Review Article

Varuna (*Crataeva nurvala* Buch. Ham.): A brief review on Phytochemistry, Pharmacological profile and uses in various ailments

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Abstract

Crataeva nurvala Buch Ham (Capparidaeae), commonly known as Varuna, is an evergreen tree indigenous to India. It grows widely in all parts of world. Traditionally, it is as anti-periodic for waste elimination, breathing problems, metabolic disorders, joint lubrication, skin moisture, wound healing etc. Barkis cytotoxic, useful in urinary disorders, kidney, bladder stones, fever, vomiting, gastric irritation, contraceptive and oxytocic; bark-juice is given post-pregnancy. Leaves are rubefacient (external application), anti-rheumatic; internally used as febrifuge and tonic. Phytoconstituents present in the plant include lupeol, lupeol-acetate, spinasterol acetate, taraxasterol, 3-epilupeol, cadabacine, cadabacine acetate, catechin, epicatechin-5-glucoside, epifzelechin and glucocapparin, pentadecane, octanamide, 12-tricosanone and friedelin etc. Reported activities included antidiabetic, antibacterial, anthelmintic, anti-nociceptive, contraceptive, antiurolithiatic, anti-fertility, anti-inflammatory, antidiarrhoeal, wound-healing, analgesic, cardioprotective and antimalarial properties of *C. nurvala*. This review includes detailed exploration of the botany, phtyochemistry and pharmacologial aspects of *C. nurvala.* This is an attempt to provide a direction of further research.

Keywords: *Crataeva nurvala*, pharmacology, phytochemistry, toxicity

Introduction

Medicinal plants play an important role in the development of potent therapeutic agents. There are over 1.5 million practitioners of traditional medicinal system using medicinal plants in preventive, promotional and curative applications (Verma and Singh, 2008). Plants are used as a source of therapeutic agents to isolate bioactive compounds for direct use as drugs to produce bioactive compounds of novel and known structures as lead compounds, for semi-synthesis to produce patentable entities of higher activities and/or lower toxicity, to use agents as pharmacological tools and to use the whole plant or part of it as a herbal remedy.

The main traditional system of medicine in India includes Ayurveda, Unani and Siddha. Ayurveda, literally meaning the "science of life and longevity" in ancient Sanskrit, is the one of the oldest healing system of India, based on lifestyle diet and herbs (Shah et al., 2010; Gupta and Shaw, 2009). In Ayurvedic system of medicine the general health and well-being of an individual is governed by a balance of the five major elements of nature, space, air, fire, water and earth (Mhaskar et al., 2000). Any imbalance in these elements present in the body leads to different types of diseases. There are a number of Ayurvedic preparations which are used to treat various ailments.

Plants have an advantage in this area based on their long term use by humans. Fossil records date human use of plants as medicines at least to the middle Palaeolithic age some sixty thousand years ago (Solecki et al., 1975). From that point, the development of traditional medical systems of medicine incorporating plants as a means of therapy can be traced back only as far as recorded documents of their likeness. However, the value of these systems is much more than a significant anthropologic or archaeological fact. Their value is as a

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methodology of medicinal agents, which according to the world health organisation, almost 65% of the world's population have incorporated into their primary modality of health care (Verma and Singh, 2008).

WHO has estimated that 80% of the population of developing countries being unable to afford pharmaceutical drugs, rely on traditional medicines mainly plant based to sustain primary health care needs (World Health Organization, fact sheet 134). India, one of the most medico-culturally diverse countries of the world, has a respected time honoured tradition of using medicinal plant in health care and because of its biggest repository of medicinal plants in the world may maintain an important position in the production of raw materials either directly for crude drugs or as the bioactive compounds in the formulation of pharmaceuticals and cosmetics (Tiwari, 2008).

According to Ayurveda, all body processes are regulated by equilibrium among the three doshas (Vata, Pitta and Kapha). *C. nurvala*is considered valuable in treating Vata (blood flow, waste elimination and breathing), Pitta (fever and metabolic disorder), Kapha (joint lubrication, skin moisture, wound healing, strength and vigour, memory loss, heart and lung weakness and weak immune systems) (Mhaskar et al., 2000).

Toxicity Study

Topical application of the leaves of *C. nurvala* causes reddening and blistering in rodents. The decoctions of the root bark and stem bark are well tolerated. The LD50 of 50% ethanolic extract of stem bark is found to be around 1000 mg/kg i.p. for adult rats (Farnsworth et al., 1985). *C. nurvala* consumption is safe for use in the human body.

