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ETHNOBOTANY, PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES OF *ZANTHOXYLUM NITIDUM*: A SYSTEMIC REVIEW

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ABSTRACT

Zanthoxylum nitidum (Roxb.) DC (Rutaceae), is a large prickly shrub, mainly found in South-east Asian and Australian region which is commonly known as *Tez-mui* in Assam. Its stem bark, small branches, leaves and fruits are ethnomedicinally prescribed in North-East India for treatment of various disease and ailments. The main objective behind this review article is to compile the updated information regarding the phytochemical constituents and pharmacological as well traditional uses of this plant. An extensive literature search regarding the underlying objective were carried out by using keywords '*Zanthoxylum nitidum*, or phytochemicals or pharmacological activities, or traditional uses or ethnomedicinal properties or herbal medicinal plants in North-eastern region on the search engine like Google Scholar, PubMed, Web of Science, Scopus etc. The investigation and deep studies revealed that *Zanthoxylum nitidum* contain various phytochemicals such as alkaloids, coumarins, flavones, terpenes etc. The plant is extensively used in treatment of gingivitis, toothache, diarrhoea, paresis, boils, rheumatism, fever, cholic, vomiting, cholera, snake bite etc. Meanwhile, preclinical investigation has also taken place for different activities such as anti-inflammatory, analgesics, anti-microbial, anti-viral, anti-cancer, haemostatic and so forth. This systemic review studies on its phytochemistry and pharmacological studies will contribute in further research about *Z. nitidum* plant for drug development.

KEYWORDS: *Zanthoxylum nitidum*, Phytochemical constituents, Pharmacological activity, Ethnomedicine, Traditional use.

INTRODUCTION

Medicinal herbs have been an integral part of society since the beginning of human civilization which is valued for their culinary and medicinal properties. Herbal medicines are known as the phytomedicines or phytopharmaceuticals.[1] Phytochemical rich plants are significantly use in the diet-based therapies to cure various maladies due to which their impact and rate of utilization has risen exponentially.[2] The plant *Zanthoxylum nitidum* Roxburgh (Roxb.) DC (*Z. nitidum*) is an aromatic prickly climbing herbs or shrubs belonging to the family Rutaceae. It is distributed pan-tropically and mainly found in North-east region of India (Sikkim, Assam and Nagaland) which is commonly known as *Tez-mui* in Assamese.[3] It is also a morphologically variable plant found in south-east Asian countries, Molucca Islands, Vietnam, Guinea and Australia.[4–6] Traditionally, different parts of the plants are used for different medicinal purposes. Generally, the roots are used in promote blood circulation, cure snake bite, stomachache, toothache, fever, rheumatism, paresis, boils, as a piscicides and insecticides. Whereas, fruits are used in treatment of cough, colic, diarrhoea, as an aromatic, stimulants and piscicides. For treatment of fever, cholera and diarrhoea small branches, seeds and stem bark are used.[7–10] In Assam, the rural peoples used to chew the stem and barks for the treatment of gingivitis and toothache.[3]

Previously worked researchers mentioned that, the root of non-Indian origin *Z. nitidum* which is mainly occurs in China, Taiwan and Japan are being used as anti-tumor, antifungal, antispasmodic, antioxidant, analgesics, anti-inflammatory agents.[11–13] Currently, *Z. nitidum* is use in preparation of some daily use item such as toothpaste, mouthwash, soap, hand sanitizer and shampoo. Among these, most widely use item is *Z. nitidum* which can eliminate toothache, breathing freshness, reduce gingival swelling and redness, and enhance oral problem.[14] Although several reports have been published on this plant, the complete exploration regarding the phytoconstituents still remains a challenging task for researchers.

Plant profile

Scientific name: *Zanthoxylum nitidum;* English name: Shiny leaf-prickly-ash

Vernacular name: *Tez-mui*(in Assamese); *Liang-Mian-Zhen* (in Chinese)

Taxonomical classification

Kingdom: Plantae

Division: Tracheophyta

Class: Magnoliopsida

Order: Sapindales

Family: Rutaceae

Genus: *Zanthoxylum*

Species: *nitidum*

Distribution and habitat

Z. nitidum (Roxb.) DC (Rutaceae) is widely distributed in south-east Asian countries and Australia. Mainly, in North-east India, this ethnomedicinally important herbal plant found in Sikkim, Assam and Nagaland.[15] Across the globe, this shrub can also occur in warm places of Japan, China including Guangxi, Guangdong, Yunnan, Fujian and Taiwan and it's very common to observe in forest and shrubs of hill and mountain. The best quality of *Z. nitidum* is cultivated in Guangxi province of China.[14]

Ethnobotanical description and Traditional uses

Z. nitidum is a woody climber shrub which rise up to height of 1-2 m. Stem, branches, both side of mid vein of leaves containing hook like prickles. The main root is thick and it possesses many branched roots whose outer side appears as muddy yellow and inner side as Sulphur yellow. The length and width of leaves are 3-12 cm and 1.5-6 cm respectively whose opposite leaves are leathery and ovoid in shape. Sessile like petiole are there whose length is 2-5 mm. It has 4 basic flowers whose sepals are purplish green, broadly ovate and about 1 mm wide. Petals of *Z. nitidum* are somewhat yellowish green, oblong and 3 mm long. The flowering and fruiting period of *Z. nitidum* is from March-May and September-November respectively. Mature seed has dormancy and seed coat is bright black and rich in oil.[3,14]

Z. nitidum is a large prickly shrub which is very important from traditional point of view. The whole plant is used for various diseases. Because of its bitter and pungent flavour and mild property it is used for liver and stomach problems.[16] Traditionally the root of *Z. nitidum* is widely used in toothache, stomach-ache, rheumatic arthralgia, fever, boils and as an insecticide. *Z. nitidum* is also used to treat traumatic injury because it promotes blood circulation to remove blood stasis. In different parts of the world, it is used to treat venomous snake bites because it can remove toxicity to achieve detumescence.[10,17] The folk people of

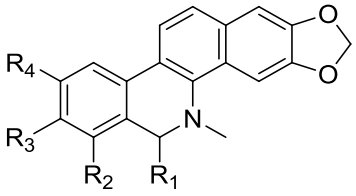
China and even Southeast Asia use *Z. nitidum* for various purposes since the time immemorial. Stewing pork leg bone with *Z. nitidum* helps in the treatment of chronic lumbar muscle strain. Also, decoction of root bark of *Z. nitidum* and egg can be useful against rheumatic bone pain.[18] The root of *Z. nitidum* is used to treat scald and aphtha and as a carminative, depurative, antiphlogistic and febrifuge.[14] The small branches stem bark and seeds are used in diarrhoea, fever and cholera.[9] Some people eat the leaf as a green vegetable. The people of Assam use the bark and stems as chewing material in the treatment of gingivitis and toothache.[7] The fruit of *Z. nitidum* is useful in the treatment of vomiting, colic and diarrhoea and also use as a piscicide and aromatic stimulant, anthelmintic, astringent, diaphoretic, carminative.[8] A decoction of leafy branches is useful in the treatment of inflammation of throat. The resin present in *Z. nitidum* has powerful stimulant and tonic property.[19] The fruits are used also used as condiment in India and Nepal. Sometimes the roots, fruits and leaves show some toxicity depending on their dose while the dose of 40g *Z. nitidum* leaves considered to be lethal dose.[20]

