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CRATAEVA NURVALA (VARUNA): PHARMACOGNOSY, PHYTOCHEMISTRY, AND THERAPEUTIC PROPERTIES

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ABSTRACT

Crataeva nurvala Buch-Ham (*Varuna*), a plant from the *Capparidaceae* family, has been extensively studied for its pharmacognostical and pharmacological properties. It is traditionally used in *Ayurvedic* and other medicinal systems for various therapeutic purposes, particularly in treating urinary tract disorders, inflammation, and metabolic conditions. Phytochemical analysis reveals the presence of compounds like lupeol, flavonoids, and saponins, contributing to its pharmacological activities. This review summarizes the macroscopic and microscopic characteristics of *C. nurvala*, its traditional uses, and its pharmacological effects, including anti-inflammatory, anti-urolithic, anti-fertility, wound healing, antidiabetic, and hepatoprotective activities. Additionally, the plant's potential for developing modern therapeutic agents is discussed.

KEYWORDS: *Crataeva nurvala* Buch-Ham(*Varuna*), Morphology, Pharmacognostical, Pharmacological, Phytochemistry, Therapeutic Properties.

1. INTRODUCTION

Medicinal plants play a significant role in developing effective therapeutics, with over 1.5 million people relying on traditional medicine. These plants have preventive, promotional,

and curative applications, providing bioactive compounds for drug production. Whether new or well-known, these substances can be employed as lead compounds, semi-synthesized to produce patented goods with improved activity and decreased toxicity, or utilized as herbal cures or pharmacological instruments.[1]

Crataeva nurvala, known as *Varuna*, is an important medicinal plant used in traditional *Ayurvedic* practices. Known for its wide distribution across India and its association with urinary health, this plant has been used to treat ailments such as urolithiasis, diabetes, and inflammatory conditions. The pharmacognostical characteristics of *C. nurvala*, including its anatomy and phytochemical constituents, provide insights into its medicinal potential. Recent pharmacological studies have confirmed the plant's multifaceted therapeutic properties, validating its long-standing use in traditional medicine. This review aims to compile the botanical, pharmacognostical, and pharmacological data on C. *nurvala* to assess its therapeutic potential.[2]

Although ancient Indian medical texts like *Charak Samhita* did not list this plant among the *Mahakashay*, the *Sushrut Samhita* recommends *Varunadi Gana* for treating *Ashmari* and *Mutrakrichha (S.S.Su. 38/8)*, additionally, *Astanga hridaya* by *Vagbhata* mentions *Varunadi Gana (A.H.Su.* 15/21-22).[3] This study aims to compile published data on the pharmacognostic and pharmacological properties of *Crataeva nurvala*.

2. Botanical description

- **Morphology**

Crataeva Nurvala Buch-Ham, commonly known as *C. magna*, *C. religiosa*, or *C. roxburghii*, is a medium-sized deciduous tree that may grow to be around 30 meters tall. This plant has a massively branching crown. The leaves are trifoliate, with petioles ranging from 3.8 to 7.6 cm in length. The leaves are ovate, whole, lanceolate to obovate, acute to acuminate, and veined reticulate. The petioles on the transverse petals are 69 mm long.[4-5]

- **Vernacular name**

Table 1: Vernacular name of *Crataeva nurvala.*

Sanskrit	*Varun, Tiktshaak*
Hindi	*Baruna, Barna*
Bengali	*Varne, Borun*
English	Three-leaved caper
Kannada	*Bitusi, Holenekki, Holethumbe, Maavilanga, Mata maavu, Naaram bele,*

	Vitasi, Neervaala mara, Sethu bandhana, Vaayu varuna, Nervaala
Malyalam	*Nirmatalam, Nirval*
Marathi	*Haravarna, Karvan, Kumla, Nirvala, Ramala, Varun, Vaayuvarna*
Tamil	*Mavilingam, Narvala, Varanam, Maavilangam, Maaredu, Peddamaagalingam, Peddavulimidi, Thellavulimidi.*[6-7]

- **Taxonomy**[8]