Botanical Description

C. nurvala (Family: Capparidaceae) is commonly known as Barna. It is an evergreen tree indigenous to India (Patil et al., 2010; Suksamrarn et al., 2003; Khalid et al., 1986; Ghani, 2003). It grows widely in all parts of Bangladesh, Pakistan, India, Philippine, South America, China, and Africa (Ghani, 2003). It requires dry hot climate and shady places to grow effectively (Kumar *et al* 2012). It is a leafy, moderate sized deciduous tree with soft wood, fragrant whitish to milky white coloured, polygamous flowers, 5-8 cm in diameter. Inflorescences appear as dense terminal corymbs; bracts minute. Fruit is berry, globes with woody rind, embedding seeds in yellow pulp. The outer surface of bark is wrinkled and grey white in colour, covered with large number of lenticels.

The flowering and fruiting season of this tree is December-May and June-August (Sikarwar and Patil, 2010). It grows at river banks of Southern India and other tropical and sub-tropical countries of the world, wild or cultivated (Kirtikar and Basu, 2005; Soosamma et al., 2010).

Traditional Uses

The bark of *C.nurvala*is cytotoxic especially useful in urinary disorders, kidney, bladder stones, fever, vomiting and gastric irritation. It also acts as contraceptive and oxytocic; juice of bark isgiven to women post-pregnancy (Ghani, 2003; Gagandeep and Kalidhar, 2006). Root and bark are laxative, lithontriptic, increase appetite and biliary secretion (Malini et al., 1995).

Leaves are rubefacient when applied externally, anti-rheumatic; internally used as febrifuge and tonic (Walia et al., 2007; Sanayaima et al., 2006). The tree is traditionally being used as anti-periodic, waste elimination and breathing problems, fever and metabolic disorders, joint lubrication, skin moisture, wound healing, memory loss, heart, lung weakness and weak immunity (Patil et al., 2010). In Unani system of medicine, the bark is used as appetite stimulant and to decrease the secretion of bile and phlegm (Mhaskar et al., 2000).

Folkloric Uses: It is potentially oxytocic, diuretic, laxative, anti-periodic, and bitter tonic (Md. Inamul et al., 2008). In tribal areas of Muzaffarnagar (UP), India: The bark is used against urinary disorders including kidney and bladder stones, antiemetic and as antidote in snake bite (Chauhan et al., 2009). Tribes of Eastern India (Assamese, Khashi, Garo) use the leaf paste in treatment of different types of joint disorders. Roots and barks are used as laxative and increase appetite and biliary secretions (Chidambaram et al., 2011). Varunal, a traditional Ayurvedic poly-herbal formulation containing *C. nurvala* is used against hepatitis, edema, ascites, and arthiritis (Mhaskar et al., 2000). Pallaypatty villagers of Tamil Nadu, India, use leaves and bark to cure jaundice, eczema, rabies, fever and to control birth (Ganesan et al., 2009; Sukumaran and Raj, 2010). In Philippines, leaves are prescribed during irregular menstruation whereas the bark is used to cure convulsions and tympanites (Bopana and Sexana, 2009). The tribes of Kango and Yurubas of Africa use leaf paste as counter irritant (Latifau et al., 2011).

Phytochemistry

Many medicinally important compounds including friedelin, diosgenin, sitosterol, betulinic acid and betulinaldehyde are being reported from *C.nurvala* (Gagandeep et al., 2006; Malini et al., 1995; Lakshmi et al., 1975; Hossain et al., 2008). Previous phytochemical investigations of different species of *Capparidaceae* result in the isolation of essential oils, sugars, alkaloids, steroids and terpenoids (Gagandeep and Kalidhar, 2006). In the isolated chemical constituents, the major bioactive triterpenoid is lupeol (**1**) (Mohammad, 2009),other

