

An overview of ethnobotanical and pharmacological study of *Embelia ribes* (Baobarang): a potential unani herbal drug

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ABSTRACT

Plant, animal and mineral products are used in unani system of medicine as drugs, which is a natural system of healthcare. The fruits of *Embelia ribes* are used as herbal drug under the name Baobarang. It is a climbing shrub, used as herbal drug not only in unani system of medicine but also in Ayurveda. It possess various medicinal properties but the plant is highly valuable as anthelmintic and it has been discussed as krimighna in Ayurveda classical text, Charaka Samhita. In this review an attempt has been made to discuss its geographical distribution, macro and microscopic properties, powder characteristics as dose, temperament, various pharmacological actions and therapeutic uses. Besides this phytochemistry of the fruits has also been explored to find out the chemical constituents present in the fruits responsible for its physiological properties. The review has also highlighted the need for the use of Baobarang in Unani system of medicine and future prospect for further research.

Key words: Baobarang, Anti Anthelmintic activity, Pharmacological Activities, *Embelia ribes*

RESUMEN

Los productos vegetales, animales y minerales se utilizan en el sistema de medicina unani como medicamentos, que es un sistema natural de atención médica. Los frutos de *Embelia ribes* se utilizan como droga a base de hierbas con el nombre de Baobarang. Es un arbusto trepador, utilizado como medicamento a base de hierbas no sólo en el sistema de medicina unani sino también en Ayurveda. Posee varias propiedades medicinales, pero la planta es muy valiosa como antihelmíntico y se ha mencionado como krimighna en el texto clásico de Ayurveda, Charaka Samhita. En esta revisión se ha intentado discutir su distribución geográfica, propiedades macro y microscópicas, características del polvo como dosis, temperamento, diversas acciones farmacológicas y usos terapéuticos. Además de esta fitoquímica de los frutos, también se ha explorado para descubrir los constituyentes químicos presentes en los frutos responsables de sus propiedades fisiológicas. La revisión también destacó la necesidad del uso de Baobarang en el sistema de medicina Unani y las perspectivas futuras para futuras investigaciones.

Palabras clave: Baobarang, Actividad antihelmíntica, Actividades farmacológicas, *Embelia ribes*

INTRODUCTION

Dried fruits of *Embelia ribes* Burm.f. belongs to the family of Myrsinaceae. It is one of the most significant plant used from the ancient period in the form of Baobarang, Barang, kabuli or Vidanga. It has been used as an ingredient of various Unani and Ayurvedic formulations for the treatment of various diseases. Baobarang has wide range of pharmacological activities like anthelmintic, analgesic, anti diabetic, anti-bacterial and anticonvulsant activities. Besides these its dried fruits have also been found to possess antiproliferative, antihyperlipidemic, antihyperhomocysteinemic, Chemotherapeutic and anti-inflammatory properties. *Embelia ribes* fruits could be a good source of alternative medicine for antitumor and anti-cancer activity. The in vitro antifungal activity was also exhibited by baobarang extracts on various fungal strains. The fruits of *Embelia* has also been shown to have a significant Antioxidant property by inhibiting free radicals. Apart from these Molluscidal, wound healing, antifertility and antispermatogenic activity were also exhibited by fruits of baobarang. The main active medicinal component in dried fruits of *Embelia ribes* is Embelin.^{1,2,3,4,5,6}

Vernaculars of Baobarang are given below -

Vernaculars

Arabic	:	Biranj Kabuli, Baranj
Persian	:	Baranj Kabuli, Barang
Assamese	:	Silgilla
Bengali	:	Biranga
Gujarati	:	Vavading, Vayavadang
Hindi	:	Wowrung, Viranga
Kannada	:	Vayuvidang, Vayuvilanga
Kashmiri	:	Babading
Malayalam	:	Vishalam, Tiruvittikanni
Marathi	:	Karkannie
Oriya	:	Bidongo
Punjabi	:	Babrunj, Vavlring
Sanskrit	:	Jantughna, Kirmighna, Vidanga, Amogha, Vella, Vrishanasana, n