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnolipsida

Family: *Capparidaceae*

Genus: *Crataeva*

Species: *Nurvala*

- **Distribution**

This plant is native to Karnataka, Kerala, and Tamil Nadu and grows in the southernmost Himalayan mountains. Usually, it can be found in streams and rivers or close to temples. It is commonly grown in Assam, Bengal, Central India, Kanara, and Malabar.[8]

3. Macroscopic characteristics

The developed bark measures 6-15 cm in length, 3-10 cm in width, and 5-15 mm in thickness. The bark has two sides: rough and greyish brown on the outside and smooth and whitish brown on the inside. The flower of *Crataeva nurvala* can be whitish cream, pale yellow, or reddish-yellow, appearing before or alongside the leaves. The fruits vary in shape, being spherical, oval, hard, slim or scaly. Within these fruits are numerous reniform seeds embedded in their yellow, fleshy pulp.[9-10]

4. Pharmacognostical structure of the leaf

- **Transverse section of Leaf**

This is a dorsiventral leaf. Transverse sections of the midrib and lamina revealed the following tissues:

a. Midrib

A hump can be seen on the adaxial side of the midrib when sectioned. The midrib consists of 3-5 layers of collenchyma beneath the upper epidermis. The conducting tissue system (xylem and phloem) forms a crescent shape in the centre of the midrib. Parenchymatous cells are typically found at the centre of the ring. The inner ring consists of xylem and phloem.

Sclerenchymatous cells as bundle caps near the phloem were also found. Depicts the presence of parenchymatous cells, 3-4 layers of collenchyma, and lower epidermis beneath the vascular tissue.

b. Transverses section of petiole

A transverse section of a *C. nurvala* leaf reveals a single-layered, compact epidermis. The epidermis is then followed by the hypodermis, which is composed of four. Collenchymatous cells are organized in 5 layers with no intercellular spaces. Ground tissue is located beneath the hypodermis. The structure is made up of thin-walled parenchymal cells. Vascular bundles form a complete ring within ground tissue. The vascular bundle includes the xylem and phloem. Sclerenchymatous cells as bundle caps near the phloem were also observed.

c. Transverse section of petiolule

C. nurvala leaf petiolules have two winged projections on the upper side and are round on the lower side. The epidermis is followed by the ground tissue, which is made up of parenchymatous cells. Vascular tissue is shaped like a crescent ring. The inner ring consists of xylem and phloem. Sclerenchymatous cells were found in bundle caps near the phloem.[11]

d. Anatomy of the leaf

The leaf exhibits a distinct midrib and a uniformly thick lamina. The midrib is broadly conical on the upper (adaxial) surface and semicircular on the lower (abaxial) surface (Plate I a). It measures 750 µm vertically and 700 µm horizontally. The epidermis on both sides consists of small, square-shaped cells with prominent circular outgrowths on the outer tangential walls. Beneath the epidermis are two to three layers of collenchyma cells, while the remaining area is filled with parenchymatous ground tissue.

The vascular system in the midrib features a broad arc of several discrete, collateral vascular bundle segments. These bundles are radially elongated, and their shapes range from cylindrical to elliptical (Plate I a). There are approximately nine bundles with narrow spaces between them, each containing clusters of wide, circular or ovate, thick-walled vessels. The protoxylem vessels are oriented towards the adaxial side, while the metaxylem elements measure about 30 µm in width. On the lower side of the xylem segment, large, semicircular, compact phloem elements are present. The phloem elements are angular, thick-walled, and arranged in vertical rows.

e. Lateral Vein

The lateral vein is flat on the abaxial side and slightly elevated on the adaxial side. It contains a single, semicircular vascular bundle, which includes a cluster of wide, circular, thick-walled vessels. Approximately five groups of phloem elements are positioned at the lower end of the xylem.

f. Lamina

Both sides of the lamina are smooth and even. The lamina is dorsiventral, measuring 170 µm thick. The adaxial epidermal layer is made up of rather thick, rectangular, and squarish cells with a noticeable cuticle. Mesophyll tissue is made up of an adaxial ring of palisade cells arranged in two horizontal rows. It also has an abaxial zone composed of approximately five layers of spongy parenchyma cells. These are tiny elliptical vascular bundles that run along the midline of the lamina. The vascular bundles are collateral bundles, with a uniform covering of parenchymatous bundle sheath cells. The lamina is hypostomatic, with stomata appearing on the abaxial epidermal layer. Stomata are located slightly beneath the epidermis. The guard cells have single beak-shaped acute stomatal ledges.

