Semecarpus anacardium Linn.: A review

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ABSTRACT

Semecarpus anacardium Linn. (*Family: Anacardiaceae*), commonly known 'Ballataka' or 'Bhilwa', has been used in various traditional system of medicines for various ailments since ancient times. Its nuts contain a variety of biologically active compounds such as biflavonoids, phenolic compounds, bhilawanols, minerals, vitamins and amino acids, which show various medicinal properties. The fruit and nut extract shows various activities like antiatherogenic, antiinflammatory, antioxidant, antimicrobial, anti-reproductive, CNS stimulant, hypoglycemic, anticarcinogenic and hair growth promoter. The article reviews the various activities of the plant.

Key words: Antiinflammatory, bhilawanols, hypoglycemic, nut extract, *Semecarpus anacardium*

INTRODUCTION

The Indian knowledge of herbal medicines is gaining widespread acceptance globally. In Ayurveda, almost all medicinal preparations are derived from plants, whether in the simple form of raw plant materials or in the refined form of crude extracts, mixtures and so on.[1] In other parts of the world, the term Complementary and Alternative Medicine (CAM) is used for various forms of traditional drugs. Complementary and Alternative Medicine (CAM) can be defined as any treatment used in conjugation (complementary) or in place of (alternative) standard medical treatment. In alternative medicine, medicinal plant preparations have found widespread use particularly in the case of diseases not amenable to treatment by modern method.[2]

Semecarpus anacardium Linn. (Family: *Anacardiaceae*) is distributed in sub-Himalayan region, tropical and central parts of India. The nut is commonly known as 'marking nut' and in the vernacular as 'Ballataka' or 'Bhilwa'. It has high priority and applicability in indigenous system of medicine.[3,4]

Semecarpus anacardium Linn. (Family: Anacardiaceae) is a plant well-known for its medicinal value in Ayurvedic and Siddha system of medicine. Chemical and phytochemical analyses of its nut reveal the presence of biflavonoids, phenolic compounds, bhilawanols, minerals, vitamins and amino acids. A variety of nut extract preparations from this source are effective against many diseases, viz., arthritis, tumors, infections and so on. However, the mechanism of the pharmacological action of its nut can be greatly aided by the isolation of its active principle and determination of structure–function relationship.

The aim of this review is to further highlight recently discovered effects and applications of *S. anacardium*.

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TAXONOMICAL CLASSIFICATION

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

BOTANICAL DESCRIPTION

It is a moderate-sized deciduous tree found in the outer Himalayas and hotter parts of India up to 3500 ft. height. The plant is found in abundance in Assam, Bihar, Bengal and Orissa, Chittagong, central India and western peninsula of East Archipelago, Northern Australia.[5]

It is a medium-to-large size tree, 15–25 m in height with grey bark exfoliating in small irregular flakes, leaves simple alternate, obviate – oblong, 30–60 cm long and 12–30 cm broad, rounded at

the apex coriaceous glabrous above and more or less pubescent, beneath. The flowers are greenish white, in panicles and appear with new leaves in May and June, easily recognized by large leaves and the red blaze exuding resin, which blackens on exposure. The nut is about 2.5 cm long, ovoid and smooth lustrous black [Figure 1]. It is frequently found in drier rather than damp localities. The fruit ripens from December to March and are 2–3 cm broad. No specific soil affinity. It is a moderate shade bearer, obliquely ovoid or oblong drupe, 2.5 to 3.8 cm long, compressed, shining black when ripe, seated on an orange-colored receptacle form of the disk, the base of the calyx and the extremity of the peduncle. The bark is grey in color and exudes an irritant secretion on incising.[6]

SYNONYMS

Common names in Sanskrit: Antahsattva, Arusharah, Aruskara (Arukara), Arzohita, Balla´ta (Bhallata, Ballata), Bhallataka (Bhalltaka), Bhallatakah, Viravrksa, Visasya; in English: Indian Marking Nut Tree, Marsh Nut, Oriental Cashew Nut; in Hindi: Bhela (Bhel), Bhelwa, Bhilawa (Bhilv), Bhilwa; in Tamil: Erimugi (Erimuki); in Telugu, Nallajeedi; in Gujarati: Bhilamu; in Russian: Semekarpus Anakardii.

