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Prajakta Jagtap

a) Department of Pharmaceutics,
MCE's Allana College of
Pharmacy, K. B. Hidayatullah
Road, Azam Campus, Camp,
Pune, Maharashtra, India.

b) Department of
Pharmaceutical Sciences,
Jawaharlal Nehru Technological
University, Kukatpally,
Hyderabad, India.

Kiran Bhise

Department of Pharmaceutics,
MCE's Allana College of
Pharmacy, K. B. Hidayatullah
Road, Azam Campus, Camp,
Pune, Maharashtra, India.

Vijayalakshmi Prakya

Department of Pharmaceutics,
Siddhartha Institute of
Pharmacy, Ghatkesar,
Hyderabad, India.

Correspondence:

Prajakta Jagtap

a) Department of Pharmaceutics,
MCE's Allana College of
Pharmacy, K. B. Hidayatullah
Road, Azam Campus, Camp,
Pune, Maharashtra, India.

b) Department of
Pharmaceutical Sciences,
Jawaharlal Nehru Technological
University, Kukatpally,
Hyderabad, India.

A Phytopharmacological Review on *Garcinia indica*

Prajakta Jagtap, Kiran Bhise, Vijayalakshmi Prakya

Abstract

Medicinal plants are gifts of nature to cure limitless number of diseases among human beings. Various plants have been identified to possess medicinal properties in various parts namely, leaves, fruits, seeds, bark and roots. Among them, *Garcinia indica*, a small to moderate sized plant belonging to the Clusiaceae family. It is a traditional home remedy in case of flatulence, heat strokes and infections. Many therapeutic effects of the fruit have been described in traditional medicine based on Ayurveda. These include its usefulness as an infusion, in skin ailments such as rashes caused by allergies; treatment of burns, scalds and chaffed skin; to relieve sunstroke; remedy for dysentery and mucous diarrhoea; an appetizer and a good liver tonic; to improve appetite and to allay thirst; as a cardiogenic and for bleeding, piles, dysentery, tumours and heart disease. This plant is also pharmacologically studied for its anti-oxidative, chelating, free radical scavenging, anticancer, anti-inflammatory, and antiulcer activities. The present review has been primed to describe the existing data on the information on traditional, medicinal uses Pharmaceutical applications and Bioactive constituent present in the kokum fruit that will be helpful to create interest towards *Garcinia indica* and may be useful in developing new formulations with more therapeutic and economical value.

Keywords: Kokum, *Garcinia indica*, anticancer, antimicrobial, antihyperlipidemic

1. Introduction

Garcinia indica (dried rind known as 'kokum'), a tropical fruit, can be viewed as a wonder berry that has a pleasant, tangy-sweet taste and a myriad of health benefits. It is an Indian spice used in many parts of the country for making several vegetarian and non-vegetarian 'curry' preparations like chutneys, pickles and the popular 'solkadhi'. The fruits are steeped in sugar syrup to make 'Amrutkokum', a healthy soft drink to relieve sunstroke, which is popular during summer. Aqueous Kokum extract also has 4% sugar which can be fermented to make excellent quality wine. Kokum seed is a good source of fat called Kokum butter that is used in chocolate and confectionary industry as well as pharmaceutical and cosmetic industry as surfactant Kokum fruit is a potential source of hydroxy citric acid, anthocyanins and a polyisoprenylated benzophenone derivative, garcinol^[1]. Recently, hydroxyl citric acid has been found to be used as a potent metabolic regulator of obesity and lipid abnormalities in mammalian system. Kokum is loaded with B-complex vitamins, and minerals like potassium, manganese and magnesium, that help in controlling heart rate and blood pressure, offering protection against stroke and coronary heart diseases. This versatile fruit has been used to counter digestive problems such as indigestion, flatulence, acidity and constipation. Kokum fruit possess useful antioxidant, chelating, anti-cancer, anti-fungal, anti-inflammatory, anti-bacterial, cardio protective and anti-ulcer activities^[2-3].

