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## ***Vrikshamla (Garcinia indica Choisy): Ethnobotanical Significance And Pharmacological Insights.***

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### **ABSTRACT**

A fruit tree with culinary, medicinal, and nutraceutical uses is kokum. Kokum has been used for many years in Ayurvedic medicine to treat ear infections, digestive issues, dermatitis, diarrhea, dysentery, and wounds. The rind fruit, fruit, and seeds oil of this plant has been found to have several pharmacological properties including anti-inflammatory, anti-microbial activity, anti-helminthic activity, anti-oxidative activity, cardioprotective activity, anti-ulcer activity, anti-depressant, and anti-anxiolytic activity, etc. This review article aims to provide an overview of the current scientific evidence on the efficacy and safety of *garcinia indica*. The article summarizes the available data on the phytochemical study, kokum butter extraction, traditional uses, traditional products, and its potential pharmacological actions. In addition, the article provides a comprehensive analysis of the current studies on *garcinia indica* and their results. The article concludes with a discussion of the future directions for research on *garcinia indica* and its potential as a safe and effective therapeutic agent.

**Keywords:** *Vrikshamla*, *Garcinia indica*, Kokum butter, Traditional uses

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## INTRODUCTION

*Garcinia indica* Choisy, also known as *G. purpurea* Roxb. and *Brindonia indica* Dupetit-Th., belongs to the Clusiaceae family and is widely recognized as *Vrikshamla*, a prominent herbal medicine in classical Ayurvedic texts. The species was first described by Dr. Garcia in 1574, which is why the genus is named *Garcinia* and the species is termed *indica*, as it is native to India. The term *purpurea*, derived from the Latin word "purpura," means purple, reflecting the color of its ripe fruit.[1,2] The family Clusiaceae includes the *Garcinia* genus, which has around 50 genera and 600 species.[3] In which the most well-known species in the genus *Garcinia* is *Garcinia mangostana*, also referred to as mangosteen and also known as the "queen of tropical fruits" due to its distinct, delicious flavor and crown-like appearance. The fruit's seeds and pericarps have long been used in the area's traditional medical practices, and drinks made with mangosteen pulp and pericarps are marketed as dietary supplements all over the world.[4] *Garcinia* is known by several names, including *sap trees*, *kokum*, *garcinias mangosteens*, and *monkey fruits*, they are native to Asia to Africa. In addition to being ornamental, *garcinia* plants have industrial pharmaceuticals, medicinal, and culinary uses.[5] *Garcinia indica* Choisy is an under-exploited fruit species that is high in anthocyanins.[6] In India, it is popularly known as *puranpulli*, *murgal*, *Ansil*, *bhirand*, or *kokum*. Although it is currently found growing in other parts of peninsular India, it is primarily found in the western peninsular coastal regions and the adjacent western ghats in the states of Maharashtra, Goa, Karnataka, and Kerala, as well as parts of Eastern India in the state of West Bengal, Assam, and North Eastern hill region. [7,8]

Indians found this beautiful ornamental fruit tree in Mumbai thousands of years ago, and they used it for many different purposes. For these people, kokum has always been essential, and it has long been employed in Ayurvedic therapy.[9] The dried fruits add a unique flavor and aroma to sambar and non-vegetarian curries, especially those made with fish, and are a great alternative to tamarind and lime. In Goa and Karnataka, it is used to prepare syrup during the summer months. [10,11]

Despite its amazing nutritional and therapeutic qualities, kokum is typically not grown on an orchard scale as systematically as cashew nuts, mangos, and other fruits. It is typically found as a wayside plant or in forests, as a mixed crop in coconut and areca nut plantations, or as a kitchen garden plant. Since they are not planted as orchards, there are few studies on the precise statistical data about kokum cultivation area, production, and productivity. According to a 2010 survey, there were around 1000 hectares of kokum in the Konkan region, with an annual fruit production of 4500 MT. According to a previous survey by the chief forest conservator, there were 46,600 kokum trees in Maharashtra overall, with roughly 43,000 of those trees located in the districts of Ratnagiri and Sindhudurg.[12]

The oldest known kind of medical treatment is the use of medicinal plants as medicine, which has been practiced in all communities throughout history. Through the investigation of numerous biologically active natural products, this indigenous knowledge which has been passed down from generation to generation in various parts of the world has greatly aided in the development of traditional medical systems and provided a scientific basis for their traditional uses.[13]