PHYTOCHEMISTRY

The most significant components of the *S. anacardium* Linn. are bhilwanols, phenolic compounds,[7,8] biflavonoids,[9] sterols and glycosides.[8,10] Bhilwanol from fruits was shown to be a mixture of cis- and transisomers of ursuhenol; this compound consists mainly of 1,2,dihydroxy-3(pentadecadienyl 8',11')benzene and 1,2,hydroxy-3(pentadecadienyl 8')benzene.[11] Other components isolated are, anacardoside,[12] semecarpetin,[13] nallaflavanone,[14] jeediflavanone,[15,16] semecarpuflavanone,[17] galluflavanone,[18,19] anacarduflavone[20] mono-olefin I, diolefin II, bhilawanol-A, bhilawanol-B, amentoflavone tetrahydroamentoflavone semicarpol, anacardic acid, tetrahydrobustaflavone, O-trimethyl biflavanone A1(21), O-trimethyl biflavanone A2,[21] O-tetramethyl bifl avanone A1, O-hexamethyl bichalcone A, O-dimethyl biflavanone B, O-heptamethyl bichalcone B1, O-hexamethyl bichalcone B2, O-tetramethyl biflavanone C., phenolics.[21]

Figure 1: Plant of semecarpus anacardium showing the nuts

Figure 2 shows the chemical structures of various constituents of the plant. Besides this the proximate principles, minerals and vitamins contents in *S. anacardium* are given in Table 1.

PHARMACOLOGY

Antiatherogenic effect

The imbalance between the pro-oxidants and antioxidants is the main cause of development of atherosclerosis. To prevent such condition, antioxidant therapy is beneficial. *Semecarpus anacardium* (SA) shows such antioxidant property. It has capacity to scavenge the superoxide and hydroxyl radicals at low concentrations. The process of atherogenesis initiated by peroxidation of lipids in low-density lipoproteins was also found inhibited by SA.

Sharma *et al.* demonstrated the cardiac activity of SA, as it generally reduces the tissue and serum hyperlipidemia by the inhibition of intestinal cholesterol absorption coupled with peripheral disposal thus possessing anti-artherosclerotic activity.[22]

It is possible that the beneficial antiatherogenic effect may be related to its antioxidant, anticoagulant, hypolipidemic, platelet anti-aggregation and lipoprotein lipase releasing properties. The mechanism of hypotriglyceridemic effect has also been shown to be partly due to stimulation of lipoprotein lipase activity.

Antiinflammatory activity

Ramprasathet *et al.* investigated the antiinflammatory effects of SA nut extract on developing and developed adjuvant arthritis. *Semecarpus anacardium* significantly decreased the carrageenan-induced paw edema and cotton pellet granuloma. These results indicate the potent antiinflammatory effect and therapeutic efficacy of SA Linn. Nut extract against all phases of inflammation is comparable to that of indomethacin.[23]

Table 1: Proximate principles, minerals and vitamins contents in *S. anacardium* nuts

Nutrient	Nutrient composition (in 100 g²) (edible portion)
Moisture, g	3.8
Energy, Kcal	587
Protein, g	26.4
Fat, g	36.4
Carbohydrate, g	28.4
Fiber, g	1.4
Ash, g	3.6
Calcium, mg	295
Iron, mg	6.1
Phosphorus, mg	836
Zinc, mg	-

