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Research Article

Embelin: A potential Benzoquinone

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ABSTRACT

Embelin is a benzoquinone compound, present mainly in Embelia species. Embelin is also reported in Lysimachia punctate, Ardisia humilis, Rapanea umbellate, Cannarus richiei, Myrsine Africana and Myrsine capitellata. Embelin has demonstrated wide range of pharmacological activities including; antidepressant, anticancer, antifertility, antidiabetic, antioxidant and analgesic. Embelin shown other activities also such as antihyperlipidemic, antifungal, antihyperhomocysteinemic, anthelminthic, anticonvulsant, antibacterial, hepatoprotective, wound healing and anxiolytic activity. Recent studies, have thrown light on anti-arthritis and antiulcer activities of the benzoquinone. The present review, discusses pharmacological investigations on embelin, with potential for drug-development.

Keywords: Embelin, Benzoquinone, Quinone, Medicinal plant, *Embelia ribes*.

INTRODUCTION

Embelin, chemically known as 2, 5-dihydroxy-3-undecyl-2, 5-cyclohexadiene-1, 4 benzoquinone (Molecular weight: 294.38) is one of the bioactive compound found in oldest medicinal plant known as *Embelia ribes*. Orange coloured embelin consists of dihydroxyquinone core and long hydrophobic tail (alkyl substitute)[1]. About 4.33% of the embelin content has been observed in the fruits of *Embelia ribes*. Embelin showed antifertility, anti-implantation, antitumour, analgesic, antioxidant, hepatoprotective, wound healing, antibacterial and anticonvulsant activities. Ayurvedic formulation i.e. Sunder Vati (contains *E.ribes* as one of key ingredient) exhibited a significant efficiency to treat inflammatory and non-inflammatory lesions patients with Acne vulgaris. There are number of indication but embelin have highly known for its potent oral contraceptive, anthelmintic and anticancer activity[2]. It is contraindicated in pregnancy.

Molecular mechanism of action

Novel XLIA inhibitor, induce the apoptosis in cancer induce mice[3]. Embelin block proliferation of cancer cells and induces apoptosis by inhibiting NF-κB in human glioma cells[4]. Molecular docking and in-vitro experimental approach showed that the embelin has potential to inhibit TNF-α converting enzyme and malignant properties in breast cancer cells through inactivation of metastatic signalling molecules include MMPs, VEGF and hnRPN-K[4].

Solubility

Embelin soluble in organic solvent like Dimethylsulphoxide (DMSO), chloroform, alcohol and insoluble in water.

Pharmacokinetic

Pharmacokinetics study of embelin for 30 days in rats depicted the highest levels in the kidney followed by the testis and intestine. Significant levels were observed in the brain, heart and spleen. After 15 days treatment, embelin concentration increased in all of the organs with time, levels slowly declined, that indicate slow elimination of embelin from the body. T1/2 was 21.86 h. Embelin after s.c dosing for 30 days depicted the highest concentration in the heart, followed by the testis, epididymis, kidney and brain. Low levels of embelin were observed in the spleen, seminal vesicles, liver, intestine, prostrate and lung. About 30 days after embelin withdrawal, 20 - 75 mg/g levels were observed with T1/2 of 16.5h[1].

Naturally occurring embelin (Quinone) from *E. ribes* has poor aqueous solubility and shows limited oral bioavailability. Therefore, various techniques has been reported to make embelin more oral bioavailable[2].

Pharmacological Activity

Anticancer activity

Embelin shows promising anticancer activity by directly inhibit X Linked apotosis (XLIA), inhibited cell growth induced apoptosis and activated caspase-9 in prostate cancer cells with high XIAP levels in comparison to control cells. Modified embelin has two fold higher affinity than the original one[5]. Embelin induced apoptosis in human glioma cells by inhibiting NF-κB, which is a crucial transcription factor associated with several human diseases including cancer and controls multiple genes. It has no inhibitory effect on XIAP in glioma cells even though discovered as an XIAP inhibitor, but instead inhibited NF-κB activity by reducing nuclear translocation of p65 through decreasing phosphorylation and proteasomal degradation of IκBα in glioma cells[6].

Embelin enhances TRAIL induced cell apoptosis through DR4 and DR5 upregulation, showing that combination of low-toxicity Embelin and TRAIL may become a novel antileukemia strategy[7]. The area of solid tumour bearing

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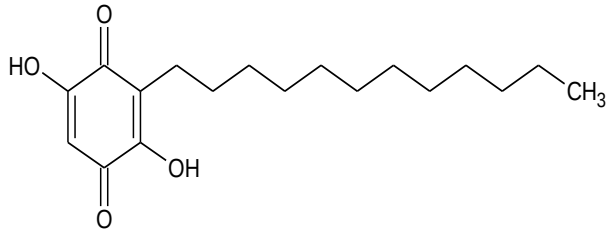

Structure of Embelin

mice was subjected to PDT (photodynamic therapeutic) with different concentration of embelin, significant cytotoxicity observed in dose dependented manner[8].

