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Phytochemistry, Pharmacological Activities, Nanoparticles Synthesis, Commercial Exploration and Valorization of Endangered Medicinal Plant *Embelia ribes* Burm.: A Review

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ABSTRACT: *E. ribes* Burm. is a medicinally important woody climber belonging to the family Myrcinaceae. It is also known as "Vidanga" and has been used for various medicinal purposes since ancient times. It has always been a significant part of history in the ayurvedic system of medicine in various forms like churna, asava, aristha, lauha, and taila. It has been extensively used as a curative agent for stomach aches, leprosy, nervous debility, dyspepsia, flatulence, colic tumors, asthma, fever, ascaris, infestation, and skin diseases. The main chemical constituent of *E. ribes* is "Embelin," and other chemical constituents are volatile oils, tannins, christembine, resinol, embeliol, embelinol, quercitol, vilangin, potassium embelate, aryl substituted benzoxadiazine, 5-O-ethylembelin, 5-O-methylembelin (derivatives), 2-hydroxy-5-substituted-3-undecylcyclohexa-2,5-diene-1,4-diones (derivatives), and phenolic acids like caffeic acid. Among the many promising pharmacological effects demonstrated by the essential oils, extracts, and isolated chemical constituents were those of antioxidant, wound healing, antidiabetic, central nervous system (CNS) disease, antiobesity, antibacterial, antiviral, cardioprotective, antifungal, and antifertility. Various applications of *E. ribes* are reported, as well as its phytochemical and phytochemical composition, pharmacological activities, and nanoparticle fabrication. More thorough, state-of-the-art preclinical research is needed to learn about its efficacy and safety profileapproaches are needed to examine the efficacy and safety profile of *E. ribes* as itmay be a good candidate for the introduction of novel drugs because of their potential utility in both traditional and contemporary medical settings. Our primary goal is to describe the current state of knowledge concerning the historical use, phytochemistry, and pharmacology of *E. ribes*. Further, the scientific connotation of traditional uses has been highlighted, and the value and importance of considering both modern therapeutically known actions and traditional uses in folk medicine have been described, through research into the therapeutic potential of essential oils/extracts and isolated compounds obtained from *E. ribes*, correlated with their antioxidant potential. This article provides a concise overview of the studies that have been conducted on the pharmacological properties and potential uses of the phytochemical substances extracted from *E. ribes* plants.

Keywords: Embelia, phytochemicals, pharmacology, nanotechnology, valorization.

INTRODUCTION

E. ribes Burm. is a red-listed medicinally important dioecious woody climber belonging to the family Myrsinaceae (Sudhakaran, 2016), which is sparsely distributed in the moist deciduous forest in India, Malaysia, South China, Cambodia, and Vietnam (Dang *et al*., 2015). *E. ribes*, commonly known as "Vidanga" has been used in traditional medicine. It has been extensively used as a curative agent for dyspepsia, flatulence, colic tumors, asthma, stomachache, leprosy, nervous debility, fever, ascaris, infestation, and skin diseases (Dang *et al.*, 2015; Mishra & Lal 2013; Sudhakaran, 2016). It has been said that the fruit pulp is applied to black pepper to make it stronger, and the fresh juice is used as a laxative, diuretic, and cooling agent (Mohandas *et al*., 2013). The root bark of *E. ribes* is unpleasant and has mordant, anthelmentic, infertility, antioestrogenic, diaphoretic, digestive, laxative, soothing, stimulant, and muscle-building properties. The leaves of this species possess depurative, thermogenic, demulcent, and astringent properties. Leprosy, pruritus, sore throat, mouth ulcers, indolecent, and skin problems are treated by them. The cooked tender leaves and fruits are reported to be used against infections of the kidney, ringworm, and other skin diseases and as a carminative to prevent flatulence in children (Choudhary *et al*., 2021). According to Rout et al. (2021), the berries of the *E. ribes* plant contain embelin, unstable oil, fixed oil, sap, tannin, and phenolic acids (Rout *et al*., 2021). In addition to having analgesic, anti-inflammatory, and antioxidant properties, it also has antibacterial and anti-protozoan activity and can be used to treat infertility, stomach

issues, lung illnesses, constipation, indigestion, fungal infections, mouth ulcers, sore throats, pneumonia, heart disease, and obesity. Embelia's high market value comes from the abundance of medicinally valuable compounds found throughout the plant, including embelin and its derivatives, embeliol, 5-O-Methylembelin, and vilangin, all of which find usage in herbal formulations. Interestingly, the use of the same plant parts varies from region to region. The World Health Organization (WHO) advocates for the prudent use of raw materials in traditional and complementary medicine based on evidence and strategic research in order to enhance global health. In this review, comprehensive information on the phytochemical/phytochemistry, pharmacological activities, nanoparticle fabrication from various *E. ribes* parts, and some other uses is reported.

MORPHOLOGICAL FEATURES OF *EMBELIARIBES*

Ribes is a large shrub with long branches up to 10 m high at maturity, measuring about 45–72 cm in diameter. The stem is a whitish gray in color, with tiny black spots representing intercellular spaces. There are lenticels all over the bark. Intercellular gaps give the stem a white-grey appearance. Leaves are ovate or oblong-lanceolate, the base rounded or cuneate and are 6–14 cm long and 2-4 cm wide. Flowers are small, pentamerous or tetramerous, light green with a yellow undertone, and borne in lax racemes of a panicle. The tiny, round fruits range in thickness from 2.4 to 4.0 microns; they are smooth, tasty, and each contain just one seed. The seeds are globose with a hollowed base. The flowers bloom in the month of February (Rout *et al.*, 2021).