Chitrotandula Janthu-neshan

Tamil : Vayuvilangam, Vayuviddangam



Baobarang (*Embelia ribes*) fruit



Baobarang (*Embelia ribes*) powder

Habit and Habitat

A shrub or a small deciduous tree, found in Malabar, Madhya Pradesh and Bihar regions.²

Geographical Distribution

It is distributed throughout India in areas upto 1,500 m elevation in hilly regions. The distribution of *Embelia ribes* in peninsular India is mainly in the states of Kerala, Maharashtra and Tamil Nadu in Eastern Ghats and Karnataka in Western Ghats. The species is reported to be vulnerable in Karnataka and Maharashtra, and at a low risk status in Kerala. It grows in like Medicinal Plants Conservation Areas (MPCAs)⁷, Malawar, Madhya Pradesh, and Bihar regions.²

Description of fruit and seed

Macroscopic : Obovate to subglobular, blackish- brown coloured fruit , 2 to 4 mm in diameter, with anastomosing wrinkled surface, beak like projection on the remnants of style at apex and occasionally with remains of 2 to 3 calyx lobes at the base ; pedicel very short or absent, a circular hole left by it often seen at the base; pericarp brittle , easily separable from the single/occasionally two seeded fruit; seed brownish- black with longitudinal furrows. Embryo lies at the centre just above the basal cavity of the seed.⁸

Microscopic : The detailed TS of the fruit shows a layer of epicarp consisting of dome shaped, three sided thickened cells covered with striated cuticle, underneath this layer lies tangentially elongated, 2 to 3 rows of thick-walled cells of hypodermis filled with dark brown contents; remaining parenchymatous cells of the mesocarp are traversed with groups of thick-walled stone cells, vascular strands and sclereids, the later forming discontinuous ring adjacent to the row of palisade like, radially arranged, compact, walled, dark brown coloured cells of the endocarp. Testa composed of a layer of tangentially running, narrow, rectangular cells, underneath which lies a row of broad squarish cells of thee pigment layer. Endosperm cells are filled with aleurone grains and fixed oil. About 4, oval to circular, dark brown coloured buildings of the perisperm, varying in size and consisting of radially arranged rod shaped cells, penetrate inside the endosperm.⁸

Safoof (Powder)

Shows lignified stone cells, abundant pitted, sclereids of numerous size and thickness, in groups or isolated, groups of rich fragments of dark brown coloured palisade like cells of endocarp, rich fragments of endosperm filled with fragments of perisperm; and pentagonal to hexagonal thick-walled cells of epicarp with striated cuticle.⁸

Hasa's Mustamala (Parts Used)

Roots, Leaves and Berries (fruit).^{3,9}

Fruit.^{2,10,11,12}

Mizaj (Temperament)

Hot and Dry ^{5, 11,12,15}

Hot and Dry ^{10,12}

Hot and moist¹⁴

Miqdar Khuraq (Doses)

6 Masha- 1 tola ¹²

1-3 gm ^{10,19}

1-2 Masha ¹³

Muzir (Adverse Effects)

Intestine ^{10,12,19}

Musleh (correctives):

Mastagi (*Pistacia lentiscus Linn*), Kateera (*cochlospermum gossypium*) and gums¹²

Kateera (*Cochlospermum gossypium*) ¹⁰

Badal (Substitutes)

Turmus (*Lupinus albus*) and half dose of kamela (*Mallotus phillippinensis*) ¹²

Turmus (*Lupinus albus*) ^{10,13}

Afa'al (Pharmacological action)

Mukhrij-e-Kiram-e-Shikam. ^{5,6,10}

Mild Appetizer, Mukhrij-e-Kirma-e-Shikam
(vermifuge). ¹⁵

Tapeworm (Vermicidal). ¹¹

Vermifuge, Purgative, Balgum sauda. ¹³

Purgative (Balgum-wa- sauda), Daf-e-Kiram-e-Shikam.