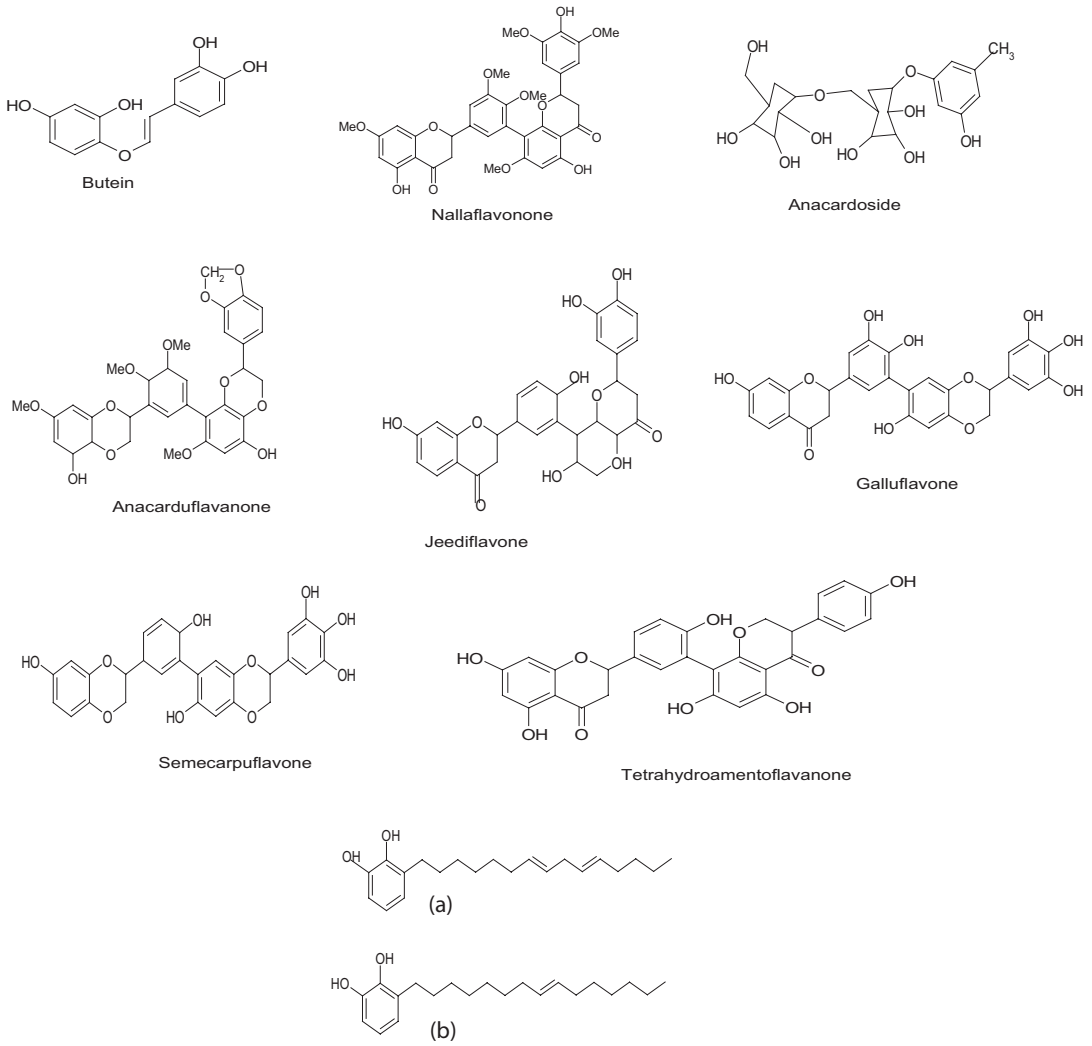

Figure 2: Biochemical constituents of *S. anacardium*. (a) and (b)) are cytotoxic compounds

Salvem *et al.* investigated that ethyl acetate extract of SA led to the isolation of major active principle, tetrahydroamentoflavone (THA), a biflavonoid. The *in vitro* cyclooxygenase (COX-1)-catalyzed prostaglandin biosynthesis assay of THA gave an IC50 value of 29.5 μM (COX-1) and 40.5% inhibition at 100 g/mL (COX-2). The *in vivo* carrageenan-induced paw edema assay resulted in dose-dependent antiinflammatory effect of THA and the activity was comparable to that of ibuprofen.[24]

Bhitre *et al.* prepared the methanolic, ethanolic, chloroform, ethyl acetate and petroleum ether extracts of fruits of SA and tested to study the antiinflammatory activity using the technique of carrageenan-induced paw edema in albino rats. The extract showed significant antiinflammatory activity comparable to the reference standard aspirin.[25]

Satayavati *et al.* and Bajpai *et al*, reported the antiinflammatory activity of SA for both immunological and non-immunological origin.[26]