2. Geographical distribution

Kokum is a tropical evergreen tree of moderate to large size. It is found at an altitude of about 800 meters from sea level. It is a slender tree with drooping branches. It grows to a height of 15-20m. The canopy is dense with green leaves. It is a native of the Western Ghats region of India. It is distributed throughout Konkan, Goa, North & south Karnataka, North Malabar, Coorg & Wynad as well as in West Bengal and Assam. It is androdioecious tree producing male and bisexual flowers on separate plants^[4].

3. Morphology of plant^[5]

The tree grows up to 10-18 meters with drooping branches. It flowers from November to February with fruits ripening from April to May. After 15 years, a properly cared single plant yields about 30 to 50 kg of fruit. The ripe Kokum fruit is red or dark purple colored containing 3-8 large seeds. The fruit is spherical, 2.5 to 3.0 cm in diameter. Seeds are usually connected to

The rind by tissue and embedded in a red acidic pulp. High content of malic acid and little amounts of tartaric and citric acids give pleasant tart taste to the fruit. At present, India produces 10,200 metric tons of Kokum with productivity of 8.5 tons/ha. Because of the sweetish acidic taste and its typical flavor. Different products like dried ripe Kokum rind (Amsul), Kokum syrup are made from the fruit and rind. The normal shelf life of fresh fruit is about 5 days at room temperature. Kokum fruits have longer shelf life at low temperatures. Traditionally, the fruit rinds are sun dried to reduce water activity and increase shelf-life.

4. Composition of fruit

Garcinia is a rich source of active compounds including garcinol, xanthochymol, isoxanthochymol and Hydroxycitric acid. These are flavonoids, benzophenones, xanthenes, lactones and phenolic acids [6]. The fruits contain citric acid, acetic acid, malic acid, ascorbic acid, hydroxycitric acid and garcinol. The major constituent of Kokum rind is garcinol, a polyisoprenylated benzophenones, isogarcinol and camboginol. Garcim-1, Garcim-2 and cambogin are the chief oxidative products of garcinol, along with isogarcinol, gambogic acid, mangostin, clusianone, macurin, oblongifolin (A, B, C), guttiferone (I, J, K, M, N). Kokum fruit is naturally very acidic with a pH between 1.5 to 2.0. The rind of ripe Kokum fruits consists of hydroxyacetic acid and hydroxycitric acid. It also contains 2.4% pigment as a mixture of two anthocyanins namely, cyanidin-3-sambubioside and cyanidin-3-glucoside in the ratio 4:1. Studies have shown that the fresh rind of Kokum contains 80% moisture, 2% protein, 2.8% tannin, 5% pectin, 14% crude fiber, 4.1% total sugars, 1.4% fat, 2.4% pigment, 22% hydroxycitric acid, 0.06% ascorbic acid⁷. Kokum leaves are reported to contain L-leucine, 75% moisture, protein 2.3g, fat 0.5g, fiber 1.24g, carbohydrates 17.2g, iron 15.14mg, calcium 250mg, ascorbic acid 10mg and oxalic acid 18.10mg per 100g. Hydroxycitric acid lactone and citric acid are present in leaves and rinds in minor quantities¹⁷. Kokum seeds are rich in glycerides of stearic acid (55%), oleic acid (40%), palmitic acid (3%), linoleic acid (1.5%), hydroxyl capric acid (10%) and myristic acid (0.5%). Kokum seed contains about 25% edible fat commonly known as Kokum butter. It is extracted mostly by crushing seeds, boiling them in water and removing fat from top or by churning the seeds in water. Sometimes it is also separated by solvent extraction. It is used as edible fat or adulterant of ghee. Crude Kokum butter is yellowish, while when refined, it is white in colour. Refined Kokum butter is comparable with high quality hydrogenated fats. Free fatty acids are present up to 7.2% of total Kokum butter¹⁸. It is an excellent emollient used by the cosmetic industry for preparations of lotions, creams, lip-balms and soaps. It has relatively high melting point and is considered as one of the most stable exotic butter which does not need any refrigeration.