**Table 1: Description Of Plant Kingdom**

Kingdom	Plantae
Subkingdom	Viridiaeplantae
Division	Magnoliophyta
Subdivision	Angiospermeae
Class	Magnoliopsida
Subclass	Dilleniidae
Order	Malpighiales
Family	Clusiaceae
Subfamily	Garcinieae
Tribe	Garcinia
Genus	Garcinieae
Species	<i>Garcinia indica</i> Choisy

### Geographical Distribution Of *Garcinia Indica*

The kokum tree is a moderately large tropical evergreen. It is located at 800 meters above sea level. The tree is slender and its branches are drooping. It can grow up to 15–20 meters in height. Green leaves are abundant under the canopy. It is indigenous to India's Western Ghats. It is spread in the Konkan, Goa, North and South Karnataka, North Malabar, Coorg and Wynad, West Bengal, and Assam. This Androdioecious tree produces flowers on distinct plants that are male and bisexual.[16]

### Morphology Of *Garcinia Indica* Plant



**Figure 1: *Garcinia indica* tree**

Flower - Flowers are polygamous.[14] These are pale yellow in color, borne either singly or in clusters. The flowers may be fascicled and umbelled. Flowers usually have 4 to 5 sepals, which form the outer layer of the unopened flower bud. Four to five imbricate petals are generally present.

- a) In the male flowers, the stamens exist either free or joined to form a ring or lobular mass that surrounds a rudimentary ovary.
- b) In the female flowers, the staminodes are free or joined together. The female flower has a largely conspicuous but varied stigma, which is sub-sessile. The trees flower annually in the month of November to February.

Fruit -Fruits, commonly known as kokum fruits, are globose and resemble a small apple in size, not furrowed/grooved.[15] Yellow-marbled and brownish-gray in color, the fruit is crowned by a stigma that is 4-parted and stalkless. The pulp is juicy, white, and has a wonderful taste and odor. It contains six to eight seeds. It is around orange in size. The berry, which is protected by a hard rind, rests on the calyx. Hundreds of fruits are produced by an average Kokam tree every summer. Their color changes to green when they are tender. Beautiful purple is the color that is reached upon maturation.[15]



**Figure 2: *Garcinia indica* fruit**

The two primary varieties of kokum are red and yellow, and they are primarily found in Uttara Kannada district's Western Ghat central region. While yellow kokum is a distinct variety and is typically referred to as "*bilimurughi*" (white kokum by native people), red kokum is the most frequent type.[16]

Leaves -*Garcinia* species have thick, oppositely oriented leaves that are shiny on both the upper and lower surfaces. Mature leaves are dark green, whereas juvenile leaves are light to dark brownish red. Typically, the leaves are oblong, rounded, lanceolate, sharp sharply acuminate, and constricted at the base. [17,18] Petiole is up to 0.7 cm long. [15]

Seeds- The seed is about one-fourth of the total weight of the fruit. Seeds contain about 23-26% oil, which remains solid at room temperature and is known as Kokum butter.[16]

**Kokum Butter Extraction**

Tribal people gather the kokum fruit that is harvested from the trees by producers or collectors. Cutting fruit by hand or using a kokum cutter separates the fruit's rind, pulp, and seeds. The kernels are then treated using one of the two different traditional methods. There are numerous ways to extract the seed, including boiling, cold extraction (which involves churning the crushed seeds with water), or simple extraction. The seed contains roughly 32–35% fat. Traditionally, dried kokum kernels are used to make kokum butter, which is then sold domestically or in villages in local market places. Traditionally, "unrefined kokum butter" refers to kokum butter that is extracted using the conventional method without a refining step.[19]

**Traditional Uses Of *Garcinia Indica***

Kokum is traditionally used in herbal remedies to treat rheumatic pains, dermatitis, digestive issues, diarrhea, and inflammatory diseases, and to stop excessive perspiration. The rind's kokum juice is used to treat diarrhea, piles, colic, and dysentery. Fruit rind decoction has been used historically to treat diabetes. Kokum fat is used in the making of confections. They use it to make candles, ointments, and soaps. Kokum fruit extracts reduce gastric issues such as indigestion, constipation, acidity, and flatulence. Additionally, it has anti-helminthic qualities and also acts as a stimulant for cravings. Infusions of kokum are used in Ayurvedic medicine to treat infections, piles, and diarrhea. Kokum strengthens the cardiovascular system and stabilizes liver function.[20]

