Chapter 4

Phytochemical and Pharmacological Review of Selected Plants: *Adhatoda zeylanica* Nees and *Embelia ribes* Burm.f.

4.1 INTRODUCTION

It is always necessary to carry out thorough survey of scientific literature to determine what is known about the study and to eliminate unnecessary duplication of research. To achieve these objectives, a strategy was developed several years ago, which comprises of (i) A survey of information on the use of a particular plant as well as its preparations in traditional medicine (i.e., field studies of classical texts), (ii) A survey of modern scientific literature and (iii) experimental research which is projected on the basis of data collected in the preceding phases (Simons, 1989).

In this section, an overview of *Adhatoda zeylanica* and *Embelia ribes* with respect to botany, traditional and contemporary use, pharmacological properties and phytochemistry are given.

4.2 ADHATODA ZEYLANICA NEES

4.2.1 Botanical identity

*Adhatoda zeylanica* Medic. Syn. *Adhatoda zeylanica* Nees; Family: Acanthaceae

4.2.2 Distribution

Throughout India upto an altitude of 1300 m

4.2.3 Classical names

*Vasa, Vasaka, Simhasya, Shimhaparna, Tamra, Vaiska, Vajidanta, Atarusha, Atarushka, Shimhika, Vrisha*

4.2.4 Vernacular names

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<td>Adusoge, Kurchigida, Pavate, Bansa</td>
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4.2.5 Botanical description

Perennial, evergreen shrub, 1.2 – 2.5 m high. Leaves elliptic-lanceolate or ovate-lanceolate, entire, leathery. Flowers white with red or yellow barred throats, in spikes with large bracts. Capsules clavate, longitudinally channelled, 1.9 - 2.2 cm long. Seeds globular.

4.2.6 Parts used

Root, leaf, flower, fruit are used for therapeutic use.

4.2.7 Traditional uses

*A. zeylanica* has been most frequently used for the treatment of respiratory complaints and for cough, asthma and colds (Maikhuri and Gangwar, 1993). It is used as an expectorant, bronchodilator and to liquefy sputum (Dymock et al., 1890; Kirtikar and Basu, 1975; Nadkarni, 1976; Pushpangadan et al., 1995; Salalamp et al., 1996). *A. zeylanica* as an expectorant and antispasmodic agent was described and an alkaloid with a bitter taste was identified and named vasicine (Dymock et al., 1890). Jain et al (1994) observed that the Neterhat people in Bihar used a decoction of the leaves to stimulate and heal before and after delivery. Nath et al (1997) observed the use of *A. zeylanica* as an abortifacient in the Gora village of Lucknow, Uttar Pradesh. They found that 70% of the pregnant women use the leaves of *A. zeylanica* to induce abortion. The macerated roots of the Vasak (*A. zeylanica*) are applied on the pubic region and the vagina to help parturition (Pathak 1970). It is also described in the Gazetteer of Bombay State (Agharkar, 1953) and by Kirtikar and Basu, (1975) that ‘root facilitates the expulsion of foetus’. Pushpangadan et al. (1995) stated the use of the whole plant of *A. zeylanica* for treating impotence and sexual disorders. The use of *A. zeylanica* leaves for checking postpartum haemorrhage was also mentioned. The leaves were toxic to ‘all forms of lower life’ and have insecticidal effect (Dymock et al.,
1890; Drieberg, 1935; Agharkar, 1953; Agarwal, 1986). It was used in intermittent, typhus fevers, febrifuge and diphtheria (Wren, 1932). It was also used for stomach catarrh with constipation, rheumatism, gout, and urinary stone (Madaus, 1938).

Decoction of leaves is used for fever (Jain, 1965). Ash of leaves, smoke from leaf and wood are used for cough and asthma (Shah and Joshi, 1971). Leaves and seeds are used for asthma, cough, colds, dysentery and diarrhea (Jain and Verma, 1981). Externally warmed leaves used for rheumatic pains and dislocation of joint (Rao and Jamir, 1982). Yellow leaves are used for cough (Lal and Yadav, 1983). Decoction and ash of leaves is used for bronchial complaints such as cough, asthma, tuberculosis and antipyretic (Jain and Puri, 1984; Bhattarai, 1989). Leaf juice orally is used for coughs, fever, malarial fever (John, 1984). Plant juice is used for cough, asthma and bronchitis (Kapur and Sarin, 1984). Leaf powder is used for cough and jaundice (Reddy et al, 1988). Leaf powder boiled in sesame oil is used to stop bleeding, ear aches, and pus from ears (Reddy et al., 1989). Leaf extract is used for bronchial troubles (Sharma et al., 1992). Root decoction is used for gonorrhoea (Siddiqui and Husain, 1993). Water extract of leaf is used to relieve acidity (Manandhar, 1993). Leaf is used for urinary trouble.