4.1 Nutraceuticals properties of Kokum

Kokum contains two major active compounds with nutraceuticals properties namely garcinol and hydroxyl citric acid. Both of these compounds are present in the rinds of Kokum. They play beneficial role in human health since they have anti-cancer and anti-obesity properties¹⁹.

4.2 Garcinol

Garcinol is a yellow colored, fat soluble pigment found in the rinds of Kokum at level of 2-3%. In fact all Garcinia species

have some amount of garcinol^[10-12]. Garcinol can be separated from the fruit rinds by ethanol or hexane extraction. Garcinol has been studied for its anti-cancer, anti-ulcer, anti-oxidative and antiglycation activity. The antioxidant activity of Kokum syrup, aqueous and boiled extract has been measured by various techniques such as ORAC, FRAP, ABTS etc. and it is shown that these preparations have very good antioxidant potential due to presence of garcinol and anthocyanins. Garcinol also showed antimicrobial activity against *Staphylococcus aureus* which was comparable to traditional antibiotic Vancomycin. Yoshida and coworkers reported garcinol fortified diet decreases the incidence of tongue neoplasms and pre-neoplasms^[13]. It also induces apoptosis through the activation of caspases and thus works as antitumor agent. There are numerous reported mechanisms through which garcinol acts as antioxidant, anti-inflammatory or anti-cancer agent as explained above.

4.3 Hydroxy citric acid

Hydroxy citric acid (HCA) is a major acid found in Kokum. HCA is also found in other Garcinia species such as *G. cambogia*, *G. atroviridis*^[14]. Kokum can contain up to 23% of HCA on dry basis. The major part is found in leaves and rinds as HCA and some quantity is present as HCA lactone. HCA which is also called as Garcinia acid can be separated from rinds by thermal as well as non thermal methods. HCA has been separated as sodium salt by combination of aqueous NaOH and methanol extraction and then neutralizing with HCl. Acetone is used to obtain pure crystals of HCA. HCA has also been separated by a thermal method in which HCA is extracted with deionized water and then concentrated by membrane distillation with hydrophobic polypropylene membrane. This method being non thermal avoids degradation of HCA and also HCA lactone formation. HCA, in some cases, has been observed to stimulate fatty acid synthesis. HCA inhibits lipogenesis only when cytoplasmic acetyl-CoA is produced by citrate cleavage enzyme otherwise if the alternate source of acetyl-CoA is available, for activate fatty acid synthesis^[15]. Since HCA regulates the ATP-citrate lyase enzyme and thus citrate cleavage reaction it acts as an anti-obesity agent. Due to its regulatory effect it is also known as weight controlling agent. HCA can be used to increase activity of carnitine palmitoyl transferase (CPT 1). CPT 1 is a rate limiting factor in fat burning and thus weight loss.

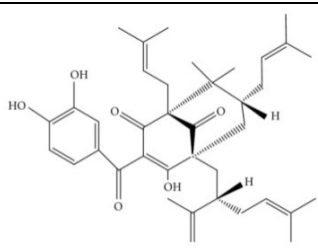
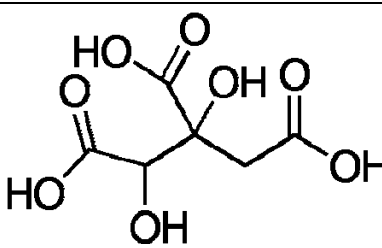
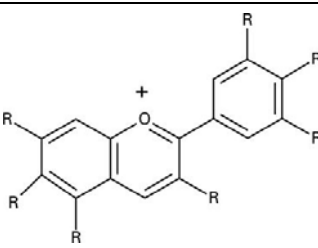
4.4 Anthocyanins