**Table 2: Traditional uses of *Garcinia indica***

Plant part used	Traditional uses
Fruit	Digestive
	Anti-obesity
	Anthelmintic
	Anti-asthmatic
	Cardiotonic
	Hepatoprotective
	Anti-tumor
Fruit, rind, and leaves	Anti-dysentery
	Anti-diarrheal
	Anti-piles
Kokum butter	Wound healing
	Demulcent
Kokum, rind, and leaves	Antacid
Leaves	Anti-hyperplasia
Leaves, fruit, and roots	Astringent
Rind	Anti-ulcer
	Anti-inflammatory
	Anti-dermatitis
	Antiperspirant
Rind and leaves	Anti-colic
Rind and fruit	analgesic

### Phytochemical Properties Of *Garcinia Indica*

The traditional classification of phytochemicals into primary and secondary metabolites is based on how they function in plant metabolism. The common sugars, amino acids, proteins, purines, and pyrimidines of nucleic acids, and chlorophylls are examples of primary metabolites. Secondary metabolites are the residual plant compounds, which include alkaloids, terpenes, flavonoids, lignans, plant steroids, curcumines, saponins, phenolics, and glucosides.[24]

Garcinol, xanthochymol, isoxanthochymol, and hydroxycitric acid are among the many active ingredients found in garcinia. These include phenolic acids, lactones, xanthenes, benzophenones, and flavonoids. Citric acid, acetic acid, malic acid, ascorbic acid, hydroxy citric acid, and gallic acid are all present in the fruits. The main components of Kokum rind are camboginol, isogarcinol, and garcinol, which are polyisoprenylated benzophenones. In addition to isogarcinol, gambogic acid, mangostin, clusianone, macurin, oblongifolin (A, B, C), and guttiferone (I, J, K, M, N), the main oxidative products of garcinol include garcim-1, garcim-2, and cambogin. Ripe Kokum fruits contain hydroxy acetic and hydroxy citric acids in their rind.[21]

**Table 3: Active constituents of different parts of *Garcinia indica*** (Ananthakrishnan & Rameshkumar, 2016) [22]

<b>Leaves</b>	D-Leucine isogarcinol, xanthochymol, isoxanthochymol, HCA and HCA lactone, Cambogic acid, mangostin, garcinol, fukugicide, GB-1, GB-2, and amentoflavone
<b>Fruit and fruit rinds</b>	i HCA, HCA lactone JGarcinol, isogarcinol, citric acid, oxalic acid, xanthochymol, isoxanthochymol, anthocyanin, glucose, xylose, cyanidin-3-glucoside, cyanidin-3-sambubioside, and deoxyisogarcinol.
<b>Bark</b>	Euxanthone (1,7-dihydroxy xanthone), volkensiflavone, and morelloflavone Xanthochymol, isoxanthochymol, and camboginol
<b>Seed</b>	Isoxanthochymol, camboginol, palmitic acid, stearic acid, oleic acid, and linoleic acid

**Table 4: Traditional Products Of Kokum And Their Application [23]**

S. no.	Products	Preparation and uses
1.	<b>Kokum butter (Bhirndel tel)</b>	The black outer shells and the white interior seeds were removed from the seeds after they had been sun-dried, diced, and ground into a fine paste. To extract the butter, they are then boiled and dried. One specific remedy for diarrhea and dysentery is kokum butter. In addition, kokum butter is preferred over cocoa as a potent skin moisturizer.
2.	<b>Kokum syrup (Amrit kokum)</b>	Cane sugar is added 1:2 to fresh, ripe kokum rind to make this product. After being packaged in a glass container, the mixture should ideally be left in the sun for eight days while being constantly stirred. After that, the mixture is placed in a jar after being drained through muslin fabric. If necessary, an additional preservative, such as sodium benzoate, is added. Before consuming, this substance must be diluted five to six times with water.
3.	<b>Kokum agal (salted juice)</b>	A salty fruit juice made from Kokum. Along with the four levels of varying pulp concentrations, salt was added. that is, (14,16,18, & 20%). Then, for seven days, the mixture was mixed every day. Following seven days, the entire mixture was filtered using a 1 mm stainless steel sieve, and the juice was then transferred into pasteurized bottles.
4.	<b>Kokum fruit bar</b>	After boiling the kokum pulp, it is dried and combined with additional ingredients and a suitable amount of sugar to make a fruit bar.
5.	<b>Sol kadi (Sol curry)</b>	Fresh kokum fruit is used in its preparation, along with fresh coconut milk, salt, sugar, and spices added in different amounts. The combination is then dried in a tray dryer.
6.	<b>Kokum wine</b>	Commercial baker's yeast is added to the traditional process used in Goa to produce kokum wine. About 4% of the red kokum juice has sugar, which causes it to ferment to produce kokum wine.