4.2.8 Chemistry

Leaves of Vasaka contains pyrroloquinazoline alkaloids, chiefly vasicine (1,2,3,9-Tetrahydropyrrolo[2,1-b]quinazolin-3-ol, C_{11}H_{12}N_{2}O) (Haq et al., 1967) and vasicinone (3-hydroxy-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one, C_{11}H_{10}N_{2}O_{2}) (Amin and Mehta, 1959). It also contains adhatodine, anisotine, vasicoline and vasicolinone (Johne et al., 1971). β-sitosterol, tritricontane and vasicinine (Haq et al., 1967), vasicinol identical with 6-hydroxypeganine; 6-hydroxypeganine isolated from leaves. A quinazoline alkaloid isolated from leaves and characterised as 1,2,3,9-tetrahydro-5-methoxypryrolo[2,1-b]quinazolin-3-ol (Chowdhury & Bhattacharyya, 1985), adhavasinone isolated and characterised (Chowdhury & Bhattacharyya, 1987).
(1) Vasicine: 1,2,3,9 – Tetrahydropyrrolo[2,1-b] quinazolin-3-ol (Haq et al., 1967)
(2) Vasicinone: 2,3-(α- hydroxytrimethylene)-4-quinazoline (Amin and Mehta, 1959)

1,2,3,9,-tetrahydro-5-methoxypyrrolo[2,1-b]quinazolin-3-ol
R = H,H
Adhavasinone
R = O

(3) 1,2,3,9,-tetrahydro-5-methoxypyrrolo[2,1-b]quinazolin-3-ol (Chowdhury & Bhattacharyya, 1985)
(4) Adhavasinone (Chowdhury & Bhattacharyya, 1987)

(5) Adhatodine (Johne et al., 1971)
(6) Anisotine (Johne et al., 1971)
(7) Vasicoline (Johne et al., 1971)
(8) Vasicolinone (Johne et al., 1971)
4.2.9 Pharmacology

Essential oil from the leaves showed smooth muscle relaxant activity in the isolated guinea-pig tracheal chain (D’Cruz et al., 1979). Methanolic extract from the plant has been shown to possess anti-allergic and anti-asthmatic activities in guinea-pig after inhalation or intragastric administration at doses of 6 mg per animal or 2.5 gm/kg, respectively (Muller et al., 1993). Ethanolic extract from the leaves showed hypoglycaemic activity after oral administration in rats and rabbits (Modak and Rao, 1966; Dhar et al., 1968). The water extract was shown to be active against the microbial flora isolated from patients with gingivitis (Patel and Venkata-Krishna-Bhatt, 1984). Vasicine showed bronchodilatory activity both in vitro and in vivo. Although vasicinone, the main metabolite of vasicine, which is also present in A. zeylanica extract, showed bronchoconstriction in vivo. The two alkaloids in combination showed a bronchodilatory activity both in vitro and in vivo (Atal, 1980). Vasicine was found to have uterotonic activity in different species including human beings. It was shown that the effect was influenced by the degree of priming of the uterus by estrogens. Vasicine initiated rhythmic contractions of human myometrial strips from both non-pregnant and pregnant uteri. The effect was comparable with that of oxytocin and methergin (Atal, 1980). The antiinflammatory activity of the methanol extract, the non-alkaloid fraction, the saponins and the alkaloids was evaluated by the modified hen's egg chorioallantoic membrane test. Alkaloid fraction showed potent activity at a dose of 50 µg/pellet (Chakraborty and Brantner, 2001). Leaf showed significant hepatoprotective effect at doses of 50-100 mg/kg, p.o., on liver damage induced by D-galactosamine in rats (Bhattacharyya et al., 2005). Adhatoda zeylanica extract was shown to have a good antitussive activity in anaesthetized guinea pigs and rabbits and in unanaesthetized guinea pigs. Intravenously, it was 1/20-1/40 as active as codeine on mechanically and electrically induced coughing in rabbits and guinea-pigs. After oral administration to the guinea-pig the antitussive activity of Adhatoda zeylanica was similar to codeine against coughing induced by irritant aerosols (Dhuley, 1999). Leaf extracts orally in rats were 100% abortive at doses equivalent to 175 mg/kg of starting dry material (Nath et al., 1992). Ethanolic extract of leaf showed 60-70% anti-implantation activity in female albino rats (Prakash et al., 1985). Oral administration of A. zeylanica leaf extract (800 mg /kg body weight) in Swiss albino mice prior to whole body irradiation showed a significant protection in terms of survival percentage and hematological parameters.
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(Kumar et al., 2005). Leaf powder showed considerable degree of anti-ulcer activity in experimental rats in ethanol-induced, and pylorus ligation plus aspirin-induced models (Shrivastava et al., 2006). It also showed wound healing (Bhargava and Singh, 1988), antiallergic (Chatterjee, 1999) and antibacterial activity (Brantner and Chakraborty, 1998).