¹²

Astringent, Carminative, Stimulant and tonic
properties. ¹⁶

Vermifuge (seeds), toothache (Roots). ¹⁷

dyspepsia. ¹⁸

skin diseases.¹⁸

Qatil-e- Kiram-e-Shikam toothache, lithotric¹⁹
kidney and uretur, diuretic and anti spasmotic

Qatil-e-Kiram-e-Shikam²⁰

Mahalle Istemal (Therapeutic uses)

Qatil-wa-Mukhriz

Deedan-e-Ama(Vermicidel).⁸

Musleh balgham-o-sauda (Bilogue).⁸

It is used in cough and ishaal (Diarrhoea).¹⁶

Mushtahi (Appetizer).¹⁵

Daaf-e-dard (Analgesic).¹⁵

Mshil e balgham wa sauda (Phlegmagogue and
melanogogue).¹³

Dard -e-dandan (Toothache).^{10,13}

Hazim (Digestive).¹⁰

Mudir-e-bol (Diuretic).^{17,21}

Stop excess menstrual flow.²²

Murakkabat (Compound formulations)

Unani

Itrifal qambeel¹¹

Habb-e-deedan^{11, 13}

Itrifal deedan¹¹

Habbe -e- kabid Naushadri^{11,14}

Qurse deedan¹⁰

Majoon e Sarkhas¹⁰

Uses in Folk Medicine

Zimmad (Paste)

For avoiding cavities used as mouth wash and also used in skin problems.

Safoof (Powder)

It is being used in infections in body, indigestion, constipation, worm infestation, epilepsy, convulsions, paralysis etc. It is also used as blood purifier.

Roghan (Oil)

Wound infections and skin related problems.

Kheshanda (Decoction)

Heart diseases and decoction of the roots is given in insanity.

16 tola powder of baobarang with curd is used in worm infestation.

Decoction of leaves is used as vermicide.

It is used as blood purifier, so useful in great variety of skin problems.

It has contraceptive effect, along with Pippali (long pepper)

It is used for rejuvenation purpose and improves skin complexion.

Its water decoction is used for oil pulling to relieve dental caries and bad breath in skin diseases,

It is used both externally and orally in the form of paste.

It has mild diuretic action.

It is useful against vomiting, bloating, indigestion, gastritis and constipation.

It is widely used in weight loss treatment.^{10,11,15,18}

PHYTOCHEMISTRY

Chemical constituents

Baobarang contains 2-3% hydroquinone.

Embelin (2,5-dihydroxy-3-lauryl-p-benzoquinone), tannins, quercitol and minute amount of volatile oil.

¹⁶ Besides these some other components are also present in Baobarang like Acids, Volatile oil, Tannins, Embelic acids, Embelin, Christembine and Tannin etc.¹⁴

Embelin, Vilangin (methyl embis-2,5-dihydroxy-4-undecyl-3,6-benzoquinon), Quercitol, Tannins, Volatile oil⁵, Embelin, Christembine, Embelin dimer, Embelin desalts, Embelinol, embelianbyl ester, Embeliol, Homoembelin, homorapanone, monopotassium embelate, Quarvital-1%, Quercitol, Rapanone, Resins, Oleic, Linoleum acid, Sitosterol, Stable oil, Tannins, Daucosterol, Vidangin, Vilangine etc.^{11,18} were also present in fruits of baobarang.

PHARMACOLOGICAL ACTIVITY

ANALGESIC ACTIVITY

Embelin has non-opiate pain relieving property which acts centrally. It has a different central site of action and is not threatened by naloxone. It is more worthy than morphine due to high therapeutic index, high oral efficacy and absence of abstinence syndrome.²³ Naloxone is known to antagonize mu (μ)-receptor mediated activity associated with narcotic analgesics.²⁴

The mixed mu (μ) and kappa (κ) agonists (such as EKC and bremazocine) and pure kappa (κ) agonist like 488H, U50 causes significant displacement of potassium embelate. This indicates that potassium embelate has high affinity for mu (μ) and kappa (κ) binding sites which may be involved in the modulation of potassium embelate induced analgesia in the rat brain.²⁵