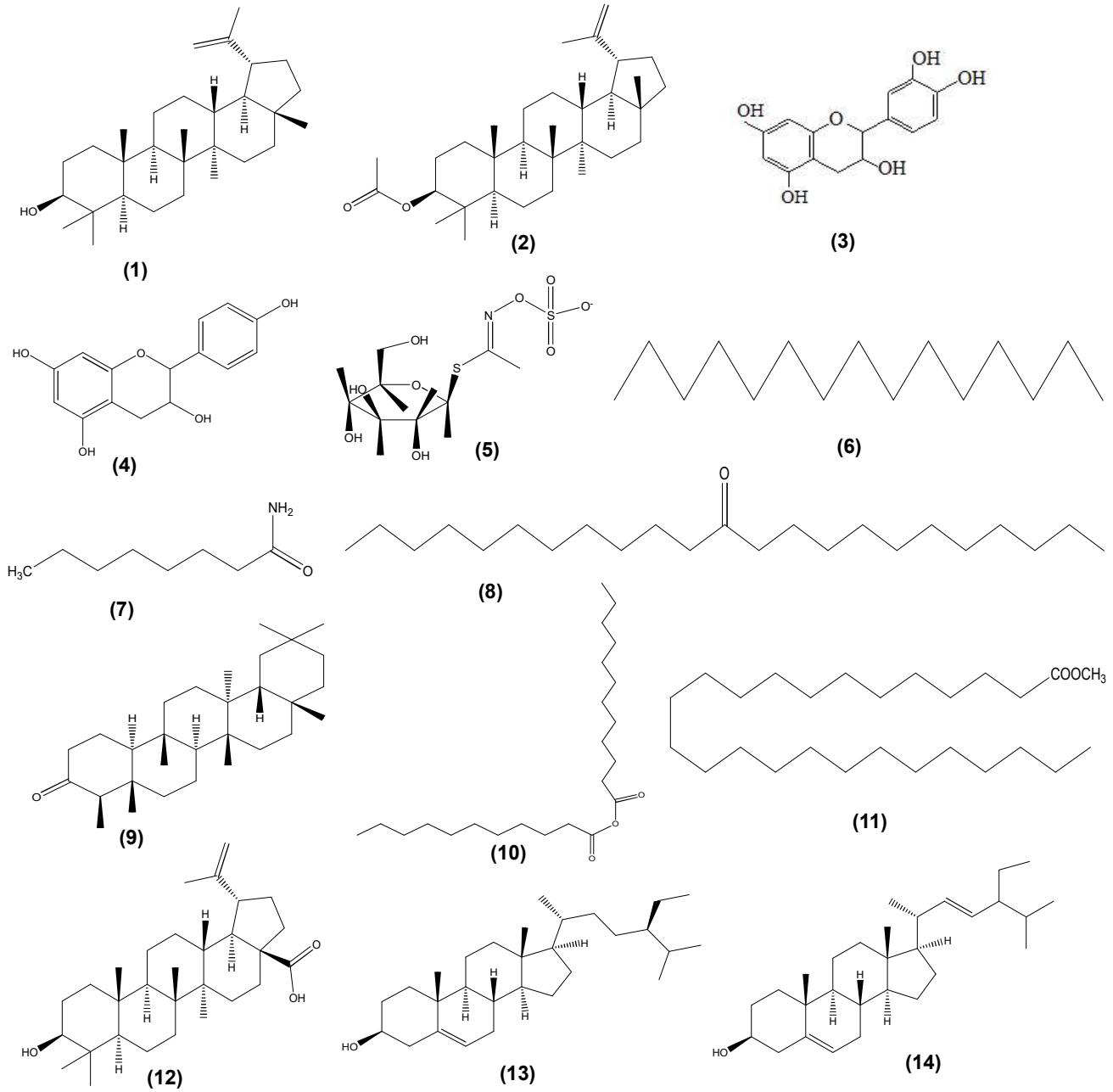

Figure 1. Structures of major chemical constituents present in *C. nurvala*

constituents isolated include lupeol acetate (**2**), spinasterol acetate,taraxasterol, 3-epilupeol,cadabacine, cadabacine acetate, catechin (**3**), epicatechin-5-glucoside, epifzelechin (**4**) and glucocapparin (**5**). Isolation of succinic acid, mannitol and lactic acid from the butanol partitioned aqueous extract of the stem has also been reported lately.Chemical investigation of fruits reveals the presence of four known compounds namely pentadecane (**6**), octanamide (**7**), 12-tricosanone (**8**) and friedelin (**9**) (Gagandeep et al., 2009).

Similarly, the chemical investigation of leaves result in the isolation of four compounds namelydodecanoic anhydride (**10**), methyl pentacosanoate (**11**), kaempferol-3-O-*α*-D-glucoside and quercetin-3-O-*α*-D-glucoside (Mhaskar et al., 2000). The chloroform fraction yield four compounds namely betulinic acid (**12**), *β*-sitosterol (**13**) and stigmasterol (**14**). The stem bark of *C. nurvala* has a rich source of tri-terpenoids and steroids (Parvin et al., 2011).