Phytochemistry

Most of the medicinal herbs contain large number of therapeutically important phytochemicals. Similarly, *Z. nitidum* is also very rich in phytochemicals like alkaloid, lignans, coumarins, terpenes, steroids, alkylamides etc.[21] Various researches are going on for extraction and identification of phytochemicals. A team from Hong Kong carried out researches on *Z. nitidum* from 1959 and they have isolated and identified large number of phytochemicals including alkaloid, lignans, coumarins, terpenes, steroids etc. Among these, alkaloids are considered to be main phytoconstituents which is responsible for its therapeutic potential.[14]

Alkaloids

Alkaloids are the major family of phytoconstituents present in *Z. nitidum* which comprises 88 alkaloids and associated glycosides. Due to wide range of biological activities, identification of alkaloids and other chemicals was an important task for researchers. Previously worked authors mentioned that, the content and quantity of benzophenanthridine alkaloids **(1-52)** were present in greater amount, so they are being considered as important alkaloids of *Z. nitidum*.[22,23] Further studies by different authors revealed that, some other class of alkaloids were also found, such as quinolines **(53-88)**, berberines **(74-77)**, aporphines **(78-81)**, indoles **(82-86)**, tetrahydroisoquinoline **(87)** and protopine **(88).**[24–27]



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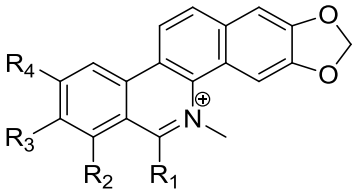
1	O	OCH_3	OCH_3	H
2	O	H	OCH_3	OCH_3
3	OCH_3	OH	OCH_3	H
4	2H	H	OCH_3	OCH_3
5	OCH_2CH_3	OCH_3	OCH_3	H
6	OCH_3	OCH_3	OCH_3	H
7	O	H	-OCH_2O-	
8	$CH(OH)CH_3$	OCH_3	OCH_3	H
9	2H	OCH_3	OCH_3	H
10	CH_2COOH	OCH_3	OCH_3	H
11	O	OCH_3	OH	H
12	CH_2OH	H	OCH_3	OCH_3
13	CH_2OH	OCH_3	OCH_3	H
14	OCH_3	H	OCH_3	OCH_3
15	CH_2COCH_3	H	-OCH_2O-	
16	CH_2COCH_3	OCH_3	OCH_3	H
17	CH_2COCH_3	H	OCH_3	OCH_3
18	CH_2COCH_3	OCH_3	OH	H
19	O	H	OH	OCH_3
20	CH_2CHO	OCH_3	OCH_3	H
21	OH	OCH_3	OCH_3	H



Sl. No.	R1	R2	R3	R4
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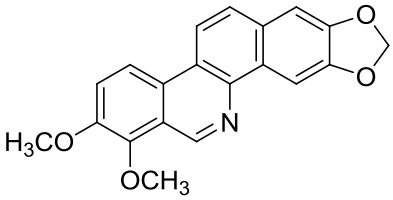
23	H	OCH_3	OH	H
24	H	OCH_3	OCH_3	H
25	OCH_3	H	OCH_3	OCH_3
26	H	-OCH_2O-		H
27	OCH_3	-OCH_2O-		H
28	H	H	-OCH_2O-	H
29	H	H	OCH_3	OCH_3



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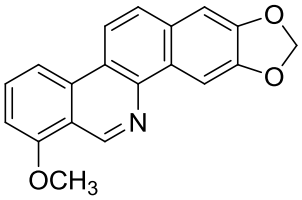

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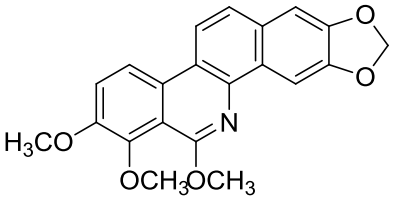

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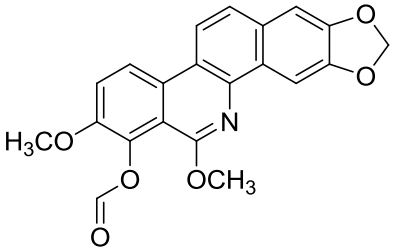

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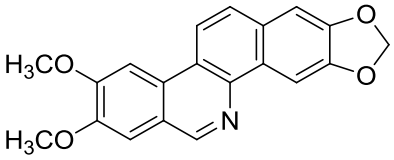

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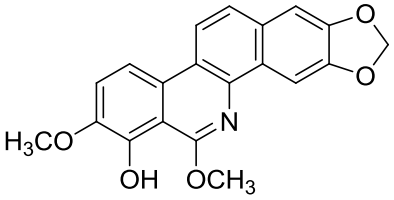

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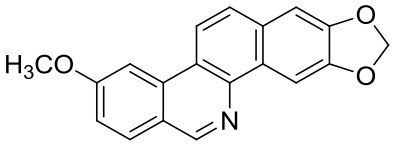

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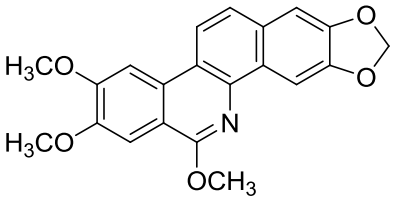

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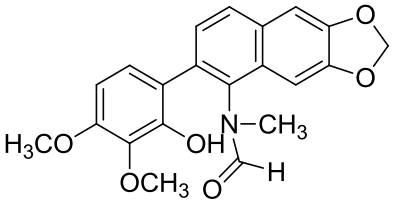

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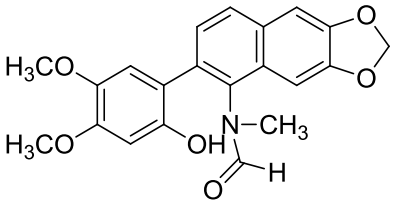