ANTHELMINTIC ACTIVITY

Embelia ribes seed oil when administered at different doses like 10 mg/ml, 50 mg/ml and 100 mg/ml reported death of the worms (*Pheretima posthuma*). But response of worms to different doses altered in the time of paralysis parameter. Increment in dose revealed a decreased time of paralysis and the values are noteworthy when compared with standard piperazine citrate (10 mg/ml).⁴² *Embelia ribes* fruit extract in combination with *Veronica anthelmintica* seed extract administered at 1g / kg exerted a considerable decrease in the fecal eggs per gram (EPG) count in goats suffering from mixed gastrointestinal nematode infections.²⁶

ANTI BACTERIAL ACTIVITY

Embelia ribes at a concentration of 500 mg/50ml reported 12 mm diameter of zone of inhibition when compared to the standard drug nitrofurazone which has 22 mm diameter of zone of inhibition against test organism *Bacillus subtilis*. It did not produce any inhibitory /anti-microbial activity against *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Escheresia coli*.²⁷

Alcoholic and acetone extract of *Embelia ribes* seeds show mild antibacterial property against *Enterobacter aerogenes* and *Klebsiella pneumoniae*. and the standard used is Amoxicillin.²⁶ Embelin, the main constituent of the fruit of *Embelia ribes* is proved to have antibacterial property against both gram +ve and gram

-ve bacteria, depending on the dose and bacteria test for the response alters. At 100 mg/disc dose embelin reported more diameter of zone of inhibition than standard (kanamycin) used at 39 mg/disc

when tested against *Staphylococcus aureus*, *Shigella flexneri* and *Shigella sonnei*. same kind of response greater than standard (ciprofloxacin 5 mg/disc) is observed in *Pseudomonas aeruginosa* when embelin is used at high dose of 100 mg/disc, considerable antibacterial property is shown against test organisms like *Shigella boydii*, *Proteus mirabilis*, *Streptococcus pyogenes*, *Salmonella typhi*. Very mild antibacterial activity has been reported when tested against *Streptococcus faecalis* and *Vibrio cholera*.²⁸

ANTIOXIDANT PROPERTY

Aqueous extract of *Embelia ribes* administered orally at doses 100 mg/kg and 200 mg/kg body weight significantly decreased the levels of glutathione and catalase pancreatic superoxide dismutase, in the streptozotocin (at a dose of 40 mg/kg, intravenously as a single dose) induced diabetic rats. This antioxidant activity further protects the pancreatic β -cells against loss in streptozotocin induced diabetic rats.²⁹

Free radical scavenging reactions and antioxidant activity of embelin has studied and discovered that embelin scavenges DPPH radical and inhibits hydroxyl radical induced lipid peroxidation and restores impaired Mn-superoxide dismutase in liver mitochondria of rat. Further examinations on the kinetics and mechanism of reactions of embelin with hydroxyl, one electron oxidizing, organo-haloperoxyl and thiyl radicals using nano second pulse radiolysis technique recommends that embelin can act as a competitive antioxidant in physiological conditions. In test diabetes, *E. ribes* shows its antioxidant potential and protection of pancreatic cells. Total glutathione activity was reduced by 69.13% in pancreatic tissue of diabetic rats as compared to normal control animals. The levels were significantly ($P < 0.01$) increased with Ethanolic extract of *E. ribes* (in a dose of 200 mg/kg).^{18,30}

ANTIDIABETIC ACTIVITY

Aqueous extract of *Embelia ribes* fruits at doses 100 and 200 mg/kg orally fed for forty days produced significant ($p < 0.01$) decrease in heart rate, systolic blood pressure, blood glucose, blood glycosylated haemoglobin, serum lactate dehydrogenase, creatine kinase and increase in blood glutathione levels in streptozotocin (administered at a dose of 40 mg/kg, intravenously single dose) induced diabetic rats. Gliclazide is used as standard in this study.

