

Semecarpus anacardium Linn. nuts—A boon in alternative medicine

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In alternative medicine, medicinal plant preparations have found widespread use particularly in the case of diseases not amenable to treatment by modern methods. Chemical and phytochemical analyses of *Semecarpus anacardium* nut reveal the presence of biflavonoids, phenolic compounds, bhitawanols, minerals, vitamins and amino acids. A variety of nut extract preparations from this source are effective against many diseases, viz. arthritis, tumours, infections etc. and non-toxic even at high dose of 2000 mg/kg. However understanding of the mechanism of the pharmacological action of *S. anacardium* nut can be greatly aided by the isolation of its active principle from the nut and determination of the structure-function relationship. Also, the potent curative effect of *S. anacardium* nut extract against human ailments need to be verified by controlled clinical studies.

Although there has been considerable progress in the modern medical field, there remain many diseases where we cannot effect any cure. Alternative medicines were able to cure many diseases that were not amenable to treatment by Western methods. Traditional Indian medicine with its evolution many centuries ago has always fascinated practitioners and researchers for the depth of analytical research and practical application. This medicine emphasizes health as the perfect state of physical, psychological, social and spiritual component of a human being. Its fundamental principles successfully eliminate harmful side effects without losing beneficial medicinal properties.

Nature is the foremost physician. Abuse of nature's law upsets the human system leading to occurrence of disease. It is again nature that effects cure. Medical information referred in the old Indian literature include uses of medicinal plants and the role of alchemy (chemistry), astrology, philosophy, yoga etc. for curing various ailments. Only few medicinal plants have attracted the interest of scientists and been the subject of scientific investigation. A research undertaken on *S. anacardium* nuts for the past twenty years has thrown some light on its suitability to conquer hitherto incurable diseases.

Semecarpus anacardium Linn.

Semecarpus anacardium Linn. (Family: *Anacardiaceae*) is distributed in Sub-Himalayan region, tropical and central parts of India, Western peninsula and N. Australia¹. The fruit is kidney-shaped, drupaceous nut with a fleshy pear-shaped receptacle². The nut is commonly called 'marking nut' and in the vernacular as 'Ballataka' or 'Bhilawa'³.

Historical background

In Ayurveda and Siddha (Indian systems of medicine) classics, copious references regarding the properties and uses of *S. anacardium* nuts are found⁴. The fruit of *S. anacardium* is acrid, hot, sweetish, edible aphrodisiac, anthelmintic, causes looseness of bowels, removes ascites, alleviates skin diseases, piles, dysentery, fever; loss of appetite, urinary discharges, heals ulcers, strengthens the teeth and is useful in insanity and asthma¹. It is popularly known as 'Ardha Vaidya' (multipurpose medicine).

Phytochemistry

A review of literature reveals the presence of biflavanoids⁵, phenolic compounds^{6,7}, bhitawanols⁸, sterols and glycosides⁹ in *S. anacardium* nuts. The chemical examination of *S. anacardium* nuts has been carried out in India by Pillai and Siddiqui¹⁰. The crushed pericarp of the marking nut on extraction with acetone gives 28% dark brown oil which on distillation gives three fractions i.e (a) light yellow oil known as semecarpol, a monophenol, (b) a golden yellow oil termed bhitawanol with a C₁₅H₂₇ side chain at position-3¹⁰. Bhitawanol is shown to be a mixture

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of phenolic compounds consisting mainly of 1,2-dihydroxy-3-(pentadecenyl-8')-benzene and 1,2-dihydroxy-3-(pentadecadienyl-8', 11')-benzene^{7,11}. Bhilawanol on dry distillation give rise to catechol and a hydrocarbon and (c) a tarry non-volatile residue (54% of extract)¹⁰. On the basis of chemical and spectral data several biflavanoids (Fig. 1) have been characterised, viz. semecarpufavanone (I)¹², jeediflavanone (II)¹³, gallufavanone (III)¹⁴, nallaflavanone (IV)¹⁵, semecarpetin (V)¹⁶ and anacardufavanone (VI)¹⁷, the first biflavanone to occur with a methylendioxy group.

