https://doi.org/10.47552/ijam.v16i1.5404 ISSN No: 0976-5921

International Journal of Ayurvedic Medicine, Vol 16 (1), 2025; 11-22

Scientific Basis for the Therapeutic Uses of *Semecarpus anacardium* Linn. (*Bhallataka*): A Systematic Review

Review Article

Abhijeet Sarjerao Shirkande[1,3], Soumya Basu[2], Ankita Abhijeet Shirkande[1,3], Hazel Samuel[2], Sangeeta Ballav[2], Jayashree V Changade[1*]

1. Dr. D. Y. Patil College of Ayurved and Research Center, Pimpri. Pune.
2. Cancer and Translational Research Center, Dr. D. Y. Patil Biotechnology and Bioinformatics Institute, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
3. Shree VishwAngad Ayurved, Panchakarma & Yoga Clinic, Pune, India.

Abstract

The present review highlights the chemical qualities, therapeutic benefits, toxicity profile of *Semecarpus anacardium Linn.* (*Bhallataka*) which is a commonly used plant in Ayurvedic medicine. While there has been some scientific research conducted on the potential therapeutic effects of the plant, more studies are needed to confirm its effectiveness and safety. Due to the generally different approaches taken by each examination, no factual pooling of results or assessment of the nature of the investigations was carried out. Some studies have found that compounds found in *Semecarpus anacardium Linn.*, such as anacardic acid, have anti-inflammatory, antioxidant and anticancer properties. However, further research is needed to understand the full range of therapeutic uses and potential side effects of the plant. *Semecarpus anacardium Linn.* (*Bhallataka*) is widely used plant in Ayurvedic medicine, with numerous reported therapeutic benefits. This review provides an overview of the plant's chemical composition, therapeutic effects, and toxicity profile. While some scientific studies have investigated its potential therapeutic effects, further research is necessary to validate its efficacy and safety. Due to the heterogeneity of the studies reviewed, no meta-analysis was conducted. However, several studies have reported that *Semecarpus anacardium Linn.* contains compounds, such as anacardic acid, with anti-inflammatory, antioxidant, and anticancer properties. Further research is required to fully elucidate its therapeutic uses and potential side effects. Preliminary research suggests that *Bhallataka* may have beneficial effects on the cardiovascular system, glucose metabolism, circulatory system, and digestive system, with low toxicity. These findings are promising and support the potential use of *Bhallataka* as a therapeutic agent.

Keywords: *Bhallataka, Semecarpus anacardium Linn., Bhilava, Bibba*, Semecarpin, Marking nut.

Introduction

Semecarpus anacardium Linn. (*Bhallataka*), a common plant in Ayurvedic medicine, can be found in central and sub-Himalayan India. It is a genus of roughly 60 species that Carl Linnaeus the Younger introduced in Supplementum Plantarum in 1782 (1). *Semecarpus anacardium Linn.* (*Bhallataka*, SA) is broadly utilized in Ayurvedic traditional medicine. It's content of many formulations & recommended for musculoskeletal conditions, neuromuscular problems, Respiratory issues, Hepatic issues, diabetes, Metabolic issues, Aphrodisiac and as an overall tonic to expand energy, work on general wellbeing and longevity.

By addressing chemical characteristics, restorative benefits, and toxicity, it seeks to serve the purpose. *Bhallataka* has been shown in studies to have anti-inflammatory, analgesic, anti-diabetic, anti-tumour, anti-biofilm, anti-bacterial, anti-oxidant, anti-hyperlipidemic, cytoprotective, acaricidal, cardioprotective, anti-arthritis, and wound healing activities. The cardiac activity, glucose metabolism, and circulatory and digestive systems, all exhibit a favourable effect. Toxicological studies also demonstrate that *Bhallataka* appears to be a harmless product of nature. This systematic review chronicles current understanding of clinically significant investigations while attempting to develop a rationale for the beneficial application of *Semecarpus* species. Our goal in writing this review is to give a thorough overview of the medicinal applications of *Semecarpus* genus with a special emphasis on the *anacardium* species to assist in identifying potential areas for further research.

*** Corresponding Author:**

Jayashree V Changade

Professor, Dr. D. Y. Patil college of Ayurved and Research centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India – 411018.

Email Id: jayshreeulemale28@gmail.com

Materials and Methods

The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement was used to design the protocol for conducting this

investigation. Two independent reviewers conducted all the steps and a third reviewer helped to settle disagreements.

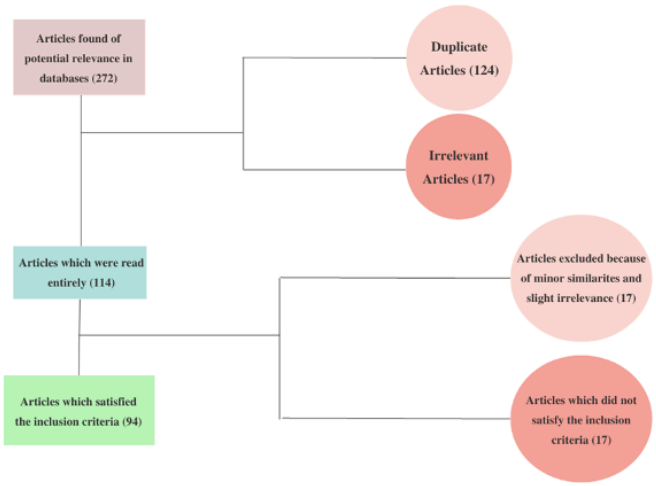
Data Sources

The literature search was carried out using MEDLINE (via PubMed), Cochrane, and PubChem databases from Jan 2010 to July 2022. The descriptors used in the search bar were *"Bhallataka", "Semecarpus anacardium", "Bhilava", "Bibba", "Semecarpus",* "semecarpin", and "marking nut". Additionally, we included literatures through our manual search of the reference lists of the studies that were included as a second search method. Unpublished data and conference proceedings were also incorporated into this study.

Study Selection

Biological processes, conventional applications, and, isolation and identification of chemical constituents were all covered in articles on *Semecarpus* species. The following articles were excluded from consideration: (1) titles and abstracts lacking the search terms; (2) reviews or systematic reviews; and (3) extraction of biologically active chemical components were not performed during the investigation but rather bought commercially. In addition, contradictory articles were eliminated.

Figure 1: Flowchart of the articles satisfying inclusion/exclusion criteria



Two impartial reviewers (Soumya Basu (SB) and Sangeeta Ballav (SB)) completed all phases of the procedure after getting the articles, and any disagreements were settled by consensus. Without a consensus, the help of a third reviewer (JVC) was solicited. The PRISMA Model was used to help choose studies: (a) all articles were acquired and screened based on titles and abstracts; (b) the articles deemed relevant were examined in-depth by the two reviewers while adhering to the eligibility criteria; and (c) articles that satisfied all the criteria were included for data collection (inclusion). The articles that raised questions during the screening stage were included and proceeded on to the eligibility stage for in-depth analysis. The whole text of each selected article was read. Data on biological activities, methods of extraction, isolation, and identification of chemical constituents, as well as measures of the primary outcome, were extracted by the first author, and validated by the second.

Data Extraction

Periodical, plant collecting site, traditional *Semecarpus* usage, separated chemicals, and biological activity were the variables of interest in each study. Discussion among the reviewers was used to settle disagreements.

Results

Figure 1: displays Schematic design of the workflow. After examining the databases we discovered 272 articles that might be relevant; however, 124 of them were duplicates, and 17 articles contained irrelevant titles or abstracts which were hence removed. The remaining 131 items were moved on to the following round, of which 114 articles were fully read since the remaining 17 again had minor similarities or were slightly irrelevant. There were 20 articles not fitting the inclusion requirements, therefore, only 94 were included. The manual searching turned up no additional articles.