g. Leaf-margin

The marginal region of the lamina is semicircular, straight, and slightly bulging. The epidermal cells in this area are smaller, thick-walled, and covered by a thick cuticle. Inside the margin, there is a compact mass of large, circular, thick-walled cells. The thickness of the leaf margin measures 220 µm.

h. Stomata

The epidermal cells and stomata were visible in the paradermal region of the lamina. The epidermal cells are polyhedral, with thick, straight anticlinal walls. Stomata are distributed sparsely. Guard cells are elliptical in shape and measure 20-30 µm in size. Stomatal pores are small, slit-like. The stoma is surrounded by five subsidiary cells, which are cyclocytic in nature. Four radiating subsidiary cells produce actinocyclic stomata.

i. Venation pattern of the lamina

Venation is extensively reticulate. The veinlets' thicknesses are uniform. The veins are thick and wavy. The vein islets are slender. Their shape and size vary greatly. Some of its vein islets include vein termination, while others lack it. There are two forms of vein terminations: simple and unbranched and branched once or twice. The terminations are thick and wavy.

The lamina contains several dark spherical entities. They are quite huge, having a spiky surface. These round spiny bodies are calcium-oxalate rich.[12-13]

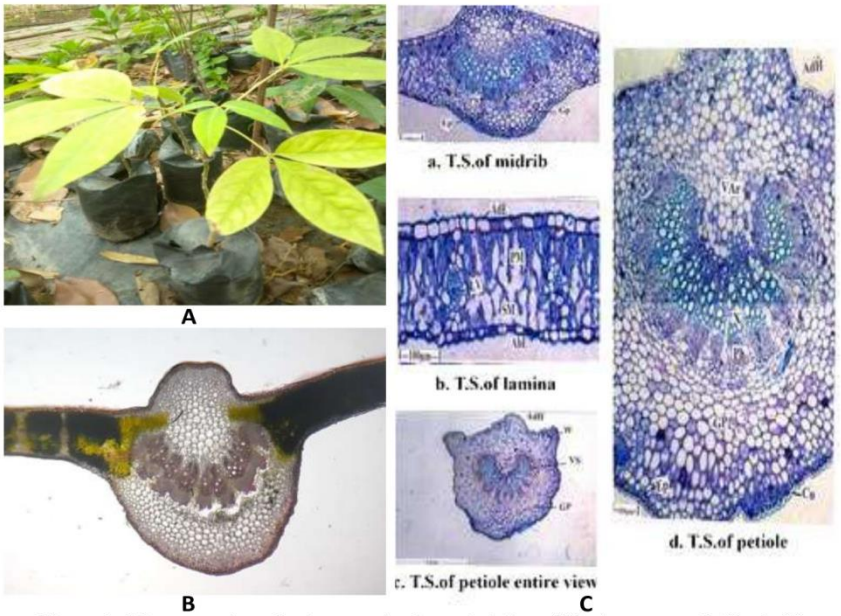

Figure 1: Marcoscopic and microscopic characteristics of Crataeva nurvala Buch. Ham
A: Plant of Crataeva nurvala **B**: TS of Midrib **C**: Ep-Epidermis; GP- Ground parenchyma; X- Xylem; Ph- Phloem; AdE- Adaxial Epidermis; AdH- Adaxial Hump; Var- Vascular Aec; Cu-Cuticle; W- cell wall; VS- Vascular strand