A. Geographical distribution

This species (Fig. 1) is found in the tropical regions of China, Southeast Asia, Australia, the Polynesian islands, Africa, and Madagascar, where it thrives in semi-evergreen and deciduous woods to an elevation of 1500 m.(Dubéarnès *et al*., 2015), it is found in the center and lower Himalayas, Arunachal Pradesh, Assam, Meghalaya, Maharashtra, Andhra Pradesh, Karnataka, Kerala, Bengal, Odisha, Madhya Pradesh, and Tamil Nadu, as well as Sri Lanka, Singapore, Malaysia, and South China(Asadulla & Rajasekharan 2013; Rout *et al.*, 2021).

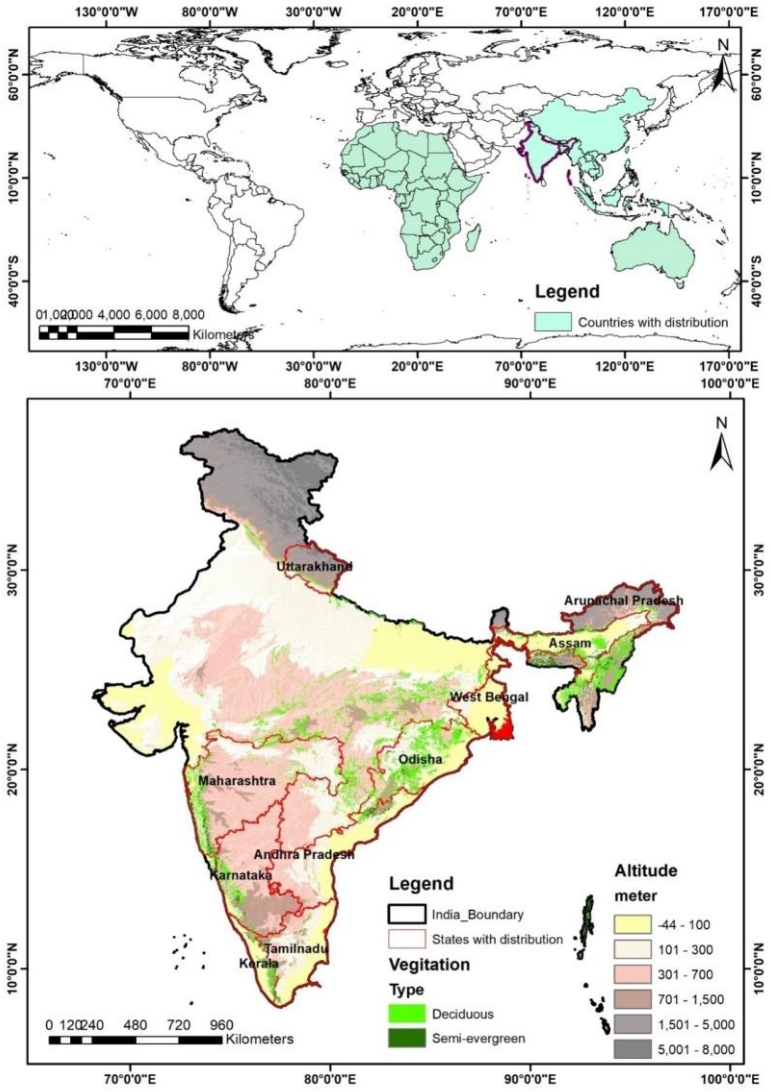

Fig. 1. Geographical distributions of *E. ribes*.

CHEMICAL COMPOSITION AND ISOLATED COMPOUNDS

The fruits, seeds, leaves, etc., of this species comprise active principal compounds such as embelin, embeliaribyl ester, embelinol, and embeliol (Haq *et al.*, 2005). Rigorous phytochemical and pharmacological studies have been carried out on the fruits of this species (Khan *et al.*, 2010), and they have been reported to contain a quinine derivative, embelin (3-undecyl-2,5-dihydroxy-1,4-benzoquinone), an alkaloid, along with christembine and quercitol. Fatty ingredients include a resinoid, tannins, and a volatile oil, vilangin (Asadulla & Rajasekharan 2013; Shankarmurthy *et al.*, 2004). Caffeic acid, vanillic acid, chlorogenic acid, and cinnamic acid are only some of the phenolic acids found in *Embelia berries*; additional phenolic acids, as well as unstable oil, fixed oil, sap, tannin, and embelin, may be found in this fruit as well. Embelin, potassium embelate, daraprim, quercitol, fatty components, vilangin, and other compounds make up 4.33 percent of the berry's total chemical makeup (Rout *et al.*, 2021). A total of 56 compounds, including 4 coumarins, 16 flavonoids, 16 phenolics, and 16 flavonoids, were discovered. There was an additional evaluation of the total phenolic and flavonoid content. A good source of phenolics and flavonoids was said to be the acetic ether or ethyl acetate extract of *E. ribes*. Furthermore, the acetic ether extract showed a strong antioxidant effect (Guo *et al.*, 2020).