Antibacterial activity

Antibacterial activity of embelin against both gram positive and gram negative bacteria determined by disk diffusion method, micro dilution method and agar diffusion methods and it has been reported that embelin with concentration of 100µg/ml, significantly exhibited antibacterial activity[9,10]. Embelin reported to have effective against the following gram positive and gram negative bacteria.

Gram negative (bacteriostatic): *Shigella flexneri, Shigella sonnei, Pseudomonas aerugenosa, Salmonella typhi, Shigella boydii, Proteus mirabilis, Klebsiella pneumonia, Escherichia coli.*

Gram positive (bactericidal): *Staphylococcus aureus, Streptococcus pyogenes, Bacillus aureus, Micrococcus luteus.*

Anti- inflammatory activity

Anti -inflammatory activity was determined by carrageenin induced hind paw edema in mice. Embelin showed significant decreases edema weight. Embelin salts also exhibits anti-inflammatory activity in carrageenan-induced paw edema and cotton pellet granuloma formation in mice. Embelin exhibited anti-inflammatory activity against both in acute and chronic irritant contact dermatitis in vivo[11,12].

Anticonvulsant activity

Embelin significantly inhibited seizure induced by electroshock and pentaprazole in dose dependent manner. The study suggest that the embelin effective against both grand mal and petit mal epilepsy[13].

Antidepressant activity

Antidepressant activity was carried out by administration of embelin (2.5 and 5 mg/kg), via Intraperitonial route to mice, 30 min prior to induction of experimental depression by subjecting mice to tail suspension test (TST) and forced swimming test (FST). The effect of embelin at the dose of 5 mg/kg in both experimental models was compared with the standard antidepressant drug, imipramine administered at the dose of 15 mg/kg. It was found that embelin, have therapeutic potential to treat the mental depression[14].

Anxiolytic activity

Anxiolytic activity was done by using behavioural parameter in elevated plus maze test, open field test and light and dark test. In elevated plus maze, the number of entries and percentage of time spend increased in open arm. Embelin exhibited significant increase in number of rearing, assisted rearing and number of square crossed in open field test. In light and dark model, increase in number of Crossing and time spent and decrease in the duration of immobility was observed in light box[15].

Antioxidant activity

Embelin act as natural antioxidant against hepatotoxicity induced in rats. At the dose of 25 mg/kg, embelin showed a significant elevating effect on CCl4-induced depleted levels of hepatic antioxidants[16]. It is reported that the embelin exhibited free radical scavenging activities towards diphenyl-picrylhydrazyl (DPPH) radicals with 50% inhibitory concentration (IC50) of 23.3 ± 0.5 µM[17]. Another study shows that embelin inhibit lipid peroxidation and restore impaired Mn-superoxide dismutase in rat liver mitochondria[18].

Antifertility activity

Embelin with concentration of 50,100 and 200 mg/kg significantly reduced the sperm count and motility and also the weight of the testes in albino rats (Seth et al., 1982). Embelin also significantly reduce motile sperm count[19]. Embelin with dose of 60 and 120 mg showed regressed implants with hard uterine swelling simulating underdeveloped implants in female albino rats at 15, 30, 60, and 120 mg/kg of body weight, but the effective dose of embelin in achieving 100% implantations was uncertain[20]. Another study showed that embelin exhibited 100% anti- implantation activity with oral dose of 10mg/kg in albino rat. With the same dose, embelin exhibited highly significant anti-ovulatory activity but no significant estrogenic activity in rabbits or anti-estrogenic activity in rats[21]. Embelin at subcutaneous dose of 0.3, 0.4 and 0.5 mg/kg was given to male rats for 35 days, resulting in altered testicular histology and anti-androgenic activity[22].

Antiulcer activity

Embelin exhibited protective effect against acetic acid-induced ulcerative colitis in rats. It also consider that the protective effect of embelin might be due to its antiinflammatory and antioxidant activities[23].

Analgesic activity

Analgesic activity of embelin determined by acetic acid induced model, with dose of 50-100mg/kg, and the study revealed that embelin significantly prevent writhing in rat[24].

Wound Healing Activity

Wound healing activity of Embelin demonstrated by incision, excision, and dead space wound models on Swiss albino rats. Embelin treated group and was significantly showed wound healing activity[25].

Toxicity

Oral dose of 10 mg to 3 g/kg of embelin given to rats and mice did not show any toxic effects and sub acute toxicity on 10 weeks of embelin to rats also indicated the drug to be free from toxic effects on different organs. Embelin has not showed any known toxicity. The recommended dose of embelin is 5-10 gm in official Ayurvedic Pharmacopoeia and Indian Herbal Pharmacopoeia, which are considered safe without any side effects (Ayurvedic pharmacopeia, 2002). A short-term toxicity of embelin was observed in female rats after 120 mg/kg oral

administration. Acute toxicity studies of 6 weeks oral administrated embelin showed no significant body weight change, mortality, signifying its safety profile[1].

CONCLUSION

In the present review, it is clear that embelin offers a remarkable Pharmacological activity. Due to its pharmacological action embelin finds potential application in pharmaceutical and cosmeceutical industries.

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CONFLICT OF INTEREST

No conflict

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