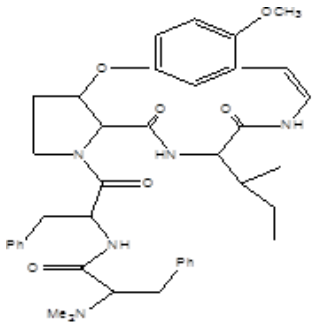
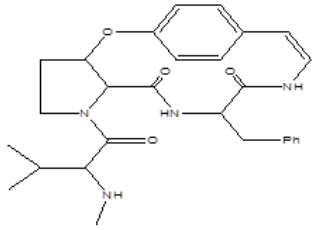
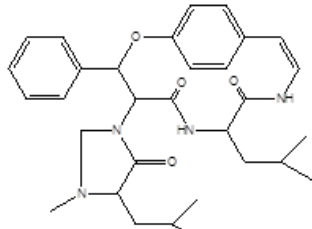
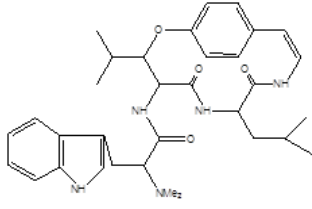
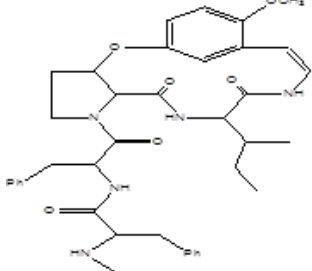
Nummularine N

[15]



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Table 1 continued

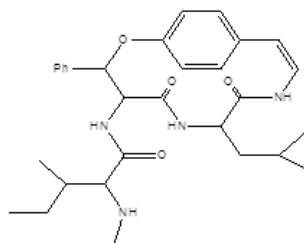
Root Bark	Jubanine A	[17]
		
	Mauritine C	[17]
		
	Nummularine G	[18]
		
	Nummularine K	[18]
		
	Nummularine H	[18]
		

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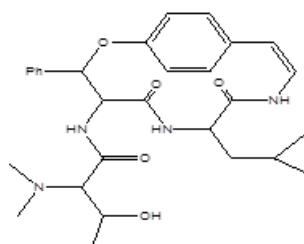
Nummularine D

[19]



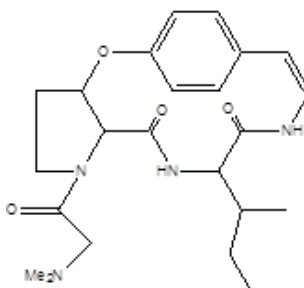
Nummularine E

[19]



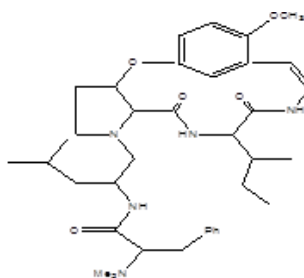
Nummularine F

[19]



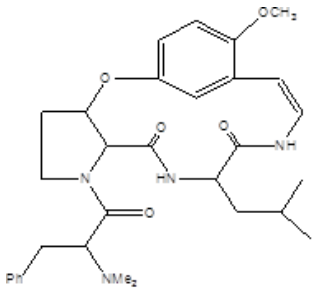
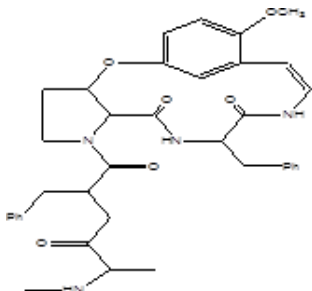
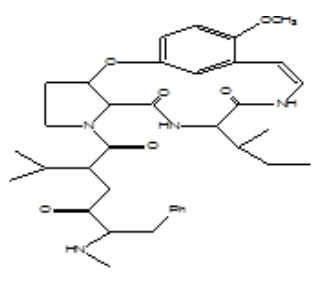
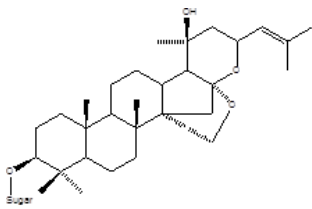
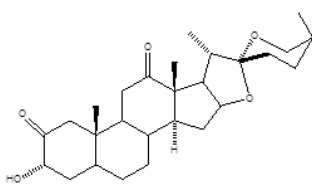
Mucronin-D

[20]



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Table 1 continued

	Nummularine C		[20]
	Nummularine B		[20]
	Nummularine A		[20]
Leaves	Zizymin		[21]
Whole plant	Nummularogenin		[22]

against *A. flavus*. Alcoholic extract was found to be more active than aqueous extract[29].