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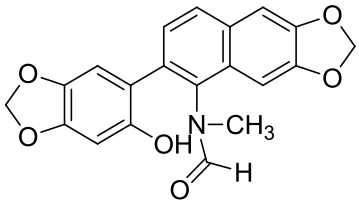

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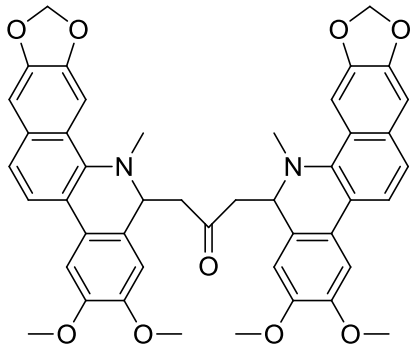

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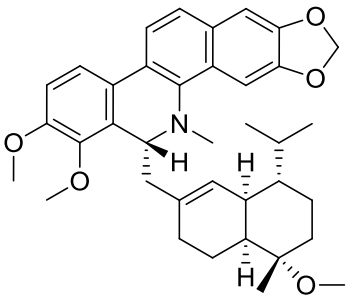

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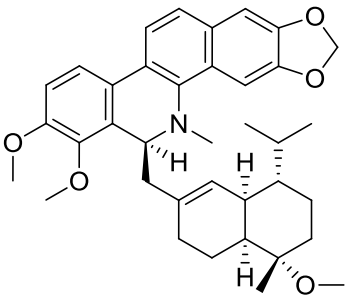

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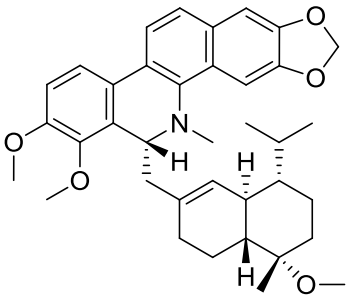

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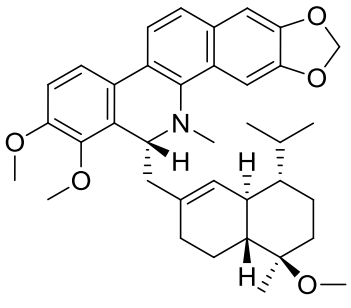

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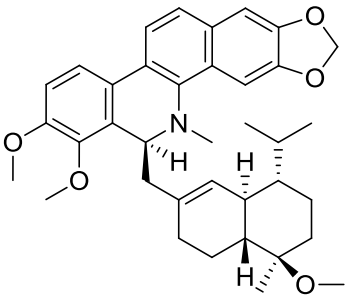

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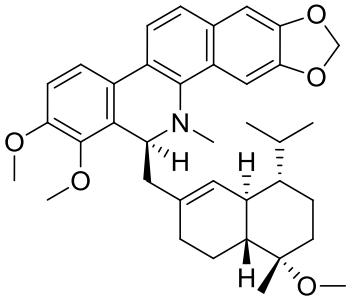

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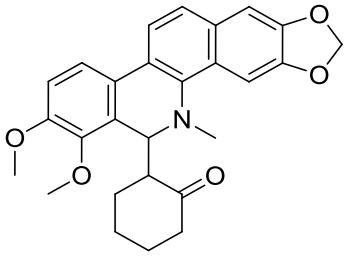

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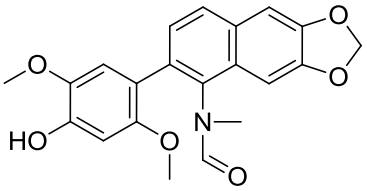

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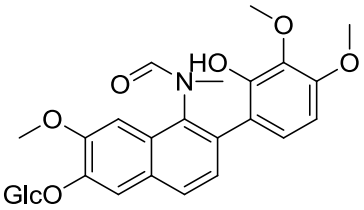

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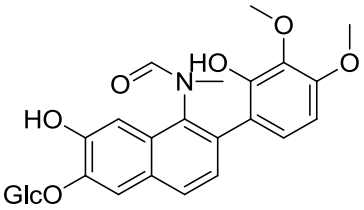

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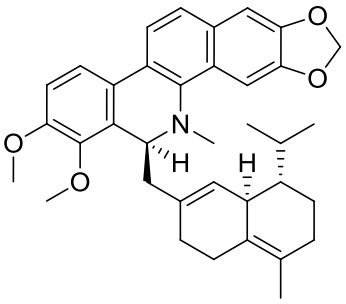

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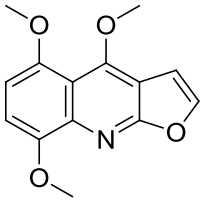

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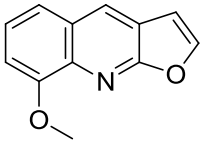

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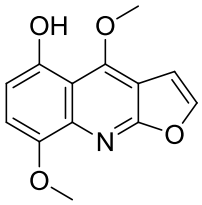

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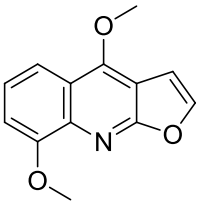

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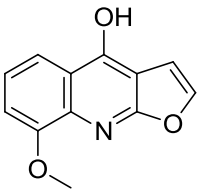

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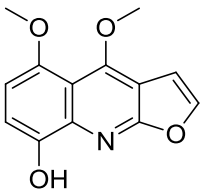

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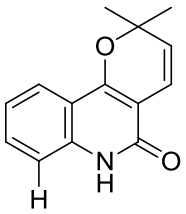

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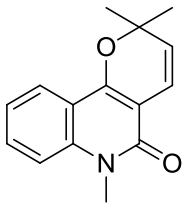

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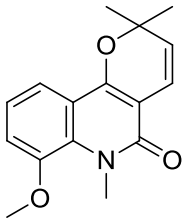

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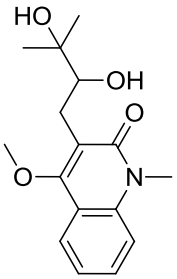

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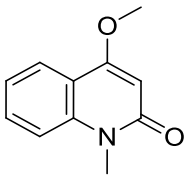

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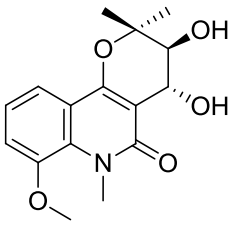

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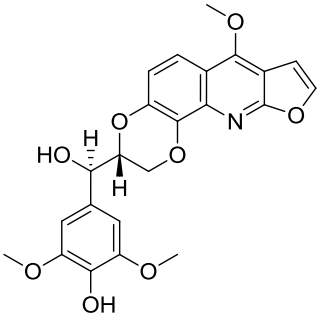