Table 1: Isolated compounds from *Embelia ribes.*

Isolated compounds/phytoconstituents	Parts used	References
Embelin	Fruits of *E. ribes*	(Arthanareeswari *et al.*, 2021)
Embeliaribyl ester	Seeds of *E. ribes*	(Alam *et al.*, 2018)
Embelinol	Seeds of *E. ribes*	(Aishwarya, 2018)
Embeliol	Seeds of *E. ribes*	(Wankhade *et al.*, 2021)
Christembine	Seeds of *E. ribes*	(Agrawal *et al.*, 2021)
Quercitol	Plants of *E. ribes*	(Wankhade *et al.*, 2021)
Tannins	Seeds of *E. ribes*	(Agrawal *et al.*, 2021)
Volatile oil	Plants of *E. ribes*	(Dwivedi *et al.*, 2019)
Vilangin	Plants of *E. ribes*	(Nijsure *et al.*, 2016)
Caffeic	Seeds of *E. ribes*	(Dwivedi *et al.*, 2019)
Potassium embelate	Fruits of *E. ribes*	(Wankhade *et al.*, 2021)
Aryl substituted benzoxadiazine	Fruits of *E. ribes*	(Wankhade *et al.*, 2021)
5-O-ethylembelin, 5-O-methylembelin (derivatives)	Fruits of *E. ribes*	(Wankhade *et al.*, 2021)
2-hydroxy-5-substituted-3-undecylcyclohexa-2,5-diene-1,4-diones (derivatives)	Fruits of *E. ribes*	(Wankhade *et al.*, 2021)

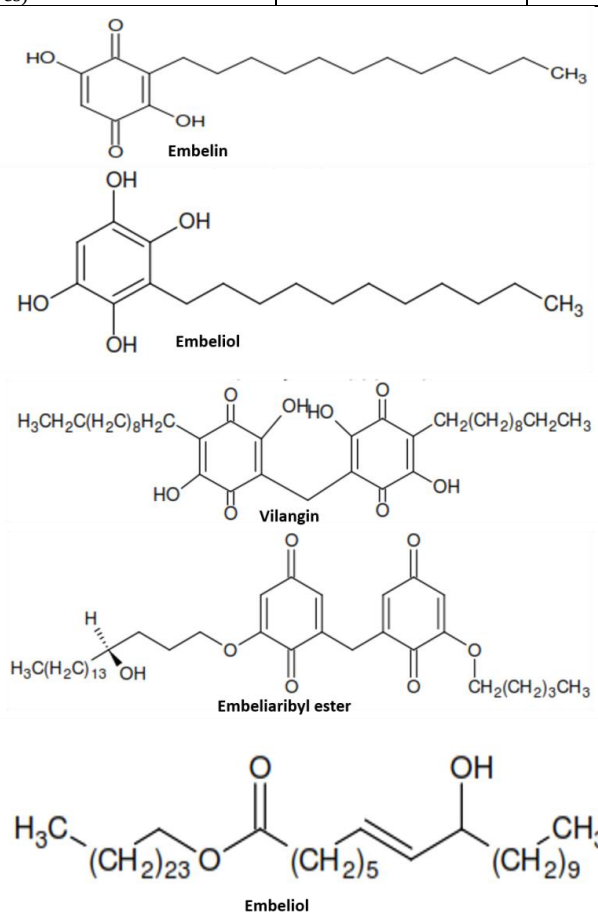

Fig. 2. Some important phytoconstituents of *Embelia ribes*.

Pharmacological activities. Since there is such a wide selection of phytochemical compounds present in virtually all plant tissues, *E. ribes* also proves to be a potent medicinal herb (Fig. 3). According to Acharya Sushrut, the fruit of *E. ribes* is anti-helminthic and a tonic for strength. To treat skin infections, paste is utilized. An infusion of the roots is helpful for treating coughs and diarrhea. It also helps to eliminate extra fat by increasing the body's metabolism. *E. ribes* is also utilized to remove vata (the characteristics of the elements ether and air constituting the vatadosha) from the gut, nerve impulses, and our energy and mobility. Vata turns up in the breath, speech, blood flow, and digestion. Additionally, it raises rasdhatvaagni, which speeds up the body's metabolism and helps remove extra fat. *E. ribes* fruits have antibacterial properties that are effective against *E. coli* and *Staphylococcus aureus*. It is an Ayurvedic tonic and energy booster that also aids in digestion and treats anorexia. Its fruits are reputed to treat insomnia, bleeding, rhinitis, headaches, and other conditions (Wankhade *et al*., 2021).

Embelin has effective antimicrobial, antipyretic, and antifertility activities. It can be taken as a purgative to eliminate tapeworms by mixing it with milk as a powder. It is also used as a fat burner and for the treatment of TB, chronic cough, snake bites, and a variety of dental problems; it helps stop nose bleeding and relieves constipation because of its laxative properties. Sore throats and mouth ulcers can be treated with the astringent leaves of this plant (Ananth, 2019; Hossan *et al.*, 2018).