Singh *et al.* evaluated that SA extract can inhibit proinflammatory cytokine production. Crude ethanolic extract of SA nuts was studied for its antiinflammatory activities *in vitro* using peripheral blood and synovial fluid mononuclear cells of healthy individuals and rheumatoid arthritis (RA) patients. *Semecarpus anacardium* extract inhibited the spontaneous and LPS-induced production of proinflammatory cytokines IL-1beta and IL-12p40 but had no effect on TNF-alpha and IL-6 production, both at protein and mRNA level. The crude extract also suppressed LPS-induced nuclear translocation of transcription factors, NF-kappaB and AP-1; the inhibition of NF-kappa B was through the inhibition of I kappa Bα phosphorylation. The extract also suppressed LPS-activated nitric oxide production in mouse macrophage cell line, RAW 264.7.[27]

Premlatha *et al.* have been reported for immunomodulatory potency, antioxidative, membrane stabilizing, tumors marker regulative, glucose level restoring and mineral regulation properties of nut extract in hepatocellular carcinoma and found

to detoxify a potent hepatocarcinogen aflatoxin B_1 and causes its metabolites to excreted in urine.[28]

In other case they explained the therapeutic effects of extract on the changes associated with collagen and glycosaminoglycan metabolism in adjuvant arthritic Wistar rats. Decreased levels of collagen and glycosaminoglycans (GAGS) components (chondroitin sulfate, heparan sulfate, hyaluronic acid) and increase in the levels of connective tissue degrading lysosomal glycohydrolases such as acid phosphatase, beta-glucuronidase, beta-*N*-acetyl glucosaminidase and cathepsin-D observed in arthritic animals were reverted back to near normal levels upon treatment with SA.

Ramprasath *et al.* found that nut milk extract modulates reactive oxygen/nitrogen species levels and antioxidative system in adjuvant arthritic rats. A significant increase in the levels of lipid peroxides (LPOs), ROS (superoxide radical, hydroxyl radical, H_2O_2 and myeloperoxidase) and RNS (nitrate + nitrite) observed in adjuvant arthritic animals were found to be significantly decreased on administration of the drug at 150 mg/kg body weight/day. Treatment with SA recouped the altered antioxidant defense components to near normal levels. These evidences suggest that the SA preparations are mainly used for irregularities caused during arthritis and to cure arthritis.[29]

Kalpaamruthaa (KA), an indigenous-modified Siddha formulation, consists of SA nut milk extract and fresh dried powder of *Emblica officinalis* (EO) fruit along with honey. Kalpaamrutha was found to be nontoxic up to the dose level of 2000 mg/kg. Further, KA has been reported for its potent antioxidant analgesic, antipyretic and non-ulcerogenic properties. Mythilypriya *et al.* studied the antiinflammatory activity of SA in adjuvant-induced arthritic rat (AIA) model with reference to mediators of inflammation (lysosomal enzymes) and its effect on proteoglycans. The activities of various enzymes and levels of plasma protein bound carbohydrate components of glycoproteins were determined and were found to be elevated in arthritic rats when compared to control animals.[30]

Antioxidant activity

Semecarpus anacardium has been reported in various studies to possess potent antioxidant activity. Verma *et al.* investigated antioxidant activity of the aqueous extract of nuts of medicinal plant SA in AKR mouse liver during development of lymphoma. Administration of the aqueous extract of SA to lymphoma-transplanted mouse leads to increase in the activities of antioxidant enzymes, whereas LDH activity is brought down significantly indicating a decrease in carcinogenesis.[31]

Sahoo *et al.* investigated the antioxidant activity of ethyl acetate extract of stem bark of SA. Ethyl acetate extract showed the stronger antioxidant activity (due to presence of highest total phenolic content of 68.67% measured as pyrocatechol equivalent) compared to the other (hexane, chloroform and methanol) extracts. The isolation of the ethyl acetate extract of SA stem bark yielded a bright-yellow solid crystal, which was identified as butein. This compound exhibited antioxidant activity (IC50 values of 43.28 ± 4.34 μg/ml), which was comparable to rutin, taken as a standard.[32]