Phytochemical examination² revealed 3.68% of total ash, 0.33% of acid insoluble ash, 11.27% alcohol soluble extractive, 11.84% water soluble extractive and 12.71% moisture content in *S. anacardium* nuts. The proximate principles, minerals

and vitamin content are given in Table I. Analysis by Bose *et al.*¹⁸ revealed the presence of iron, copper, sodium, calcium and aluminum in traces. Phenolic substances and resins were also detected. Vijayalakshmi *et al.*¹⁹ have reported the presence of carbohydrates, phenols and flavanoids in the Siddha preparation of *S. anacardium* nut milk extract.

Pharmacological evaluation

Bose *et al.*¹⁸ have reported the pharmacological and allergic properties of the nut extract. The nut is used internally in asthma and bruised nut is applied to the *os uteri* by some women to induce abortion¹.

Satyavati *et al.*³ and Bajpai *et al.*²⁰ have reported the antiinflammatory activity of *S. anacardium* nuts in acute inflammation of both immunological and non-immunological origin. Reports from

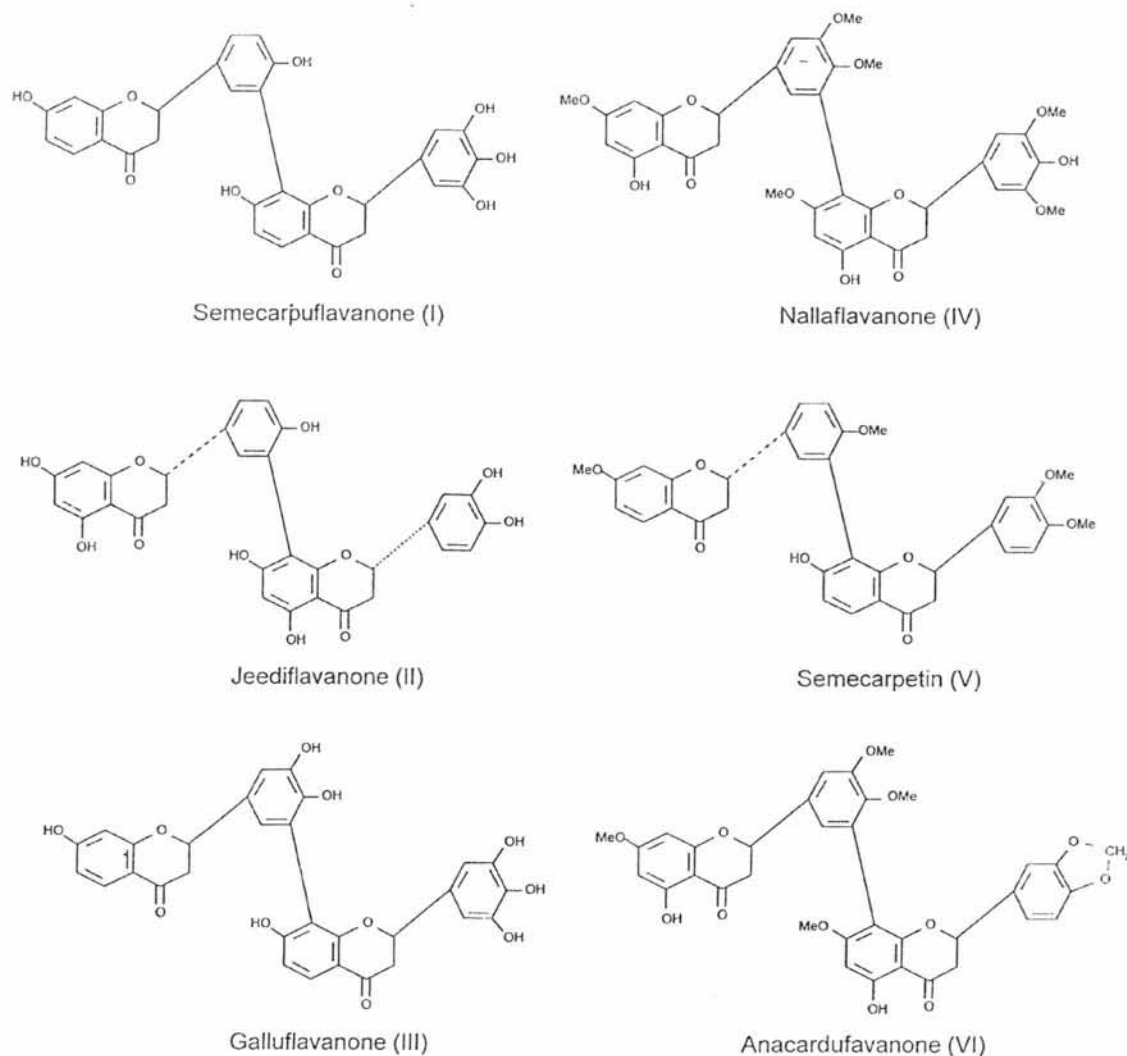


Fig. 1—Structure of biflavanoids from *Semecarpus anacardium* nuts

Vijayalakshmi *et al.*²¹ on the curative potency of *S. anacardium* nut milk extract in adjuvant induced arthritis bearing animals support the observations of the present clinical trial. The suppression of the development of secondary inflammation in experimental arthritis by the nut extract suggests its immunosuppressive activity and this property might be the reason for its effectiveness against rheumatoid arthritis²².

A variety of marking nut preparations are used in traditional medicine against numerous tumours. Ghothoskar and Ranadive²³ have found that, even a single injection of *SAN-AB*, another marking nut preparation could bring about complete inhibition of tumour growth in 14/15 rats. The chloroform extract of *S. anacardium* nut possess antitumour action against L1210, P388, advanced P388 leukemia, B16 melanoma and glioma²⁴ and increase in life span was observed in these cases²⁵. *In vitro* effect of acetyl derivative from *S. anacardium* nut indicated that the incorporation of radiolabelled precursors into DNA, RNA and protein was considerably inhibited at a concentration ranging from 40-75 µg/ml within 2 hr and thereby biosynthesis of DNA, RNA and protein was significantly inhibited²⁶. *Anacartin forte*, an Ayurvedic marking nut preparation, exhibited not only a broad spectrum of anticancer properties in clinical and animal studies but also a wide margin of safety in therapeutic dosage even when used for long periods. It has shown very gratifying results in the cases of the cancer of oesophagus, urinary bladder, liver and chronic leukaemia by giving subjective and objective improvement, alleviation or disappearance of troublesome symptoms and clinical benefit with extension of survival time. This preparation has selective action, attacking only the cancer cells without harming the normal cells²⁷.