The two major anthocyanin pigments found in Kokum are characterized as cyanidin-3-glucoside and cyanidin-3-sambubioside. They have been identified by thin layer chromatography as well as HPLC, mass and NMR spectroscopy^[16]. Anthocyanins constitute approximately 2.4% of the total fruit biomass. These pigments can scavenge free radicals and are water soluble. They can be extracted from the fruit rind by hydraulic press using 1% acidified water as a solvent^[17]. The monomeric anthocyanins in Kokum can be measured using pH differential method. Anthocyanins have been shown to possess strong antioxidant activity. Given their wide distribution in nature, daily intake of anthocyanins is 25 to 215 mg/person depending upon gender and age^[18]. Anthocyanins prevent ascorbic acid oxidation, scavenge free radicals, show inhibitory effects against oxidative enzymes and reduce the risk of cancer and heart diseases^[19]. The 3' and 4'-OH in B-ring determine radical scavenging capacity with a saturated 2, 3-double bond. Different glycosylation and

hydroxylation positions determine their potential as an antioxidant [20]. With increase in hydroxyl groups in B ring, antioxidant activity increases. Corresponding aglycones have weaker activities. Anthocyanins are better agents against lipid peroxidation than α -tocopherol. They also have scavenging properties against-OH and Oxygen. Bioflavonoids such as

leucoanthocyanidins, catechins, flavonols, along with anthocyanins such as cyanidin-3-glucoside have shown activity to improve permeability and strength of capillaries, to accelerate the ethanol metabolism and to reduce inflammations and edematous reactions [21].

Table 1: Composition of *Garcinia indica* Fruit

Chemical Constituent	Garcinol	Hydroxy citric acid	Anthocyanins
Structure			
Pharmacological properties	Antioxidant, Anti-inflammatory Anti-cancer agent	Antihyperlipidemic	Anti-inflammatory Cardioprotective

5. Pharmacological and biological properties

5.1 Antioxidant and Hepatoprotective activity

Deore *et al.* studied antioxidant and hepatoprotective effect of aqueous and ethanolic extract of *Garcinia indica* Linn fruit rind on carbon tetrachloride (1.5 ml/kg) induced liver toxicity on Wistar albino rats [22]. The degree of liver protection was measured by using biochemical parameters such as aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALKP) and serum bilirubin (SBRN). Whereas antioxidant effect was determined by using biochemical parameters like sulphoxide dismutase (SOD), glutathione (GSH), lipid peroxidation (LPO) and catalase (CAT). Gogoi *et al.* evaluated methanolic fruit rind extract of *Garcinia indica* fruit rind for determination of free radical inhibition property and total phenolic content [23]. Selvi reported the free radical scavenging property of chloroform extract of kokum rind by using DPPH assay and β -carotene linoleate assay. Marketed concentrated syrup, cold and hot aqueous extract of kokum also exhibited free radical scavenging activity [24]. Methanolic extract of kokum fruit showed potent antioxidant activities comparable to standard ascorbic acid [25-26]. Garcinol was found to have superoxide anion scavenging activity in phenazine methosulphate/ NADH nitroblue tetrazolium system [27].

5.2 Anti-neoplastic activity

Garcinia indica fruit rind extract exhibited dose dependent cytotoxic activity by inhibiting cultured Balb/c 3T3 mouse fibroblasts. Previous reports showed that garcinol elicited inhibitory effect on Azoxymethane (AOM) - induced colonic aberrant crypt foci (ACF). Moreover, garcinol also improved liver glutathione-S-transferase and Quinone reductase levels, reflecting hastening of detoxification mechanisms. Garcinol showed significant suppression in 4-NQO induced oral carcinogenesis. It also diminishes tongue carcinoma. Garcinol prevented DNA damage, by scavenging the hydroxyl radical and inhibit carcinogenesis. Furthermore, garcinol and its derivatives, cambogin, garcim-1, and garcim-2 showed potent growth-inhibitory effects on the neoplastic colon cancer cells, as well as in normal immortalized intestinal cells. Antiproliferative effects of garcinol was elicited in HeLa cells, human colorectal cancer cell line, human leukemia HL-60 cells, human breast cancer cells, prostrate and pancreatic cancer cells [28-29]. Isogarcinol and xanthochymol induce

apoptosis through activation of caspase-3 in neoplastic cells. In vivo studies predicted reduction in number of non-malignant and malignant skin tumors per mouse in skin carcinogenesis model by Cyanidin-3-glucoside. Cyanidin-3-glucoside provided protection to Caco-2 colon cancer cells against the peroxy radical (AAPH)-induced oxidative damage and reduce its cytotoxicity [30].