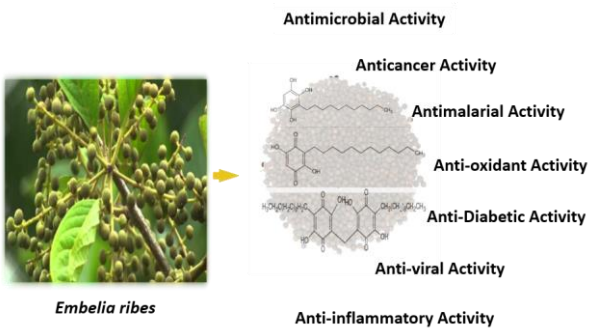

Fig. 3. Pharmacological activities of *Embelia ribes*.

Traditional pharmacological uses of *Embelia ribes.* Since ancient times, peoples of respective localities having access to *E. ribes* have used its different parts for the treatment of health issues and also for guarding their health (Sharma *et al.*, 2022). Plant parts such as fruits, leaves, roots, and seeds (Table 2) have been mostly used. That traditional knowledge is only the real booster to take the modern pharmacological exploration of *E. coli* to the newer drug developments. Fruits, seeds, root barks, and leaves were all employed for different purposes in traditional medicine. Various techniques of application (including paste, powder, oil, and decoction) were proposed by traditional applications. The oil was used for dermatologic disorders and wound infections; the paste was used for mouthwashes in preventing cavities, but also for skin-related disorders; and decoction of the roots was administered in cardiac diseases and insanity the powder was used for various types of infections, indigestion, constipation, epilepsy, and as a blood purifier. Additionally, *E. ribes* has been used for weight reduction therapy and as a contraceptive, as well as for rejuvenation, nausea, vomiting, gastritis, and bloating. Carminative, anti-malignant, diuretic (e.g., fruit), anthelmintic (e.g., seeds), antibacterial, and pneumoprotective (e.g., leaves, root bark) are some of the most often reported effects from traditional applications (Bist & Prasad 2016; Souravi & Rajasekharan 2014). Different pharmacological effects have been investigated through experimental investigations to elucidate mechanisms of action, doses, precautions, etc., for the purposes of translating traditional applications into modern medicine. Embelin, vilangin, embeliaflavosides, and embelialkylresorcinols are some of the most promising phytocompounds.

Antioxidant activity. Swamy *et al.* (2007) showed that the wound healing activity of embelin is effective and was relatively easily tested with the standard ointment Framycetin (Swamy *et al.*, 2007). Albino rats were tested for their responsiveness to ethanol leaf extract (30 mg/ml) and embelin (4mg/ml) extracted from *E.ribes* for their ability to speed up the healing process. Experimental evidence by Nazish *et al.* (2012) revealed improved insulin tolerance in rat models with HFD-induced obesity by treatment with a H_2O extract of *E. ribes* (Nazish *et al.*, 2012). In rats, the embelin treatment decreases the thiocyanate reactive oxygen species contents and also mitigates pancreatic antioxidant enzyme conditions (Afzal *et al.*, 2012). Bhandari *et al.* (2013) also showed a significant anti-obesity effect, decreased fat-fed myocardial lipid peroxidation, and increased antioxidant levels with *E. ribes* ethanol extract (ERE)(Bhandari *et al.*, 2013). According to the *insilico* molecular docking analysis, the receptor-binding domain of the viral hemagglutinin is where embelin binds. The findings of the study also indicate that *E. ribes* has potential as a source for a new plant-based anti-influenza agent. Three new flavonoid glycosides, embelia flavosides, were isolated from the fruits of *E. ribes*. The methanolic extract of the berries of *E. ribes* from Nagavelli genotypes was found to have the highest total phenolic content, whereas the ethanolic extract of the berries showed the highest total flavonoid content (Kamble *et al.*, 2020). According to the various extraction methods carried out for the berries from NAG accession, microwave-assisted extraction exhibited a 3-fold enhancement in embelin content. These findings suggest that the NAG accession is a precious asset for the pharmaceutical industry as a potential source of natural antioxidants and emulsifiers. Rout *et al. (*2021) revealed that when streptozotocin-induced diabetic rats are given an oral fluid concentrate of *E. ribes*, the levels of superoxide dismutase, catalase, and glutathione in the pancreas decrease(Rout *et al.*, 2021). Their anti-cancer agent movement protects pancreatic cells from damage in streptozotocin-induced diabetic rodents.