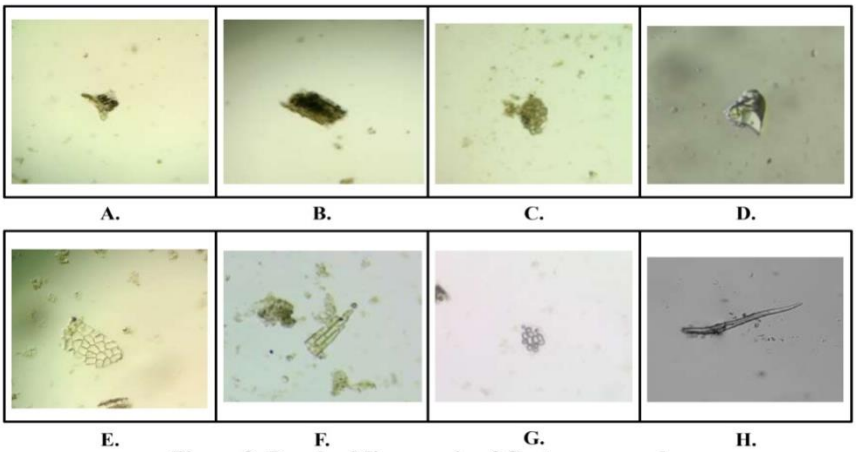

Figure 2: Powder Microscopic of Crataeva nurvala
A. Epidermis and palisade layer; B. Spiral xylem vessels; C. Spongy parenchyma tissue; D. Prismatic crystal; E. Parenchyma cells; F. Trichome; G. Starch grains; H. Fiber.

5. Traditional Therapeutic Uses

a) Bark

- This decoction is particularly effective in alleviating painful micturition.
- When combined with *Apamarg, Punarnava, Yavakshara, Gokhura,* and *Yastimadhu, Varun* bark decoction proves beneficial for conditions such as diabetes, painful bladder, urolithiasis, and various other urinary tract ailments.

- According to Yunani medicine, The bark acts as an appetizer, reduces bile and phlegm secretion, and addresses urinary tract issues.
- A decoction of *Varuntwak, Sonth*, and *Gokshur* mixed with *Yavakshara* and Jaggery (Gud) is used to treat urolithiasis.
- *Vataja Asmari* includes *Snehapakas* for *Varuntwak, Pasanaveda, Agastya, Satavari, Asmantaka, Gokshuru, Kachanar, Yava, Kulathi*, and more.
- "*VarunadyaGhrita*" is used to treat *KaphajaAsmari*.
- In *Vyanga*, goat milk is used to apply Varun's stem bark externally. (C.D)[14-15]

b) Root Bark

- External application of *kalka* (root paste) to *gandamala*.
- *Varun* root bark decoction was used to treat urolithiasis.[16]

c) Leaves

- In *Udarasula*, a cold infusion (*Phanta*) made from fresh *Varun* leaves alleviates abdominal pain.
- Consuming fresh leaves can help reduce media (fat) in the body.
- Both the bark and the leaves are ineffective antidotes for snake bites.
- In *Kikkisa*, the suprapubic area is first rubbed with dried cow dung and then anointed with *Varuna* leaf paste.[17-18]

d) Flowers

- The flowers are known as *Grahi* and *Pittarechak*.[19]

6. Phytochemical constituents

Phytochemical studies revealed that the plant's stem bark, fruits, leaves, and root bark contain distinct constituents.

- The bark contains saponins, flavonoids, sterols, glucosinolates, ceryl alcohol, fridelin, cadabicinediacetate, lupeol, and betulinic acid diosgenin.[20]
- Fruits are rich in glucocapparin, beta-sitosterol, tricontanol, ceryl and ceryl alcohol pentadecane, octanamide, 12-tricosanone and friedelin.[21]
- Leaves contain L-stachydrine, dodecanoic anhydride, methyl pentacosanoate, kaemferol-0-a-D-glucoside and quercitin-3-0-a-D-glucoside.[22]
- Rutin, quercetin, lupeol, varunol and a-sitosterol are found in root bark. Bark and stems have been found to contain alkaloids.[23]

7. Pharmacological Activity

a. Anti-inflammatory effect

In rat macrophages, *C. nurvala* ethanol extract inhibits the inflammatory response triggered by lipid polysaccharides by negatively controlling signal transduction and extracellular kinase signals. The extract's non-cytotoxic concentrations significantly reduce nitric oxide and interleukin-6 production in macrophages activated by lipid polysaccharides. After using the extract to reduce the production of inflammatory mediators, mitogen-activated protein kinase, specifically extracellular signal transduction, regulates kinase activity. Lupeol, when applied topically, reduces inflammation caused by 12 Otetradecanoylphorbol acetate in a mouse ear model and cell invasion in inflammatory tissues of mice by lowering myeloperoxidase levels (neutrophil-specific markers). Applying lupeol (5 to 9.37 mg kg−1) results in the highest inhibition of inflammation (57.14%).[24-25]

