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Semecarpus Anacardium: A Review of Its Phytochemistry, Traditional Uses, Pharmacological and Toxicological Properties

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Abstract

Semecarpus Anacardium is also known as Bhallataka or Bhilwa which belongs to Anacardiaceae family and is traditionally used in treating obstinate skin illnesses and counter poisoning in the traditional system of medicine. It contains many active constituents like biflavonoids, phenolic compounds, bhilawanols, minerals, vitamins and amino acids which show many various medicinal properties Shodhana has been studied in this review to detoxify the nut extract. It discusses this review discusses the recent scientific literature on the phytochemistry, traditional uses, pharmacological activities, and toxicological aspects of S.anacardium. The potential applications of bhallataka in the pharmaceutical, cosmetic, and food industries are also discussed, along with future research directions.

Keywords

Semecarpms Anacardium; Phytochemistry; Pharmacological activities; Traditional medicine; Toxicology.

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1. INTRODUCTION:

Semecarpus anacardium Linn, known as "marking nut" (Family: Anacardiaceae), is a plant that was traditionally utilised for therapeutic purposes in Ayurvedic and Siddha systems of medicine. In Ayurvedic classics, it falls under the Upavisha (toxic but not lethal to human health) group. In the Drugs and Cosmetics Act (India), 1940, it is classified as a poisonous medicinal plant [1]. The tree is deciduous. The gigantic leaves and the red blaze of resin that exudes from the blossoms—which become black when exposed—make it easy to identify the greenish-white panicles of flowers that develop with new leaves in the months of May and June [2].

The fruit of *Semecarpus anacardium*, known as the marking nut (also called the washerman's or dhobi's nut), has been used in India to mark laundry and heal skin conditions. "Dhobi mark" dermatitis may result from it [3, 4]. The marking nut, or nut of S. anacardium, contributes for many conditions, including fever, rheumatism, dysentery, asthma, ulcers, and enlargement of the spleen, alopecia, leucoderma, leprosy, haemorrhoids, and cancer. The fruits and oil are also very effective in treating

helminthic infection, neuritis, leprosy, and venereal disorders [5].

The fruit's pericarp holds tarry oil that contains anacardic acid, which contains urushiols causing blisters when they come into encounters. Thus, there is a significant chance that unintentional intoxication during Bhallataka shodhana (purification of Semecarpus Anacardium Linn) could end up in contact dermatitis in people of all ages. Semecarpus anacardium Linn. is known to have a number of biologically active substances, including alkaloids, phenolic compounds, and biflavonoids. It has also been demonstrated that this medication has anti-inflammatory, antioxidant, antimicrobial, neuro-protective, anti-spermatogenic, analgesic, hypoglycemic, anti-ulcer, antiatherogenic and anti-carcinogenic properties [6, 7, 8]. This study looked to alleviate knowledge deficits, evaluate future research opportunities, and illustrate the therapeutic potential of phytoconstituents by providing a comprehensive summary that focused on their phytoconstituents, traditional medicinal uses, pharmacological and toxicological properties.

2. PLANT PROFILE:

2.1. Taxonomical classification:

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

2.2. Botanical description:

A small tree native to Himalayan and subtropical parts of India, reaching a height of 12 m; leaves are somewhat crowded at the ends of the branches, lanceolate-obovate to oblong-obovate, 10–25 cm long, hairy, whitish beneath, rounded or somewhat pointed at the tip, and usually pointed at the base. Flowers are whitish, glomerate, 2–2.5 mm long and are borne on panicles which are usually longer than the leaves. Fruit, borne in clusters, resemble in shape the cashew but is much smaller. The fruit is of the size and shape of a broad bean, black in color, and quite hard and dry externally, but upon breaking the outer skin with a knife, the central cellular portion of the pericarp is full of a brown oily acrid juice; inside the pericarp is a thin shell conforming to it, and containing a large flat kernel, which has no acrid properties. They are glabrous above and pubescent beneath. The flowers are greenish white, in panicles. Fruits are ripe between December to March 2-3 cm broad, ovoid and smooth with a lustrous black [8, 9].