4.2.10 Therapeutic evaluation

Clinical trials of a drug containing vasicine and vasicinone have not revealed any side effects while treating bronchial asthma. Drug is known to possess abortifacient activity and hence not to be used during pregnancy.

4.3 EMBELIA RIBES BURM. F.

4.3.1 Botanical identity

*Embelia ribes* Burm. f., Family: Myrsinaceae

4.3.2 Distribution

It is found throughout India up to an altitude of 1600 m, from Central Himalaya to Konkan, Deccan, Western Ghats and South India.

4.3.3 Classical names

*Vidanga, Krimighna, Chitratandula, Jantunashana, Vella, Amogha, Kitashatru, Kitari, Krimijit, Krimiripu, Krimihara, Krimihrit, Jantughna, Jantuhrit.*

4.3.4 Vernacular names

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4.3.5 Botanical description

A large, scandant shrub with long slender, flexible, terete branches; bark studded with lenticles. Leaves simple, alternate, elliptic-lanceolate, gland dotted, short and obtusely acuminate, entire, shiny above. Flowers small, white or greenish, in both terminal and axillary panicles. Fruits globose, wrinkled or warty, dull red to nearly black, a short pedicel often present, usually one seeded; seeds globose.

4.3.6 Parts used

Fruit, root, leaf

4.3.7 Traditional uses

The dried fruit was considered anthelmintic, astringent, carminative, alternative and stimulant. It has been employed in India, since ancient times, as anthelmintic and is administered as powder, usually with milk, followed by a purgative. It was effective in the treatment of ascariasis, and for this purpose it was better than Santonin and as good as Oil of Chenopodium (Anonymous, 1952).

4.3.8 Chemistry

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\text{(1) Embelin : 2,5-dihydroxy-3-undecyl-2,5-cyclohexadiene-1,4-dione (Hao et al., 2005)}
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\text{CH}_2\text{(CH}_2\text{)}_2\text{CH}_2\text{OC(CH}_2\text{)}_9\text{CH=CHCH(CH}_2\text{)}_9\text{CH}_3 \\
\end{align*}
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\[
\text{(2) Embeliaribyl ester : n-pentacosanyl-n-nonadeca-7'-en-9'-alpha-ol-1'-oate}
\]
(3) Embelinol: 3-(4"-hydroxyoctadecanyloxy)-p-quinonyl-5-methylene-8-(10-pentanyloxy)-p-quinone

(4) Embeliol: 1,2,4,5-tetrahydroxy 3-undecanyl benzene


(6) Potassium embelate, 2,5-dihydroxy, 3-undecyl-1, 4-benzoquinone, from Embelia ribes Burm. (Johri et al., 1990).
4.3.9 Pharmacology

Aqueous *E. ribes* extract showed a significant blood glucose and blood pressure lowering potential. The same extract increased endogenous antioxidant defense against free radicals produced under hyperglycaemic conditions and thereby, protected the pancreatic β-cells against loss in streptozotocin induced diabetic rats (Bhandari and Ansari, 2008). Ethanolic *E. ribes* extract treatment increased the antioxidant defense against methionine-induced hyperhomocysteine and oxidative stress in brain (Ansari and Bhandari, 2008). Aqueous *E. ribes* extract (100 mg/kg) pretreatment orally for 40 days in isoproterenol (ISO)-treated rats significantly decreased the heart rate, systolic blood pressure, increased levels of serum lactate dehydrogenase, serum creatine kinase and myocardial lipid peroxides and significantly increased the myocardial endogenous antioxidants (glutathione, superoxide dismutase and catalase) levels. Thus *E. ribes* extract pretreatment improved myocardial injury and enhanced the antioxidant defense against ISO-induced myocardial infarction in rats and exhibited cardioprotective property (Bhandari et al., 2008). Chronic treatment with ethanolic *E. ribes* extract enhanced the antioxidant defense against MCAO-induced focal cerebral ischemia in rats and exhibited neuroprotective activity (Ansari et al., 2008). Embelin, major compound present in the *E. ribes* showed good wound healing property (Kumara Swamy et al., 2007). Extract of berries showed antifertility activity in rats and also anti-oestrogenic activity (Prakash & Mathur, 1979). It also showed encouraging antifertility activity. Embelin was found to be a NF-kappaB blocker and potential suppressor of tumorigenesis (Ahn et al., 2007). Embelin showed chemopreventive effect against DENA/PB-induced hepatocarcinogenesis in Wistar rats (Sreepriya et al., 2005). Embelin showed significant antibacterial activity mostly at the higher concentration (100 mg). The inhibition was highly significant against *Staphylococcus aureus*, *Streptococcus pyogenes*, *Shigella flexneri*, *S. sonnei* and *Pseudomonas aeruginosa*; moderate against *Salmonella typhi*, *S. boydii* and *Proteus mirabilis* (Chitra et al., 2003). Methanol and aqueous extract of *E. ribes* showed moderate activity against multi-drug resistant *Salmonella typhi* (Rani and Khullar, 2004). Potassium embelate showed potent centrally acting analgesic activity (Zutshi et al., 1989). Embelin showed antispermatogenic effect both in vivo albino rats and in vitro (Gupta et al., 1989). Embelin altered the testicular histology and glycogen, gametogenic counts and accessory sex gland fructose at the dose levels 0.3, 0.4 and 0.5 mg/kg body weight
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administered subcutaneously for 35 days. The compound showed antiandrogenic activity (Agrawal et al., 1986).