Antimicrobial activity

S Gautam *et al.* (2011), investigated the aqueous and alcoholic extract of *Zizyphus nummularia* leaves for antibacterial efficacy using agar disc diffusion method and revealed no activity against *B. subtilis* and significant activity against *S. aureus* and *P. aeruginosa*. Antifungal activity was determined against *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans* and *Trichophyton rubrum* using Dry weight method. In fungi maximum efficacy was recorded in alcoholic extract against *C. albicans* (67.25%) and *T. rubrum* (52.75%) while minimum against *A. flavus*. Alcoholic extract was found to be more active than aqueous extract[29].

VB Pandey *et al.* (1990), isolated many cyclopeptide alkaloids from Rhamnaceae family and also investigated their antimicrobial activity. Frangulofolin was active against both Gram positive and Gram negative bacteria while Nummularine R, S and B at 10 µg showed antibacterial activity against Gram negative bacteria only. The alkaloids also found to be ineffective against *Candida albicans* and possess significant antifungal activity against *Aspergillus niger*[30].

Sedative and hypnotic activity

Rauf A *et al.* (2016), evaluated the methanolic extract of *Zizyphus nummularia* roots for sedative-hypnotic, antipyretic and analgesic properties. Marked dose-dependent ($p < 0.05$) sedative hypnotic, analgesic and antipyretic activities was exhibited by various extracts at dose 50 and 100 mg/kg[31].

Hypoglycemic and hypolipidemic activity

Rajasekaran S *et al.* (2013), estimated the hypoglycemic action of ethanolic and aqueous leaves extract of *Zizyphus nummularia* (250mg/Kg & 500mg/Kg) in dexamethasone-induced diabetic rats. Animals were treated orally and showed significant ($p < 0.01$ & $p < 0.05$) anti-hyperglycemic and hypolipidemic activity as compared to diabetic control[32]. In their previous study they showed the same activity when diabetes was induced by Alloxan (150 mg/kg of body weight- i.p.). Significant ($p < 0.01$) anti-hyperglycemic and hypolipidemic activity was found on oral administration of the extracts to the animals. Lowering of elevated blood glucose, low density lipoprotein (LDL), very low density lipoprotein (VLDL), triglycerides (TGL), total cholesterol (TC) was observed along with elevation of reduced level of high density lipoprotein (HDL) and body weight maintenance in both cases[33].

Antioxidant activity

Gupta D *et al.* 2011 investigated the antioxidant activity of fruit along with its nutritional and phytochemical content analysis. Various extracts were evaluated for antioxidant activity of *Z. nummularia* fruits using DPPH radical scavenging assay, FRAP assay, ABTS radical scavenging assay and metal chelation activity. Antioxidant potential is found to be maximum in acetone extract followed by dichloromethane, methanol and least in petroleum ether extract. Antioxidant potential was correlated to the high phenolic content of fruit[34].

Anti tumor activity

Kumar A and co-workers (2002), isolated Lapachol (2-hydroxy-3-(3-methyl-2-butenyl)-1, 4-naphthoquinone) for the first time from the plant of *Z. nummularia*. Its anti tumor property alone and in combination with radiation was evaluated in female Swiss albino mice, 6-8 weeks old, bearing sarcoma-180 (S-180) ascetic tumor cells[35].

Abortifacient action

Shah GM *et al.* (2009), studied many plants for abortifacient and antifertility properties. Abortion is induced when root bark powder of *Zizyphus nummularia* mixed with candy sugar is taken with milk (3-5 g twice a day)[36].

Molluscicidal activity

Shah *et al.* (2013), investigated the ethanolic and n-hexane extract of leaves for the phytotoxicity and molluscicidal activity. They stated that both the extracts are potential molluscicidal and phytopromoters and can be used as fertilizers[37].

Conclusion

The plant is reviewed for phytochemistry, traditional and bioactivities and has potential to develop drugs against diabetes, inflammation and microbial infections. This encourages us for further exploitation of the plant for developing newer novel uses of *Z. nummularia*.

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