



## SEMICARPUS ANACARDIUM LINN AND THEIR ANTICANCER ACTIVITY

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### ABSTRACT

Semecarpus anacardium Linn. of the family Anacardiaceae. is a well known medicinal plant in ayurvedic and siddha medicine. It has been found to have lot of medicinal properties, particularly for its anti-cancerous activity. semecarpus anacardium, commonly known as the marking nut tree, has been investigated for its potential anti-cancer properties. research has shown that the plant exhibits various pharmacological activities, including anti-inflammatory, anti-arthritis, anti-diabetic, and anti-tumor effects. The active compounds isolated from semecarpus anacardium, such as bhilawanol, cardol, ant anacardic acids, have demonstrated cytotoxic effects against various cancer cell lines these compounds have shown potential in inhibiting cancer cell proliferation, including apoptosis, and preventing angiogenesis. Semecarpus anacardium linn. f. nuts were extracted by using non polar and polar organic solvents. Hot methanol extract and resinous fraction, isolated from it, showed antitumor activity against P388 phocytic leukemia in BDF<sub>1</sub> mice as judged by their median survival time.

**KEYWORDS:** Medicinal plant, Anti-cancer, Cytotoxicity, Apoptosis.

### INTRODUCTION

Semecarpus anacardium linn.f.deciduous tree distributed in the sub Himalayan tract and in hotter parts of india. In vernacular language, it is known as Bibba (Marathi), Bhilawa (Hindi), Bhallataka (Sanskrit). The fruit is known as the marking nut, since the juice of pericarp is used for marking cotton clothes. The nut of S. anacardium is reported useful, particularly in the treatment of lepra nodules, warts and rheumatism.

S. anacardium has been under investigation for its anti-tumor properties and certain extracts of S. anacardium have exhibited promising antitumor properties. It has been observed that chloroform extract of nut, designated as "SAN-AB", gives symptomatic relief to patients suffering from oesophageal cancer and myeloid leukemia. In view of such observations, fractionation studies on S anacardium were undertaken with a view to isolating and characterizing the active principal in the plant.

### Pharmacological activity

S. anacardium has been used in the treatment of a number of diseases. A vast number of clinical and pharmacological studies on different type of preparations

and also on the different parts of S. anacardium have been carried out.

1. Anti-inflammatory activity
2. Anti-arthritis effect
3. Anti-septic activity
4. Anti-microbial activity
5. Anti-tumor, Antineoplastic, Cytotoxic, Cytostatic activity.
6. Lipoxygenase inhibitory activity
7. Hypolipidemic and Hypocholesterolemic activity
8. Antistress activity

### MATERIALS AND METHOD

#### Preparation of the extracts

Authentic samples of S. anacardium were procured from the local market. The extracts of freshly crushed material were obtained by employing to methods.

#### Methods: 1

The crushed material was extracted with methanol in Soxhlet apparatus for 32 hr. the solvent from the extract was removed under reduced pressure (10 mm).the methanol extract (200 g) was transferred to a separating funnel and partitioned between chloroform (2 lit) and water (2 lit containing 200 ml methanol). The contents

were shaken vigorously for 20 min, then occasionally and kept overnight. The chloroform layer (2 lit) was separated, concentrated and again partitioned between petroleum ether (2 lit) and methanol (2 lit containing 200 ml water). the methanol-partitioned fraction (method-1) was subjected to chromatography on silica gel (60-120 mesh, BDH) and the column was eluted with different solvents. The benzene-eluted fraction yielded a brown-coloured resinous material (yield 0.5%).

### Method: 2

Consisted of initial cold extraction of fruits with petroleum ether by percolation, followed by Soxhlet extraction of the residue with petroleum ether, benzene chloroform, ethyl acetate and methanol in succession. The solvent from these extracts were removed under reduced pressure to get the corresponding extract.

### Isolation of oil

Petroleum ether extract obtained by cold percolation (method 2) (67 g) was transferred to petroleum ether (60-80<sup>o</sup>). And chromatographed on silica gel (60-120 mesh, BHD). The major benzene eluted was collected and concentrated under reduced pressure (10 mm), when an oily material was obtained (yield, 34 g). On distillation under reduced pressure, this benzene eluate yielded an orange-coloured oil, (b.p. 200-20/ 2-3 mm) (yield, 17 g). It gave characteristics ferric chloride test indicating the presence of a phenolic hydrpxy group in the oil.

### Preparation of the derivatives of *S. anacardium* oil

Acetyl, methyl and benzoyl derivatives of the oil were prepared as soon as the oil (b.p 200-20/2-3 mm) was freshly obtained (yield, 17 g). Bhilawanol was obtained by redistillation of the oil under reduced pressure when a light yellow oil (b.p.215-17<sup>o</sup>/3 mm) was obtained (yiled 13 g), its diacetate and dimethylate were obtained following the usual procedures. A compound, m.p.70-72<sup>o</sup>, was obtained by hydrogenating acetylated bhilawanol in the presence of freshly prepared raney nikel as catalyst. the derivatives were characterized by qualitative tests and physico-chemical methods.