b. Antiurolithic Effect

The plant decoction was found to prevent stone formation in albino rats and reduce the pH of urine, indicating its potential for reducing the recurrence of urolithiasis. Lupeol (50 mg/kg) demonstrated significant anti-urolithiatic activity in a previous study. Decoction of this plant (800 mg kg−1) improves contractile strength and decreases urine load in patients with enlarged prostates.[26]

c. Anti-fertility activity

When tested on rats, the dried stem bark of *C. nurvala* showed anti-fertility properties. The ethanolic fraction at 300 mg/kg body weight and the aqueous fraction at 600 mg/kg body weight resulted in partial and complete implant reabsorption, respectively. In the estrogenic activity study, both extracts increased uterine weight and caused vaginal opening and cornification in immature rats. This study examines the effectiveness of fractions in preventing pregnancy in all rats at various dose levels. The effect is most likely due to the action of lupeol.[27]

d. Wound healing activity

nurvala root bark ethanol extract (150 and 300 mg kg−1, p.o.) effectively heals wounds in both vivo and in vitro. More research is needed to understand the molecular mechanisms behind the observed pharmacological activities of bioactive phytochemicals.[27]

e. Antipyretic activity

The ethanolic extract of *C. nurvala* (200 and 400 mg/kg) effectively reduced pyrexia caused by the typhoid vaccine in rabbits. The result was comparable to Paracetamol (100 mg/kg p.o.), a standard antipyretic.[28]

f. Antidiabetic Activity

nurvala stem bark extracts (500 mg/kg) effectively treat alloxan-induced diabetes in vivo. Results were comparable to standard glibenclamide (600 µg/kg). The effect could be because Increased glucose utilization by peripheral tissues leads to increased insulin secretion from β-cells in the islets of Langerhans or the release of bound insulin.[29-30]

g. Hepatoprotective Properties

It has been demonstrated that lupeol shields the liver's cells from aflatoxin B1, a carcinogenic and toxic fungal metabolite. Hepatocyte deterioration was significantly lowered by lupeol treatment. In addition, it has been shown that lupeol may improve the activity of antioxidant enzymes in mouse livers that have been harmed by oxidative stress caused by DMBA.[31-32]

h. The Nootropic Process

Ethanolic extracts *of C. nurvala* reduced acetylcholinesterase activity in rat brain stem bark; this effect was similar to that of the prescription medication piracetam. According to this study, an ethanolic *C. nurvala* extract may function as a nootropic, possibly delaying and reducing Alzheimer's disease and dementia symptoms.[33]

i. Analgesic activity

Mice administered acetic acid were made to write in order to test the potential of the leaves of the medicinal plant *C. nurvala*, which were extracted in ethanol. The raw extract demonstrates that 200 and 400 mg/kg body weight orally produced a significant analgesic effect, causing writhing to be inhibited by 68.4% and 76.3%, respectively, in contrast to 67% for the positive control.[34]

j. Antimicrobial Activity

At a 30 ug/100 ul concentration, luteol inhibits the growth of Pseudomonas aeruginosa and Klebsiella pneumoniae, two Gram-negative bacteria. There were noted inhibition zones. In Salmonella typhi and Escherichia coli cultures, luteal-impregnated disks at a concentration of 10 mg/ml were found to be effective.[35]

k. Gastroprotective Activity

Lupeol has demonstrated a gastroprotective effect against gastric mucosal damage induced in rats by intragastric ethanol. When treated with lupeol suspended in tween 80 at concentrations of 3, 10, 30 and 100 mg/kg, the rats exhibited gastroprotection rates of 21%, 60%, 79% and 77%, respectively. Given this medicinal property of lupeol, a principal constituent of *C. nurvala* and a pentacyclic triterpene, it could be further derivatized to enhance its potency.[36]

l. Antiprotozoal activity

Extract of *Crataeva nurvala* and the active ingredient lupeol has been shown by in-vitro tests to have anti-protozoal potential against trypanosomiasis, leishmaniasis and malarial brought on by different plasmodium, leishmania and trypanosome species.[37]