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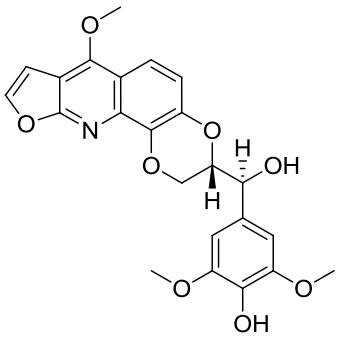

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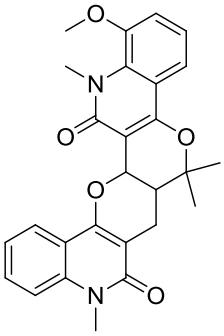

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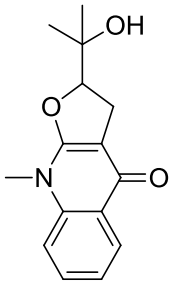

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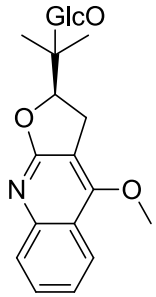

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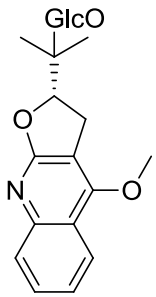

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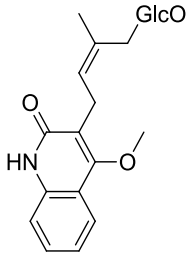

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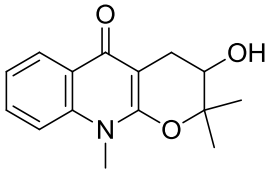

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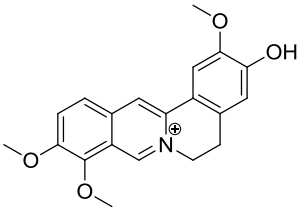

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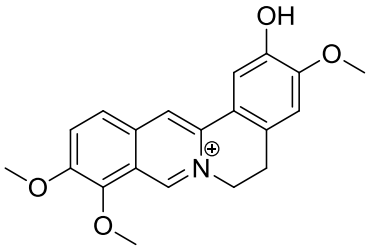

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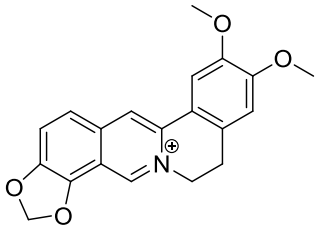

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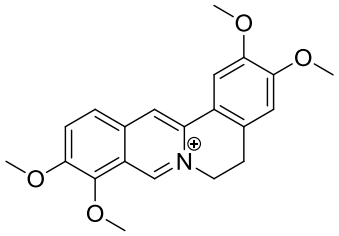

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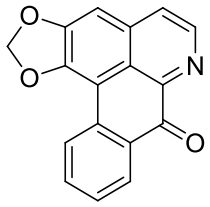

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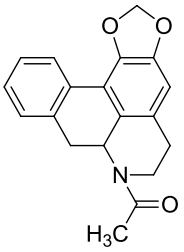

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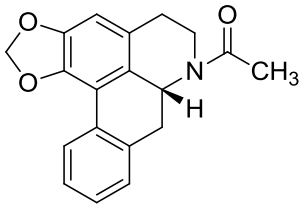

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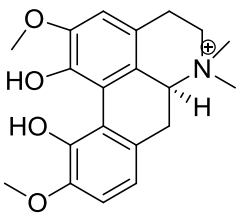

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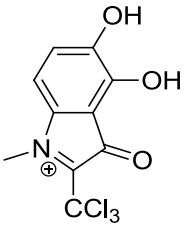

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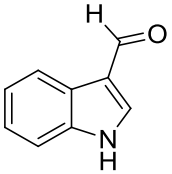

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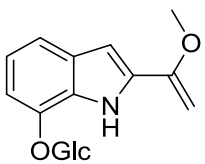

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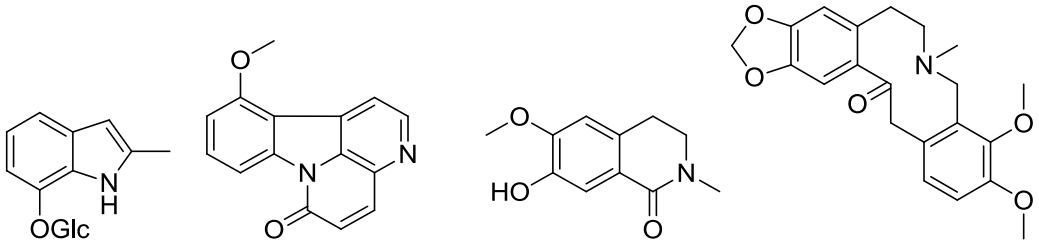
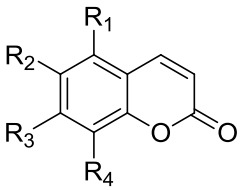


84 **85** **86** **87**

Coumarins

Phytochemical studies have found that *Z. nitidum* contain few numbers of coumarins. A team of researchers from China mentioned that, up to February 2020, 19 compounds **(90-108)** which contains 15 simple coumarins and 4 furanocoumarins have been isolated and identified. All the coumarins have the similar characteristics of linking oxygen containing functional group at C-7.[28,29] Among these, four oxygenated coumarins **(92, 97, 105, 106)** exhibit certain antibacterial property as like alkaloids.[23]



	R1	R2	R3	R4
88	OCH_3	H	OCH_3	H
89	OCH_3	H	OCH_3	OCH_3
90	OCH_3	H	OCH_3	**M**
91	OCH_3	OCH_3	OCH_3	H
92	H	OCH_3	OCH_3	H
93	H	OCH_3	OCH_3	OCH_3
94	H	OCH_3	OH	H
95	**X**	H	OCH_3	H
96	OCH_3	**Y**	OCH_3	H

