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A SYSTEMATIC REVIEW: ANTI-INFLAMMATORY AND ANTI-CARCINOGENIC ACTIVITIES OF *SEMECARPUS ANACARDIUM* Linn.

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ABSTRACT:

The traditional medicinal herb *Semecarpus anacardium*, which is utilized extensively in many indigenous medical systems, has drawn interest due to its possible therapeutic uses. The purpose of this review is to compile and assess the available scientific data on *Semecarpus anacardium*'s potential anti-inflammatory and anti-carcinogenic properties. The plant's active ingredients include a variety of bioactivities and are mostly found in the fruit and nut. According to studies, *Semecarpus anacardium* has strong anti-inflammatory properties. These benefits may be related to its capacity to block important inflammatory mediators and enzymes. This involves the control of nuclear factor-kappa B (NF- κ B) signaling pathways and the inhibition of pro-inflammatory cytokines. These results validate its conventional application in the treatment of inflammatory diseases. Research suggests that *Semecarpus anacardium* has anti-carcinogenic qualities and may be useful in preventing cancer. Apart from its ability to reduce inflammation, *Semecarpus anacardium* has demonstrated potential in the field of cancer prevention and treatment. According to experimental research, its components have strong anti-carcinogenic properties, including the capacity to stop the formation of tumors, cause apoptosis in cancerous cells, and lessen the likelihood of metastatic spread. The fundamental processes seem to entail alterations in the course of the cell cycle, intensification of oxidative harm to cancerous cells, and disruption of signaling networks inside tumor cells.

Keywords: *Semecarpus anacardium*, Plant extract, Anti-inflammatory, Anti-carcinogenic,

INTRODUCTION

Semecarpus anacardium, commonly known as "marking nut," is a medicinal plant that has been traditionally used to treat a variety of ailments such as snake bites, skin diseases, and rheumatism. Recent scientific research has focused on the anti-inflammatory and anti-carcinogenic properties of *Semecarpus anacardium*, making it a promising candidate for the development of new therapeutic drugs. In this text, we will explore the latest findings on the mechanisms behind these activities and the potential applications of *Semecarpus anacardium* in modern medicine. (Arumugam, G., et.al., 2013)

Semecarpus anacardium is a plant species that belongs to the family Anacardiaceae. It is a deciduous tree found in several parts of India, Sri Lanka, and other tropical regions. The plant has been used for centuries in traditional medicine to treat a range of illnesses and health disorders, such as skin conditions, snake bites, and fever. The various parts of *Semecarpus anacardium*, including leaves, fruit, and seeds, contain several bioactive compounds such as tannins, flavonoids, and anacardic acid, which are responsible for its therapeutic properties.

Recent studies have shown that *Semecarpus anacardium* both anti-inflammatory and anti-carcinogenic activities. Inflammation is the body's response to injuries and infections, but chronic inflammation is associated with many chronic diseases such as cancer, arthritis, and cardiovascular diseases. Several studies have reported that *Semecarpus anacardium* extracts and its bioactive compounds have anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines and enzymes. (Kumar P, et.al., 2011)

Furthermore, research studies have also demonstrated that *Semecarpus anacardium* exhibit anti-cancer properties by inhibiting cell proliferation and promoting apoptosis in various cancer cell types. The potential anti-cancer effect of *Semecarpus anacardium* is partly attributable to its chemical constituents, which have been shown to induce cell cycle arrest, activate the immune system, and inhibit signaling pathways involved in cancer development.

In this text, we will review in detail the current state of knowledge on the anti-inflammatory and anti-cancer effects of *Semecarpus anacardium*, including the underlying mechanisms and the potential applications of this plant in the development of novel therapeutic drugs. We will also discuss the challenges and