Fig 1: Seed of *Semecarpus Anacardium*

2.3. Geographical distribution:

Semecarpus Anacardium (Anacaridiaceae), Most of the species of genus Semecarpus are distributed in the tropical Asia to Oceania and the plant is distributed at the outer Himalayas from Sutlej to Sikkim and fairly at hotter parts of India to the altitude of 3500 feet and in places such as Assam, Maharashtra, Karnataka, Konkan, Bihar, West Bengal, Orissa, Kanara Forest of Tamil Nadu, Madhya Pradesh, etc. S. anacardium is found in various parts of the world right from the outer. Himalayas to the Coromandel Coast Africa, East Asia to Indian subcontinent, Indo-Malaysian region, western peninsula, North Africa and in China, Nepal, India, Burma, Malaysia, N. Australia. It grows naturally in the tropical Moist deciduous and semi evergreen forests having dry climate [10, 11].

3. CHEMICAL CONSTITUENTS:

The most significant bioactive components of the *S. anacardium* Linn. are bhilwanols, phenolic compounds [12, 13], Bioflavonoids [14], sterols and glycosides [15], Anacardoside [16], Semecarpetin [17], Nallaflavanone [18], Jeediflavanone[19], Semecarpuflavanone [20], Galluflavanone [21], Anacarduflavone [22], anacardic acid, O-hexamethyl

bichalcone A, O-dimethyl bi-flavanone B, O-heptamethyl bichalcone B1, O-hexamethyl bichalcone B2, O-hexamethyl bichalcone C [23], 3,4,2',4'-tetrahydroxychalcone (butein) and 7,3',4'-trihydroxyflavone [24] and l-O-ß-Dglucopyranosyl- (1 6)-ß-D-glucopyranosyloxy-3-10hydroxy-5-methylbenzene [25].

Table 1: Nutritive value of the marking nut kernel.

S.NO.	Constituent	G/100g
1	Calories	587
2	Carbohydrates	28.4
3	Protein	26.4
4	Fat	36.4
5	Moisture	3.8
6	Fibre	1.4

Table 2: Minerals and vitamins:

S.NO	Minerals and vitamins	Mg/100g
1	Iron	6.1
2	Phosphorus	836
3	Calcium	295
4	Thiamine	0.38
5	Riboflavin	0.17
6	Nicotinic acid	1.06

4. PHARMACOLOGICAL PROPERTIES:

Semecarpus anacardium is an exceptional plant each of its components has been associated with distinct medicinal activity. Extensive research has unveiled the plant's potent antioxidant, antimicrobial, anticancer, hypoglycaemics, Neuro-protective, anti-ulcer, anti-inflammatory, analgesic, antiatherogenic and antispermatogenic activities**.**

4.1. Anti –oxidant Activity:

The stem bark ethanolic extract of S. anacardium exhibited 69.45% superoxide scavenging capacity compared to the control, whereas acknowledged antioxidant Quercetin showed 72.45% at 1000 µg/ml. Quercetin and stem bark extract revealed IC50 values of 215 and 240 µg/ml, respectively. These results show that the stem bark's crude methanolic extract demonstrated properties substantially comparable to the natural component quercetin [26]. With an IC50 of 72.24 µg/ml, the ethanolic bark extract demonstrated DPPH radical scavenging activity in comparison to ascorbic acid, which had an IC50 of 17.81 µg/ml [27].

The potential of S. anacardium's aqueous and ethanolic leaf extracts to donate hydrogen is considered to be the explanation for their effect on DPPH scavenging increased as the extracts' concentration increased from 50 to 250 µg/ml [28]. The antioxidant property of the aqueous extract of SA nuts was studied by Verma et al. in the liver of an AKR mice model during the development of lymphoma. When the aqueous extract of SA is administered to mice with lymphoma transplants, antioxidant enzyme activity increases while LDH activity dramatically decreases, suggesting a reduction in carcinogenesis [29]. The antioxidant activity of SA stem bark ethyl acetate extract was studied by Sahoo et al. After the SA stem bark's ethyl acetate extract was isolated, a crystalline crystal with a bright yellow color was found and identified as butein. With IC50 values of 43.28 ± 4.34 µg/ml, this substance demonstrated antioxidant activity which was comparable to the activity of rutin as a reference [30].