7.	<b>Kokum RTS beverage</b>	The clear juice from kokum pulp was used to make this, along with the addition of enough sugar that was developed through pasteurization and cooling.
8.	<b>Kokum rind powder</b>	First, the kokum rind was ground after being dried at a specific temperature in a tray dryer. Additionally, to obtain uniform particle size, the ground product is sieved in a sieve. This powder can be used as an ingredient in various mixtures, such as Sarbat and Solkadhi, or as a raw material for various curry dishes.
9.	<b>Cosmetic application of kokum</b>	Due to its emollient qualities, kokum is used as a natural moisturizer to keep skin smooth and supple. It's beneficial for treating extremely dry skin as well as ulceration and fissures of lips, hands, feet, etc.

### Substitutes And Adulterants

In south India *Garcinia cambogia* (Gaertn.) Desr. is used as *Vrikshamla*. [24]

### Pharmacological Activity

#### Antihyperlipidemic activity

Methanolic Extract of *Garcinia indica* was used to evaluate the antioxidant and antihyperlipidemic activity using the cholesterol-induced hyperlipidemic model in Albino Wistar rats. In comparison to lovastatin, it showed a significant decrease in total cholesterol, triglycerides, LDL-C, VLDL-C, and a rise in HDL-C. Additionally, there was a considerable decrease in the LDL-C: HDL-C ratio and the Atherogenic index. The polyphenols present in *Garcinia*, such as garcinol and hydroxy citric acid, may have significant antioxidant and antihyperlipidemic effects. [25]

The anti-dyslipidemic effects of *Garcinia indica* fruit juice were evaluated in the cafeteria diet-fed obese rat model. Body weight decreased after four weeks of *G. indica* fruit juice treatment, and metabolic parameters such as glucose sensitivity, dyslipidemia, insulin and leptin levels, and lipid metabolizing levels improved without producing toxicity. Oral dosage of *G. indica* fruit juice for 4 weeks exhibits anti-obesity potential in cafeteria diet-fed dyslipidemic rats. [26]

In experimental animals fed a modified high-fat diet, Garcinol Enriched Fraction demonstrated a dose-dependent improvement in hyperlipidemia, a risk factor for atherosclerosis, as well as a modification of the underlying pathogenic mechanisms, including oxidative stress and inflammation. [27]

#### Hypoglycemic activity

A variety of fruit rind extracts of *Garcinia indica*, including acetone, alcohol, and aqueous, were prepared and evaluated for their ability to lower blood sugar levels in alloxan-induced rats. Alcoholic extract demonstrated an anti-diabetic effect that was comparable to that of the common standard drug glibenclamide. [28]

*Garcinia indica* aqueous extract was administered orally to streptozotocin-induced type 2 diabetic rats for four weeks at doses of 100 and 200 mg/kg. In mice with type 2 diabetes, an aqueous extract of *G. indica* markedly reduced blood glucose levels in fasting and postprandial. [29]

In Streptozotocin STZ-induced hyperglycaemic rats, the aqueous extract of *Garcinia indica* whole fruit at a dose of 400 mg/kg twice daily demonstrated considerable hypoglycemic effect, whereas treatment with methanol and chloroform extracts did not cause significantly lower blood sugar levels. [30]

*Garcinia indica* exhibits significant hypolipidemic and hypoglycemic activity of methanolic extract of seeds of *Garcinia indica* on blood glucose levels in Streptozotocin-induced diabetic albino rats. The extract alone and in combination with glibenclamide showed significant hypoglycemic activity in comparison to the diabetic control group. [31]