future prospects of integrating traditional medicine with modern pharmacology to improve global healthcare. (Ramprasath VR, et.al., 2005) Plants are the basis of life on earth and are of vital importance to human life. People usually depend on nearby forest areas for their needs such as medicines, timber, firewood, and wild plants. For thousands of years, cultures around the world have used herbs and plants to treat disease and maintain good health. As a source of medicinal properties, higher plants continue to play a major role in maintaining human health since ancient times. (Jain and Sharma, 2013) Traditional medicine, especially herbal medicine, has seen increasing use worldwide over the past two decades. (Mukherjee, 2013) *Bella Semecarpusanacardium* is one of the finest and most versatile medicinal plants in Ayurvedic medicine and belongs to the Anacardiaceae family. Commonly known as Mark Nut, Bella, Balataka and Birawa. The plant is common in sub-Himalayas, tropical regions, Bihar, Bengal, Orissa and central India. Known to the world since ancient times as one of the most powerful and fast-acting Ayurvedic plants, it is known in Ayurveda as 'HALBÄRZT'. (Poornima et al., 2013) This paper attempts to examine the available information on historical background, botanical description, chemical composition, pharmacological activity, therapeutic evaluation, breeding and current status in order to unlock the potential of this crop in this region. (Katoch, P., et.al., 2016) Herbs have been consumed by humans since time immemorial as part of their diets to prevent and treat various diseases. Plants are rich with various bioactive components that are very beneficial for the maintenance of good health. Increasing globalization, exposure to toxic chemicals, unhealthy lifestyles, environmental pollution, etc., the biological burden of diseases is increasing. In such a context, herbal medicine has become an integral part of the global healthcare system. Although modern medicines are available, the traditional way of making it is still popular due to its cultural value. Several scriptures and manuals available to this day list herbs with their medicinal value. Drugs such as ataxol, quinine, vincristine, epinephrine, etc. are founded from medicinal plants. Therefore, further studies on these important traditional herbs are needed to develop a more powerful and effective treatment for deadly diseases. *Semecarpus anacardium* commonly known as bhallataka, is one of the ancient traditional herbs of importance mentioned in the Valmiki Ramayana, one of the most sacred books of North India written.

HISTORICAL BACKGROUND

Before 3000 BC it is a powerful medicinal plant called Ardha-Vaidya in Ayurveda which means half doctor as it can cure almost any disease and the fruit was considered a golden acorn in the days of Galen and Avicenna in the society. However, it is deadly and toxic if consumed without detoxification. It has been used in both Ayurvedic and Siddha systems of medicine to treat various ailments like cancer, asthma, arthritis, myocardial infarction, diabetes, hemorrhoids, worm infections, hives, etc. In this review, an attempt was made to combine the details of this medicinal plant together with its pharmacological uses to highlight its role in the treatment of various types of cancer. *Semecarpus anacardium* has a long history of traditional use in various cultures, particularly in India, where it is native. Here is a brief historical background of *Semecarpus anacardium*: (Ali, M.A., et.al., 2015)

1. **Ayurvedic Medicine:** *Semecarpus anacardium* has been an integral part of Ayurvedic medicine for centuries. Ayurveda, the traditional system of medicine in India, considers the plant to have potent medicinal properties. It is believed to balance the doshas (vital energies) and has been used for treating conditions such as skin disorders, joint pain, digestive issues, and respiratory ailments.
2. **Traditional Remedies:** In Indian folklore, various parts of the *Semecarpus anacardium* tree, including the nuts, oil, and leaves, have been used in traditional remedies. The oil extracted from the nuts has been used topically for treating skin disorders, rheumatic conditions, and even toothache.
3. **Cultural and Religious Significance:** *Semecarpus anacardium* holds cultural and religious significance in India. The marking nut tree is associated with Lord Shiva, one of the major deities in Hinduism. The nuts, known as "Bhallataka" or "Shivalingi," are considered sacred and are offered during religious ceremonies. Besides its toxicity, the immobilized oil of *Semecarpus anacardium*. Insoluble in aqueous media due to its highly lipophilic nature. Therefore, the bioavailability of the binding oil is limited by oral administration. For a better therapeutic effect, a larger dose of the drug must be taken, which can lead to unwanted side effects. Therefore, the development of pharmaceutical dosage forms for the immobilized oil of *Semecarpus anacardium* is required to achieve improved water solubility and similar pharmacological activity at lower doses with minimal side effects.

GEOGRAPHICAL SOURCE:

Semecarpus anacardium, also known as marking nut tree or bibba, is a plant

species that is native to various regions of Asia. Its natural habitat includes tropical and subtropical regions of India, such as the states of Maharashtra, Kerala, Tamil Nadu, Karnataka, and Andhra Pradesh. The plant is also found in other countries in Southeast Asia, including Sri Lanka, Myanmar, Thailand, Malaysia, and Indonesia. *Semecarpus anacardium* has been an important part of traditional medicine and cultural practices in these regions for centuries. Its use in Ayurvedic medicine and various indigenous remedies is well-documented. The marking nut tree is also associated with Lord Shiva in Hinduism, and the nuts are considered sacred in religious ceremonies. (Upreti, S., et.al., 2016) While *Semecarpus anacardium* has been introduced to other parts of the world, it is important to note that its natural range is limited to specific geographical regions in Asia. The plant's natural habitat provides the ideal conditions for it to grow and thrive, and its cultural and medicinal significance in these regions is a testament to its importance.