	R1	R2	R3	R4
97	OCH_3	**Z**	OCH_3	H
98	OCH_3	**P**	OCH_3	H
99	H	H	OCH_3	OCH_3
100	OCH_3	H	OCH_3	**Y**
101	H	H	OH	H

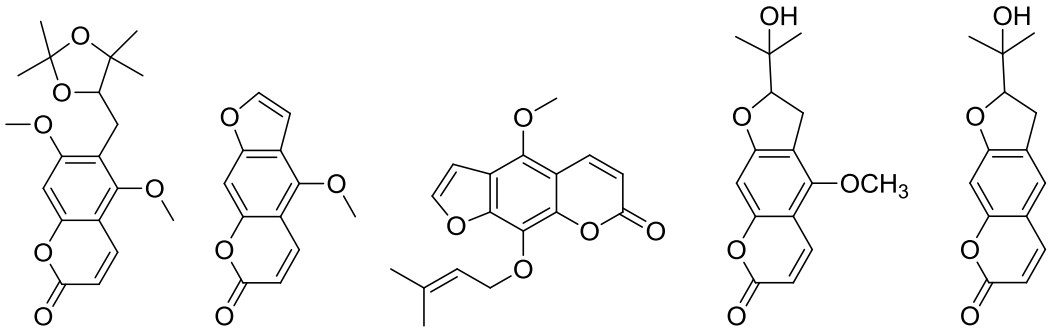
M: $OCH_2CH=C(CH_3)_2$

X: $OCH_2CH=C(CH_3)$ $CH_2CH_2CH=C(CH_3)_2$

Y: $CH_2CH(OH)C(CH_3)_2OH$

Z: $CH_2COCH(CH_3)_2$

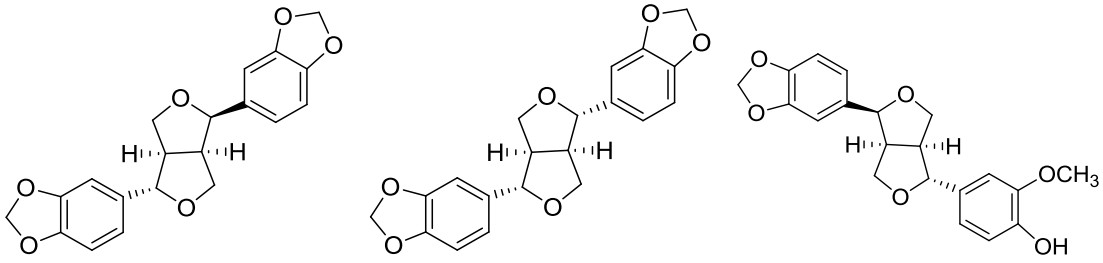
P: $CH_2CH=C(CH_3)_2$



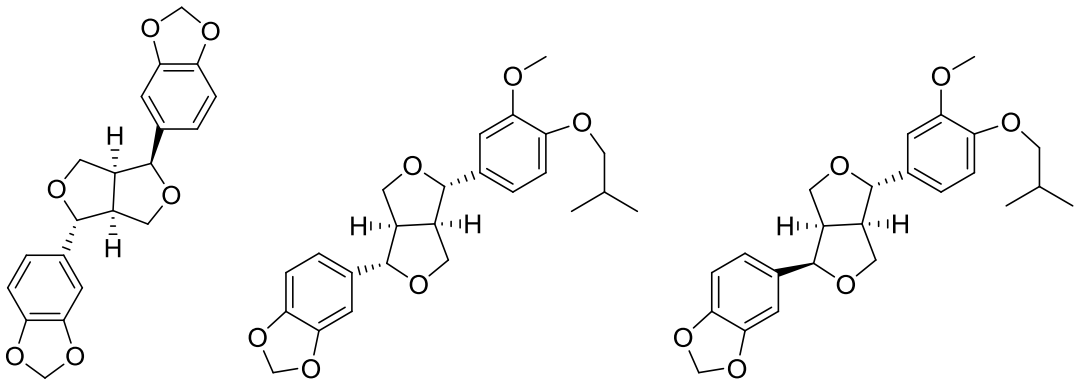
102 **103** **104** **105** **106**

Lignans

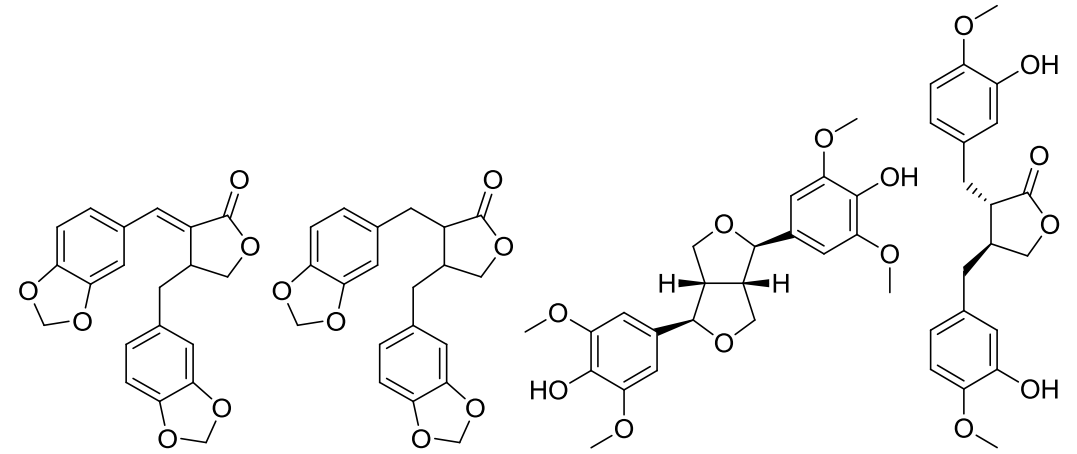
Researchers have isolated 15 lignans **(108-121)** from the stem and roots *Z. nitidum*. Among these, most of the lignans are belongs to furfuran lignans **(108-113, 116, 119).**[23,27,29]