### **Cardioprotective activity**

The ethanolic extract of *Garcinia indica* at a dose of 250mg/kg b.w., 500mg/kg b.w. for 30 days produced significant protective activities in group III and IV rats when compared to isoprenaline hydrochloride-induced rats (group II). In a dose-dependent manner, *Garcinia indica* fruit extract exerts equipotent cardioprotective activity in the experimental model of isoprenaline hydrochloride-induced myocardial necrosis in rats.[32]

*Garcinia indica* fruit rind (GIE) hydroalcoholic extract's cardioprotective and antioxidant properties in rats with isoproterenol (ISO)-induced cardiac necrosis. To cause myocardial damage, at dose levels of 400 and 800 mg/kg, po daily for 30 days, and ISO (85 mg/kg, sc) in the final two days at 24-hour intervals. GIE oral treatment for ISO-challenged rats increases the rat heart's natural antioxidants, improves free radical scavenging, and prevents membrane lipid peroxidation, protecting the myocardial from ISO's harmful effects.[33]

The cardioprotective effect of *Garcinia indica* Linn. fruit rind aqueous extract was assessed in Wistar albino rats that had myocardial infarction caused by isoprenaline. Administration of *G. indica* in both the doses 250mg/kg and 500mg/kg did not significantly recover the altered electrocardiogram, cardiac injury markers, oxidative stress markers, and histopathological myocardial damage as compared to the disease control group.[34]

In another study, high-dose garcinol treatment (100 mg/kg) reduced the mRNA and protein levels of pro-apoptotic markers (cleaved caspase-3, caspase-3, and Bax) while increasing levels of the anti-apoptotic marker Bcl-2. This indicates that garcinol effectively prevents apoptosis in rats with isoproterenol-induced heart failure and in cardiac H9C2 cells.[35]

### **Anti-microbial activity**

*Garcinia indica* fruit rind extract demonstrated an inhibitory effect on cultured 3T3 mouse fibroblasts; the cell concentration decreased with increasing extract concentration. The extract's cytotoxic and antifungal qualities were demonstrated by its cytotoxic effects on Balb/c 3T3 mouse fibroblasts and its minimum inhibitory concentrations against bacteria were 0.5 mg/ml in *Escherichia coli*, 5 mg/ml in *Bacillus subtilis* and *Enterobacter aerogenes*, and 50 mg/ml in *Staphylococcus aureus* and against fungi were 50mg/ml for both *Candida albicans* and *Penicillium sp.* The *G. indica* extract shows both antifungal and antibacterial properties.[36]

The four dried kokum extracts (50 µl volume)—water, ethanol, methanol, and acetone extract—were used against *Salmonella typhimurium*, *Bacillus megaterium*, *Micrococcus aureus*, *Micrococcus luteus*, *Escherichia coli*, and *Pseudomonas aeruginosa* to investigate the antimicrobial properties. As the volume of extracts increases, the antimicrobial activity of all kokum extracts against gram-positive organisms increases. Significant zones of inhibition against gram-negative organisms were demonstrated by water and ethanolic extracts. While *Salmonella typhimurium* and *Escherichia coli* were not suppressed in methanolic extract, *Pseudomonas aeruginosa* displayed the same outcome. Gram-negative bacteria are not inhibited by kokum acetone extract. The main cause of the antimicrobial action in kokum extract is the presence of furfural.[37]

### **Parkinson's disease**

*Garcinia indica* methanolic extract (GIM) was found to be effective in preventing 6-hydroxydopamine (6-OHDA) neurotoxicity in rat striatal dopaminergic neurons. The extract was tested using various behaviour and biochemical assays, showing a significant preventative impact on dopamine and its metabolites.[38]

### **Anti-bacterial activity**

The antibacterial activity of polyphenols isolated from the ethyl acetate soluble methanol extract of stem bark of *Garcinia indica* against *Staphylococcus aureus*, *Salmonella typhi*, and *Escherichia coli* by paper disc method. Flavononyl flavone exhibited no activity against *E. coli*, even at greater concentrations, but it did exhibit good antibacterial activity against *S. aureus* at higher concentrations, moderate

antibacterial activity against lower concentrations, and moderate antibacterial activity against *S. typhi* at higher concentrations. With proanthocyanin *S. Aureus*, *S. Typhi* and *E. coli* showed good antibacterial activity at higher concentrations only.[39]