4.2. Anti-cancer Activity:

Anacardic acid and cardanol have both been shown to have anticancer properties [31, 32]. Derivatives of anacardic acid have been suggested as possible antitumor agents against liver cancer, prostate cancer, and numerous additional cancers [33]. In leukemic mice administered SA nut milk extracts, Sugapriya et al. demonstrated the restoration of energy metabolism. In comparison to control animals, leukemia-bearing mice exhibited a large rise in LPOs, and glycolytic enzymes, a fall in gluconeogenic enzymes, and a significant drop in TCA cycle and respiratory chain enzyme activity. Imatinib mesylate, a common medication, was contrasted with the treatment of Semecarpus anacardium. Leukemic cells were removed via the bone marrow along with internal organs of leukemic animals after being administered Semecarpus anacardium. [34].

In mice with Ehrlich Ascites Carcinoma (EAC)-induced peritoneal ascites, purified samples (SA-II & SA-III) demonstrated a significant and highest degree of

protection at the dosage level of 200 mg/kg, p.o. A significant dose-dependent anticancer activity was additionally observed [35]. Banuhaseena et al assess the Semecarpus ancardium's apoptotic and cytoprotective effects on the breast cancer cell line MCF-7. The trypan blue exclusion approach was used to investigate the SA's apoptotic impact on MCF-7 cells, and the lactate dehydrogenase (LDH) assay was used to determine its cytotoxicity [36].

The anti-cancerous effectiveness of milk extract from Semecarpus Anacardium (SA) nuts was demonstrated by Joseph et al. in rats with hepatocellular carcinoma. During the trial, neoplastic alterations in the liver contributed to elevated liver enzymes and HCC marker in the hepatocellular carcinoma control group, while these same markers were lowered in the group treated with Semecarpus Anacardium nut milk extract [37]. The dose-dependent inhibitory effects of methanolic extract on PA-1 cell growth remain less prominent at different concentrations (0.1, 1, 10, 100 µg/ml). There was a rise in the inhibitory rate of cell growth that was dose-dependent. The methanolic SA nut extract's IC50 value was found to be 250 µg/ml [38].

4.3. Analgesic activity:

For 20 minutes, 73.33±1.16 writhing was seen in the control group. In comparison to the petroleum ether extract (51 ± 2.62) and the chloroform extract (45 ± 1.81), the methanol extract (28.33 ± 2.25) exhibited a significantly greater analgesic efficacy. However, it was found that the acetylsalicylic acid (2.33 ± 0.3), was more potent than all of the stem bark preparations [39].

4.4. Anti-microbial Activity:

Nair et al. demonstrated that the dry nuts of SA (Bhallatak) alcoholic extract had bactericidal action against two-gram positive pathogens (Staphylococcus aureus and Corynebacterium diphtheriae) and three-gram negative microorganisms (Escherichia coli, Salmonella typhi, and Proteus vulgaris) in vitro. In the mouse skin irritant assay, no dermatoxic impact (irritant property) was observed [38]. Synthesis of AgNPs through plant extract from S. anacardium. The half-life (MIC) of these AgNPs were 33.77±0.2 388 µg/ml, 12.9±0.2 µg/ml, and 23.49±0.2 µg/ml for S. aureus, P. aeruginosa, and E. coli, in that order. At 60 µg/ml for S. 390 aureus, 40 µg/ml for P. aeruginosa, and 50 µg/ml for E. coli, 389 S. anacardium produced AgNPs exhibited >99% inhibition [41]. Semecarpus anacardium has been shown to have antifungal activity against four different fungi: Fusarium oxysporum, Rhizctonia solanii, Alternaria spp., and Sclerotium rolfsii. The LC50 values for these four fungi are 62.5, 8.125, 31.25, and 30 µg/ml[42].