Table 2: Traditional Uses of *Embelia ribes.*

Plant Parts Used	Ethno-Medicinal Uses	References
Plants	Chandraprabhavati, Vidangataila, Vidangaadichruna, Vidangarishta, Sarvajwaralouha, Agnitundivati, Yograjagugglu and Kaishorgugglu.	Current Study
Fruits and Leaves	It has been used to cure a wide variety of ailments, such as ascariasis, sore throat, gastrointestinal, inflammatory, and mental problems, constipation, headache, flatulence, indigestion, jaundice, snake bite, skin illnesses, leprosy, nerve debility, dyspepsia, colic, tumours, asthma, and general debility.	(Jaiswal, 2019; Kuspraningrum *et al.*, 2020)
Root Bark	Useful in preventing and treating infections caused by intestinal parasites and worms. It is prescribed for a wide variety of conditions, including gastrointestinal issues, fungal skin infections, bloating, headache, haemorrhoids, lung diseases, obesity, piles, pneumonia, mouth ulcers, constipation, indigestion, toothache, and sore throat. The decoction is helpful for mental illness and cardiovascular issues.	
Root	Root boiled in water and the decoction is effective against chest pains. Roots grounded with lime juice and taken orally with honey against cough.	
Leaf	The leaves have astringent, thermogenic, demulcent, and depurative properties. Paste of powdered leaves, mixed with honey is consumed to treat ulcers of mouth.	
Leaves and fruits	Anti-diarrheal, also used against intestinal worm infection.	(Jaiswal, 2019)
Fruits	The ethnological features include brain tonification, carminativeness, contraception, diureticness, febrifugeness, laxativeness, stimulation, and thermogenesis.	(Saikia *et al*., 2021)
Fruits	Used in Liver disorder, worm infestation	(Tripathi, 2017)
Plant	Tender leaves and shoots eaten as cooked vegetable and is said to act as stomachic	(Arya *et al.*, 2020)
Dried Leaf	Dried leaf of *Embelia ribes* taken with *Allium sativum*, *Acoruscalamus*, *Trachyspermum ammi* ground into paste with honey bee as a medicine with water for worm infestation. *Embelia ribes* leaf can be taken as food with *Trachyspermum ammi*, popcorn of *Oryza sativa* (Laja), *Zingiber officinale* mixed with treacle of *Cocos nucifera* and taken in the morning. Dried leaf of *Embelia ribes* mixed with jaggery of *Caryotaurens* taken on empty stomach in the morning Powder of dry leaves of *Embelia ribes* (after frying alone), *Zingiber officinale*, *Oryza sativa* (after frying alone) mixed with treacle of *Cocos nucifera* taken in the morning. Powdered dried leaves of *Embelia ribes* (after frying alone), powdered Oryza sativa (after frying alone) mixed with treacle of Cocos nucifera. 30g of powdered *Embelia ribes*, *Triphala*, *Trikatu*, *Trivarga*, *Aconitum heterophyllum*, *Allium sativum*, *Cumin umcyminum*, *Trachyspermum ammi*, *Baliospermum montanum*, *Cassia fistula* from each mixed with 10g each from powdered *Operculina turpethum* and leaves of *E. moonii* and given 2.5g with bee honey as medicine to treat anemia in a person.	(Perera & Rabinarayan 2020)

Table 3: Antioxidant activities of *Embelia ribes.*

Parts used	Type of extract	Method used	Responsible phytochemicals	Reference
Embelia ribes fruits	Aqueous	Superoxide scavenging activity	Embelin	(Bist & Prasad, 2016)
Embelia ribes seed	Gold and Silver nanoparticles	DPPH, PMA assay	Seed extract	(Dhayalan *et al.*, 2017)
Embelia ribes seed	Aqueous	DPPH	Embeliaribyl ester	(Aishwarya, 2018)
Embelia ribes seed	Acetone, petroleum ether, water, methanol, and chloroform	DPPH and ABTS assays	Alkaloids, Tannins, Flavonoids, steroids, Phenols, Diterpenes, Saponins, Glycosides, Proteins and amino acids	(Thyloor, 2018)
Embelia ribes fruits	Herbal formulation	DPPH	Embelin	(Nanthini et al., 2019)
Embelia ribes seed	Silver nanoparticles	DPPH and MTT assays	Embelin	(Othman & Sekar, 2019)
Embelia ribes plants		DPPH	Embelin	(Bashir & Kumar, 2019)
Embelia ribes fruits	Ethanolic	DPPh and ABTS radical scavenging activity	flavonoid glycosides, Embelia flavoside	(Qin *et al.*, 2021)
Embelia ribes fruits	Methanolic, Ethanolic	DPPH. FRAP, Antioxidant activities	Embelin	(Kamble et al., 2020)
Embelia ribes plants	Ethanolic		Embelin	(Zeeshan *et al.*, 2018)
Embelia ribes plants	Embelin N,O-CMC nanoparticles	DPPH and MTT assay	Embelin	(Ghazali *et al.*, 2020)

Antibacterial activity. A high antibacterial efficacy was shown by embelin against *Staphylococcus aureus*, *Streptococcus pyogenes*, *Shigella flexneri*, *S. sonnei*, and *Pseudomonas aeruginosa* at the higher concentration (100 mg); a modest effect was shown against *Salmonella typhi*, *Shigella boydii*, and *Proteus mirabilis*(Radhakrishnan *et al.*, 2011). Antibacterial activity against *Pseudomonas aeruginosa*, *Escherichia*

coli, Streptococcus faecalis, and *Bacilus subtilis* was determined by the ethanol and aqueous extracts of *E. ribes* (Bist & Prasad 2016).

Antifungal activity. Antifungal activity against *Candida species* was determined by petroleum ether, solvent ether, methanolic, and aqueous extracts of *E. ribes,* and it was found that embelin showed excellent inhibitory activity against *C. tropicalis* (Bist & Prasad 2016; Rathi *et al*., 2010).

Antiviral activity. Hossan *et al.* (2018) demonstrated that *E. ribes* has the potential to be utilized in the production of a brand-new plant-based anti-flu drug (Hossan *et al.*, 2018). Five plants native to Bangladesh were tested for their ability to fight influenza A and B. The A/mallard/Pennsylvania/10218/84 (H5N2) avian influenza virus was the most sensitive to embelin, while the A/Aichi/2/68 (H3N2) virus had the highest tolerance.