MORPHOLOGY:

Semecarpus anacardium is a small to medium-sized tree that belongs to the family Anacardiaceae. It is also commonly known as the marking nut tree or the Bhilawa tree. Here is a botanical description of *Semecarpus anacardium*: (Mona, S., et.al. 2010)

- **Leaves:** The leaves of *Semecarpus anacardium* are simple, alternate, and oblong in shape. They are about 5-12 cm long and 2-6 cm wide. The leaves are dark green in color and have a smooth, glossy surface. They are attached to the stem by a short stalk.
- **Flowers:** The flowers of *Semecarpus anacardium* are small and greenish-yellow in color. They are borne in clusters on long, slender stalks that arise from the axils of the leaves.
- **Fruits:** The fruits of *Semecarpus anacardium* are drupes that are about 2-3 cm long and 1.5-2 cm wide. They are kidney-shaped and have a hard, woody shell. The shell contains a single seed, which is surrounded by a fleshy, edible pulp.
- **Bark:** The bark of *Semecarpus anacardium* is dark brown or grayish brown in color and has a rough, fissured surface. The inner bark is pinkish-brown in color.
- **Wood:** The wood of *Semecarpus anacardium* is hard, heavy, and durable. It is dark

brown in color and has a fine texture. *Semecarpus anacardium* is native to India and is widely distributed in the tropical and subtropical regions of Asia and Africa. It is commonly used in traditional medicine for its various health benefits.(Jain, P. and Sharma, H.P., 2013)

Taxonomy Classification

- **Kingdom** : *Plantae*
- **Subkingdom** : *Tracheobionta*
- **Super division** : *Spermatophyta*
- **Division** : *Magnoliophyta*
- **Class** : *Magnoliopsida*
- **Subclass** : *Rosidae*
- **Order** : *Sapindales*
- **Family** : *Anacardiaceae*
- **Genus** : *Semecarpus*
- **Species**: *Anacardium*



Fig .1 Plant & fruit of S. Anacardium

Synonyms

- Hindi : Bhilwa, Billar, Bhelwa, Bhilawa
- Sanskrit : Bhallataka, Antahsattva, Arusharah, Aruskara, Arzohita, Bhallata, Viravrksa, Vishasya, Bhallatakah
- English : Marking Nut Tree, Marsh Nut, Oriental Cashew Nut
Tamil : Erimugi
- Telugu : Nallajeedi, Bhallatamu
Gujarati : Bhilamu, Bhilamo
Marathi : Bibba, Bhillava
- Oriya : Bhollataki, Bonebhalia,
Amberi Urdu : Baladur, billar,
bhilavan Assamese : Bhala
- Nepali : Bhalaayo

CULTIVATION AND PROPAGATION:

Semecarpus anacardium is propagated by seeds, cuttings, and grafting. Here's a brief overview of its cultivation and propagation:

1. Seed propagation: *Semecarpus anacardium* a deciduous forest tree, is a potent source of medicinal compounds prescribed for a variety of ailments. Trees bear seeds in winter. Seasonal fruiting and poor viability limit the use of conventional propagation techniques. Use of in vitro techniques to overcome these limitations has not yet been reported. Microbe-free seedlings of *Semecarpus anacardium* could not be raised in vitro due to poor seed viability, acute seed-borne microbial contamination, and leaching of phenolics. Seed viability (30-35%) reduced with time and was completely lost in 6 months.
2. Cutting propagation: Stem cuttings of *Semecarpus anacardium* are taken from mature trees during the dormant season (December-January). The cuttings should be about 30-45 cm long with 2-3 nodes. They are treated with a rooting hormone and planted in pots filled with a mixture of sand and soil. The cuttings should be kept in a shady area and watered regularly. After about 6-8 weeks, the cuttings will develop roots and can be transplanted to the field.
3. Botanical description: This medium-sized deciduous tree can reach a height of 3,500 feet and can be found in the hotter regions of India and the outer Himalayas. The plant is widely distributed in Bengal, Assam, Bihar, and Chittagong, Orissa, central India, and the eastern peninsula of the Northern Australian Archipelago. This medium-to-large tree reaches a height of 15 to 25 meters. Its grey bark peels off in little, uneven flakes, and its leaves simply alternate oblong: oblong, glabrous above, round at the apex, 30-60 cm long, 12-30 cm