Although the nut extract has been used for the treatment of malignant growth, the biochemical basis for its anticancer activity had been lacking. Hence, a Siddha preparation called '*Serankottai nei*' which is a milk extract of *S. anacardium* nuts was subjected to biochemical screening by Premalatha *et al.* The antioxidative^{28,29}, membrane stabilizing^{30,31}, tumour marker regulative³²⁻³⁴, glucose level restoring (via modulation of carbohydrate metabolizing enzymes)³⁵ and mineral regulation³⁶ properties in experimental hepatocellular carcinoma (HCC) were observed. Also, *S. anacardium* nut extract is found to detoxify a potent hepato carcinogen, aflatoxin B₁ and causes its

Table I—Proximate principles, minerals and vitamins in *Semecarpus anacardium* nuts (in 100g)²

1.	Moisture (g)	3.8
2.	Protein (g)	26.4
3.	Fat (g)	36.4
4.	Minerals (g)	3.6
5.	Fibre (g)	10.4
6.	Carbohydrates (g)	28.4
7.	Energy (Kcal)	587
8.	Calcium (mg)	295
9.	Phosphorus (mg)	836
10.	Iron (mg)	6.1
11.	Thiamine (mg)	0.38
12.	Riboflavin (mg)	0.15
13.	Niacin (mg)	2.7

metabolites to be excreted in urine³⁷. Considering the pessimistic prospect in case of primary HCC, for which the prognosis is grim with an expected six months span of life, the results achieved in these experiments hold out great promise for future. The nut extract also potentiates the efficacy of widely used anticancer drugs, viz. mitomycin-C, 5-fluorouracil and methotrexate³⁸.

The observed antitumour activity of this natural product indicates that it might have potential antineoplastic active principles. Unfortunately, bhlawanols and their epoxides have no role to play in the observed anticancer property³⁹. But the marking nut contains K40. Besides possible effective radioactivity, the complex nut probably has other active principles with specific differential effect on the malignant cells²⁴.

The nut extract has direct depressant effect on the isolated frog heart and rabbit intestine and antagonism to the spasmogenic effects of carbachol, histamine, barium chloride and pitocin¹⁸. Delayed type of hypersensitivity induced in mice by sheep red blood cells as an antigen was potentiated by the nut extract²³. Immunomodulatory potency of the nut extract in hepatocellular carcinoma was also reported from our laboratory⁴⁰.