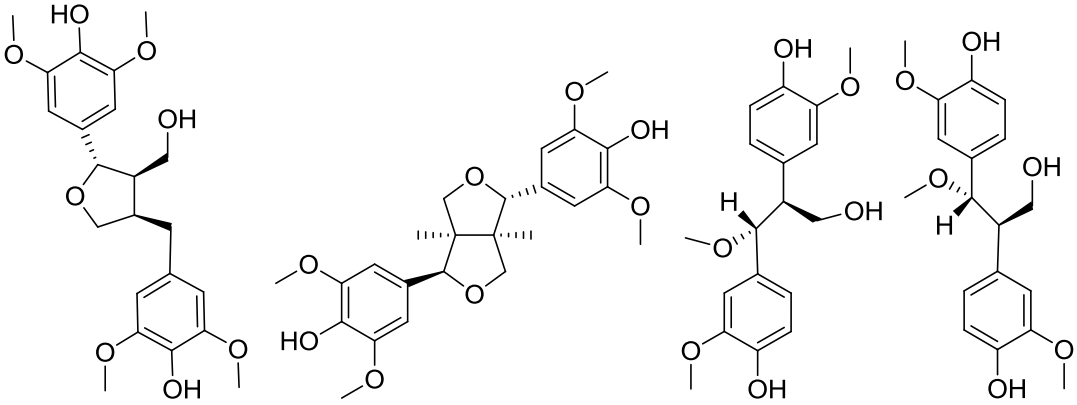
107 **108** **109**



110 **111** **112**



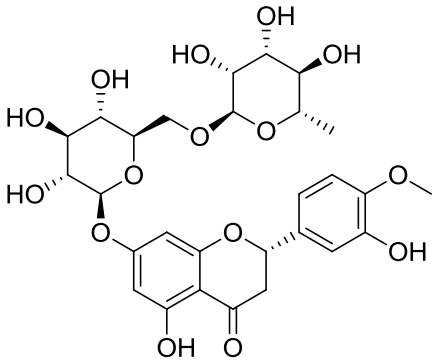
113 **114** **115** **116**



117 **118** **119** **120**

Flavonoids

Flavonoids are important class of compound which exhibits various activities like antibacterial, anti-inflammatory as well as antidiabetic properties also. Previously worked authors mentioned that, 4 therapeutically potential flavonoids namely hesperidin **(121)**, diosmin **(122)**, vitexin **(123)** and apigenin **(124)** were isolated, purified and characterised from roots and stems of *Z. nitidum*. Previously worked authors mentioned that flavones of *Z. nitidum* possess potential antimicrobial properties and can be useful in development of new chemotherapeutic drugs which will inhibit microbial infections.[14,23]



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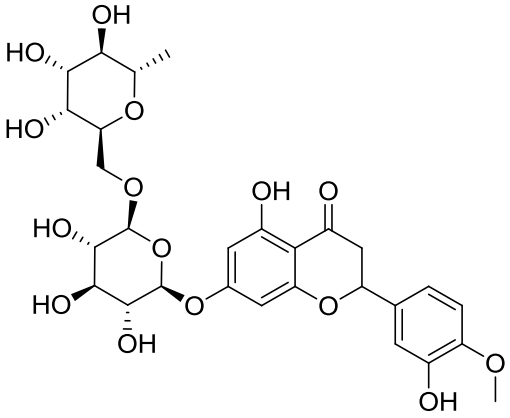

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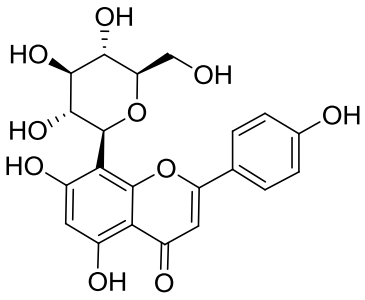

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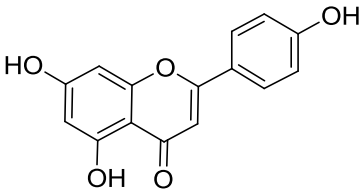
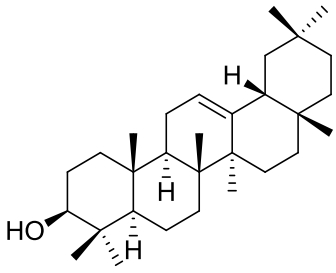


128

Terpenes

Terpenes are mainly found in the volatiles oil containing plants. A total of 17 terpene containing compound **(129-141)** has been isolated and identified from *Z. nitidum* plant. Among them, two compounds **(130-131)** belongs to monoterpenes, one triterpenoid compound **(129)** whereas rest of the compounds **(133-141)** belongs to sesquiterpenes.[14]



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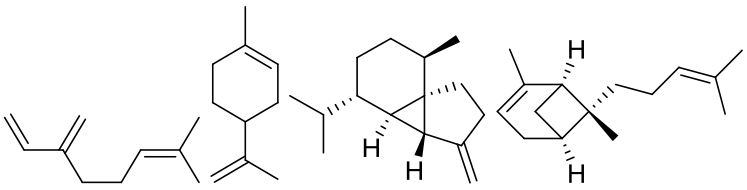
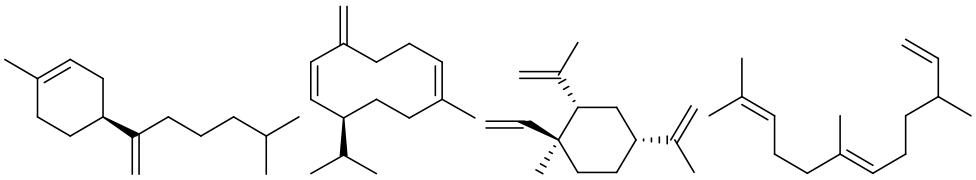
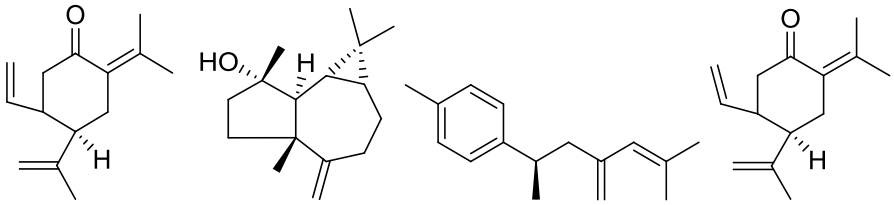