Traditional Uses

Semecarpus anacardium Linn., commonly known as "marking nut" and locally referred to as "*Bhallataka*" or "*Bhilwa*," holds significant value in traditional medicine. Its fruit and nut extracts exhibit multiple pharmacological properties, including anti-atherogenic, anti-inflammatory, antioxidant, antibacterial, anti-reproductive, anticancer, CNS stimulant, hypoglycemic, and hair growth-promoting effects. In Ayurveda, the mature fruit is widely used for treating various ailments, including cancers. The reported anticancer activity is attributed to its potent antioxidant properties and its ability to enhance the in vivo antioxidant defense system.(10). The fruits of *Semecarpus anacardium Linn.* contain 28–36% oil and possess therapeutic properties, including aphrodisiac, rubefacient, anti-irritant, and astringent effects. Traditionally, the fruit's pericarp juice was used to mark cotton fabrics. It has shown notable effects against coronary heart disease, various cancers, and other ailments. Studies using *Bhallataka* milk extract in adjuvant-induced rheumatoid arthritis in rats revealed the presence of flavonoids, phenols, and carbohydrates, demonstrating protective effects against lead acetate-induced toxicity. An antibacterial compound isolated from the seeds supports its use in treating infections and holds potential for development in novel antibacterial drug research.

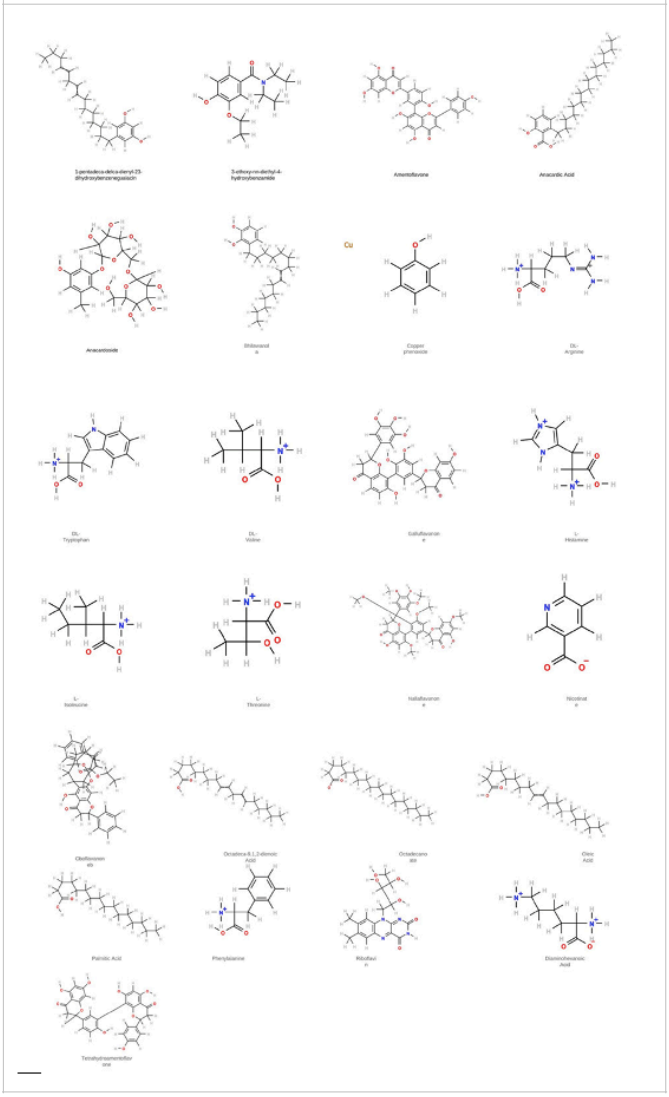
Phytochemical Investigation

The therapeutic application of *Bhallataka* has yet to receive formal scientific validation, leading to skepticism regarding its efficacy in various diseases. In Ayurveda, *Bhallataka* is classified among rejuvenative and aphrodisiac herbs. The phytochemistry of *Semecarpus anacardium Linn.* has been extensively

https://doi.org/10.47552/ijam.v16i1.5404 ISSN No: 0976-5921

International Journal of Ayurvedic Medicine, Vol 16 (1), 2025; 11-22

Figure 2: Chemical Constituents of *Semecarpus anacardium Linn.*



studied, with over thirty bioactive compounds identified, isolated, and characterised. Key constituents include 3-ethoxy-N,N-diethyl-4-hydroxybenzamide, amentoflavone, anacardic acid, anacardoside, bhilawanol A, cardol, guaiacin, copper(I) phenoxide, various amino acids (e.g., DL-arginine, L-leucine, L-methionine), flavanones (e.g., galluflavanone, jeediflavanone, nallaflavanone), fatty acids (e.g., oleic, palmitic, tetradecanoic acids), and other compounds such as riboflavin, pyrocatechol, and tetrahydroamentoflavone.(55).

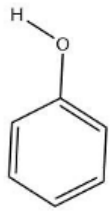
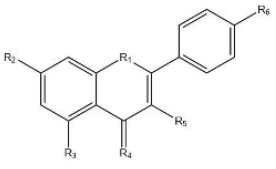
Shodhana Process (Ayurvedic purification/ processing technique)

Shodhana, the Ayurvedic detoxification or purification process, involves transforming toxic substances into safe and therapeutically beneficial forms. *Bhallataka* is a notable example of a toxic plant still used in traditional Indian medicine following this process. Shodhana reduces toxic constituents, often enhancing therapeutic efficacy. During this process, polar components are diminished, while total flavonoid and carbohydrate levels remain largely unaffected. However, a significant reduction in total phenolic content has been observed post-purification. Shodhana improves the safety profile of *Bhallataka* by eliminating toxic phenolic oils, though it may reduce antioxidant activity. Despite this, the plant retains its anti-arthritic efficacy after purification(51).

Phenolic and Flavonoid Compounds

Phenolic compounds, synthesised via the phenylpropanoid pathway derived from the pentose phosphate and shikimic acid pathways, are characterised by hydroxylated aromatic rings. Glucose metabolism through the PPP yields NADPH, erythrose-4-phosphate, and phosphoenolpyruvate, which serve as precursors for phenylalanine synthesis via the shikimate pathway, leading to phenolic biosynthesis (9). These secondary metabolites, including phenolic acids, flavonoids, and anthocyanins, play vital roles in plant defence, stress adaptation, pigmentation, and antimicrobial activity (10). Their bioactivity is attributed to antioxidant, anti-inflammatory, anti-mutagenic, and anti-carcinogenic properties (1).

Flavonoids, a major class of polyphenolic compounds, have garnered interest due to their cardioprotective potential and preventive effects against chronic diseases. Despite unclear mechanisms, they exhibit diverse biological activities. Current research emphasises their isolation, functional roles, and therapeutic applications, supported by molecular docking and bioinformatics approaches (9). Found in fruits, vegetables, grains, tea, and wine, flavonoids contribute to disease prevention, including cancer, Alzheimer's, and atherosclerosis (3). Due to their broad pharmacological potential, flavonoids are increasingly explored in nutraceutical, therapeutic, and cosmetic applications (2).

Figure 3: Phenol	**Figure 4: A base structure for a flavonoid**
	

Pharmacological effects of *Semecarpus anacardium* extracts and isolated compounds.

Table 1 summarises the pharmacological actions of different parts of *Bhallataka* plant studied in various researches.

Anti-diabetic activity

Diabetes mellitus is a metabolic disorder marked by hyperglycemia due to impaired insulin secretion or action. The liver regulates glucose homeostasis via glycolysis, gluconeogenesis, and glycogenesis, with decreased glucokinase and increased glucose-6-phosphatase activity observed in diabetic states. *Semecarpus anacardium Linn.* (SA), an Ayurvedic