Table 4: Antimicrobial activities of *Embelia ribes.*

Parts used	Type of extract	Activity against	References
Fruits	Aqueous	*Pseudomonas aerugenosa, Escherichia coli, Streptococcus faecalis, Bacilus subtilis*	(Bist & Prasad, 2016)
Seeds	Gold and Silver nanoparticles	*E. coli* and *S. aureus*	(Dhayalan *et al*., 2017)
Seed	Aqueous	*E. coli* and *S. aureus*	(Aishwarya, 2018)
Seed	Acetone and methanolic	*E. coli* and *P. aerugenosa*	(Thyloor, 2018)
Plants	Formulated ointment	*E. coli, Pseudomonas aeruginosa, Staphylococcus aureus, S. epidermidis.*	(Mahendran *et al.*, 2011)
Fruits	Ethanolic	*pseudomonas aeruginosa*	(Asokan & Kabilan Natarajan, 2019)
Plants	Methanolic, Ethanolic	*Aspergillus niger, Aspergillus terreus, Rhizopus oryzae, Cladosporium species, Armillaria mellea, Colletotricum capsici, Colletotrichium crassipes and Candida albicans, Klebsiella pneumoniae, Salmonella typhii, Shigella flexneri, Shigella boydii, Shigella somnei, Proteus mirabilis, Vibrio cholerae and Pseudomonas aeruginosa.*	(Bashir & Kumar, 2019)
Plants	Ag nanoparticles	*Propionibacterium*	(Pathak *et al*., 2020)
Plant	Aqueous and Ethanolic extract	*S. aureus, E. coli, P.aeruginosa and B. subtilis*	(Wankhade *et al.*, 2021)

Anti-diabetic activity. Durg *et al*. (2017) have well documented the efficacy of embelin against diabetes (Durg *et al.*, 2017). Bhandari *et al.* (2008) have reported that under hyperglycemic conditions, a considerable blood glucose-lowering potential and the aqueous extract of *E. ribes* produced an increased endogenous antioxidant defense against free radicals (Bhandari *et al.*, 2008). The extract thus protected pancreatic beta-cells against loss in streptozotocin-induced diabetic rats and methionine-induced hyperhomocysteinemia, as well as oxidative stress in the brain. Embelin from *E. ribes* showed a significant anti-diabetic effect by improving body weight and reducing fasting serum blood glucose levels against alloxan (Mahendran *et al.*, 2011).

Anthelminthic activity. When compared to other plants such as *Gynandropsis gyanandra, Impatiens balsamina, Celastrus paniculata*, and *Mucuna pruriens, E. ribes* demonstrated the most effective anthelmintic property (Jalalpure *et al*., 2007). Seed extracts of *E. ribes* treated *Rhabditis pseudoelongata* very effectively (Bora *et al*., 2017; Choudhary, 2012) as a helminth (roundworm). The anthelmintic activity of *E. ribes* seed oil was tested on *Pheritima posthuma,* and it was found to cause the worms to die off significantly (Choudhary *et al.*, 2021). The anthelmintic activity of *E. ribesembelin* was much stronger and more effective than that of albendazole against *Pheretima posthuma* (Bora *et al.*, 2017; Ghugarkar *et al.*, 2015). Against the adult earthworm *Pheritima posthuma,* the plants *Embelia ribes, Hordeum vulgare, Mallotus philippinensis*, and *Terminalia chebula* showed potent in vitro anthelmintic activity (Bora *et al.*, 2017; Mohandas *et al.*, 2013). According to Bora *et al.* (2017); Kekuda *et al.* (2009); Bora *et al*. (2017); Kekuda *et al.* (2009), an aqueous extract of the fruit of *E. ribes* exhibited strong anthelmintic activity against the adult Indian earthworm *Pheretima posthuman.*

Analgesic activity. Embelin is an oral, non-narcotic analgesic with a central action. It differs from naloxone in its core site of action and is not antagonistic to it. Due to its higher oral effectiveness, higher therapeutic index, and lack of abstinence syndrome, it is more bearable than morphine (Lal & Mishra 2013). The receptor-mediated action is known to be blocked by naloxone (Lal & Mishra 2013).

Anti-cancer activity. Embelin has been suggested to exhibit anti-cancerous properties based on the origin of cancer by inducing apoptosis by targeting several signaling pathways(Ko *et al.*, 2018). Experimental validation using photodynamic therapy (PDT)(Joy *et al.*, 2014) revealed embelin as an efficient photodynamic curative candidate against the malignant tumor. Embelin has also been reported to act as a bioactive molecule, revealing a significant potency against breast cancer (Kaur *et al.*, 2015). Embelin is also used in rats with experimental fibrosarcoma to minimize tumor size and interrupt the transmission of serum enzymes like acid phosphatase, glutamyl transferase, lactate dehydrogenase, aldose, and others from increasing. In tumor-bearing mice, embelin alters the metabolism of glucose and amino acids (Rout *et al*., 2021).

Anticonvulsant activity. When given intraperitoneally, embelin reduces seizures caused by electroshock and pentylenetetrazol. A noticeable decrease in mobility indicated depressant effects on the central nervous system. Research suggests that embelin has

anticonvulsant effects in both grand mal and petit mal forms of epilepsy (Rout *et al.*, 2021).