Administration of ethanolic extract of *Embelia ribes* berries orally for 6 weeks at a dose of 100 mg/kg and 200 mg/kg significantly ($p < 0.01$) reduced the levels of blood glucose, heart rate (HR) and systolic blood pressure (SBP) in streptozotocin induced diabetic Wistar albino rats. Gliclazide at a dose 25 mg/day is the standard used in this study²⁸. Further studies revealed that ethanolic extract of *Embelia ribes* fruits significantly ($p < 0.01$) reduced the pancreatic thiobarbituric acid-reactive substances (TBARS) in pancreatic tissue of diabetic rats.²⁹

ANTICONVULSANT ACTIVITY

Administration of Embelin at doses 2.5, 5 and 10 mg/kg body weight intraperitoneally automatically inhibited seizures induced by electroshock and pentylenetetrazole in a dose dependent manner and the activity was comparable to phenytoin and diazepam. C.N.S depressant activity was revealed by significant decrease in locomotion. The observation suggests that embelin possess anticonvulsant activity against both grand mal and petit mal epilepsy.³¹

ANTI CANCER ACTIVITY

Embelin is reported to decrease tumor size and inhibit the increase in activity of serum enzymes, viz. Aldose, acid phosphatase, τ -glutamyl transferase, lactate dehydrogenase etc in rats with experimental fibrosarcoma. Embelin interferes with carbohydrate and amino acid metabolism in tumor bearing animals.

Embelin 50 mg/kg/day in combination with curcumin 100 mg/kg/day prevented the induction of hepatic hyper plastic nodules, body weight loss, increase in the levels of hepatic diagnostic markers, and hypoproteinemia induced by N-nitrosodi-ethylamine in adult male Wistar rats. The osteoclasts are responsible for the osteolysis observed in bone metastases of the tumor. RANKL(Receptor Activator for Nuclear Factor κ B Ligand), a member of the TNF superfamily and an activator of the NF- κ B signaling pathway, has emerged as a major mediator of bone loss, commonly associated with cancer and other chronic inflammatory diseases. Embelin has been reported to bind and inhibit XIAP protein and inhibit inflammatory pathways. The investigations whether embelin could inhibit osteoclastogenesis - associated bone loss induced by RANKL and by tumor cells in vitro reported that embelin suppressed the RANKL-induced differentiation of monocytes into osteoclasts. Thus, inhibitions of RANKL - induced NF- κ B activation have great potential as therapeutic agents for osteoporosis and cancer -linked bone loss.³²

Nuclear factor-kappa B (NF-kappaB) regulates several genes associated with proliferation, carcinogenesis, inflammation and apoptosis. It was found that embelin inhibited Tumor Necrosis Factor (TNF) alpha-induced NF-kappa B activation. Both inducible and constitutive NF-kappa B activation were abolished by embelin. In addition, NF-kappa B activated by diverse stimuli such as lipopolysaccharide, interleukin-1beta, , phorbol myristate acetate, hydrogen peroxide, okadaic acid, and cigarette smoke condensate also was suppressed. Embelin inhibited sequentially the TNFalpha-induced activation of the inhibitory subunit of NF-kappa B alpha (Ikappa Balpha) kinase¹⁸ (Ikappa Balpha phosphorylation, Ikappa Balpha degradation, and P65 phosphorylation and nuclear translocation).

Embelin also suppressed NF-kappa B-dependent reporter gene transcription induced by TNF alpha, TNF receptor-1 (TNFR1), TNFR1-associated death domain protein, TNFR-associated factor-2, NF-kappa B-inducing kinase, and Ikappa Balpha kinase but not by P65. Furthermore, embelin down-regulated gene products involved in cell survival, proliferation, invasion, and metastasis of the tumor. This down-regulation was associated with enhanced apoptosis by cytokine and chemotherapeutic agents. Together, the results indicate that embelin is a novel NF-kappaB blocker and potential suppressor of tumorigenesis.⁴¹ In assessing the drug-induced cell toxicity,

a fibrosarcoma cell line was exposed in vitro to increasing concentrations of embelin and simultaneously inoculated with [3H]-thymidine. The cells were examined for incorporation of the labeled thymidine in DNA, lipid peroxide and glutathione levels for regular intervals. A dose- dependent decrease in labeled thymidine uptake, lipid peroxide and glutathione levels were observed on embelin administration.²⁸

CHEMOTHERAPEUTIC ACTIVITY

Embelin, recognize basically from the *Embelia ribes* plant, is one such compound show anti-inflammtory, chemopreventive and apoptic activities through an unknown mechanism. Because nuclear factor-kappa B directs a few qualities with apoptosis, it was proposed that the embelin may intervene its action through modulation of NF-kappa B activation.