Table 1: Pharmacological actions of different parts of *Bhallataka* plant

Plant Parts	Pharmacological actions	Reference(s)
Fruit (resin)	Anti-cancer, anti-tick and anti-inflammatory	(3-7)
Nut Extract (milk, oil, shell)	Anti-cancer, anti-cholestrolemic, anti-inflammatory, anti-oxidant, anti-diabetic, anti-fungal, anti-arthritic, anthelmintic activities and protein inhibition	(8), (9-10)
Seeds	Anti-bacterial, anti-microbial, anti-oxidant, anti-inflammatory	(11-14)
Stem Bark Extract	Anti-diabetic, anti-oxidant, anti-inflammatory, wound healing and toxicity studies	(15-18)
Sap	Toxicity studies	(19)
Pericarp Juice	Toxicity studies	(20)

plant, exhibits antidiabetic activity, especially in streptozotocin (STZ)-induced diabetic models (21). SA treatment improves plasma insulin, reduces HbA1c, enhances glucose tolerance, and increases HOMA-β while lowering HOMA-IR (9). It elevates glucose-6-phosphate dehydrogenase activity, promoting NADPH production and reducing oxidative stress (9). SA modulates glycolytic and gluconeogenic enzymes, increases hepatic glycogen, and regulates GSK-3 expression (9, 23). Bioflavonoids in SA mimic insulin by enhancing key glycolytic enzymes like phosphofructokinase and hexokinase, reducing hyperglycemia in high-fat diet/STZ-induced models (24). SA normalizes plasma glucose, insulin, HbA1c, and body weight, showing efficacy comparable to metformin and atorvastatin (24). It also inhibits gluconeogenesis and improves mitochondrial function (25). SA upregulates PI3K/AKT expression in skeletal muscle, enhancing glucose uptake (22, 25). It improves lipid profiles by increasing HDL and reducing LDL, VLDL, TG, cholesterol, phospholipids, and FFAs (25). SA-treated rats also show increased pancreatic islet numbers (22, 25). SA provides cardioprotective effects by restoring altered enzyme levels, improving renal markers (urea, creatinine, uric acid), and reducing oxidative stress (26). Hematological parameters and cardiac histopathology improve with treatment (27). SA enhances energy metabolism by stimulating TCA cycle enzymes, reducing gluconeogenesis, and boosting mitochondrial activity (28). SA bark extracts reduce blood glucose, TC, TG, LDL, and elevate hepatic glycogen in alloxan-induced diabetic rats (21, 26). Polyphenols in SA lower LDH, suppress ROS, and increase electron transport chain activity, indicating strong antioxidant and cardioprotective effects in diabetic CVD models (20, 30).

Anti-Rheumatic clinical activity

The Indian traditional medicine system recommends several herbal and mineral-based formulations for treating inflammatory and arthritic conditions, though only a few have been scientifically evaluated for anti-arthritic activity (31). *Semecarpus anacardium Linn.* (SA), known as Sanjivani or *Bhallatak*, has been traditionally used for rheumatic disorders and gout. While its efficacy in managing rheumatoid arthritis (RA) has been documented, the underlying mechanisms remain partially elucidated (31). Crude ethanolic extracts of SA seeds exhibit immunomodulatory activity by reducing inflammatory cytokine production. In adjuvant-induced arthritis models, SA extract significantly reduced paw edema in both early and established disease stages (32). SA also demonstrated dose-dependent inhibition of carrageenan-induced acute paw oedema, indicating anti-inflammatory potential via immunosuppressive modulation (31). A randomised, investigator-blind, three-arm multicenter clinical trial compared standardised Ayurvedic formulations, including SA as a key ingredient, with hydroxychloroquine sulfate (HCQS). Results revealed superior efficacy of the Ayurvedic regimen in controlling active RA symptoms (33). Mechanistically, SA extract suppresses IL-1 and IL-12p40 expression, both spontaneously and LPS-induced, without affecting TNF-α and IL-6 levels. It also inhibits NF-κB and AP-1 nuclear translocation and LPS-induced IκB phosphorylation—key pathways in RA pathogenesis (32). These transcription factors regulate genes such as MMPs, iNOS, and COX-2, contributing to inflammation and tissue damage in RA. The downregulation of these mediators by SA suggests its role in modulating MAPK pathway activation and suppressing inflammatory gene expression. The extract also demonstrated suppression of regulatory suppressor cells, potentiation of delayed-type hypersensitivity (DTH) response, and reduction of secondary inflammation in adjuvant arthritis models, further confirming its immunosuppressive potential (31). Overall, these findings support the therapeutic promise of *S. anacardium* in RA through modulation of key proinflammatory pathways.

Anti-inflammatory activity

Inflammation is a vital defence mechanism; however, chronic inflammatory responses often result in unintended tissue damage (34). In rheumatoid arthritis (RA), key pathological processes—intracellular signalling, cell proliferation, adhesion, matrix degradation, and angiogenesis—perpetuate joint destruction (35). Herbal medicines, including *Semecarpus anacardium Linn.* (SA), are widely used in Ayurveda and Siddha systems for arthritis management. Studies show SA's anti-inflammatory potential is comparable or superior to indomethacin in acute and chronic inflammation models such as carrageenan-induced paw oedema, cotton pellet granuloma, xylene-induced ear oedema, and formalin tests (36). SA significantly reduced edema and granuloma formation across all phases of inflammation and demonstrated both central and peripheral analgesic effects in hot plate and acetic acid-induced writhing models (34). Tetrahydroamentoflavone (THA), a flavonoid from SA, is a potent xanthine oxidase inhibitor, supporting its

traditional use in treating gout and inflammation. THA exhibited IC_{50} and K_i values (92 nM and 0.982 μM, respectively), comparable to allopurinol (37). SA treatment also showed immunomodulatory effects by significantly reducing antibody titres, plaque-forming cells, and immunoglobulin levels in arthritic animals (38). It normalised inflammatory cytokines, including TNF-α, and decreased ROS/RNS markers such as H_2O_2, superoxide, hydroxyl radicals, and MPO activity (14, 38). SA reduced lysosomal enzyme levels in neutrophils and lowered neutrophil infiltration at inflammation sites (14). SA's efficacy in attenuating chronic inflammation and modulating immune responses highlights its potential as a pharmacological anti-inflammatory and anti-arthritic agent (34, 36).

Anti-hypercholesterolemic

A study evaluated the effects of acyclic isoprenoid on high-fat diet-induced hyperlipidemic rats. Oral administration of acyclic isoprenoid at doses of 20, 40, and 80 mg/kg body weight for 30 days significantly reduced elevated cardiac and inflammatory markers in hypercholesterolemic rats. Treatment also increased lecithin cholesterol acyltransferase (LCAT) activity and decreased 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase activity, suggesting its potential antihypercholesterolemic and anti-inflammatory effects (40).

Wound healing

The wound healing potential of *S. anacardium* stem bark methanolic extract was evaluated using excision, incision, and dead space wound models in Wistar albino rats. Although less effective than standard treatment, the extract demonstrated significant wound healing activity, supporting its traditional ethnomedicinal use (15).

Hypolipidemic activity

The hypolipidemic effect of SA was demonstrated in STZ-induced diabetic rats, showing a significant reduction in LDL, cholesterol, VLDL, TG, phospholipids, and free fatty acids, along with increased HDL levels and improved lipid-metabolizing enzyme activity in the liver and kidney (25). Additionally, in high cholesterol-fed hypercholesterolemic rats, SA exhibited potent hypolipidemic activity, likely attributed to its intrinsic antioxidant properties (41).

Anti- Cancer Activity

In India, the mature fruits and seeds of *Semecarpus anacardium Linn.* (SA) are traditionally used in Ayurvedic and Siddha medicine to treat various diseases, including cancer (42). LC-MS analysis of raw and purified *Bhallataka* samples revealed enhanced anticancer activity in purified forms. Using the Ehrlich Ascites Carcinoma (EAC) mouse model and 5-fluorouracil as a standard, SA-II and SA-III significantly reduced tumour volume and weight, improved survival, and showed higher efficacy at 200 mg/kg p.o., whereas raw SA (SA-I) showed minimal activity (44). The improved activity of purified SA was attributed to chemical alterations enhancing the potency and reducing toxicity of active constituents. Anacardic acid and cardanol derivatives, known anticancer agents, demonstrated efficacy against prostate and liver carcinomas. Further studies indicated that SA-3C, isolated from the kernel, exhibits strong anticancer potential through inhibition of angiogenic and hypoxia markers such as HIF-1α, VEGF, and iNOS (42). Additionally, SA nut oil exhibited cytotoxicity selectively against leukemic cell lines (K-562, HL-60), but not in epithelial-derived cancers (HeLa, MCF-7, CEC), supporting its selective anticancer action (44).