Antihyperlipidemic activity. The antihyperlipidemic activity of the ethanolic extract of *E. ribes* has proven to lower serum total cholesterol and triglycerides while increasing HDL levels in diabetic rats (Bist & Prasad 2016).

Antihyperhomocysteinemic activity. Bhandari *et al.* (2008) in their study to evaluate the antihyperhomocysteinemia property of *Embelia ribes*, showed the levels of homocysteine, LDH, total cholesterol, triglycerides, LDL-C, and VDL-C were decreased, and the HDL-C levels in serum were increased (Bhandari *et al.*, 2008).

Mollusicidal activity. Molluscicides, including *Azadirachta indica* and *Cedrus deodara* oil, were utilized against *Lymnea acuminata* in binary and tertiary combinations with synergists MGK-264, piperonylbutoxide (PB), and the fruit powder of *E. ribes*. There was an increase in toxicity when plant-derived molluscicides were combined with synergists in binary and tertiary mixes, compared to when they were used alone(Bhandari *et al*., 2008).

Wound healing property. Significant wound healing activity of *E. ribes* and embelin ethanolic extract was reported by Swamy et al. (Swamy *et al.*, 2007). Histological analysis of embelin-treated granulation tissue revealed increased cross-linking of collagen fibers and the absence of monocytes, in contrast to the standard skin ointment framycetin. A medicated hydrogel with 0.2% embelin, 10% PVA, and 5% PEG 400 was developed by Shrimali *et al.* (2019). The embelin-loaded hydrogel initiates the healing process more quickly.

Anti-fertility activity. he root aqueous extract of *E. ribes* possessed anti-fertility activity (Bist & Prasad 2016; Rout *et al.*, 2021).

Antispermatogenic activity. When given daily subcutaneous injections, embelin inhibits sperm motility in male albino rats (Rout *et al*., 2021).

Antinematodal activity. Brahmeshwari and Kumaraswamy (2012) in their study, reported the antinematodal action of a combination of *Veronica anthemintica* seed (Kali zeeri) and *E. ribes* fruit (Babrang) (Brahmeshwari & Kumaraswamy 2012). Reuter *et al*. (2010) performed an EPG (egg per gram) count in feces before and on subsequent treatment days with *E. ribes* powder, which showed safety and efficiency in treating natural gastrointestinal nematodes in local goats(Reuter *et al.*, 2010).

Anti-inflammatory activities. In a carrageenan-induced paw edema model, the anti-inflammatory properties of *E. ribes* fruits were assessed, as well as embelin (Bist & Prasad 2016).

Contraceptive activity. A study on the contraceptive potential of *Embelia ribes* extracts, reported by Kholkute's group, used rats, mice, and hamsters as models. The *E. ribes* extracts in various solvents (ether, methanol, chloroform, and benzene) were injected into the uterus. In another study, Prakash's group administered the extracts of *E. ribes* through the oral route and observed that uterine tissues were not able to progress with pregnancy, and when male albino mice were administered with the extracts, the acid levels in the testis and prostate glands increased significantly. Hence, the extracts of *E. ribes* were found to possess excellent contraceptive properties with some additional unwanted side effects (Chauhan *et al.*, 1979; Kholkute *et al.*, 1978; Prakash & Mathur, 1979).

MOLECULAR PROFILE OF *EMBELIA*

The lack of basic biological information such as morphological descriptions of the plant due to minute phenotypical variation among species, species-distribution maps, approximate population size, and limited information on the molecular profiling of *E. ribes* are major constraints in assessing the genetic variation in this species. Devaiah and Venkatasubramanian (2008) suggested using RAPD-PCR and SCAR markers to identify genuine *E. ribes* and differentiate it from common substitutes and adulterants (Devaiah & Venkatasubramanian 2008). Gowda *et al.* (2010) reported immense potential in the pharmaceutical industries for *E. ribes* and *E. tsjeriam-cottam*(Gowda *et al.*, 2010). The active component embelin performs the same actions but shows polymorphism in up to 88.65% of its genetic makeup, as revealed by AFLP analysis. DNA fingerprinting may be used to create species-specific markers that can be employed in any species-identification dispute. This study showed that AFLP is a robust tool for establishing the degree of similarity and variation between species of medicinal plants. Chrungoo *et al.* (2018) have used molecular markers ITS, matK, and ISSR to reveal a distinct separation of the three species of *E. ribes*, *E. floribunda*, and *E. subcoriacea*, which revealed low genetic variation among the species, which contributes to the current threatened status of the plants (Chrungoo *et al.*, 2018). The molecular identification of 13 distinct *Embelia* species was confirmed by using RAPD, according to Nagamani and Rani (Nagamani & Rani, 2018). They reported a significant observation that *E. ribes* showed distinct separation as one cluster, though they belong to different geographic areas and do not group with other *Embelia* species.

