

The biochemical alterations following administration of Kalpaamruthaa and *Semecarpus anacardium* in mammary carcinoma

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Abstract

Background: Breast cancer is one of the most common cancers in women of developed and developing countries. Lipids, lipoproteins and lipid-metabolizing enzymes have been associated with the risk of breast cancer. Kalpaamruthaa (KA) is a modified Siddha preparation, which contains *Semecarpus anacardium* Linn. (SA), *Embllica officinalis* (EO) and honey.

Objective: The present study was embarked to study the variations in lipids, lipid-metabolizing enzymes and lipoproteins in cancerous animals and the effect of KA on the lipid metabolism.

Materials and methods: Breast cancer was induced in rats by administering 7,12-dimethylbenz(a)anthracene orally (25 mg/kg body weight). After 90 days of induction, KA (300 mg/kg body weight) and SA (200 mg/kg body weight) were administered for 14 days, by gastric intubations. The levels of lipids and lipid-metabolizing enzymes were analysed in control and experimental animals.

Results and conclusion: 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. In mammary carcinoma bearing animals, the activities of total lipase, cholesterol ester synthase, and cholesterol ester hydrolase were significantly ($p < 0.05$) increased whereas lipoprotein lipase and lecithin cholesterol-acyl transferase were decreased. The levels of very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) were increased and the level of high-density lipoprotein (HDL) was decreased. These alterations were recouped back upon treatment with KA as well as SA when compared to cancer animals. The effects of KA were found to be more effective than SA. No significant alterations were observed in herbal preparation control animals when compared to control animals.

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1. Introduction

Worldwide, breast cancer is the most common cancer among women after skin cancer, and it is also the second leading cause of cancer death (after lung cancer) in women [1]. The mechanisms of action through

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which the lipids participate in the growth of breast cancer are beginning to be known. Breast tumour cells require lipids as a metabolic fuel. In this respect it has been described that fatty acid synthase, a major enzyme of fatty acid biosynthesis, is produced in primary breast tumours and certain human and murine cancer cell lines. In human tumours its over expression is associated with poor prognosis [2]. Furthermore, genes whose function is to activate final genes of fatty acid synthesis have been found both amplified and expressed in several breast cancer-derived cell lines [3]. Conversely, the pharmacological inhibition of fatty acid synthesis in breast cancer cells with fatty acid synthase over expression caused reduced growth and programmed cell death, an effect that was reversed by addition of fatty acids to the growth media [4].

Peroxidation of lipids in biomembranes and tissues causes the leaking of these lipids into circulation, and consequently leads to hyperlipidemia. The direct relationships between lipid peroxidation and subsequent alteration in lipid metabolism have already been well established [5].

Both benign and malignant proliferation of breast tissue in women has been associated with changes in plasma lipids and lipoprotein levels. Lane et al. [6] reported that prior to diagnostic biopsy, serum lipid and apolipoprotein components of low-density lipoproteins were increased in women with fibrocystic disease and early stage breast cancer but decreased in women with early recurrence.

Various compounds characterized from natural antioxidants, such as vitamins and flavonoids, have been tested for their potential to cure diseases by reducing oxidative stresses. Kalpaamruthaa (KA) is a modified Siddha preparation, which has been formulated in our laboratory. It contains *Semecarpus anacardium* Linn. (SA), *Emblica officinalis* (EO) and honey in different ratio. The components studies of this herbal preparation reveal the presence of flavonoids, ascorbic acid, polyphenols, tannins, sugars, sterols, etc. Dose-dependent study of Kalpaamruthaa was carried out in mammary carcinoma bearing rats, which showed fixed 300 mg/kg body weight as the effective dosage levels [7].

S. anacardium Linn. (Family: *Anacardiaceae*) (SA) is distributed in Sub-Himalayan region, tropical and central parts of India. The nut is commonly called 'marking nut' and in the vernacular as 'Ballataka' or 'Bhilawa' [8]. Due to its wide therapeutic utility and easy availability, the chemistry of *S. anacardium* nut extract was extensively studied. Many pharmacological properties such as antirheumatic [9] and anticancer [10,11] have been

attributed to the nuts of the plant. Phytochemical studies of Siddha preparation of *S. anacardium* nut extract from our laboratory, reported by [12] was found to contain phenols, flavonoids and carbohydrates.

E. officinalis (syn. *Phyllanthus emblica* L.) Eupherbiacase is used therapeutically in Indian system of medicine. Fruits of EO are used for the treatment of a number of diseases like antibacterial [13], anti-inflammatory agent [14] and modify metal-induced clastogenic effects [15].

Researchers now believe that ascorbic acid, a major component of EO prevents cancer [16]. Extensive animal, clinical and epidemiological studies were carried out on the role of ascorbic acid in the prevention of different types of cancers. Vitamin C has an ability to convert cancerous cells to normal ones. There is evidence that vitamin C has beneficial effects on lipid-metabolizing enzymes, as it promotes the activities of lipoprotein lipase [17] and implications are that, Vitamin C inhibits abnormalities.

Flavonoids are members of large chemical groups, polyphenols, which have known preventive activities against degenerative diseases, e.g. cancer and coronary heart disease [18]. Flavonoids are biosynthesized by plants and have strong antioxidant activity such as scavenging free radicals that are involved in cell damage and tumour promotion [19]. The current investigation has been carried out to study the effects of KA and SA on the alterations in the lipid metabolism caused by mammary carcinoma.

2. Materials and methods

2.1. Animals and diet

Female albino Sprague–Dawley rats of Wistar stain, 50–55 days, were obtained from the National Institute of Nutrition, Hyderabad. The animals were housed in spacious hygienic plastic cages in an air-conditioned room controlled for temperature ($27 \pm 1^\circ\text{C}$), humidity ($60 \pm 5\%$) and lighting 12h: light–dark cycle) and they were given food (Gold Mohur rat feed, Hindustan lever Limited, Mumbai, India) and water ad libitum.

2.2. Chemicals

7,12-Dimethylbenz(a)anthracene (DMBA), was obtained from Sigma Chemical Company, St. Louis, USA. Ammonium molybdate, silicic acid, sodium metaperiodate, *p*-nitrophenyl acetate were obtained from Sisco Research Laboratories Pvt. Ltd., Mumbai, India.

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