Hepatocarcinoma

Hepatocellular carcinoma (HCC), responsible for 15% of global cancer mortality, is a highly aggressive tumour with an annual incidence ranging from 250,000 to 1,000,000 cases worldwide (45). Aflatoxin B1 (AFB1), a potent hepatotoxic and carcinogenic mycotoxin produced by *Aspergillus flavus*, is a key etiological factor in HCC, particularly in regions with high dietary aflatoxin exposure (46). AFB1-induced hepatocarcinogenesis in rats is a well-established model for evaluating anticancer therapies. *Semecarpus anacardium Linn.* (SA) nut extracts have demonstrated significant anticancer potential against AFB1-induced HCC. Chloroform and milk extracts of SA exhibited tumour-suppressive effects by enhancing antioxidant defence mechanisms, modulating tumour marker enzymes, reducing lipid peroxidation, and reversing cancer-induced hypoglycemia (45, 46). SA treatment normalized levels of cytochrome P450 and b5, stimulated phase I and II detoxification enzymes (e.g., glutathione-S-transferase, UDP-glucuronyl transferase), and stabilised lysosomal enzymes, preventing rapid enzyme leakage in cancer conditions (46). The extract's bifunctional induction of detoxification pathways may prevent DNA, RNA, and protein adduct formation by AFB1, thus inhibiting tumour progression. Moreover, SA significantly restored altered liver enzyme levels (ALP, γ-GT, LDH, AST, ALT) to near-normal values in treated groups (45). Enhanced GST activity in SA-treated groups correlated with reduced AFB1-DNA binding and improved antioxidant levels (GSH, TSH, NPSH, vitamins C & E) (47). Silver nanoparticles synthesized using SA nut and *Andrographis paniculata* extracts (SaAgNPs and ApAgNPs) also exhibited hepatoprotective and anticancer activity in diethylnitrosamine (DEN)-induced liver cancer models. SaAgNPs significantly reduced serum ALT, AST, SGPT, and SGOT levels while increasing glutathione-S-transferase activity, suggesting their potential as nanodrugs against HCC (45, 48). Furthermore, SA nut extract enhanced the efficacy of doxorubicin, indicating possible synergistic effects when used alongside chemotherapy (45). Additional studies also revealed cytotoxic effects of SA-derived silver nanoparticles against liver (HepG2) and prostate (PC3) cancer cell lines (48).

Mammary Carcinoma

Breast cancer, accounting for 20% of all female cancers worldwide, remains the most prevalent malignancy among women and the second leading cause of cancer-related mortality globally, following lung cancer (49). Despite advances in modern treatments, plant-based traditional medicine continues to play a vital role, with approximately 80% of the global population relying on such practices (50). In a mammary carcinoma model, SA nut milk extract showed promising anticancer effects. Treatment for 14 days resulted in a significant increase in glucose-6-phosphatase and fructose-1,6-diphosphatase activities, alongside a notable decrease in glycolytic enzymes such as hexokinase, aldolase, and phosphoglucoisomerase ($P < 0.05$), indicating an inhibitory effect on tumor glycolysis (51). These effects may be attributed to the flavonoid content in SA, which disrupts tumour energy metabolism by inhibiting glycolysis and enhancing oxidative phosphorylation and the TCA cycle (52, 53). SA nut extract also enhanced mitochondrial enzyme activity and restored normal metabolic enzyme levels in mammary carcinoma-bearing rats (52). The structural resemblance of SA flavonoids to glycosylated polyphenols and purine analogs may contribute to hexokinase inhibition and tumour growth suppression (53). Another study confirmed that SA helps maintain glutathione redox balance, protecting antioxidant enzymes from oxidative damage. GSH and GSSG levels were normalised in the liver and kidney of SA-treated tumour-bearing animals (54). Additionally, elevated plasma, liver, and kidney lipid profiles—including total cholesterol, free cholesterol, triglycerides, and phospholipids—were restored to near-normal levels following SA treatment, reflecting its role in lipid metabolism modulation and tumour growth inhibition (54). SA also exhibited strong antiangiogenic effects, reducing vascularisation and expression of markers such as carbonic anhydrase IX and glucose transporter 1. It further down regulated hypoxia-inducible factor-1 (HIF-1), vascular endothelial growth factor (VEGF), and inducible nitric oxide synthase (iNOS), contributing to tumor suppression (55). The suppression of pro-survival cytokines and inhibition of endothelial cell growth also support SA's antiangiogenic potential (56). In a biomarker-based study, erythrocyte protoporphyrin fluorescence was used to assess oxidative stress and antioxidant enzyme status in dimethylbenz(a)anthracene (DMBA)-induced mammary carcinoma rats. SA effectively restored antioxidant levels in erythrocytes, reducing oxidative stress damage and highlighting its potential for diagnostic and therapeutic applications (57, 58). A separate study evaluated the antiangiogenic effects of SA and *Kalpaamruthaa* (KA) in DMBA-induced mammary carcinoma models. Histopathological analysis confirmed tumor induction after 90 days, and subsequent treatment with SA and KA significantly reduced expression levels of angiogenic mediators like cyclooxygenase-2 (COX-2), proteases, and VEGF (59).This reduction was attributed to phenolic compounds—such as tannins and flavonoids—present in SA, which are known for their chemopreventive properties (60).

Leukemia

Chronic Myeloid Leukemia (CML) is a malignant clonal disorder characterised by the BCR-ABL gene fusion, which results in the overproduction of myeloid lineage cells at various stages of maturation and the synthesis of a 210 kDa chimeric tyrosine kinase protein. CML typically progresses through two clinical phases. The initial chronic phase is marked by an increased myeloid-erythroid ratio in the bone marrow, a rise in mature leukocytes in peripheral blood, and splenomegaly. If untreated, CML advances to the blast phase, an aggressive stage that responds poorly to conventional therapy (61). The antileukemic potential of *Semecarpus anacardium* Linn. nut milk extract (SA), a Siddha herbal formulation, has been explored in experimental leukemia models. Acetylated SA oil has shown enhanced efficacy when used in combination with standard chemotherapeutic agents such as mitomycin, fluorouracil, and methotrexate. Furthermore, SA-based Ayurvedic preparations have demonstrated cytotoxicity against leukemic cell lines K562 and HL-60. With growing global interest in herbal medicines, SA has attracted attention for its antioxidant, anticancer, and non-toxic properties (61). In another study, leukemia was induced in BALB/c mice via intravenous injection of BCR-ABL+ 12B1 murine leukemia cells. SA administration led to the clearance of leukemic cells from the bone marrow and internal organs, as confirmed by histological examination and RT-PCR analysis for p210 mRNA expression. SA treatment significantly restored levels of lipid peroxides (LPO), glycolytic enzymes, gluconeogenic enzymes, and mitochondrial enzymes, suggesting a normalization of energy metabolism in leukemic mice (61). The therapeutic effects observed may be attributed to the presence of flavonoids, polyphenols, and other bioactive compounds in SA. The study model closely mimics human CML in blast crisis, validating its relevance. RT-PCR analysis of the spleen, liver, and peripheral blood confirmed leukemic induction in 12B1-injected animals. Notably, SA-treated mice showed a gradual increase in body weight and no signs of toxicity, indicating the safety of the extract. A significant reduction in LPO levels in SA-treated groups (Group IV), as well as those treated with imatinib (Group III), suggests a protective antioxidant effect. Flavonoids in SA may contribute to the decreased glycolytic enzyme activity and improved mitochondrial function by preventing oxidative damage and enzyme inactivation. SA treatment likely impedes tumor progression by modulating mitochondrial activity, reducing energy metabolism in cancer cells, and promoting apoptosis. Elevated activities of gluconeogenic and TCA cycle enzymes, along with reduced glycolysis, indicate a shift in energy pathways that may impair leukemic cell survival. In addition to scavenging free radicals, SA has demonstrated potent inhibition of lipid peroxidation. These findings support the hypothesis that SA extract exerts antileukemic

effects by altering energy metabolism and inducing apoptosis in malignant cells. Overall, SA nut milk extract emerges as a promising and accessible phytotherapeutic agent with significant potential in leukemia treatment due to its chemoprotective, antioxidant, and metabolic regulatory properties (61).