It was discovered that embelin restrained tumour necrosis factor (TNF) alpha-induced NF-kappa B activation was repealed by embelin. In addition, NF-kappa B activated by diverse stimuli such as interleukin-1 beta, phorbol myristate acetate, lipopolysaccharide, hydrogen peroxide, okadaic acid and cigarette smoke condensate also was suppressed. Found that embelin inhibited sequentially the TNF alpha-induced activation of the inhibited subunit of I kappa B alpha phosphorylation, p65 phosphorylation, nuclear translocation and NF-kappa B alpha (I kappa B alpha) kinase and I kappa B alpha degradation. Embelia also restrains NF-kappa B-dependent reporter gene transcription induced by TNF alpha, TNF receptor-1 (TNFR1), TNFR-associated factor-2, TNFR1-associated death domain protein, I kappa B alpha kinase and NF-kappa B-inducing kinase but not by p65.

Besides this, it was found that embelin down-managed gene products involved in invasion, cell survival, proliferation, and metastasis of the tumour. This down-regulation was associated with enhanced apoptosis by cytokine and chemotherapeutic agents. Together the results indicate that embelin is a novel NF-kappa B blocker and potential suppressor of tumorigenesis.³³

ANTIPROLIFERATIVE ACTIVITY

Biological activities of the 1, 4-benzoquinone subsidiaries 5-O-ethylembelin (1) and 5- O-4-methylembelin (2) were researched. Both of these exhibited antiproliferative activity against a panel of human tumour cell lines upon comparison to normal marsupial kidney cells (Ptk2). They captured HL-60 cells in the G (0)/G (1) phase of the cell cycle in dose- and time-dependent manner. In HeLa cells, exposure to 100 micro M of 1 or 2 for 6h induced a complete disassembly of the microtubule network and an increased number of cells blocked in mitotic stages. Treatment with 10 micro M of 1 and 2 for 24h induced apoptosis in HL-60 cells. This evidence suggested that both 1 and 2 are promising novel antimitotic and anticancer molecules targeting microtubular proteins.³⁴

ANTITUMOR AND ANTI INFLAMMATORY ACTIVITY

A plant-based benzoquinone derivative Embelin, has been found to show significant antitumor activity in methylcholanthrene-induced fibrosarcoma in albino rats besides increasing their survival time. The drug also

has an important action on pain and inflammation. The changes in DNA, RNA and RNA and protein levels in various organs in the tumor-treated animals were also studied.²⁸

ANTIHYPERLIPIDEMIC ACTIVITY

Alcoholic extract of *Embelia ribes* administered orally at a dose of 200 mg/kg for 20 days reported significant ($p < 0.01$) decrease in serum, total cholesterol and triglycerides, blood glucose level, and increase in HDL-cholesterol levels when compared to pathogenic diabetic rats which are induced by streptozotocin (at a dose of 40 mg/kg intravenously). The extract further lowered the liver and pancreas thiobarbituric acid reactive substances (TBARS) values ($p < 0.01$) when compared to TBARS values of liver and pancreas of the pathogenic diabetic rats.³⁵

ANTIFUNGAL ACTIVITY

Antifungal activity assessment of *Embelia ribes* utilizing standard in vitro method was studied by test technique NCCLS (The national committee for clinical laboratory standard M27-A2 Protocol).