CNS activity

Farooq *et al.* evaluated the beneficial effect of nuts of SA, extracted with milk, on CNS, mainly for its locomotor and nootropic activities in different experimental animal models. The extract tested but a slight CNS depressant effect was noted with only 150 mg/kg of the extract and it was found to possess nootropic activity.[33]

Antimicrobial activity

Mohanta *et al.* prepared the aqueous and organic solvent extracts of the plant and screened for antimicrobial (disc diffusion method) and phytochemical properties. The petroleum ether (PEE) and aqueous extract fractions (AQE) showed inhibitory activity against *Staphylococcus aureus* (10 mm) and *Shigella flexneri* (16 mm) at 100 mg/ml, respectively. While chloroform extract showed inhibition against *Bacillus licheniformis*, *Vibrio cholerae* and *Pseudomonas aeruginosa*, the ethanol extract showed inhibition to *Pseudomonas aeruginosa* and *S. aureus*.[34]

Nair *et al.* found that the alcoholic extract of dry nuts of SA (Bhallatak) showed bactericidal activity *in vitro* against three gram negative strains (*Escherichia coli, Salmonella typhi* and *Proteus vulgaris*) and two gram positive strains (*Staphylococcus aureus* and *Corynebacterium diphtheriae*). Subsequent studies have shown that the alcoholic extracts of different parts of the plant (leaves, twigs and green fruit) also possess anti-bacterial properties, especially the leaf extract. No dermatoxic effect (irritant property) was observed in the mouse skin irritant assay.[35]

Hypoglycemic effect

Arul *et al.* studied the effect of ethanolic extract of dried nuts of SA on blood glucose and investigated in both normal (hypoglycemic) and streptozotocin-induced diabetic (antihyperglycemic) rats. The ethanolic extract of SA (100 mg/kg) reduced the blond glucose of normal rats The blood glucose levels were measured at 0, 1, 2 and 3 h after the treatment and antihyperglycemic activity of SA was compared with tolbutamide, a sulfonyl urea derivative used in diabetes mellitus.[36]

Krishnamurthy *et al.* developed Kalpaamruthaa (KA), a modified Siddha preparation, which contains SA Linn., EO and honey, and studied for the variations in lipids, lipid-metabolizing enzymes and lipoproteins in cancerous animals and the effect of KA on the lipid metabolism. The increased levels of total cholesterol, free cholesterol, phospholipids, triglycerides and free fatty acids and decreased levels of ester cholesterol in plasma, liver and kidney found in cancer-suffering animals were reverted back to near normal levels on treatment with KA and SA. The effects of KA were found to be more effective than SA.[37]

Anti-carcinogenic activity

Mathivadhani *et al.* studied SA nut extract for inhibitory effect on human breast cancer cells (T47D). Cytotoxicity analyses suggested that these cells had become apoptotic. *Semecarpus anacardium* was discovered to induce rapid Ca(2+) mobilization from intracellular stores of T47D cell line, and its cytotoxicity against T47D was well correlated with altered mitochondrial transmembrane potential. At the molecular level, these changes are accompanied by decrease in Bcl(2) and increase in Bax, cytochrome c, caspases and PARP cleavage, and ultimately by internucleosomal DNA fragmentation. Taken together, our results provide unprecedented evidence that SA triggers apoptotic signals in T47D cells.[38]

Arulkumaran *et al.* investigated the protective efficacy of preparation named as Kalpaamruthaa (KA) (includes SA nut milk extract, dried powder of Phyllanthus emblica fruit and honey) on the peroxidative damage and abnormal antioxidant levels in the hepatic mitochondrial fraction of 7,12-dimethylbenz(a) anthracene (DMBA)-induced mammary carcinoma rats. DMBA-treated rats also showed decline in the activities of mitochondrial enzymes. In contrast, rats treated with SA and KA showed normal lipid peroxidation antioxidant defenses in mitochondrial enzymes, and indicate the anticarcinogenic activity of KA during DMBA-initiated mammary carcinogenesis. On the basis of the observed results, KA can be considered as a readily accessible, promising and novel cancer chemopreventive agent.[39]