Analgesic activity

The tail-flick and writhing assays are among the most widely employed experimental models to evaluate the analgesic efficacy of drugs, natural compounds, and crude extracts in rodents. In a few studies investigating the analgesic properties of *Semecarpus anacardium* (SA) extracts, these methods were utilised effectively. The abdominal constriction response induced by glacial acetic acid is a particularly sensitive method for detecting peripherally acting analgesics, as this response is believed to be mediated by local peritoneal receptors (62). In this study, the analgesic effects of SA extracts prepared using chloroform, methanol, and petroleum ether were evaluated using the tail-flick and writhing assays. Acetylsalicylic acid was used as the standard reference drug. All three SA extracts demonstrated consistent analgesic activity across both experimental models. Among the tested extracts, the methanolic extract exhibited the most significant analgesic effect, surpassing the petroleum ether and chloroform extracts in potency, although it remained less effective than acetylsalicylic acid. The methanol extract of SA significantly delayed the onset of writhing and reduced the number of abdominal constrictions when compared to the control group. In contrast, the petroleum ether and chloroform extracts showed only moderate analgesic activity. These findings corroborate the traditional ethnomedicinal claims regarding the analgesic potential of *S. anacardium* (63). In conclusion, the results of this investigation confirm that all SA extracts possess analgesic properties, with the methanol extract demonstrating superior efficacy. Although it was less effective than the standard analgesic drug, it was notably more potent than the other extracts tested. This study supports the therapeutic potential of *Semecarpus anacardium Linn.* as a medicinal plant for pain relief and provides scientific validation for its use in traditional medicine.

In silico study

The acetylcholinesterase (AChE) inhibitory activity of catechol alkenyl compounds from *Semecarpus anacardium Linn.* was investigated using both in vitro and in silico methods. Active compounds were isolated from a dichloromethane extract through activity-guided fractionation and identified by mass spectrometry, along with one- and two-dimensional ^1H and ^13C NMR spectroscopy. Two major compounds, dihydroxy-1,2,3-pentadec-8-enylbenzene (A) and 1,2,3-pentadec-8,11-dienylbenzene (B), showed selective inhibition of AChE with IC50 values of 12 µg/mL and 34 µg/mL, respectively, and showed no significant activity against butyrylcholinesterase (BChE). Molecular docking studies using GOLD 3.1 software were conducted with AChE structures from Torpedo californica and Electrophorus electricus (retrieved from the Protein Data Bank), which confirmed the interaction of compounds A and B with the AChE active site. HPLC analysis revealed that compounds A and B were present at concentrations of 1.85% and 1.88%, respectively, in the fruit extract. These findings suggest that A and B are the key bioactive components responsible for the AChE inhibitory activity of *Semecarpus anacardium Linn.* fruit resin (4).

Antibacterial

Semecarpus anacardium Linn., traditionally used in Ayurvedic and Siddha medicine for its antibacterial, antidiabetic, and antiarthritic properties, has been evaluated for its antimicrobial potential. The present study focused on isolating bioactive compounds from the seeds of S. anacardium using column and thin-layer chromatography, followed by structural characterisation through IR, high-resolution mass spectrometry, and ^1H and ^13C NMR spectroscopy. The isolated compound was identified as a non-cyclic isoprenoid (C21H32O), which exhibited significant antibacterial activity (11). The compound demonstrated notable inhibition against clinical bacterial strains, including Gram-positive Bacillus cereus and Gram-negative pathogens such as Staphylococcus aureus, Escherichia coli, and Acinetobacter baumannii, showing comparable activity to standard antibiotics like tetracycline. These findings support the traditional therapeutic use of *S. anacardium* and suggest its potential as a source for novel antibacterial agents. However, further pharmacological, toxicological, and mechanistic studies are required to explore its therapeutic applications in detail (11).

Antibiofilm

Biofilm-associated infections pose significant challenges due to their resistance to conventional antimicrobial therapies and represent a major health concern. Nanotechnology has emerged as a promising approach to combat biofilm-forming pathogens. In this context, the present study explored the eco-friendly synthesis and characterisation of biocompatible silver nanoparticles (AgNPs) using leaf extracts of *Semecarpus anacardium Linn.* The biosynthesised AgNPs demonstrated potent antibacterial and anti-biofilm activity against several clinically relevant human pathogens (65). The study emphasised the role of naturally occurring phytoconstituents such as phenolic compounds, flavonoids, glycosides, and phytosterols as effective reducing agents in the green synthesis of AgNPs. UV–visible spectroscopy and attenuated total reflectance–Fourier transform infrared (ATR–FTIR) spectroscopy confirmed the involvement of these phytochemicals in nanoparticle synthesis. The AgNPs were further tested against Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa, revealing strong antibacterial and antibiofilm effects. Additional plant extracts from *Glochidion lanceolarium* and *Bridelia retusa* were also studied for comparative purposes. The findings underscore the potential of plant-derived AgNPs as effective agents in preventing and disrupting bacterial biofilms. Such biosynthesised

nanoparticles offer a safer, sustainable, and efficient alternative to conventional antimicrobial therapies, highlighting the need for further investigation into their biomedical applications (65).

Antimicrobial

The potential of *Semecarpus anacardium Linn*. nut extract as an alternative to traditional salt curing in leather processing was evaluated in a recent study. The assessment included parameters such as hair slip, putrefaction odour, volatile nitrogen content, moisture content, bacterial count, and shrinkage temperature. The findings indicated that SA nut extract effectively minimised skin degradation during pre-tanning operations. Its antibacterial constituents contributed to the preservation of freshly flayed skins for more than 30 days. The study highlights SA as a promising eco-friendly substitute for salt curing, offering a sustainable approach to leather preservation while mitigating the environmental impact associated with conventional salt-based methods (66).

Cytoprotective effect

Semecarpus anacardium Linn. contains kaempferol and 3-O-methyl quercetin, which exhibit cytoprotective effects against H_2O_2-induced oxidative stress in liver and lung cells. H_2O_2, a metabolic by-product, induces ROS generation, DNA damage, and mitochondrial dysfunction at elevated levels. The study evaluated the compounds' effects on ROS production, membrane integrity, and mitochondrial potential. Nrf2 gene expression was assessed via RT-PCR, while ELISA quantified Nrf2 and p-p38 protein levels. Western blot analysis confirmed upregulation of antioxidant enzymes SOD and catalase. Pre-treatment promoted Nrf2 nuclear translocation and enhanced antioxidant enzyme expression, indicating the potential of these flavonoids in mitigating oxidative damage through Nrf2 pathway activation (67).

Oxidative stress/nitrosative stress

Semecarpus anacardium Linn. demonstrated protective effects against oxidative and nitrosative stress in diabetic rats by reducing ROS and RNS levels, enhancing mitochondrial membrane potential, and decreasing intracellular calcium accumulation. Streptozotocin-induced diabetic rats treated with SA nut milk extract for 21 days showed significant mitochondrial protection, as observed through confocal microscopy. The antioxidant activity was attributed to metal ion chelation and free radical scavenging mechanisms (30). The non-polar hexane fraction (NPF) of SA nut oil exhibited pro-inflammatory potential by activating protein kinase C (PKC) in resting rat peritoneal macrophages. Western blot analysis confirmed upregulation of PKC protein expression, comparable to phorbol myristate acetate (PMA), suggesting that the oily component may contribute to the inflammatory response (68). In a high-fat diet and streptozotocin-induced type 2 diabetic rat model, SA nut milk extract (200 mg/kg) exhibited significant antihyperlipidemic and anti-inflammatory effects, surpassing metformin treatment. SA administration improved lipid profiles, increased expression of PPAR-γ, and reduced levels of inflammatory cytokines (TNF-α, IL-6) and C-reactive protein. The extract effectively modulated lipid metabolism and enhanced insulin sensitivity, highlighting its therapeutic potential in metabolic disorders (69). The acaricidal potential of SA fruit extract was evaluated against susceptible (IVRI-I) and multi-acaricide-resistant (IVRI-V) strains of Rhipicephalus (Boophilus) microplus. Both 50% hydro-ethanolic and 95% ethanolic extracts demonstrated significant efficacy, with the latter showing 73.3% inhibition. The extract also disrupted tick oviposition, indicating interference in reproductive physiology. Pyrocatechol was identified as a bioactive marker compound via HPTLC fingerprinting, supporting the efficacy of SA against acaricide-resistant ticks (70).