4.5. Anti-inflammatory activity:

The physiologically active components of S. anacardium, have anti-inflammatory properties. Such results imply that S. anacardium may be able to lessen the arthritic effects of FCA [43]. Tetrahydroamentofole (THA), a biflavonoid, has been demonstrated to be the primary active principle isolated from SA using an ethyl acetate extract, by research by Salvem et al. The prostaglandin biosynthesis test of THA, which is catalysed by cyclooxygenase (COX-1) in vitro, yielded an IC50 value of 29.5 µM (COX-1) and 40.5% inhibition at 100 g/mL (COX-2). THA exhibited a dose-dependent anti-inflammatory effect in the in vivo carrageenan-induced paw edema experiment; its action was similar to that of ibuprofen [44]. Using the technique of carrageenan-induced paw edema in albino rats, Bhitre et al. synthesized the methanolic, ethanolic, chloroform, ethyl acetate, and petroleum ether extracts of fruits of SA and tested the effectiveness of the anti-inflammatory activity. The extract had significant anti-inflammatory action that was on par with aspirin, the accepted benchmark [45]

A distinct combination of T. cordifolia and Semecarpus anacardium has shown considerable alleviation from arthritic symptoms in an open label randomized controlled clinical experiment [46]. The S. anacardium methanolic extract exhibited a maximal inhibition of 69.89% at 1000µg/ml and an IC50 value of 250 µg/ml. The positive control, diclofenac sodium, is an anti-inflammatory drug that showed 72.92% inhibitory action at 1000 µg/ml and an IC50 value of 220 µg/ml. Additionally, the proteinase trypsin was inhibited by the methanolic extract of S. anacardium bark in a dose-dependent manner, showing the most potent inhibitory activity at 73.95% at 1000 µg/ml (IC50 210 µg/ml). The positive control, diclofenac sodium, showed 74.42% with an IC50 of 205 µg/ml [47].

4.7. Antiatherogenic Activity:

A study by Sharma et al., SA has anti-artherosclerotic properties and typically lowers tissue and serum hyperlipidemia by inhibiting intestinal cholesterol absorption in conjunction with peripheral elimination [48].

4.8. Anti –ulcer Activity:

The level of mucoproteins was significantly and similarly raised by the extract at 200 mg/kg compared to the standard drug cimetidine ($p < 0.01$). The ulcer scores rose in the EPPL ulcer-induced group. When the extract was administered, the EPPL models significantly decreased ($p < 0.05$ and $p < 0.01$). Ethanol plus pylorus ligation procedure [EPPL] drug-treated group histological sections revealed a

hyperplastic gastric mucosa with regenerative mucosal epithelium and a decrease in ulcer focus [49].

4.9. Antispermatogenic Activity:

The aqueous extract of S. anacardium's aerial portion exhibited spermicidal action, according to Narayan et al. (1985) [50]. The effect of S. anacardium on albino rats' uteri and ovaries was investigated by Gudibanda (1968). Based on his observations, S. anacardium's cotyledons were effective in reducing the number of litters (from 12 to 3) and the size of the litters (from 7.17 to 2.67) [51]. In vitro acetylcholinesterase (AChE) inhibitory activity was investigated by Vinutha et al. for SA (stem bark), extracts comprising methanolic and successive water extracts. The results revealed that extracts with more methanol than those with water were more active. SA (stem bark) plant extracts have a potent AChE-inhibiting concentration of 38 g/ml [52]. Furthermore, it was also established that Semecarpus anacardium is effective effectively as an oral contraceptive [53, 54, 55].

4.10. Hypoglycaemic Activity:

Rats with diabetes had a reduced capability to tolerate glucose than rats in the control group. The oral administration of both metformin and SA to diabetic rats demonstrated in our study a significant reduction in the treated rats' peak blood glucose levels at 1 and 2 hours during the oral glucose tolerance test. Compared to the usual medication, SA had a more significant impact. By elevating the amount of glycogen in the liver and skeletal muscle, SA might have altered the peripheral tissues' utilization of glucose. When the medication SA was administered, HOMA-IR decreased and HOMA-beta increased [56].