NANOPARTICLE FABRICATION FROM *EMBELIA* AND THEIR APPLICATIONS

In recent years, scientists' curiosity about nanomedicine has been piqued by the development of environmentally friendly methods for synthesizing gold (GNPs) and silver (SNPs). A green, cheap, quick, and easy method for synthesizing GNPs and SNPs was developed by using *E. ribes* seed extract (SEEr) as a capping and reducing agent. The produced GNPs and SNPs were characterized through ultraviolet-to-visible (UV-Vis) spectroscopy, dynamic light scattering (DLS), high-resolution transmission electron microscopy (HR-TEM), Fourier transform infrared (FT-IR), and X-ray powder diffraction (XRD). Both GNPs and SNPs were tested for their ability to scavenge free radicals using the -diphenyl--picrylhydrazyl (DPPH) and phosphomolybdenum tests(Dhayalan *et al*.,

2017).Analysis with a UV-Vis spectrophotometer showed that a solution of silver nitrate and chloroauric acid may be used to produce both GNPs and SNPs. As metal ions have been neutralized, the color of the gold solution has deepened from yellow to a deep wine red, with a distinct peak.

A cost-effective and non-toxic method for synthesizing ZnO nanoparticles from the methanol extract of *E. ribes* seeds was reported by Mahakal *et al.* (2018). Dhayalan *et al.* (2017) reported that gold nanoparticles with greater stability were synthesized using a simple, low-cost, eco-friendly green chemistry approach, exhibiting antioxidant activity (Dhayalan *et al.*, 2017). Its antioxidant activity is at a comparatively low concentration and could be used in controlling various plant diseases caused by fungi. Leema *et al.* (2019) reported that silver nanoparticles are available by reduction using embelin, whose size and morphology depend on the concentration of embelin which showed antibacterial activity (Leema *et al.*, 2019). Othman and Sekar reported the anticancer activity of silver nanoparticles prepared from embelin isolated from *E. ribes* (Othman & Sekar 2019). Inhibitory activity against Propionibacterium was shown in an anti-acne investigation by Pathak *et al*., 2020). In addition, *E. ribes* silver nanoparticles were more effective than the extract in treating acne vulgaris. In the DPPH free radical scavenging and phosphomolybdenum experiments, AgNPs and AuNPs showed exceptional antibacterial activity against *S. aureus* and Escherichia coli, respectively (Dhayalan *et al*., 2017).

Table 5: Nanoparticle fabrication from *Embeliaribes*and their applications.

Nanoparticles	Characterization techniques	Shape	Size (nm)	Applications	Reference
Ag	UV–Vis, FTIR, XRD and HRTEM		30	Antibacterial and anti-cancer	(Manikandan *et al.*, 2019)
ZnO	UV–Vis, FTIR, XRD and SEM Analysis	haxagonal	57.57	Green synthesis of ZnO from methanolic extract of *E. ribes*	(Mahakal *et al*., 2018)
Ag	UV–Vis,Absorption spectroscopy and TEM			Antioxidant activity	(Leema *et al*., 2019)
Ag	SEM and Zeta potential measurement		19.06-22.64	In-vitro antioxidant and cytotoxic activities	(Othman & Sekar, 2019)
Ag	UV–Vis,Absorption spectroscopy and TEM			Propioni bacterium	(Pathak *et al*., 2020)
Ag	UV–Vis, DLS, FTIR, XRD and HR-TEM	Spherical	20-30	antibacterial and antioxidant activities	(Dhayalan e*t al*., 2017)
Embelin loaded N,)-CMC	FTIR, DLS, SEM Zeta potential and XRD measurements		650-850	Antioxidant and cytotoxic properties	(Ghazali *et al*., 2020)

COMMERCIAL PRODUCTS FROM *EMBELIARIBES*

Embelia ribes extract is used in both Ayurvedic medicine and conventional medicine production. Now, many medical pharmaceuticals use imported Northeast Indian fruits in their production. One year of storage is recommended before using vidanga seeds (Rout *et al.*, 2021; Sahoo *et al.*, 2020). The crop is ready for harvest and fruiting by October or November, around 5–6 months after seeding. The fruits are then shade-dried before being stored. This crop averaged 190–200 kg of seeds per hectare (Rout *et al.*, 2021). The viability of formulations is significantly affected by how they are stored, both in terms of the conditions under which the raw ingredients are kept and the packaging they are kept in. Vidanga is typically dried using a natural drying method, and the quality of the stored fruits and seeds is significantly affected by the containers used. It has been found that fruits can be stored in HDPE bags, which are inexpensive and moisture-proof, for up to 6 months with 12% moisture and only a little dip in quality (Rout *et al*., 2021).

CONCLUSION AND FUTURE SCOPE

According to the current medical literature, *E. ribes* has been used as a traditional folk medicine in several Asian countries and cultures (India, Sri Lanka, Malaya, Singapore, and China) to treat digestive, carminative, laxative, anti-helminthic, and other disorders. *E. ribes* contain embelin and other vital constituents such as tannins, christembine, resinol, embeliol, embelinol, quercitol, vilangin, and potassium embelate, which have many pharmacological properties. According to the study results, the plants need to be treated with care to prevent any unwanted side effects, and those other potential uses need to be explored. This review provides insight into the development of many phytochemical compounds in *E. ribes*, which can play an important role in the treatment of various diseases. However, medicinal research has been hampered in its efforts to find an efficient delivery method for these compounds. Persistent efforts are required to further understand their efficacy, their structural activity, and their bioavailability. The available data suggest that embelin may one day be used to treat a wide variety of diseases and conditions, including cancer. While embelin has gained significance, more extensive pharmacological studies with animal models and subsequent clinical trials are needed to establish embelin's use as a conventional therapeutic agent alone or in combination.

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