5.3 Antimicrobial and Cytotoxic Effects

Antimicrobial properties of *Garcinia indica* on certain microbes and cytotoxic properties of *Garcinia indica* on Balb/c 3T3 mouse fibroblasts. The minimum inhibitory concentrations of the water extract against bacteria were, 0.5mg/ml in *Escherichia coli*, 5mg/ml in both *Bacillus subtilis* and *Enterobacter aerogenes* and 50mg/ml in *Staphylococcus aureus*. The minimum inhibitory concentrations against fungi were 50mg/ml for both *Candida albicans* and *Penicillium sp.* *Garcinia indica* fruit rind extract showed inhibitory effect on cultured 3T3 mouse fibroblasts. The cell concentration decreased with increasing concentration of the extract [31]. The *Garcinia indica* extract has both antifungal and antibacterial properties.

5.4 Anti-fungal activity

Varalakshmi and coworkers demonstrated antifungal activity of aqueous extract of kokum rind against *Candida albicans* and *penicillium sp* [31]. Chloroform extract of kokum rind inhibited the growth of *Aspergillus flavus* and production of aflatoxin.

5.5 Anti-bacterial activity

Hexane and benzene extracts of the rinds of kokum and its active constituent garcinol possess powerful anti-bacterial activity of its own. It also potentiated the effects of clarithromycin on *H. Pylori* [32]. Even the kokum leaf extract possesses inhibitory activity against pathogenic bacteria *salmonella typhi*, *salmonella paratyphi A* and *Salmonella typhimurium*. Aqueous extract of kokum rind is reported to have highest antibacterial activity against *Bacillus subtilis*, followed by *Escherichia coli*, *Enterobacter aerogenes* and *Staphylococcus aureus*. The phytoconstituents garcinol, isogarcinol and xanthochymol exhibited inhibitory effect on the growth of methicillin resistant *S. Aureus*.

5.6 Anti-inflammatory activity

Kokum rind aqueous and ethanolic extract was investigated for its anti-inflammatory potential, by using carrageenan induced paw edema model. Both the extracts showed powerful reduction in inflammation, in acute study. Moreover, significant reduction in lysosomal enzymes acid phosphate and alkaline phosphate confirms its anti-inflammatory activity^[33].

5.7 Anti-ulcer activity

Deore *et al.* reported the ulcer protective effect of aqueous and ethanolic extract of *Garcinia indica* Linn fruit rind. The aqueous and ethanol extract of *Garcinia indica* Linn were investigated for ulcer protective activity against indomethacin induced ulcerogenesis and HCl/ethanol induced gastric lesion. Oral administration of the aqueous and ethanol extracts of *Garcinia indica* fruit rind at the dose 500 mg/kg provided significant ($p < 0.001$) reduction of ulcer index in the HCl/ethanol and indomethacin induced gastric lesion rat models^[34-35].

5.8 Anti-obesity activity

Darji and his coworkers reported that the methanolic extract of the dried fruit of kokum showed remarkable anti-hyperlipidemic activity in rats, using cholesterol induced hyperlipidemic model. Significant decrease in total cholesterol, triglycerides, LDL-C, VLDL-C levels and increase in HDL-C^[36]. Many studies have shown that intake of hydroxycitric present in kokum reduces appetite, inhibits lipogenesis and reduces body weight. In vitro studies demonstrated increase in adipocytokine secretion and up-regulation of adipocyte specific gene expression without activation of PPAR γ on treatment of rat adipocytes with

cyaniding 3-glucoside. Furthermore, in vivo studies also showed increase in gene expression of adiponectin in the white adipose tissue. Lipase inhibitory property and anti-obesity activity of isogarcinol was also shown^[37].