NCCLS technique disclose that methanol extract of *Embelia ribes* and embelin had lowest MIC50 range of 120 mg/L against *Candida albicans* (MTCC no. 183) and among four *Candida* species tested embelin had reported MIC50 values below 700 mg/L. methanol extract, petroleum ether extract and Solvent ether extract embelin reported to have MIC50 in range of 300-700 mg/L against *Candida albicans* (MTCCno.227) and *Candida parapsilosis* (MTCCno.1744). Petroleum ether extract shows lowest MIC50 range of 250 mg/L against *Candida parapsilosis* (MTCC no. 1744) and 360 mg/L against *Candida laurintis* (MTCC no. 2898) while Aqueous extract required higher MIC50 value for all species. In this way results exhibit that the percentage growth was increased with the decrease in the concentration of the plant extracts, except for the aqueous extract.³⁶

ANTIHYPERHOMOCYSTEINEMIC ACTIVITY

Anti-hyperhomocysteinemic activity of *Embelia ribes* was assessed in hyperhomo-cysteinemia induced adult male Wistar rats. Hyperhomocysteinemia was induced by methionine treatment (1 g/kg p.o) for 30 days. Administration of water extract of *Embelia ribes* (100 and 200 mg/kg p.o) for 30 days to hyperhomocysteinemic rats significantly ($p < 0.01$) decreased the levels of LDH, triglycerides, homocysteine, total cholesterol, VDL-C and LDL-C and increased the HDL-C levels in serum. The results are comparable to the standard anti-hyperhomocysteinemic drug folic acid.³⁵

MOLLUSCIDAL ACTIVITY

Molluscidal activity of *Embelia ribes* fruit powder in combination with *Cedrus deodara* oil and *Azadirachta indica* with synergists MGK-264, piperonyl butoxide (PB) in binary and tertiary combinations were used against the *Lymnea acuminata*. It was seen that the toxic effects of these mixtures were time and dose dependent. The binary and tertiary mixtures of plant derived molluscicides with synergists were more toxic with respect to the single treatment of the plant-derived molluscicides. The order of toxicity of various tertiary

combinations against *Lymnaea acuminata* was *Lawsonia inermis* seed + *Cedrus deodara* + *Embelia ribes* > *Lawsonia inermis* seed + *Azadirachta indica* + *Embelia ribes* > *Lawsonia inermis* seed + *Polianthes tuberosa* + *Embelia ribes* > *Lawsonia inermis* seed + *Allium sativum* + *Embelia ribes*. The toxicity of tertiary combination (1:1:1) of *Lawsonia inermis* seed powder with *Cedrus deodora* oil and *Embelia ribes* fruit powder against *Lymnaea acuminata* was highest (24 hr LC50 14.80 mg/l) when compared to other combinations in this study.^{18,37}

WOUND HEALING PROPERTY

Alcoholic extract of *Embelia ribes* (30 mg/ml) and embelin both reported significant wound healing activity. In embelin treated groups (4 mg/ml of 0.2% sodium alginate gel), epithelialization of the incision wound was faster with a high rate of wound contraction. The tensile strength of the incision wound was significantly increased than the alcoholic extract. Also in dead space model the weight of the granulation was increased indicating increase in collagenation. The histological examination of the granulation tissue of embelin treated group reported increased cross-linking of collagen fibres and absence of monocytes. The results are comparatively evaluated with standard skin ointment framycetin.³⁸

ANTIFERTILITY ACTIVITY

Embelin extracted from *Embelia ribes* Burm. berries altered the testicular histology and glycogen, gametogenic counts and accessory sex gland fructose at the dose levels 0.3, 0.4 and 0.5mg/kg body weight administered subcutaneously for 35 days. The compound is suggested to possess anti-androgenic activity. An oral herbal contraceptive would allow couples to control their fertility without consulting a health worker, which in turn would likely markedly increase the number of couples practicing family planning.

Other advantages of such a contraceptive would include the familiarity the rural people have with herbal medicines, the fewer side effects associated with herbal preparations, their ready availability from local sources and protection of privacy. There are many references to plants in India with antifertility properties.