- **The pharmacological activity of C. nurvala**

Various research studies have explored the therapeutic potential of different parts of *Crataeva nurvala* on various disorders. Here is a summary of the research activities conducted:

Table 2: Pharmacological activity of *Crataeva nurvala.*

S. No.	Activity	Model	Extract/formulation	Mode of action	Reference
1	Anti-inflammatory	Rat macrophage, mouse ear model	Ethanol extract, lupeol	Inhibits inflammatory response by regulating kinase activity, reducing inflammatory mediators and myeloperoxidase levels	[22-23]
2	Antiurolithic	Albino rats	Plant decoction, lupeol	Prevents stone formation, reduces urine pH, and exhibits anti-urolithiatic activity.	[24]
3	Anti-fertility	Rats	Dried stem bark extracts	Induces implant reabsorption, exhibits estrogenic activity, likely mediated by lupeol.	[25]
4	Wound healing	Rats(in-vivo & in-vitro)	Root bark ethanol extract	Promotes wound healing; specific molecular mechanisms require further research.	[25]
5	Anti-pyretic	Rabbits	Ethanol extract	Reduces fever induced by typhoid vaccine, comparable to Paracetamol.	[26]
6	Antidiabetic	Rats, alloxan-induced diabetes	Stem bark extracts	Improves glucose utilization, comparable to glibenclamide.	[27]
7	Hepatoprotective	Mice, aflatoxin B1-induced liver damage	Lupeol	Protects liver cells from oxidative damage, restores antioxidant enzyme activity.	[30]
8	Nootropic	Rats, acetylcholinesterase	Stem bark ethanolic extract	Reduces acetylcholinesterase activity, potential nootropic	[31]

		activity in brain		effects.	
9	Analgesic	Mice, acetic acid-induced writhing	leaf ethanol extract	Exhibits peripheral analgesic activity, inhibits writhing response.	[32]
10	Antimicrobial	In vitro, various bacterial cultures	Lupeol	stops the growth of bacteria that are Gram-negative, such as Klebsiella and Pseudomonas aeruginosa. pneumoniae, Escherichia coli, and Salmonella typhi). Observed inhibition zones	[33]
11	Gastro-protective Activity	Rat(in-vivo)	Lupeol suspended in tween 80	Prevention of gastric mucosal damage	[34]
12	Antiprotozoal Activity	Various protozoa(in-vitro)	Extract of *Crataeva nurvala*, Lupeol	Anti-protozoal potential against Trypanosomiasis, Leishmaniasis, and malaria.	[35]

8. DISCUSSION

The pharmacognostic analysis of *C. nurvala* reveals distinct structural features, including its dorsiventral leaf structure and the presence of specific phytochemicals like lupeol, flavonoids, and saponins, which are likely responsible for its therapeutic properties. Traditional uses of the plant in *Ayurvedic* medicine, such as in the treatment of urolithiasis, diabetes, and inflammation, align with contemporary pharmacological findings. Studies have shown that *C. nurvala* has significant anti-inflammatory effects, with its ethanol extract inhibiting inflammatory mediators in rat macrophages. Additionally, its anti-urolithic properties demonstrated through its ability to prevent stone formation and reduce urine pH, make it a valuable resource for urinary tract health. The plant also exhibits promising anti-fertility, wound healing, and antidiabetic effects, highlighting its diverse therapeutic potential. Furthermore, lupeol, a major constituent of the plant, plays a crucial role in many of these activities, suggesting the potential for developing targeted therapeutic agents based on this compound.

9. CONCLUSION

Crataeva nurvala, with its rich pharmacognostic profile and diverse pharmacological activities, offers considerable promise in the field of natural medicine. The plant's traditional uses are supported by modern scientific research, confirming its effectiveness in treating various health conditions, particularly those related to the urinary system, metabolic disorders, and inflammation. Its phytochemical constituents, especially lupeol, contribute to its broad therapeutic spectrum. Future research should focus on isolating and enhancing the bioactive compounds of *C. nurvala* to explore its full potential in clinical applications. This

plant holds great promise for the development of new drugs, contributing to both traditional and modern medicine.

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