Research indicates that there is a correlation between elevated rates of impaired glucose tolerance (IGT) along with type 2 diabetes and both high HOMA-IR and low HOMA-b [57].

Arul et al. investigated the impact of an ethanolic extract of dried SA nuts on the levels of blood glucose in rats with both streptozotocin-induced diabetes (antihyperglycemic) and normal (hypoglycemic). The blond glucose of normal rats was decreased by an ethanol extract of SA (100 mg/kg). A comparison was made between the antihyperglycemic activity of SA and tolbutamide, a sulfonylurea derivative used for the treatment of diabetes mellitus, at 0, 1, 2, and 3 hours after the therapy [58].

Lipid peroxide and protein carbonyl concentrations were dramatically reduced to near-normal levels by treatment with SA and standard drugs (metformin and atorvastatin). The activity of TCA cycle enzymes was reduced in diabetic-induced CVD animals due to irregularities in the metabolism of glucose and oxidative mitochondrial damage. When compared to control rats, treatment with the drug SA and conventional medications (metformin and atorvastatin) enhanced the activity of these enzymes in diabetic-induced CVD animals [59]. The rats in Groups SA 100, SA 200, and SA 400 showed significantly decreased glucose levels after undergoing extract therapy for 15 days. The effect was dose-dependent, with Group SA 200 and Group SA 400 exhibiting the greatest effects ($p < 0.05$) [25].

4.11. Neuro protective Activity:

Research suggests that the SA extract improves memory and cognitive function. The findings imply that the medication was effective in halting cholinesterase inhibition and hippocampus neuron deterioration. Rats' spatial identification memory appeared to be much worse in the AD group in the Y-maze test, but the SANE group's spatial recognition memory altered dramatically, according to the study [60]. The concentrations of hydroperoxides and TBARS (Thio barbituric acid reactive compounds) in the brain tissue of experimental and normal rats. Rats given NH4Cl were shown to have brain tissue with considerably higher amounts of TBARS and HP compared normal rats. In comparison to rats treated with NH4Cl, it was shown that the levels were much decreased in hyperammonaemia rats treated with SA [61].

5. TRADITIONAL USES:

In Charaka Samhitha, S. anacardium has been mentioned for various gastric and urinary disorders, curative of obstinate skin diseases and has been prescribed for counter poisoning. In Sushrutha Samhitha, plant nut preparations have been recommended for the treatment of intestinal parasites, fever, liver toxicity, menorrhagia ulcers, obesity, & pelvic inflammatory disease [62]. It is used as a blood purifier, brain tonic, and haematinic tonic. The powdered seeds of Semecarpus anacardium, Terminalia chebula, and Sesamum indicum L. combined with jaggery has excellent results in chronic rheumatic disorders. The medicated milk or its oil is salubrious in cases of dysmenorrhea (painful menstruation) and oligomenorrhea (scanty menstruation). It decreases urine output, which makes it beneficial in kapha-type diabetes. Bhallataka is the best rejuvenative (rasayana) for skin conditions, vata disorders, and as a preventive measure to increase the body's resistance [8].

The ripe, sweet fruit of Bhallataka improves digestion, cures vata-kapha dosha, heals wounds, skin anomalies, piles, inflammation, bloating, ascite infestation, improves mal-absorption, etc. The seeds

have a high nutritional value, balance vata and pitta dosha, pacify pitta dosha, stimulate the digestive system, and is very useful for hair growth. Fruits and oil are effective in treating rheumatic pain, gout, and neuritis [63]. Fruits after detoxification have been used for improving eyesight, prolonging life, and in certain skin conditions. They have also been used to treat asthma, piles, leprosy, arthritis, and skin conditions like leukoderma [64].