Since 1966, the Indian Council of medical Research (ICMR) has been conducting research to identify an herbal contraceptive, as have other organization. Plants that have exhibited antifertility activity in clinical trials include (benzene extract of the flower petals suppresses implantation); Rudrapushpaka (*Hibiscus rosa sinensis*)(extract of the flower petals prevents pregnancy); *Embelia ribes* (pregnancy prevention), *Doacus carota*, *Butea monosperma* (anti-implantation effect) and *Mentha arvensis* (leaves have anti-implantation effect). Effect of embelia on oestrous cycle, plasma levels of progesterone and oestradiol and in vitro production of oestradiol and progesterone by mixed ovarian cells was studied. Forty adults (4 months old), regularly cycling female Spargur-rats each. Groups I and II (controls) were given 1 mil.kg body weight of physiological saline or com oil (vehicle). Groups III and IV animals, and there was significant depression in plasma oestrediol)($p < 0.05$) and progesterone ($p < 0.02$) at both 10 and 20 mg/kg body weights, respectively. Isolated mixed ovarian cells from embelin treated rats produced significantly less progesterone and estradiol than controls in vitro. It is concluded that embelin probably interferes with reproductive functions in female rats by suppressing ovarian production of sex steroid hormones.

Oral administration of embelin (75 mg/kg per day, daily for 15 and 30 days) to male rats caused significant elevation in the uptake of D-glucose, L-alanine, L-leucine and calcium in small intestinal segments. Embelin also produced significant increases in intestinal brush border membrane-associated enzymes (sucrose, lactase, maltase, alkaline phosphatase and leucine amino-peptidase) in both intestinal homogenates and partially purified brush border membrane preparations.

Significant increase was also noted for microsomal glucose-6-phosphatase and cytosolic lactate dehydrogenase. Increase in brush border membrane-associated triacylglycerol, total lipids, cholesterol, phospholipids, unesterified fatty acids and ganglioside sialic acid were seen but not in the cholesterol/phospholipids molar ratio. All these changes returned to control or near control levels following withdrawal of the drug.^{18,39}

ANTISPERMATOGENIC ACTIVITY

The active principle of the seeds of *Embelia ribes* Burm, has been isolated and the purity established. Daily subcutaneous administration of the compound at a dose of 20 mg/kg body weight to male albino rats for 15 or 30 days revealed an inhibition of: a) epididymal motile sperm count, b) fertility parameters such as pregnancy attainment and litter size, and c) the activities of the enzymes of glycolysis and energy metabolism. These changes were reversible, as seen after 15 and 30 days of recovery. Addition of embelin to epididymal sperm suspensions caused a dose- and duration-dependent inhibition of spermatozoal motility and the activities of the enzymes of carbohydrate metabolism.

Light and scanning electron microscopy showed that both *in vivo* and *in vitro* treatment with the drug causes profound morphological changes in spermatozoal head, a) decapitation of the spermatozoal head, b) discontinuity of the outer membranous sheath in the mid-piece and the tail region, and c) alteration in the shape of the cytoplasmic droplet in the tail. Embelin from *Embelia ribes* significantly reduced the sperm count and motility and also the weight of the testes, in albino rats.¹⁸

INHIBITORY ACTIVITY

Seventy-six plant extracts including methanolic and successive aqueous extracts from 37 India medicinal plants were investigated for acetylcholinesterase (AChE) inhibitory activity (*in vitro*). Results indicated that methanolic extracts to be more active than water extracts. The potent AChE inhibiting methanolic plant extracts included *Embelia ribes* (root), *Nardostachys jatamansi* (rhizome), *Ficus religiosa* (stem bark), *Withania somnifera* (root), *Semecarpus anacardium* (stem bark) and *Tinospora cordifolia* (stem). The IC₅₀ values of *Embelia ribes* (Root) obtained for the extract was 23.04µg/ml.⁴⁰

CONCLUSION

Embelia ribes is a herbal drug widely used around the world to combat various ailments. The present review has confirmed its therapeutic potential by highlighting its biological properties with pharmacological and other medicinal activities like analgesic, anthelmintic, antibacterial, antidiabetic, antioxidant, anticancerous etc.

The present review is of utmost importance as it describes what has been done and how much has been explored on *Embelia ribes* so far. On the bases of this collection of information it can be concluded that Baobarang (*Embelia ribes*) is an important, promising drug and could be fruitful for further researchers. The review has suggested that presently less clinical trials are available to confirm therapeutic potency of the drug, so large scale clinical trials are required to explore its hidden potentials.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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