Pharmacological Activities

A number of pharmacological activities are being reported using various parts of the plant Varuna such as anti-diabetic, antibacterial, anthelmintic, anti-nociceptive, contraceptive, antiurolithiatic, anti-fertility, anti-inflammatory, antidiarrhoeal, wound-healing, analgesic, cardioprotective and antimalarial activity. A brief review of these activities is summarised below:

Antidiabetic activity

Different solvent extracts of *C. nurvala* show anti- diabetic activity. Compared with diabetic control, all the four extracts, aqueous extract, ethanolic extract, chloroform extract and petroleum ether extract decrease the elevated blood glucose levels only in sub-acute treatment. The ethanolic and petroleum ether extract shows more potent effect as compared to other ones (Sikarwar and Patil, 2010).

Antidiarrhoeal activity

Ethanolic extract of *C. nurvala* stem bark shows tatistically significant reduction in the severity and frequency of diarrhoea and intestinal transit produced by castor oil. The extract significantly inhibits castor oil induced intestinal fluid accumulation and the volume of intestinal content is more than atropine (Inayathulla et al., 2010). Antidiarrhoeal activity of ethanolic extract of the leaves of this plant is also tested using intestinal motility test in mice. In the motility test, the crude extract at oral doses of 200 and 400 mg/kg b. wt (body weight) shows 31.16% and 35.31% inhibition of intestinal propulsion of charcoal marker whereas positive control group exhibited 36.25% inhibition of charcoal propulsion through the intestine (Khatun et al., 2012).

Antiurolithiatic activity

Calcium oxalate urolithiasis induced by 3% glycolic acid in rats is treated using *C.nurvala* bark decoction. The decoction shows significant activity in preventing the deposition of calcium and oxalate in the kidney, the formation of vesicle calculi and also reduces the size of the preformed stones (Aggrawal et al., 2010).

Antibacterial activity

The antibacterial efficacy of ethanol extract of root bark and chloroform extract of the stem bark of *C. nurvala* is evaluated using agar well diffusion method (Malini et al., 1995). The extract inhibits the test bacteria. The extract has less potency than the standard antibiotic in inhibition of the test bacteria.

Antibacterial activity is tested against two Gram positive and four Gram negative human pathogenic bacteria using disc diffusion method. The range of zone of inhibition of the extract is found to be 8.3 to 22.1 mm (Parvin et al., 2012).

Anthelmintic activity

The ethanol extract of root bark of *C. nurvala* is investigated for its anthelmintic activity against earthworms (*Pheretima posthuma*), tapeworms and roundworms. Three concentrations (25, 50 and 100 mg/ml) of the extract are taken for activity which involves determination of time of paralysis and time of death of the worms. The ethanol extract shows anthelmintic activity in dose-dependent manner giving shortest time of paralysis (P) and death (D) with 50 mg/ml concentration, for all three types of worms. However, prominent activity is exhibited at lower concentration (10 mg/ml) against all three types of worms (Kamath et al., 2011).

Antimalarial activity

C. nurvala contains chemical constituent responsible for its antimalarial activity. This encouraged researchers to prepare semi-synthetic derivatives after isolating the constituent having antimalarial activity from the plant, for development of new antimalarial agent for better activity (Khalid et al., 1986).

Anti-inflammatory activity

Anti-inflammatory activity is present in Lupeol, isolated from the stem bark of *C. nurvala*. In adjuvant arthritis, Lupeol linoleate and Indomethacin show a reduction in paw swelling by 39, 58 and 35%, respectively (Verma and Singh, 2008; Shah et al., 2010; Gupta and Shaw, 2009; Tiwari, 2008; Suksamrarn et al., 2003). Lupeol and its linoleate ester derivative are used in ameliorating the lipidemic–oxidative abnormalities in the early stage of hypercholesterolemic atherosclerosis (Md. Inamul et al., 2008).

Anti-fertility activity

The bark extracts of *C. nurvala* are tested for anti-implantation and estrogenic properties. Ethanolic extract exhibits partial whereas aqueous extract exhibits complete resorption of implants at 300 and 600 mg/kg b. wt dose levels. In estrogenic activity study, both the extracts increased uterine weight and caused opening and cornification of vagina in immature rats (Bhaskar et al., 2009).