Toxicity studies

Semecarpus anacardium Linn. (*Bibba, Bhilwa, Bhallataka*, Black nut, Marking nut) is known for its corrosive juice and vesicant properties. Pharmacological studies using isolated frog heart and rabbit intestine revealed that the extracts exert a direct depressive effect on these tissues, indicating weak smooth muscle relaxant activity (71). In canine models, delayed hypotension was observed, and the petroleum ether extract significantly reduced cutaneous histamine levels. However, the primary limitation in its therapeutic use is its pronounced dermal toxicity, particularly in sensitive individuals (62). In a recent investigation, the antioxidant and hepatoprotective effects of SA were evaluated in a lead acetate-induced toxicity model. SA administration restored biochemical marker enzymes and normalised histological alterations in lead-exposed albino rats, suggesting that its protective effects may be attributed to phytochemicals present in the extract (72). Toxicological evaluations of catechol derivatives (I–IV) isolated from SA were conducted in Wistar albino rats. Acute toxicity studies showed no behavioural abnormalities or mortality at 800 mg/kg. However, mortality occurred at higher doses: LD50 was observed at 1250 mg/kg for derivative IV and 1600 mg/kg for derivatives I–III. In subacute studies, daily administration of 300 mg/kg for 30 days did not induce mortality or significant changes in body or organ weights. Haematological and biochemical analyses indicated beneficial effects in derivatives I and IV, including transient leukocytosis, increased HDL, and reduced LDL and tissue lipid levels, suggesting a potential role in immune modulation and cardiovascular protection (73). One study also reported that combining SA with peanut oil or similar carriers may reduce its dermal toxicity.

Cardioprotective activity

The cardioprotective effect of *Semecarpus anacardium Linn.* nut extract (SANE) and propranolol (PRO) was evaluated against isoproterenol-induced myocardial injury in rats. The study assessed serum biomarkers, antioxidant enzyme activity, histopathological changes, and electrocardiographic

parameters. Compared to the isoproterenol group, treatment groups showed significantly reduced levels of thiobarbituric acid reactive substances (TBARS), increased activities of superoxide dismutase (SOD) and catalase, and decreased lactate dehydrogenase (LDH) and creatine phosphokinase-MB (CPK-MB) levels. Electrocardiographic abnormalities were also normalised in treated groups. Both low (100 mg/kg) and high (500 mg/kg) doses of SANE exhibited cardioprotective effects, with enhanced efficacy observed when combined with PRO. The most pronounced protection was achieved with a high-dose combination of SANE and PRO. However, dose optimisation is necessary to minimise potential adverse effects from excessive pharmacological activity.

Different Case Reports treatment

Alopecia treatment case, ankle pain relief case, cause of the nephrotic syndrome (74), marking nut anaphylaxis case (75), marking nut allergic dermatitis (76), (20), acetylcholinesterase inhibition (4), (78), contact urticaria (79), atherosclerosis, facial oedema (80) are mentioned.

Limitations of the Review

This review has certain limitations. The limited number of studies and their methodological heterogeneity precluded the possibility of conducting a meta-analysis, despite the application of a rigorous process for literature search, selection, and analysis. Additionally, the absence of an appropriate assessment tool restricted the evaluation of study quality. Nonetheless, the review successfully identified key themes and research gaps, offering valuable insights to guide future investigations. While these limitations should be acknowledged, the review provides a comprehensive summary of the existing literature on the topic.

Conclusion

This review demonstrated the variety of *Semecarpus* species that are found all over the world and have therapeutic potential. *Semecarpus* is a rich reservoir of chemical compounds and an economically significant genus with easily cultivable species. The main constituents of the genus, flavonoids and phenols, have anti-cancer, anti-diabetic, and therapeutic properties that hold out a lot of promise. However, other fractions also showed significant behaviors, like potent anti-inflammatory behavior. The medicinal potential of numerous other substances, including phenols and flavonoids, was also discussed.

References

1. Balachandran I. Purification of Bhallathaka (Semecarpus anacardium L.f.) enhanced anti-cancer activity. Regul Toxicol Pharmacol. 2021 Jun;122:104898, 10.1016/j.yrtph.2021.104898.
2. Subramani S, Banu Hedyathullah Khan H, Palanivelu S, Thiruvaiyaru Panchanadham S. Restorative Effect of Semecarpus Anacardium on Altered Energy Metabolism in Type-2 Diabetes Mellitus-Induced Cardiac Dysfunction in Rats. J Diet Suppl. 2020;17(1):27-40, 10.1080/19390211.2018.148148.
3. Aseervatham J, Palanivelu S, Panchanadham S. Semecarpus anacardium (Bhallataka) Alters the Glucose Metabolism and Energy Production in Diabetic Rats. Evid Based Complement Alternat Med. 2011;2011:142978, 10.1155/2011/142978.
4. Purushothaman A, Meenatchi P, Saravanan N, Karuppaiah M, Sundaram R. Isolation and Characterization of an Acyclic Isoprenoid from *Semecarpus anacardium* Linn. and its Antibacterial Potential *in vitro*: - Antimicrobial Activity of *Semecarpus anacardium* Linn. Seeds. J Pharmacopuncture. 2017 Jun;20(2):119-126, PMID: 30087789
5. Verma N, Vinayak M. Semecarpus anacardium nut extract promotes the antioxidant defence system and inhibits anaerobic metabolism during development of lymphoma. Biosci Rep. 2009 Jun;29(3):151-64, 10.1042/BSR20080035.
6. Premalatha B, Sachdanandam P. Semecarpus anacardium L. nut extract administration induces the in vivo antioxidant defence system in aflatoxin B1 mediated hepatocellular carcinoma. J Ethnopharmacol. 1999 Aug;66(2):131-9, 10.1016/S0378-8741(99)00029-X.
7. Ghosh S, Tiwari SS, Srivastava S, Kumar S, Sharma AK, Nagar G, Kumar KG, Kumar R, Rawat AK. In vitro acaricidal properties of Semecarpus anacardium fruit and Datura stramonium leaf extracts against acaricide susceptible (IVRI-I line) and resistant (IVRI-V line) Rhipicephalus (Boophilus) microplus. Res Vet Sci. 2015 Aug;101:69-74, 10.1016/j.rvsc.2015.05.015.
8. Jaya A, Shanthi P, Sachdanandam P. Hypolipidemic activity of Semecarpus anacardium in Streptozotocin induced diabetic rats. Endocrine. 2010 Aug;38(1):11-7,
9. (9) Ramprasath VR, Shanthi P, Sachdanandam P. Semecarpus anacardium Linn. nut milk extract, an indigenous drug preparation, modulates reactive oxygen/nitrogen species levels and antioxidative system in adjuvant arthritic rats. Mol Cell Biochem. 2005 Aug;276(1-2):97-104, PMID: 16132690
10. Sundaram R, Muthu K, Shanthi P, Sachdanandam P. Antioxidant and antihyperlipidemic activities of catechol derivatives and biflavonoid isolated from *Semecarpus anacardium* seeds. Toxicol Mech Methods. 2022 Feb;32(2):123-131, 10.1080/15376516.2021.1973170.
11. Sharma A, Verma PK, Dixit VP. Effect of Semecarpus anacardium fruits on reproductive function of male albino rats. Asian J Androl. 2003 Jun;5(2):121-4, PMID: 12778323.
12. Khan HB, Vinayagam KS, Palanivelu S, Panchanadham S. Ameliorating effect of Semecarpus anacardium Linn. nut milk extract on altered glucose metabolism in high fat diet STZ induced type 2 diabetic rats. Asian Pac J Trop Med.