130 **131** **132** **133**



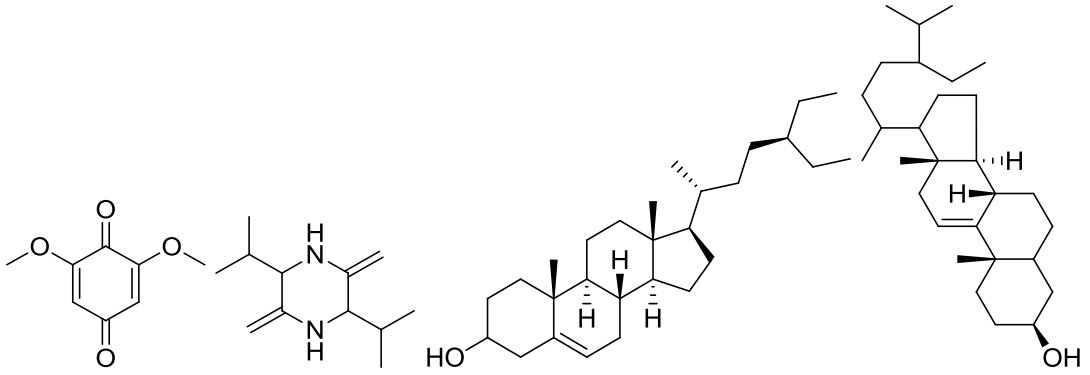
134 **135** **136** **137**



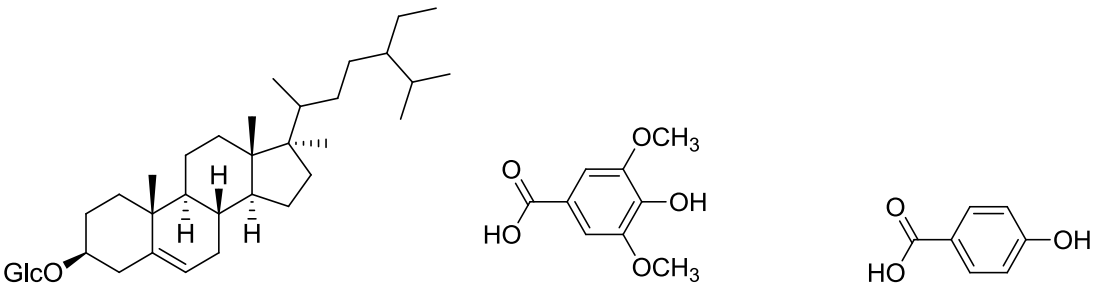
138 **139** **140** **141**

Other compounds

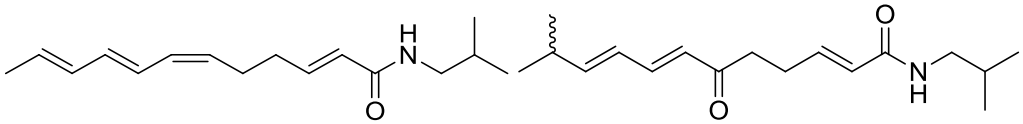
Apart from alkaloids, coumarins, lignans, flavones and terpenes, some other beneficial compound are also present. Several authors mentioned that, *Z. nitidum* contains one benzoquinone **(142)**, polypeptide **(143)**, steroids **(144-146),** organic acids **(147, 148)**, alkylamides **(149, 150)** and benzenoids **(151-153).**[24,27,29] Meng *et al.* reported that, neoherculin **(149)** is an alkylamides present in *Z. nitidum*, due to which this plant possesses analgesic activity.[14]



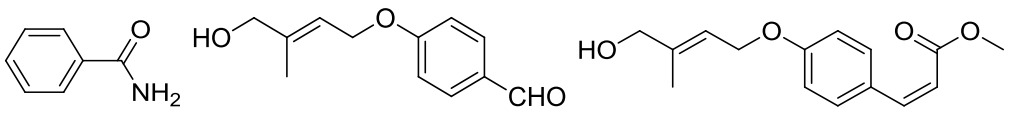
142 **143** **144** **145**



146 **147** **148**



149 **150**



151 **152** **153**

Pharmacological activity of *Zanthoxylum nitidum*

Z. *nitidum* also known as *Tez-mui* in Assamese, shows various pharmacological activities due to the presence of wide range of phytoconstituents in it. Some of the reported pharmacological activities by various researchers are as below-

Anti-inflammatory activity

Z. *nitidum* possesses anti-inflammatory activity. Bhattacharya *et al.* evaluated the anti-inflammatory activities of *Z. nitidum* against carrageenan induced acute paw oedema in rats, where it was found that extract of *Z. nitidum* was effective in exhibiting anti-inflammatory activity at a dose dependent manner. 95% of ethanol extract of *Z. nitidum* roots showed significant anti-inflammatory activity.[21] Yang *et al.* carried out the extraction of *Z. nitidum* in both ethanol and water, where it was found that, the number of phytochemicals extracted was greater in ethanolic extract. Therefore, the anti-inflammatory components of *Z. nitidum* was mainly exist in ethanolic extract not in the water extract.[6] The roots of Z. *nitidum* possess stronger anti-inflammatory activity as compared to their stems. One of the main mechanisms behind anti-inflammatory activity of Z. *nitidum* is that the total alkaloid present in Z. *nitidum* inhibits the level of both TNF-α and IL-8 (interlukin-8) in the serum of ulcerative colitis rats.[14]

The phytochemicals mainly responsible for anti-inflammatory activity of *Z. nitidum* are dihydrochelerythrine, oxyavicine, neoherculin, hesperidin, 8-methoxy dihydrochelerythrine, 8-hydroxy dihydrochelerythrine, 6-ethyoxychelerythrine, 8-acetonyl dihydrochelerythrine and nitidine chloride, which mainly acts by inhibiting the release of prostaglandin E2 (PGE_2).[14] Among them nitidine chloride exhibits strongest anti-inflammatory activity by targeting DNA topoisomerase 1 (TOP1) and increasing interlukin-10 (IL-10) levels.[6] Hu *et al.* reported that a C=N bond may be important for its anti-inflammatory activity.[30] 8-acetonyldihydrofagaridine, 8-acetonyldihydrochelerythrine, decarine, *d*-episesamin, N-methylflindersine, *l*-sesamin inhibits fMLP (N-formyl-methionyl-leucyl-phenylalanine) induced elastase release which helps in suppression of inflammation.[24]

Analgesic activity

Previously worked authors reported that, 95% of ethanolic extract of *Z. nitidum* roots possesses significant analgesic activity which was evaluated by using writhing and hot plate method. There is no significant difference between the analgesic effect of *Z. nitidum* roots and stem.[14] The main mechanism behind analgesic activity of *Z. nitidum* is that it significantly suppressed the over-expression of the phosphorylation of NF-kB (Nuclear Factor kappa-light-chain-enhancer of activated B cells) p65 and ERK1/2 (Extracellular Regulated Kinase 1/2) at both central and peripheral levels which attenuates inflammatory pain.[31]

The phytochemicals mainly responsible for analgesic activity of *Z. nitidum* are dihydrochelerythrine, neoherculin, oxyavicine, 8-methoxydihydrochelerythrine, 8-hydroxydihydrochelerythrine and nitidine chloride. Among them nitidine chloride exhibits strongest analgesic activity.[6,30] Rhiofoline A also shows some analgesic activity through NO-cGMP (Nitric Oxide cyclic Guanosine Monophosphate) signalling pathway and L-type Ca_{2+} channels.[31,32]

Haemostatic activity

Z. nitidum also possesses some haemostatic activity. The haemostatic activity can be evaluated by using capillary glass tube and glass slide method. 95% ethanol extract and ethyl acetate portion of *Z. nitidum* roots possesses strong haemostatic activity. According to Yang, 2008 report the main phytochemical which is responsible for haemostatic activity of Z. *nitidum* is neoherculin.[6,14]

Anti-microbial activity

The hot methanol extract of *Z. nitidum* possesses broad spectrum antibacterial properties as well as good inhibitory effects on MRSA (Methicillin-resistant *Staphylococcus aureus*) strains. Earlier author reported that, among different polar parts i.e. 70% ethanol extract, n-butanol, ethyl acetate and water, the ethyl acetate portion of stems exhibited strongest antibacterial activity. The flavones present in *Z. nitidum* shows strongest antimicrobial activity which is useful for the development of new chemotherapeutic agents against various microbial infections.[14] Sanjib Bhattacharya *et al.*, evaluated the anti-bacterial activity of aqueous and ethanol extract of stem bark and root of *Z. nitidum* by using disk diffusion method and minimum inhibitory concentration (MIC) was evaluated by broth dilution method.[15]