Antinociceptive activity

Ethanolic extract of *C. nurvala* exhibits moderate analgesic activity in acetic acid induced writhes. The ethanolic extract of whole plant produces 26.88% and 43.55% writhing inhibition at oral dose of 250 mg/kg and 500 mg/kg b. wt. of mice (Suksamrarn et al., 2003). Similarly, marked reduction in acetic acid-induced writhes in the animals is seen with diclofenac sodium (100 mg/kg IP).These observations suggest that crude ethanolic extract may possess centrally and peripherally-mediated analgesic activity (Alam et al., 2006).

Hepatoprotective activity

Lupeol, a pentacyclic triterpene present in *C. nurvala* is responsible for hepatoprotective activity of the plant (Preetha et al., 2006).

Antioxidant Activity

The plant extract (250 and 500 mg/kg) is effective in significantly altering the indices of cisplatin induced dysfunction of renal proximal tubule cells under oxidative stress by decreasing the concentration of blood urea

nitrogen, creatinine and lipid peroxidation. The increase in glutathione and catalase activity is indicative of the antioxidant properties of *C. nurvala* stem bark extract (Hossain and Biazid, 2008).

Anti-inflammatory Activity

C. nurvala bark is having anti-inflammatory activity due to the presence of a constituent lupeol in it (Arya and Arya, 2011).

Diuretic activity

The plant *C. nurvala* is having diuretic action which is responsible for the anti-urolithiatic activity of decoction prepared from bark of the plant (Arya and Arya, 2011). The diuretic action of Varuna attributes the metabolic correction of the serum and the urinary electrolyte levels in experimentally induced urolithiasis in albino rats (Agrawal et al., 2010).

Wound healing activity

Ethanolic extract of *C. nurvala* root bark is evaluated for its wound healing activity in ether anaesthetized wistar rats at two different doses (150 and 300 mg/kg) using incision, excision, and dead space wound model. Significant increase in skin breaking strength, granuloma breaking strength, wound contraction, hydroxyl proline content and dry granuloma weight and decrease in epithelization period is observed. Enhanced wound healing activity may be due to free radical scavenging action of the plant (Dinesh et al., 2010).

Analgesic activity

The leaves of medicinal plant *C. nurvala*, extracted in ethanol and the peripherally acting analgesic potential is tested using acetic acid induced writhing in mice. The crude extract shows significant analgesic activity at oral doses of 200 and 400 mg/kg b. wt. with an inhibition of writhing 68.4% and 76.3% compared to 67% for the positive control (Khatun et al., 2012).

Cardioprotective activity

The stem bark extract of *C. nurvala* is effective against cyclophosphamide induced cardio-toxicity (Sudharsan et al., 2005).

Conclusion

Crataeva nurvala has been ethnomedicinally used as a therapeutic agent for a variety of diseases, as we have illustrated in this article. Moreover, numerous research works have proven its uses beyond the ethno-medicinal ones in experimental animals. The plant appears to have abroad spectrum of activity on several ailments. The various parts of the plant have been explored for antidiabetic, antibacterial, anthelmintic, anti-nociceptive, contraceptive, antiurolithiatic, anti-fertility, anti-inflammatory and many other activities. It is reported to contain lupeol, lupeol acetate, spinasterol acetate, taraxasterol, 3-epilupeol, cadabacine, cadabacine acetate, catechin, epicatechin-5-glucoside, epifzelechin and glucocapparin, pentadecane, octanamide, 12-tricosanone, friedelin, succinic acid, mannitol, lactic acid, betulinic acid, *β*-sitosterol, stigmasteroland triterpenoids, which may be responsible for the different biological activities. Hence, we can isolate some purephyto-pharmaceuticals which in turn can be used as lead molecules for synthesizing novel agents having good therapeutic activity. With regard to the development of quality herbal medicine, the standardization of extracts, phytopharmacology of different extracts, isolation and characterization of active phytopharmaceuticals, elucidation of mechanism of action of the isolated compounds and clinical trial of the compounds are much needed. In the changing global scenario, the interest towards plants with medicinal value is increasing substantially in the primary healthcare system both in the developed and developing countries. Therefore, the information will help the scientists and researchers to screen the compounds responsible for different bioactivities, and to elucidate the molecular mechanism of action.

Conflicts of interest

The authors report no conflict of interest

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