Phyto-chemical components of *Semecarpus Anacardium*:

The most important component of *Semecarpus anacardium* are bharwanols, phenolic compounds, biflavonoids, sterols and glycosides. The bharwanol fruit was found to be a mixture of cis and trans isomers of ursulenol; This compound consists mainly of 1,2, dihydroxy-3(pentadecadienyl 8',11')benzene and 1,2,hydroxy-3 (pentadecadienyl

8')benzene. The other isolated constituents are anacardoside, nallaflavanone

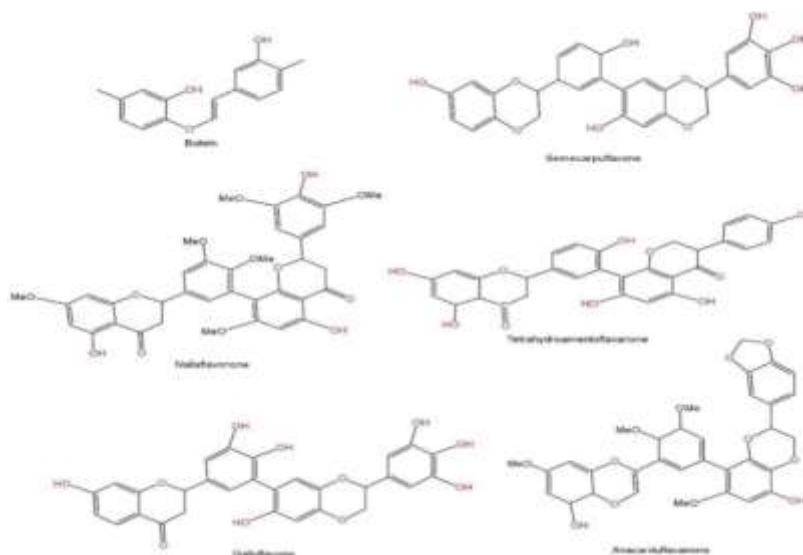


Fig.2 Chemical structures of various constituents of *Semecarpus anacardium*

ACTIVITIES OF *SEMECARPUS ANACARDIUM*

Preparation of plant extract

The stem bark was thoroughly cleaned, shade dried and powdered in a mechanical grinder. The powder was extracted with soxhlet extractor using n-hexane, ethyl acetate, methanol and water for 48 hrs. The extracts were concentrated to dryness in a desiccator.

Anti Inflammatory activities

The anti-inflammatory effects of *Semecarpus anacardium* seed extract have been studied on developing and developing adnexal arthritis. *Semecarpus anacardium* significantly reduced carrageenan and cotton ball-induced foot edema granulomatous. (Mona, S., et.al. 2010)

These results suggest the potent anti-inflammatory and therapeutic effects of *Semecarpus anacardium* Walnut extract against all stages of inflammation comparable to indomethacin. Kalpaamruthaa, a modified indigenous Siddha formulation, consists of *Semecarpus anacardium* seed milk extract and fresh dried *Emblica officinalis* fruit powder with honey. Kalpaamrutha was found to be nontoxic at a dose of 2000 mg/kg. In addition, Kalpaamrutha has been reported for potent analgesic, antipyretic, and antioxidant properties.

Mythilypriya et al. investigated the anti-inflammatory activity of *Semecarpus anacardium* in

a mouse model of adjuvant-induced arthritis associated with inflammatory mediators (lysosomal enzymes) and its effect on proteoglycans. The activities of various enzymes and the levels of the plasma protein-bound carbohydrate components of glycoproteins were determined and found to be increased in arthritic rats compared with control animals. (Ramprasath, V.R., et.al., 2006)

Methodology for anti inflammatory activity:

Experimental method (carrageenin-induced paw edema) - The anti-inflammatory effect of *Semecarpus anacardium* seed extract was determined in a rat paw edema model due to the use of carrageenan induced paw edema. Wistar rats were divided into seven groups, each containing six mice. Group 1 received saline as vehicle, group 2 received carrageenan and vehicle, group 3 received 100 mg/kg by orally. Initially, animals received drugs (means, standards, and treatments) based on the groups described above. To induce edema, 0.1 ml of 1% carrageenan solution was injected subcutaneously in the subfoot area of the right hind foot 1 hour after the for mentioned treatment. The volume of the foot increased after injection of carrageenan, which was used to quantify. We used a volumetric meter to determine leg volume at 3 and 5 hr after carrageenan treatment.