2012 Dec;5(12):956-61, 10.1016/S1995-7645(12) 60181-3.
13. Khan HB, Vinayagam KS, Renny CM, Palanivelu S, Panchanadham S. Potential antidiabetic effect of the Semecarpus anacardium in a type 2 diabetic rat model. Inflammopharmacology. 2013 Feb;21(1):47-53, PMID: 22556061.
14. Patwardhan B, Saraf MN, David SB. Toxicity of semecarpus anacardium extract. Anc Sci Life. 1988 Oct;8(2):106-9, PMID: 22557639.
15. Nair PK, Melnick SJ, Wnuk SF, Rapp M, Escalon E, Ramachandran C. Isolation and characterization of an anticancer catechol compound from Semecarpus anacardium. J Ethnopharmacol. 2009 Apr 21;122(3):450-6, https://doi.org/10.1016/ j.jep.2009.02.001
16. Joseph JP, Raval SK, Sadariya KA, Jhala M, Kumar P. Anti cancerous efficacy of Ayurvedic milk extract of Semecarpus anacardium nuts on hepatocellular carcinoma in Wistar rats. Afr J Tradit Complement Altern Med. 2013 Aug 12;10(5):299-304, PMID: 24311839.
17. Premalatha B, Sachdanandam P. Potency of Semecarpus anacardium Linn. nut milk extract against aflatoxin B(1)-induced hepatocarcinogenesis: reflection on microsomal biotransformation enzymes. Pharmacol Res. 2000 Aug;42(2):161-6, 10.1006/phrs.2000.0676 .
18. Abirami N, Raju VS, Rajathi K. Effect of Semecarpus anacardium against lead induced toxicity in rats. Anc Sci Life. 2007 Oct;27(2):24-7, PMID: 22557265.
19. Gil RR, Lin LZ, Cordell GA, Kumar MR, Ramesh M, Reddy BM, Mohan GK, Narasimha AV, Rao A. Anacardoside from the seeds of Semecarpus anacardium. Phytochemistry. 1995 May;39(2):405-7, 10.1016/0031-9422(94)00842-H .
20. Khan HB, Vinayagam KS, Sekar A, Palanivelu S, Panchanadham S. Antidiabetic and antioxidant effect of Semecarpus anacardium Linn. nut milk extract in a high-fat diet STZ-induced type 2 diabetic rat model. J Diet Suppl. 2012 Mar;9(1):19-33, 10.3109/19390211.2011.631099 .
21. Arathi G, Sachdanandam P. Therapeutic effect of Semecarpus anacardium Linn. nut milk extract on carbohydrate metabolizing and mitochondrial TCA cycle and respiratory chain enzymes in mammary carcinoma rats. J Pharm Pharmacol. 2003 Sep;55(9):1283-90, 10.1211/0022357021710 .
22. Mathivadhani P, Shanthi P, Sachdanandam P. Effect of Semecarpus anacardium Linn. nut milk extract on glutathione and its associated enzymes in experimentally induced mammary carcinoma. J Med Food. 2006 Summer;9(2):265-9, 10.1089/ jmf.2006.9.265 .
23. Lingaraju GM, Krishna V, Joy Hoskeri H, Pradeepa K, Venkatesh, Babu PS. Wound healing promoting activity of stem bark extract of Semecarpus anacardium using rats. Nat Prod Res. 2012;26(24):2344-7, 10.1080/ 14786419.2012. 656108 .
24. Ramprasath VR, Shanthi P, Sachdanandam P. Immunomodulatory and anti-inflammatory effects of Semecarpus anacardium LINN. Nut milk extract in experimental inflammatory conditions. Biol Pharm Bull. 2006 Apr;29(4):693-700, 10.1248/ bpb.29.693 .
25. Ramprasath VR, Shanthi P, Sachdanandam P. Anti-inflammatory effect of Semecarpus anacardium Linn. Nut extract in acute and chronic inflammatory conditions. Biol Pharm Bull. 2004 Dec;27(12):2028-31, 10.1248/bpb.27.2028 .
26. Mathivadhani P, Shanthi P, Sachdanandam P. Effect of Semecarpus anacardium nut extract on ECM and proteases in mammary carcinoma rats. Vascul Pharmacol. 2007 Jun;46(6):419-26, 10.1016/ j.vph.2006.12.004 .
27. Ramprasath VR, Shanthi P, Sachdanandam P. Effect of Semecarpus anacardium Linn. nut milk extract on rat neutrophil functions in adjuvant arthritis. Cell Biochem Funct. 2006 Jul-Aug;24(4):333-40, 10.1002/cbf.1243 .
28. Ali MA, Wahed MI, Khatune NA, Rahman BM, Barman RK, Islam MR. Antidiabetic and antioxidant activities of ethanolic extract of Semecarpus anacardium (Linn.) bark. BMC Complement Altern Med. 2015 Apr 29;15:138, PMID: 25925864
29. Mathivadhani P, Shanthi P, Sachdanandam P. Apoptotic effect of Semecarpus anacardium nut extract on T47D breast cancer cell line. Cell Biol Int. 2007 Oct;31(10):1198-206, 10.1016/ j.cellbi.2007.04.004 .
30. Iyappan K, Ponrasu T, Sangeethapriya V, Gayathri VS, Suguna L. An eco-friendly method for short term preservation of skins/hides using Semecarpus anacardium nut extract. Environ Sci Pollut Res Int. 2013 Sep;20(9):6324-30, PMID: 23589261.
31. Vijayalakshmi T, Muthulakshmi V, Sachdanandam P. Effect of the milk extract of Semecarpus anacardium nut on adjuvant arthritis--a dose-dependent study in Wistar albino rats. Gen Pharmacol. 1996 Oct;27(7):1223-6, 10.1016/ S0306-3623(96)00042-0 .
32. Singh D, Aggarwal A, Mathias A, Naik S. Immunomodulatory activity of Semecarpus anacardium extract in mononuclear cells of normal individuals and rheumatoid arthritis patients. J Ethnopharmacol. 2006 Dec 6;108(3):398-406, https://doi.org/10.1016/j.jep.2006.05.028 .
33. Ramprasath VR, Shanthi P, Sachdanandam P. Evaluation of antioxidant effect of Semecarpus anacardium Linn. nut extract on the components of immune system in adjuvant arthritis. Vascul Pharmacol. 2005 Mar;42(4):179-86, 10.1016/ j.vph.2005.02.001 .
34. Mathivadhani P, Shanthi P, Sachdanandam P. Effect of Semecarpus anacardium Linn. nut extract on mammary and hepatic expression of xenobiotic enzymes in DMBA-induced mammary carcinoma. Environ Toxicol Pharmacol. 2007 May;23(3):328-34, 10.1016/j.etap.2006.12.004 .