It also reduces tissue and serum hyperlipidemia by the inhibition of intestinal cholesterol absorption coupled with peripheral disposal. Thus it possesses promising antiatherosclerotic activities and its use by coronary heart disease patients may be beneficial⁴¹.

The oil of *S. anacardium* is a cardiac tonic, a powerful antiseptic, a cholagogue and general respiratory stimulant. It is good for leucoderma, coryza, epilepsy and other nervous diseases. It lessens inflammation, is useful in paralysis and for superficial

dermatological pain. Oil with milk is given in daily cough for the relaxation of uvula and palate¹. Monohydroxy phenols from *S. anacardium* are used externally in the form of dermatological pastes and ointments (1 to 10%) for the treatment of ache, psoriasis and other skin diseases².

Consideration of mechanism of action

Many of the well known properties of marking nut oils are easily explainable by the catechol half and lipid-soluble C₁₅ chain. During exposure to air, the catechol ring might be oxidised to an orthoquinone. The *vesicant* nature and indelible pigmentation may be closely connected to the rapid formation of the orthoquinoid intermediate. The absorption of the oil by the skin is obviously due to the lipid soluble C₁₅ chain⁷.

Role of anacardic acid in pharmacology

Anacardic acid from oil of nuts exhibited anthelmintic⁴² and antimicrobial⁴³ properties in the treatment of hook worm infections. Monoene and diene bhalawanols inhibit gram positive anaerobes but not gram negative anaerobes which is probably due to lipoprotein layer which prevents penetration of lipophilic agents like bhalawanols into the cell membranes. Bhalawanols are susceptible to atmospheric oxidation and complex polymerization in the presence of oxygen which makes them unable to inhibit aerobic bacteria⁴⁴.

Toxicity evaluation

S. anacardium nuts can be given orally with milk, ghee, peanut oil etc. Toxic effects are not observed by such routes of administration. On the contrary, anabolic effects are obtained. Traditional methods recommended in Ayurveda and Siddha should be closely followed so as to get therapeutic effects without toxicity. Various reports have mentioned the range of dosage from 300 to 9000mg in a graded manner⁴. Toxicity studies were carried out by Ghosh *et al.*⁴⁵ with one Siddha preparation of *S. anacardium* (coded as SKx) and they found that, in rats, there was no adverse effect or mortality up to the oral dose of 2000mg/kg. The histopathological studies on liver, lung, kidney and heart did not reveal any significant pathological lesions even when the extract was administered at a high dose of 1000mg/kg⁴⁵. The animals looked healthy and active without any physiological disturbance and loss in body weight.

Hematological picture was almost normal. The extract did affect total WBC count but there was no effect on RBC count and haemoglobin percentage⁴⁵. The LD₅₀ dose of 40g/kg in rats and rabbits was determined by Vaishnav *et al.*⁴⁶.

The toxic-side effects of the very high dose of the drug are diarrhoea and vomiting, swelling all over the body, ulceration and vesication on the skin. It should be used cautiously and in lesser doses in hot season⁴. During use, whether external or internal the least appearance of a rash or redness of the skin or an itchy or uneasy sensation in any part of the body should be considered as a manifestation of undesirable effects and use should be discontinued immediately.

Clinical trials

The therapeutic utility of *S. anacardium* has been unequivocally established in experimental animals. The results obtained at this pre-clinical stage could be extended to clinics and only then can this extract be used successfully as supplement to stronger drugs already in use. The area currently under investigation is to study the effect of nut extract against AIDS and the preliminary findings seem promising.

Conclusion and future perspective

All these indicate that the *S. anacardium* nut extract is a life saving non-toxic drug, and has its own unique character with respect to physiology, pathology, pharmacology and therapeutics. It is suggested that the claims for any therapy should be subjected to scientific analysis although, at present, we do not understand the rationale for this treatment in scientific terms. However, it is difficult, perhaps rather premature, to arrive at any conclusion regarding the mechanism of the pharmacological action of *S. anacardium* nuts. The active principles of chemical constituents are to be assayed and confirmed. Further work is in progress to isolate the active principle of the drug and to detect the mechanism of antitumour activity at clinical and pharmacological levels. Only then will the nut be recognized for inclusion in modern scientific pharmacology. It is therefore desirable that pharmacological research be based on the broad outlines of elucidating all aspects in their entirety rather than finding merely the active principles. Only then can *Semecarpus anacardium* nuts to a certain extent, compete with drugs of synthetic origin.

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