This formula is used to determine the pin thickness reduction ratio:

$$\text{Foot thickness inhibition (\%)} = 1 - \frac{V_t}{V_c} \times 100$$

Where, V is the mean relative increase or decrease in leg mass in the experimental groups and V_t/V_c is the mean relative increase or decrease in leg mass in the control group.

To evaluate the anti-inflammatory effects of *Semecarpus anacardium* seed extract, a mouse model of inflammation was used, mediated by carrageenan-induced leg edema. Male Wistar rats were divided into seven groups, each consisting of six rats. The first group received saline as vehicle, the second group received carrageenan and vehicle, the third group received 100 mg/kg newly extracted *Semecarpus anacardium*, the fourth group received 200 mg/kg extracted *Semecarpus anacardium* and the fifth group received 100 mg/kg drug by orally. We used diclofenac sodium as standard drug. Initially, animals received drugs (means, standards, and treatments) based on the groups described above. To induce edema, use 0.1 ml of 1% carrageenan solution.

B. Anti-carcinogenic activities

Semecarpus anacardium has been studied for its potential anti-tumor properties with various preparations of marking nut used in clinical practice and showing promising results against cancers of the oesophagus, liver, urinary bladder, and leukemia. The investigation of pericarp oil has revealed its anticancer activity, and the flavonoids present in the *Semecarpus anacardium* nut have been found to possess cancer-preventing abilities. (Chakraborty, S., et.al., 2004)

Semecarpus anacardium nut extract has also shown potent anticarcinogenic activity against AFB1-mediated hepatocellular carcinoma, reversing the adverse effects induced by AFB1 to near-normal cells in terms of biochemical parameters and histological pattern. *Semecarpus anacardium* oil prepared according to the Ayurvedic principle has displayed strong cytotoxic activity in human leukemia cell lines, which is attributed to its phenolic constituents, particularly biflavones. (Mona, S., et.al. 2010)

Methodology for anti-carcinogenic activities

Mathivadhani et al. investigated the inhibitory effect of *Semecarpus anacardium* seed extract on human breast cancer (T47D) cells. Cytotoxicity analyzes revealed that these cells became apoptotic. *Semecarpus anacardium* was found to induce rapid Ca^{2+} mobilization from the intracellular stores of the T47D cell line, and its cytotoxicity against T47D correlates well with its ability to penetrate altered mitochondrial membrane. At the molecular level, these changes were accompanied by a decrease in Bcl(2) and an increase in Bax, cytochrome c, caspase and PARP cleavage, and ultimately DNA fragmentation in the cell nucleus. Taken together, our results provide unprecedented evidence that *Semecarpus anacardium* activates apoptotic signaling in T47D cells. in terms of biochemical parameters and strong cytotoxic activity in human leukemia cell lines.

CONCLUSION

Semecarpus Anacardium, commonly known as "marking nut," is a medicinal plant which has been traditionally used to treat a variety of diseases such as snake bites, skin diseases, and rheumatism. Recent scientific research has focused on the Anti-inflammatory and Anti-carcinogenic properties of *Semecarpus Anacardium*. *Semecarpus Anacardium* is small to medium sized tree which belongs to the family Anacardiaceae.

The most significant components of the *Semecarpus anacardium* are bhilwanols, phenolic compounds, biflavonoids, sterols and glycosides. Bhilwanol from fruits was shown to be a mixture of cis- and trans isomers of ursuhenol. *Semecarpus anacardium* also contains the bhilawanol-A, bhilawanol-B, anacardic acid and phenolics.

Semecarpus anacardium seed extract should contain the lysosomal enzymes, biflavonoids – biflavones A, C, A1 & A2 should produce anti-inflammatory effect on developing arthritis.

Semecarpus anacardium significantly reduced the carrageenan induced foot edema. *Semecarpus anacardium* nut extract shows the inhibitory effect on human breast cancer cells.

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