Serankottai nei is a medicated ghee preparation which includes nut extract of Bhalayo is used to treat lung infections such as tuberculosis, cancer, neurological pain, and autoimmune disorders like rheumatoid arthritis and osteoarthritis [65]. Another modified Siddha formulation called Kalpaamruthaa contains nut milk extract along with dried powdered Emblica officinalis fruit and honey. This formulation has been assessed for numerous ailments like analgesic, antipyretic, ulcerogenic, anti-carcinogenic, anti-arthritic, etc [66].

For the purification of semecarpus anacardium, by using steel knife the thalamus portion of the fruit was removed. The nuts were then treated for an additional seven days with fresh cow urine every day and then a final seven days with cow milk per day. Lastly, brick powder was applied abundantly to the nuts and left for three days. Before each application of fresh cow pee or milk throughout the treatment, the nuts were thoroughly cleaned with water. The nuts were thoroughly rinsed with hot water on the eighteenth day, which was the last day of the shodhana procedure. Three repetitions of the shodhana technique ensured that the nuts were completely purified and that all poisons and impurities had been eliminated preparing them for use as therapy [67, 68].

6. TOXICOLOGY PROPERTIES:

Avoid consuming Semecarpus anacardium in infants, the elderly, expectant mothers, or anyone with a pitta-dominant constitution. This should only be used during the warmer months. Coriander leaf pulp or butter, musta (Cyperus rotundus), coconut oil, rala ointment, ghee, and stinging and swelling are instances of external therapies for allergic reactions. Limit the consumption of salt and spices, and try to stay out of the sun, the heat, and too much sexual activity while undergoing the Bhallataka therapy. The poisonous oily part of the nut should be eliminated to the extent that it fits the safety margin. It uses the irritating qualities of pericarp juice to trigger skin and ocular issues, as well as miscarriages [69].

Therapeutic formulations containing nuts could trigger dermatitis on the hands and face. Legs and foot injuries may arise from employing a pestle and mortar positioned between the knees to pound nuts [70]. Skin lesions, anuria, and spreading cortical necrosis were caused by Anacardium. Bloody urine, bowel movements, and painful micturition were the exterior effects of topical S. anacardium [71]. Based on their findings, 17 out of 70 patients showed a response to drugs. Reddish maculopapular rashes and itching in the hands and forearms are among the symptoms. Additionally, certain negative effects were described by patients treated with S. anacardium [72, 73].

Male albino rats have been employed for toxicity testing on a few blood parameters at both acute and subchronic levels using 50% w/v SA nut oil extract in ground nut oil. The immediate and long-term effects of the crude extract on the activity of particular renal enzymes, such as GOT, GPT, SDH, and LDH, and on the kidney histology in albino rats of both genders. In albino rats, significant alterations in the histological structure resulting in nephritis and activity levels of kidney marker enzymes were suggesting renal failure. The extract from SA nuts can cause nephrotoxicity, according to the results [74, 75]. The brine shrimp lethality test was utilised to determine the cytotoxicity of aqueous preparations of medicinal herbs. Within the 120 plants analyzed, SA (Anacardiaceae) exhibited the most significant level of cytotoxicity, with an LC50 of 29.5µg [76]. About their hemodynamic effects, SA toxins may outcome in acute renal failure [77].

7. CONCLUSION:

This review has provided a comprehensive overview of the plant's botany, geographical distribution, phytochemistry, traditional uses, pharmacological and toxicology properties. The pharmacological properties discussed include antiatherogenic, anti-inflammatory, antioxidant, antimicrobial, anti-spermatogenic, anti-ulcer, analgesic, hypoglycaemic, neuro-protective, and anti-carcinogenic activities. Even though Semecarpus anacardium has been the subject of several studies investigating its medicinal potential, it is important to promote the progression of studies to strengthen the current evidence with more studies, necessary to completely understand its mechanisms of action and determine its efficacious and safe ranges. Clarifying aspects related to bioaccessibility of bioactive compounds, interaction with gut microbiota, and also exploring technologies and strategies. Subsequently is vital to use cautious scientific research and regulatory control to ensure the efficacy, safety, and quality of SA products. This review serves to illustrate the potentials of the medicinal potential of Semecarpus anacardium.

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