35. Herath HM, Wazil AW, Ratnatunga NV, Badurdeen AS, Weerakoon KG. Could the latex of Semecarpus anacardium (Kiri Badulla) cause nephrotic syndrome? Ceylon Med J. 2012 Jun;57(2):92-3, http://dx.doi.org/10.4038/cmj.v57i2.4467 .
36. (36) Lingaraju GM, Hoskeri HJ, Krishna V, Babu PS. Analgesic activity and acute toxicity study of Semecarpus anacardium stem bark extracts using mice. Pharmacognosy Res. 2011 Jan;3(1):57-61, PMID: 21731397.
37. Ramprasath VR, Shanthi P, Sachdanandam P. Therapeutic effects of Semecarpus anacardium Linn. nut milk extract on the changes associated with collagen and glycosaminoglycan metabolism in adjuvant arthritic Wistar rats. Chem Biol Interact. 2006 Jul 25;162(1):43-52, 10.1016/j.cbi.2006.05.003 .
38. Sujatha V, Sachdanandam P. Recuperative effect of Semecarpus anacardium linn. nut milk extract on carbohydrate metabolizing enzymes in experimental mammary carcinoma-bearing rats. Phytother Res. 2002 Mar;16 Suppl 1:S14-8, 10.1002/ptr.777 .
39. Ramprasath VR, Shanthi P, Sachdanandam P. Curative effect of Semecarpus anacardium Linn. nut milk extract against adjuvant arthritis -- with special reference to bone metabolism. Chem Biol Interact. 2006 Apr 15;160(3):183-92, 10.1016/j.cbi.2005.11.009 .
40. Selvam C, Jachak SM. A cyclooxygenase (COX) inhibitory biflavonoid from the seeds of Semecarpus anacardium. J Ethnopharmacol. 2004 Dec;95(2-3):209-12, 10.1016/j.jep.2004.07.026 .
41. Vijayalakshmi T, Muthulakshmi V, Sachdanandam P. Effect of milk extract of Semecarpus anacardium nuts on glycohydrolases and lysosomal stability in adjuvant arthritis in rats. J Ethnopharmacol. 1997 Sep;58(1):1-8, https://doi.org/10.1016/S0378-8741(97)00074-3 .
42. Saraf MN, Ghooi RB, Patwardhan BK. Studies on the mechanism of action of Semecarpus anacardium in rheumatoid arthritis. J Ethnopharmacol. 1989 Apr;25(2):159-64, https://doi.org/10.1016/0378-8741(89)90017-2 .
43. Premalatha B, Muthulakshmi V, Sachdanandam P. Anticancer potency of the milk extract of Semecarpus anacardium Linn. nuts against aflatoxin B1 mediated hepatocellular carcinoma bearing Wistar rats with reference to tumour marker enzymes. Phytother Res. 1999 May;13(3):183-7,10.1002/(SICI)1099-1573 (199905)13:3%3C183::AID PTR420% 3E3.0.CO;2-5 .
44. Chakraborty S, Roy M, Taraphdar AK, Bhattacharya RK. Cytotoxic effect of root extract of Tiliacora racemosa and oil of Semecarpus anacardium nut in human tumour cells. Phytother Res. 2004 Aug;18(8):595-600, 10.1002/ptr.1501.
45. Selvam C, Jachak SM, Bhutani KK. Cyclooxygenase inhibitory flavonoids from the stem bark of Semecarpus anacardium Linn. Phytother Res. 2004 Jul;18(7):582-4, 10.1002/ptr.1492 .
46. Sugapriya D, Shanthi P, Sachdanandam P. Restoration of energy metabolism in leukemic mice treated by a siddha drug--Semecarpus anacardium Linn. nut milk extract. Chem Biol Interact. 2008 May 9;173(1):43-58, 10.1016/j.cbi.2008.01.013 .
47. Mathivadhani P, Shanthi P, Sachdanandam P. Hypoxia and its downstream targets in DMBA induced mammary carcinoma: protective role of Semecarpus anacardium nut extract. Chem Biol Interact. 2007 Apr 5;167(1):31-40, 10.1016/j.cbi.2007.01.003 .
48. Nagabhushana KS, Umamaheshwari S, Tocoli FE, Prabhu SK, Green IR, Ramadoss CS. Inhibition of soybean and potato lipoxygenases by bhilawanols from bhilawan (Semecarpus anacardium) nut shell liquid and some synthetic salicylic acid analogues. J Enzyme Inhib Med Chem. 2002 Aug;17(4):255-9, 10.1080/14756360210000062 43 .
49. Vijayalakshmi T, Muthulakshmi V, Sachdanandam P. Toxic studies on biochemical parameters carried out in rats with Serankottai nei, a siddha drug-milk extract of Semecarpus anacardium nut. J Ethnopharmacol. 2000 Jan;69(1):9-15, 10.1016/S0378-8741(99)00020-3 .
50. (50) Premalatha B, Sujatha V, Sachdanandam P. Modulating effect of Semecarpus anacardium Linn. nut extract on glucose metabolizing enzymes in aflatoxin B1-induced experimental hepatocellular carcinoma. Pharmacol Res. 1997 Sep;36(3):187-92, 10.1006/phrs.1997.0214 .
51. Llanchezhian R, Joseph C R, Rabinarayan A. Urushiol-induced contact dermatitis caused during Shodhana (purificatory measures) of Bhallataka (Semecarpus anacardium Linn.) fruit. Ayu. 2012 Apr;33(2):270-3, PMID: 23559802.
52. Tripathi YB, Pandey N, Tripathi D, Tripathi P. Oily fraction of Semecarpus anacardium Linn nuts involves protein kinase C activation for its pro-inflammatory response. Indian J Exp Biol. 2010 Dec;48(12):1204-9, PMID: 21250602.
53. Sharma K, Shukla SD, Mehta P, Bhatnagar M. Fungistatic activity of Semecarpus anacardium Linn. f nut extract. Indian J Exp Biol. 2002 Mar;40(3):314-8, PMID: 12635702.
54. Premalatha B, Sachdanandam P. Modulating role of Semecarpus anacardium L. nut milk extract on aflatoxin B(1) biotransformation. Pharmacol Res. 2000 Jan;41(1):19-24, 10.1006/phrs.1999.0544 .
55. (55) Mohanta YK, Biswas K, Jena SK, Hashem A, Abd Allah EF, Mohanta TK. Anti-biofilm and Antibacterial Activities of Silver Nanoparticles Synthesized by the Reducing Activity of Phytoconstituents Present in the Indian Medicinal Plants. Front Microbiol. 2020 Jun 23;11:1143, 10.3389/fmicb.2020.01143 .
56. Kesava Rao KV, Gothoskar SV, Chitnis MP, Ranadive KJ. Toxicological study of Semecarpus anacardium nut extract. Indian J Physiol Pharmacol. 1979 Apr-Jun;23(2):115-20, PMID: 489092.
57. Premalatha B, Sachdanandam P. Stabilization of lysosomal membrane and cell membrane glycoprotein profile by Semecarpus anacardium

linn. nut milk extract in experimental hepatocellular carcinoma. Phytother Res. 2000 Aug;14(5):352-5, 10.1002/1099-1573(200008)14:5%3C352::AID-PTR645%3E3.0.CO;2-C.
58. Sharma A, Mathur R, Dixit VP. Hypocholesterolemic activity of nut shell extract of Semecarpus anacardium (Bhilawa) in cholesterol fed rabbits. Indian J Exp Biol. 1995 Jun;33(6):444-8, PMID: 7590951.
59. Indap MA, Ambaye RY, Gokhale SV. Anti tumour and pharmacological effects of the oil from Semecarpus anacardium Linn. f. Indian J Physiol Pharmacol. 1983 Apr-Jun;27(2):83-91, PMID: 6885136.
60. Chitnis MP, Bhatia KG, Phatak MK, Kesava Rao KV. Anti-tumour activity of the extract of Semecarpus anacardium L. nuts in experimental tumor models. Indian J Exp Biol. 1980 Jan;18(1):6-8, PMID: 7399581.
61. Gothoskar SV, Ranadive KJ. Anticancer screening of SAN-AB: an extract of marking nut, Semecarpus anacardium. Indian J Exp Biol. 1971 Jul;9(3):372-5, PMID: 5144337.
62. Phatak MK, Ambaye RY, Indap MA, Bhatia KG. Cytotoxicity of the acetylated oil of Semecarpus anacardium Linn. f. Indian J Physiol Pharmacol. 1983 Apr-Jun;27(2):166-70, PMID: 6885130.
63. Mythilypriya R, Sachdanandam PS, Sachdanandam P. Ameliorating effect of Kalpaamruthaa, a Siddha preparation in adjuvant induced arthritis in rats with reference to changes in proinflammatory cytokines and acute phase proteins. Chem Biol Interact. 2009 May 15;179(2-3):335-43, 10.1016/j.cbi.2009.01.001.
64. Gothoskar SV, Chitnis MP, Adwankar MK, Ranadive KJ. Antitumour activity of SAN-AB: an extract of marking nut, Semecarpus anacardium. Indian J Exp Biol. 1971 Jul;9(3):399, PMID: 5144346.
65. Verma G, Tegta GR, Rattan R, Sharma R, Singh A. Airborne contact dermatitis apparently acquired as a result of using pericarp juice from an Indian marking nut as a home remedy to treat patchy hair loss. Contact Dermatitis. 2019 Sep;81(3):211-213, 10.1111/cod.13275.
66. Pal D, Mohapatra TK, Das A. Evaluation of anthelmintic activity of nuts of Semecarpus anacardium. Anc Sci Life. 2008 Jan;27(3):41-4, PMID: 22557277.
67. Maurya SK, Seth A, Laloo D, Singh NK, Gautam DN, Singh AK. Śodhana: An Ayurvedic process for detoxification and modification of therapeutic activities of poisonous medicinal plants. Anc Sci Life. 2015 Apr-Jun;34(4):188-97, PMID: 26283803
68. Ramalingam S, Karuppiah M, Thiruppathi M, Palanivelu S, Panchanatham S. Antioxidant potential of biflavonoid attenuates hyperglycemia by modulating the carbohydrate metabolic enzymes in high fat diet/streptozotocin induced diabetic rats. Redox Rep. 2020 Dec;25(1):1-10, 10.1080/13510002.2020.1722914.
69. Aseervatham J, Palanivelu S, Sachdanandam P. Cytoprotective effect of Semecarpus anacardium against toxicity induced by Streptozotocin in rats. J Exp Pharmacol. 2010 Aug 25;2:135-43, 10.2147/JEP.S11466.
70. Subramaniam S, Khan HB, Gomathy G, Palanvelu S, Panchanadham ST. Effect of Semecaprus anacardium on diabetes-induced alterations in the activities of marker enzymes and antioxidant enzymes in type 2 diabetes induced cardiac vascular damage model in rats. J Diet Suppl. 2014 Dec;11(4):347-60, 10.3109/19390211.2013.859219.

*****