Sugapriya *et al.* showed restoration of energy metabolism in leukemic mice treated by SA nut milk extract. Leukemia-bearing mice showed a significant increase in LPOs, glycolytic enzymes, a decrease in gluconeogenic enzymes and significant decrease in the activities of TCA cycle and respiratory chain enzymes as compared to control animals. *Semecarpus anacardium* treatment was compared with standard drug imatinib mesylate. *Semecarpus anacardium* administration to leukemic animals resulted in clearance of the leukemic cells from the bone marrow and internal organs.[40]

REPRODUCTIVE FUNCTION (ANTISPERMATOGENIC EFFECT)

Semecarpus anacardium extract feeding caused antispermatogenic effect evidenced by reduction in numbers of spermatogenic cells and spermatozoa in male albino rats.[41]

Vinutha *et al.* investigated for SA (stem bark), extracts including methanolic and successive water extracts for acetylcholinesterase (AChE) inhibitory activity (*in vitro*). Results indicated that methanolic extracts to be more active than water extracts. The potent AChE-inhibiting methanolic plant extracts of SA (stem bark) comes to be 38 g/ml.[42]

NEPHROTOXICITY

Choudhari *et al.* studied the toxicity study on a few blood parameters in male albino rats at acute and sub-chronic levels with SA nut oil extract (50% w/v) in ground nut oil. Albino rats (Wistar strain) were treated orally with three sub-lethal doses. There was a significant decrease in hemoglobin percent and lowering of erythrocytes, indicating 'anemia' during toxicity study. He also evaluated the acute and sub-chronic effect of crude extract on activity of some kidney enzymes GOT, GPT, SDH, LDH and histology of kidney of albino rat (Wistar strain) in either sex. Significant alteration in activity levels of marker enzymes of kidney as well as histological structure leading to nephritis were observed, indicating renal dysfunctioning in albino rat. Results exhibited nephrotoxicity inducing potential of SA nut oil extract.[43,44]

Prabhu *et al.* studied the antimutagenic effect of SA under *in vivo* condition. Mice were intraperitoneally treated with 500 and 250 mg/kg of SA, which. showed a significant inhibition of induced aberrations at the 12 h pretreatment period. The results on the reduction of induced chromosome aberrations clearly show that SA serves as an antioxidant because of the presence of flavonoids which scavenge free radicals. The action of SA oil extract has definite beneficial role against mitomycin-C induced mutagenicity and its administration may be protective and therapeutic.[45]

In this study, Krishnarajua *et al.* found that aqueous extracts of medicinal plants were screened for their cytotoxicity using brine shrimp lethality test. Out of the 120 plants tested, SA (Anacardiaceae) showed significant cytotoxicity with LC50 29.5 µg, respectively.[46]

TOXICITY

Since Bhallataka is extremely hot and sharp in its attributes, it should be used with caution. Individuals showing allergic reactions to it should stop and avoid the usage of Bhallataka. It should not be used in small children, very old persons, pregnant women and individuals of predominant pitta constitution. The use of the same should be restricted in summer season. For its allergic reactions like rash, itching and swelling, the antidotes used externally are coconut oil, rala ointment, ghee, coriander leaves pulp or butter mixed with musta (Cyperus rotundus). The salt and spices should be strictly restricted and during Bhallataka treatment, it is recommended to avoid exposure to sun, heat and excessive sex. The oily part of the nut is toxic and its degree of removal is proportional to its safety margin.

Nephropathy is associated with exposure to toxins of plant origin. It was noted that with the exception of Djenkol bean nephrotoxicity, SA toxins lead to acute renal failure due to hemodynamic effects.[47]

TRADITIONAL USES

Bhallataka is used for hair care in traditional system of medicines.

It is used for dyeing, and promoting hair growth in folk medicine.[48,49]

CONCLUSION

Semecarpus anacardium is used for various medicinal properties. The fruit and nut extract shows various activities like antiatherogenic, antiinflammatory, antioxidant, antimicrobial, anti-reproductive, CNS stimulant, hypoglycemic, anticarcinogenic and hair growth promoter. More efforts are needed to study the traditional uses of the plant and the subsequent validation of activity and the mechanism of action.[1]

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