### Preparation of test material for antitumour activity

The test materials was dissolved in refined ground nut oil (postman brand) so as to make a concentration of 40mg/ml. different doses (400,200 and 100 mg/kg/day). were tried intraperitoneally to ascertain the toxicity of the material. the tolerable single dose was administered intraperitoneally to BDF<sub>1</sub> mice, 24 hr after the tumour transplantation and treatment was given for 9 days. Different routes and schedules of administration were tried in other sets of experiments. the animal were kept on normal diet and their body weights were recorded on days 1 and 5. deaths were recorded daily.

### Anti tumour activity evaluation

The maintenance of P388 lymphocytic leukaemia in DBA/2 mice was carried out because this strain is the inbred strain in which the tumour was originally induced.

For the purpose of drug testing, this tumor is transplanted into f<sub>1</sub> hybrid as the number off-springs in f<sub>1</sub> hybrid is larger. Mice of either sex were used for experiments.

The inoculum of cells (10<sup>6</sup>/mouse) a from sevan-day-old P388 lymphocytic leukemia was given intraperitoneally in BDF<sub>1</sub> mice which caused 100% mortality between 8 and 11 days. Six mice of either sex were used to evaluate anti-tumour activity at each dose level.

### RESULTS

It can be seen that the methanol extract and resinous material from it produced anti tumour activity. Attempts to purify the resinous material were, however, unsuccessful. several fractions obtained by partitioning the methanol extract in appropriate polar and non polar solvents and subsequent chromatography over silica gel yielded sub-fractions possessing anti tumour activity. However, the TLC pattern data of these fractions were identical.

Petroleum ether extracts also produced anti-tumor activity while other successive extracts did not demonstrated any promising activity. The fractionation of petroleum-ether extract, under high vaccum, yielded an orange-coloured oils, which also produced good anti-tumour activity against P388 tumour. In order to increase the therapeutic efficacy of oil, various dose levels routes and schedules were tried. The oil has produced the maximum anti-tumour activity at 200 mg/kg when given intraperitoneally.

As regards the routes of administration, only intra-peritoneal administration produced good antitumour activity. There were variations in antitumour activity when different administration schedules were variations in antitumour activity when different administration schedules were followed. A single dose of oil (400mg/kg) compared fairly well with the dose of 200 mg/kg given for nine days.

Apart from the ground nut oils which was usually used as a vehicle, tween 80 and saline emulsion, dimethyl sulphoxide and propylene glycol could not be used due to the solubility and toxicity problems. The nuts oil on keeping outside for one year, showed decreased anti-tumour activity as compared to the freshly distilled sample. This is probably due to air-oxidation which is apparent from the change in its colour from orange to black.

### DISCUSSION

In view of the reported antitumour properties of *S. anacardium*, fractionation studies were undertaken to isolate and characterize the active principle in the nuts. The response of P388 lymphocytic leukaemia to standard anticancer drugs has been studied by several investigators and this tumour has been found to be useful model for detecting active principle which may ultimately be useful clinically.

Since the crude oils, expressed from *S. anacardium* nuts, is a powerful vesicant, its antitumour activity was not determined. The present study has indicated that a resinous material from methanol extract and an orange-coloured oils properties. From petroleum ether extract of *S. anacardium* have been found to possess antitumour properties. Although resinous material could not be further purified, the orange-coloured oil yielded Bhilawanol, a phenolic liquid containing long-chain alkenyl catechols. Qualitative tests, spectral data and preparation of certain derivatives were useful in the identification of Bhilawanol.

The derivatives were mainly prepared since the original oil was found to be unstable due to air oxidation. The extracts were also tested for *in vitro* cytotoxic activity, wherein small amounts of the material are required. Our preliminary studies indicate that *S. anacardium* oil and its acetyl derivatives possessed the most significant growth-inhibitory activity against KB cell line *in vitro*. It has also been observed that the *in vitro* exposure of P388 cells to different concentrations of *S. anacardium* oil and its acetyl derivatives are cytotoxic in nature; while acetyl derivatives inhibit the macromolecule biosynthesis *in vitro*. Hembere et al. have shown that one of the fractions isolated on the basis of cytotoxicity studies on eagle 9 KB tumour cell culture contains a mixture of closely related unsaturated pentadecyl catechols which are cytotoxic. The present investigation on *S. anacardium* has indicated that the resinous material from methanol extract possesses maximum antitumour activity. It is possible that in this instance, the activity results from the blocking of an oxidized group present in the oil.

The experiment has been in progress to prepare more derivatives of the oil and also stabilize and increase the antitumour activity using antioxidant. Since there were no effects on any change in major physiological functions and also antibacterial or antifungal activity was lacking, it could be presumed that the *S. anacardium* oil produces its antitumour effect through a mechanism which is not reflected in acute physiological disturbance.

A review of literature shows that *S. anacardium* nut contains about 30% oil, Bhilawanol, flavonoid compounds, sterols and their glycosides, have been reported in *S. anacardium*. Although the principle of antitumour constituent has not yet been reported, the present findings have given encouraging leads to the investigation on *S. anacardium*.

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