The biogenic synthesis of AgNPs using Kokum fruit extract was optimized and tested against various bacteria. The optimal parameters included 1.5 mM AgNO<sub>3</sub>, a 1:1 ratio, pH 10, and incubation at 37°C for 24 hours. The biogenic AgNPs demonstrated antibacterial activity against four of the seven tested bacteria and strong antioxidant properties, including reducing power, hydrogen peroxide, DPPH, and NO radical scavenging.[40]

Both alcoholic and aqueous extracts of Kokum demonstrated significant antibacterial activity against *Clostridium difficile* using the disc diffusion method. All tested isolates, including both toxigenic and non-toxic strains, were sensitive to these extracts. The minimum inhibitory concentration (MIC) of the Kokum extracts ranged from 2.5 µl/ml to 10 µl/ml. [41]

### Antioxidant activity

The micellar linoleic acid peroxidation system showed that garcinol has moderate antioxidative activity and nearly the same amount of chelating action as citrate. In aqueous ethanol solution, it also demonstrated about three times the DPPH (1,1-diphenyl-2-picrylhydrazyl) free radical scavenging activity by weight compared to dl- $\alpha$ -tocopherol. Garcinol inhibited protein glycation in a bovine serum albumin/fructose system and showed superoxide anion scavenging action in a phenazine methosulfate/NADH-nitroblue tetrazolium system.[42]

Using peanut powder as a model food system, the ability of a concentrated and vacuum-dried chloroform extract of *Garcinia indica* rinds to suppress the generation of aflatoxin B1 and *Aspergillus flavus* was examined. Using b-carotene-linoleate and 1,1-diphenyl-2-picryl hydrazyl (DPPH) model systems, the antioxidant activity (AA) of *G. indica* extract was assessed. At 50 ppm concentration, b-carotene-linoleate and DPPH model systems demonstrated 53% and 78% Antioxidant Activity, respectively.[43]

In addition to the commercial kokum syrup, this study investigated the antioxidant activity of boiling and aqueous extracts about their application in home remedies and cooking. In this test, kokum syrup and the two aqueous extracts demonstrated significant antioxidant properties.[44]

The antioxidant activities of *Garcinia indica* extract were investigated in vitro at different concentrations (10, 25, 50, and 100 µg/ml). The DPPH assay, reducing power ability, hydrogen peroxide scavenging assay, and hydroxyl radical (OH $\cdot$ ) scavenging activity were used to measure antioxidant activity. *Garcinia indica*'s ethanolic fruit extract showed dose-dependent antioxidant capacity, peaking at 100 µg/ml.[45]

According to the DPPH, total antioxidant activity, and FRAP assays, *Garcinia indica* resin extracts in both acetone and methanol demonstrated excellent antioxidant activity.[46]

### Anti-helminthic activity

Petroleum ether, ethyl acetate, methanol, and water were used as solvents to extract various *Garcinia indica* fruit extracts at concentrations of 25 and 50 mg ml<sup>-1</sup>. The results were compared to albendazole as a standard reference and normal saline as a control. At a concentration of 50 mg ml<sup>-1</sup>, the methanolic extract of *Garcinia indica* demonstrated dose-dependent anthelmintic action, exhibiting the shortest time for paralysis and death.[47]

The Indian earthworm *Pheretima posthuman* was used in this study to test the in vitro anthelmintic and antibacterial properties of extracts from the leaves and fruits of *Garcinia indica* (Dupetit-Thouars) Choisy and *Garcinia cambogia* (Gaertn.) Desr. At concentrations (25 and 50 mg/mL) of different extracts, including petroleum ether, chloroform, ethyl acetate, methanol, and water. The standard reference was albendazole at concentrations of 25 and 50 mg/mL. The fruits and leaves of *Garcinia cambogia* and *Garcinia indica* showed significant anthelmintic effects, and the findings were reported in terms of Earthworm paralysis and death demonstrated by all extracts in a dose-dependent manner.[48]