The phytochemicals i.e. 7-demethyl-6-methoxy-5,6-dihydrochelerythrine, nitidine chloride, 8-methoxydihydrochelerythrine, sikimmianine, lirioddenine present in *Z. nitidum* shows antibacterial activity. Dictamnine, 5-methoxy Dictamnine, γ-fagarine shows strong antifungal activity. Also, both (+)-zanthonitidine A and (-)-zanthonitidine A shows moderate antimicrobial activity.[6,26]

Anti-viral activity

The phytochemicals i.e. 6-methoxy-5,6-dihydronitidine, 5-methoxydictamnine, 5,6-dihydro-6-methoxynitidine, skimmianine isolated from roots of *Z. nitidum* possesses significant anti-HBV (Hepatitis B Virus) activity. The aqueous extract of Z. *nitidum* inhibit the growth of ERG6Δ (Ergosterol 6) yeast prion.[33]

Anti-oxidant activity

Z. nitidum possesses some anti-oxidant activity. Bhattacharya *et al.* experimentally carried out the antioxidant properties of *Z. nitidum* stem bark. The anti-oxidant properties of *Z. nitidum* was evaluated by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay and it was found that the extract of *Z. nitidum* stem bark possess significant anti-oxidant activity. The mechanism behind this anti-oxidant property is inhibition of Fe2+ cysteine induce production of malondialdehyde in liver homogenate lipids and also shows some scavenging effect on superoxide anion radical.[21] The ethanol-acid extract shows strongest inhibition and water extract shows strongest scavenging effect. These three extracts also show some degree of inhibition on the whole blood chemiluminescence.[14]

Anti-cancer activity

Z. nitidum possesses some potent anti-cancer activity. It is useful against gastric cancer, liver cancer, breast cancer, ovarian cancer and cervical cancer.[34] The phytochemicals i.e. nitidine chloride and 8-methoxydihydrochelerythrine can prolong the life span of mice with Ehrlich ascites carcinoma. Also, nitidine chloride possesses some effect on chronic myeloid leukaemia. Liriodenine has a very high activity against MCF-7, SF-268 and NCI-H460 cell lines.[14] Also 7-methoxy-8-demethoxynitidine possesses strong cytotoxic effect against KB, MCF-7, LNCaP, HepG2 human cancer cell lines.[10] 8-methoxy dihydrochelerythrine act by inhibiting STAT3 (Signal Transducer and Activator of Transcription 3) phosphorylation and its target gene expression.[35] Nitidine chloride shows anticancer activity by inhibiting breast tumour cell migration and invasion by suppressing the c-Src (cellular-Sarcoma)/FAK (Focal Adhesion Kinase) -associated signalling pathway, induces apoptosis, cell cycle arrest, by

suppressing JAK1/STAT3, ERK and SHH (Sonic Hedgehog Signaling Molecule) signalling pathway, regulating the expression of key target gene including Bcl-2, Bax, Cyclin D1, CDK4 (Cyclin-Dependent Kinase-4), VEGFR2 (Vascular Endothelial Growth Factor 2), VEGF-A (Vascular Endothelial Growth Factor-A) etc. Because of these properties nitidine chloride is one of the most important anticancer active ingredients from Z. *nitidum.*[36–38]

Anti-gastric ulcer activity

Bhattacharya *et al.* experimentally investigated the anti-ulcer activity of stem bark aqueous extract of *Z.nitidum* against chemical and stress induced ulcer in Wister Albino rats. It was found that, the extract of *Z. nitidum* shows anti-ulcer activities in a dose dependent manner as compared to standard drug Ranitidine HCl.[39] The total alkaloid presence in *Z. nitidum* can increase the content of superoxide dismutase, nitric oxide (NO) and PGE2 and reduce the activity of pepsase and the content of malondialdehyde inside the stomach in the pyloric ligation induced gastric model. It can also reduce the ulcer index induced by stress, pyloric ligation and alcohol in animal models.[14]

Anti-oral ulcer activity

Experimental studies revealed that, the effect of external use of *Z.nitidum* against oral ulcer induced by burning the cheeks with phenol on guinea pig model. It was found that, the external use of *Z.nitidum* paste and decoction has a favourable positive effect on oral ulcer.[14]

Hepatoprotective activity

Previously worked authors reported that, the water extract of *Z. nitidum* possesses hepatoprotective activity. They studied the hepatoprotective effect of water extract of *Z. nitidum* on tetrachloromethane induced experimental liver damage in Kunming mice. From that experiment they found that *Z. nitidum* notably increased the liver superoxide dismutase activity and reduced the aspartate aminotransferase, alanine aminotransferase and liver malondialdehyde content in mice. Hence *Z. nitidum* has definitely hepatoprotective effect.[14]

Anti-nociceptive and locomotor activity

Bhattacharya *et al.* evaluated the anti-nociceptive and locomotor activity of ethanol and aqueous extract of stem bark of *Z.nitidum* in mice. From their experiment they found that the ethanol extract showed strong anti-nociceptive activity by involving both central and peripheral pain mechanism while aqueous extract only inhibited peripheral pain mechanism. Also, only the ethanol extract showed significant depressed locomotor activity in mice.[40]

CONCLUSION

Recent studies have claimed that *Z. nitidum* possesses many pharmacological activities such as anti-inflammatory, analgesics, anti-microbial, anti-viral, anti-cancer, haemostatic and other activities. Apart from pharmacological use, this prickly shrub is being used traditionally in different places as blood circulation promoter, cure snake bite, stomachache, toothache, fever, cough, diarrhoea, stimulants, rheumatism, paresis, boils, as a pesticides and insecticides. *Z. nitidum* is rich in various types of phytoconstituents such as alkaloids, coumarins, lignins, terpenoids, flavonoids etc. Among these, alkaloids are considered to be most active phytochemicals in *Z. nitidum* due to which most of the pharmacological activities are shown by this plant. Roots, stem, bark are the main parts of the plant whose extracts are being used abundantly for experimental purpose. Various experiments for determine the anti-oxidants, anti-inflammatory, anti-cancer, hepatoprotective and anti-ulcer activities had carried out and proved their efficacy in controlling various disease in animal model. Meanwhile, most of the traditional uses of this plant are to be investigated experimentally. Leaves of this plant are used very less for experimental program which lead to opportunities for researchers in further preclinical investigation. All the phytoconstituents possess different activities in a dose dependent manner due to which we can conclude that there might be some serious toxicity for overdose of this plants after used traditionally.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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