5.9 Hypoglycemic activity

The whole fruit extract of kokum significantly lowered fasting blood glucose levels in streptozotocin induced hyperglycemic rats in acute as well as chronic study. The acute administration of aqueous extract at 400 mg/kg significantly improved oral glucose tolerance, revealing its anti-hyperglycemic activity. Garcinol purified from *Garcinia indica* rind was reported to have potent glycation inhibiting activity, as it suppresses protein glycation in a bovine serum albumin/fructose system^[38].

5.10 Neuroprotective Effects

Methanolic extract of kokum fruit exhibited significant neuroprotective potential against 6-OHDA, indicating its antiparkinson's activity in rats. Garcinol also reduced the expression of LPS induced anti-inflammatory mediators. iNOS and COX-2 and prevented nitric oxide accumulation in LPS-treated astrocytes^[39]. It was also found to have anticholinesterase property. Cyanidin-3-glucoside prevent the neurite outgrowth and the expression of neurofilament proteins demonstrating its neuroprotective potential.

5.11 Antiageing activity

Kokum pigments are useful in skin disorders for skin care due to its UV light absorbing properties. Kokum exhibits anti hyaluronidase and anti elastase activities which favours skin care^[40].

Table 2: Traditional uses of Kokum

Traditional uses of kokum	Plant Parts involved
Digestive	Fruit
Anti-dysentery	Fruit, Rind and leaves
Antacid	Kokum Rind and leaves
Anti-diarrheal	Fruit, Rind and leaves
Anti-piles	Fruit, Rind and leaves
Anti-ulcer	Rind
Anti-colic	Rind and leaves
Anti-obesity (Fruit)	Fruit
Anthelmintic	Fruit
Anti-asthmatic	Fruit
Cardiotonic	Fruit
Hepatoprotective	Fruit
Anti-tumor	Fruit
Anti-hyperplasia	Leaves
Wound healing	Kokum butter
Analgesic	Rind, Fruit
Anti-inflammatory	Rind
Anti-dermatitis	Rind
Anti-perspirant	Rind
Astringent	Leaves, fruits and roots
Demulcent	Kokum butter

6. Conclusion

The backbone of Indian traditional system of medication is herbal source, Ayurveda the oldest traditional medicinal system that is based on plant medicines and treatments. *Garcinia indica*, commonly known as Kokum belonging to the Clusiaceae family, is a tropical fruit native to India. It does not require irrigation, spraying or fertilizers. The *Garcinia indica* tree's major health benefits are derived from the fruit which is rich in polyisoprenylated benzophenone derivatives such as

Garcinol a yellow, fat soluble pigment and isogarcinol its colourless isomer. Garcinol possess anti-oxidative, chelating, free radical scavenging, anticancer, anti-inflammatory, and antiulcer activities. Hydroxycitric acid (HCA), a water soluble constituent that possess appetite suppressant effect and antihyperlipidemic activity. The fruit also contains other compounds including hydroxycitric acid lactones, citric acid and oxalic acid. Malic acid, polyphenols, carbohydrates, anthocyanin, pigments and ascorbic acid. Kokum seed butter

has nongreasy moisterising properties that are being used in many cosmetics, creams, conditioners, and soaps. Kokum tel is used as foot massage. It is an Indian spice used in many parts of the country for making several vegetarian and non-vegetarian 'curry' preparations like chutneys, pickles and the popular 'solkadhi'. The fruits are steeped in sugar syrup to make 'Amrutkokum', a healthy soft drink to relieve sunstroke, which is popular during summer. Kokum is loaded with B complex, vitamins and minerals which help to control heart rate and blood pressure. This is versatile golden fruit has long been used to combat digestive problems such as indigestion, flatulence, acidity and constipation. The detailed plant information and its uses could help to lead the discovery of various new plant based drugs and treatment of various disorders and diseases.

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