### **Anti-oxidant and hepatoprotective effect**

The aqueous extract of *Garcinia indica* (GI) fruit rind was studied for its hepatoprotective effects against acetaminophen (AAP)-induced acute liver damage in Wistar rats. AAP administration (750 mg/kg body weight) significantly increased biochemical markers such as SGOT, SGPT, ALP, ACP, and bilirubin levels, indicating liver damage. Pretreatment with the aqueous extract of GI fruit rind (AEGF) at doses of 250 mg/kg and 450 mg/kg significantly reduced these elevated levels, demonstrating a dose-dependent hepatoprotective effect.[49]

The antioxidant and hepatoprotective properties of *Garcinia indica* Linn's aqueous and ethanolic extracts were investigated regarding the liver damage caused by carbon tetrachloride (1.5 ml/kg) in Wistar albino rats. At a dosage level of 500 mg/kg, aqueous and ethanolic extracts exhibit strong hepatoprotective and antioxidant properties. The aqueous extract's effects were equivalent to those of silymarin, a common medication.[50]

Rats treated with carbon tetrachloride (CCl<sub>4</sub>) for seven days were given aqueous extracts of the fruit rind of *Garcinia indica* (GIE) at doses of 400 mg/kg, 800 mg/kg, and the reference drug silymarin (100 mg/kg) orally for ten days. By reducing the CCl<sub>4</sub>-depleted levels of reduced glutathione, superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase in the liver and lowering the CCl<sub>4</sub>-elevated levels of serum marker enzymes (aspartate aminotransferase and alanine aminotransferase) and malondialdehyde, GIE and silymarin produced notable hepatoprotective effects. GIE 800 mg/kg showed greater hepatoprotection than GIE 400 mg/kg.[51]

In this study, the protective effects of aqueous extracts of the fruit rind of *Garcinia indica* (GIE) on ethanol-induced hepatotoxicity were investigated in rats. The reference drugs silymarin (200 mg/kg) and GIE (400 and 800 mg/kg) were given orally to ethanol-treated rats for 28 days. GIE and silymarin demonstrated strong hepatoprotective efficacy. Compared to GIE 400 mg/kg, GIE 800 mg/kg showed more hepatoprotection.[52]

Rats were given the reference medication Liv.52 (500 mg/kg) orally for 29 days to examine the protective effects of aqueous extracts of the fruit rind of *Garcinia indica* (GIE) against antitubercular drug (ATD)-induced liver injury at dose levels of 400 mg/kg and 800 mg/kg. GIE restored the ATD-depleted levels of glutathione (GSH), superoxide dismutase, catalase, GSH peroxidase, and GSH reductase while also considerably reducing the ATD-elevated levels of aspartate aminotransferase, alanine transaminase, alkaline phosphatase, bilirubin, and malondialdehyde. GIE's antioxidant activity may be the cause of its hepatoprotective impact on oxidative damage caused by ATD.[53]

### **Anti-proliferative activity**

ZnO nanoparticles were prepared using the fruit rind extract of a *Garcinia indica* plant and the aqueous seed extract of an *Origanum marjorana* plant. With an emphasis on colon cancer, the produced nanoparticles' antimicrobial activities on bacterial pathogens and their antiproliferative effects on the HCT 116 cancer cell line were assessed on *B. cereus* and *S. typhi*, two gram-positive and gram-negative bacteria, were used. For *S. typhi* and *B. cereus*, the OM-ZnO MICs were 2 µg/mL and 2 µg/mL, respectively. 4 µg/mL for *S. typhi* and 4 µg/mL for *B. cereus* were noted for GI-ZnO. On the investigated cell lines, ZnO nanoparticles demonstrated strong antiproliferative effects and efficiently caused apoptosis and cell cycle arrest at the G<sub>2</sub>/M phase. Using plant extracts, this study effectively illustrates the synthesis of ZnO nanoparticles, emphasizing its antibacterial and antiproliferative properties.[54]

### **Anti-tumour activity**

The potential anti-tumor effects of garcinol on oral squamous cell carcinoma (OSCC) cells, using three OSCC cell lines: SCC-4, SCC-9, and SCC-25. Garcinol treatment (48 hours) significantly inhibited cell growth, proliferation, and clonogenic survival. It also induced apoptosis and caused cell cycle arrest, as assessed by MTT, clonogenic assay, propidium iodide staining, and annexin-V binding assay. Western blot analysis revealed a significant reduction in the expression of NF-κB and COX-2, while VEGF (vascular endothelial growth factor) expression was inhibited, as determined by ELISA. Garcinol showed no toxic effects on normal cells, suggesting its selective anti-tumor potential against OSCC cells by targeting key molecular pathways.[55]