4.3.10 Therapeutic evaluation

Clinical studies were conducted with alcoholic and aqueous extracts of *E. ribes* fruits on 40 children infected by ascarides. Alcoholic extract was found effective in 80 percent cases, while aqueous extract cured 55 percent cases, rendering stools free from ova. No toxic effects were observed during and after treatment.

Fruits of *Embelia ribes*, when administered in doses of 200 mg/kg to patients of worm infestation, produced good results. Marked improvement was observed in cases of tape worm, *Giardia N. nana*. A single dose up to a maximum of 8 gm was sufficient. Worms were expelled within 6 to 24 hours of taking the drug. The drug was well tolerated and safe for use.

School children (5-12 years) suffering from various helminth diseases were treated with the *Ayurvedic* preparation, *Kuberakshadi yoga*, in a dose of 200 mg per kg body wt. in two divided doses. The drug was found effective against *Enterobium vermicularis* and *Ascaris lumbricoides*. *Kuberakshadi yoga* contained *Caesalpinia bonduc*, *Embelia ribes*, *Ptychotis sp.*, *Myristica fragrans*, *Caryophyllum aromaticum* and *Curcuma cymínsum*.

Pippalyadi yoga, a composite drug containing *Piper longum*, *Embelia ribes* and borax in equal amount, was investigated in 254 women covering 4694 cycles for contraceptive property. Oral administration of the drug in a dose of 1 gm/day gave very good results. Drug failure was observed only in 4 women. Pregnancy due to drug omission was found in 26 women. Minor side effects were observed in 17 cases. Fertility appeared normal after discontinuation of the drug.

Clinical trials were conducted with *Vidangadi yoga* (a herbal preparation containing *Embelia ribes* seeds, *Hibiscus rosa-sinensis* flowers and *Ferula foetida* oleo-gum resin) for its antifertility activity. The drug was found to be very effective and showed no toxic effects.

AC-4, a composite drug containing *Embelia ribes*, *Laccardia lacca*, *Areca catechu* and *Saraca asoca* in equal parts, when administered orally (1 gm/day in two divided doses) to 281 women for 15 days (*4th* day of menstrual cycle to *18th* day) exhibited good
contraceptive activity. There was no pregnancy due to drug failure after 10th cycle. No toxic symptoms or severe side effects were noticed.

Powders of Vidanga and Tankana in a dose of 2 gm twice a day, after meals, were administered in 150 fertile women for 6 months. 58 % of women were benefitted who followed the medication for six months continuously and no pregnancy was recorded for 2 years of follow-up. However, it was noted that cycle-wise result was 80 % successful. It was concluded that Tankana, Vidanga and Pippali Churna, administered for 5 days, can be used for 6 months to prevent pregnancy for 24 months.

Solid extract prepared from the decoction of Holarrhena antidysenterica (bark and seeds), Berberis aristata (wood), Embelia ribes (fruit), Cyperus rotundus (tuber), Aegle marmelos (fruit pulp) and Butea monosperma (seeds), in a clinical trial on 25 patients of diarrhoea and dynttery, showed cure rate of 80 percent with an average 3.3 days treatment, without any toxic effect.

Gasozyme syrup (indigenous herbal drug, containing Carica papaya, Carum copticum, Coriandrum sativum, Peucedanum graveolens, Atropa belladona, Aegle marmelos, Piper nigrum and Embelia ribes seeds) was administered orally (2 teaspoonfull twice a day after meals for months) to 40 patients of gastritis. Eight cases (20 %) were completely relieved of symptoms, 16 cases showed marked improvement and 10 showed satisfactory improvement.

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ischemia/reperfusion-induced oxidative stress in rats. *Fundamental & Clinical Pharmacology* 22(3), 305-14


Chakraborty A, Brantner AH (2001) Study of alkaloids from *Adhatoda vasica* Nees on their antiinflammatory activity. *Phytotherapy research* 15, 532-4


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