### **Breast carcinoma**

The phytochemicals found in *Garcinia*, such as  $\alpha$ -mangostin, cambogin, gambogic acid [GA], garcinol, griffipavixanthone, friedolanostane triterpenoid, hexane, neobractatin, 7-Epiclusianone, xanthochymol - guttiferone E, and isoxanthochymol - cycloxanthochymol, have anticancer effects that include metastasis, apoptosis, and inhibition of proliferation.[56]

### **Human renal carcinoma**

The MTT assay was used to study the effects of aqueous leaf extracts of *Garcinia cambogia* (GC) and *Garcinia indica* (GI) on human embryonic kidney cells (HEK-293) and human renal cancer cells (A498), and the selectivity index was calculated. Compared to alkaloids and saponins, GI extract showed a higher phenolic content, but GC extract had a larger flavonoid concentration. According to the test, both plant extracts had greater antioxidant capabilities. In vitro, GC and GI leaf extracts were selectively cytotoxic to (A498) human renal carcinoma cells. Kidney cancer can be safely treated at 500  $\mu$ M for GC extract and 300  $\mu$ M for GI extract; normal renal cells did not show any discernible effects.[57]

### **Gall bladder cell carcinoma**

By downregulating mRNA levels, garcinol therapy reduced the activity of matrix metalloproteinase 2 (MMP2) and MMP9, two enzymes essential for tumor invasion. In GBC-SD cells, garcinol treatment also reduced Stat3 and Akt activity. Both the invasion of GBC-SD cells and the proliferation of GBC cells were greatly reduced by garcinol in a dose-dependent and time-dependent manner.[58]

### **Anti-inflammatory activity**

In this study, rats with carrageenan-induced paw edema were given 200 and 400 mg/kg p.o. Single doses of both aqueous and ethanolic extracts exhibited strong anti-inflammatory properties. They also significantly lower serum enzyme levels of ACP and ALP. The group treated with 200 mg/kg of aspirin showed comparable outcomes.[59]

Wistar rats with cotton pellet-induced granuloma and paw edema caused by carrageenan were used to test the anti-inflammatory properties of *Garcinia indica* fruit rind aqueous extract (GIE). To induce edema, Wistar rats were given GIE (400 mg/kg and 800 mg/kg) and the common medication diclofenac sodium (10 mg/kg) orally 60 minutes before receiving a subcutaneous injection of carrageenan (0.1 ml of 1% w/v) into their right hind paws. Comparing GIE-treated animals to those treated with carrageenan and those implanted with cotton pellets, respectively, revealed a significant decrease in paw edema and cotton pellet granuloma.[60]

The effectiveness of GEF against Complete Freund's Adjuvant (CFA)-induced arthritis in Wistar albino rats was assessed at a dose of 10 mg/kg. From the fifth to the twenty-first day of treatment, GEF significantly decreased the paw swelling and arthritis index when compared to the disease control. This suggests that GEF, which has been shown to inhibit NF- $\kappa$ B in vitro, also inhibits it in articulate chondrocytes, suppressing the inflammatory cascade and lowering paw swelling. From day 16 to day 21, GEF treatment increases the rats' ability to move about and climb stairs, suggesting that it also acts throughout the post-acute stage of inflammation.[61]

### **Human immune deficiency virus**

In the HIV-1RT-associated RNase H and DNA polymerase inhibitory assay, garcinol, and isogarcinol were evaluated and compared to the activities of efavirenz and RDS1759 as positive controls. Garcinol maintained full effectiveness against the RNase H of a drug-resistant HIV-1 reverse transcriptase form and showed more HIV-1 RNase H inhibition than the well-known inhibitor RDS1759. Garcinol's enolizable  $\beta$ -diketone moiety is crucial for its anti-RNase H activity, as isogarcinol was noticeably less effective than it. [62]

### **Anti-obesity activity**

The ethyl acetate fraction (FGIEF), butanol, chloroform, and aqueous fractions were obtained by extracting *G. indica* fruits using methanol that was treated to liquid-liquid extraction.

Due mostly to the presence of polyphenols, the fruits of *G. indica* have an antiobesity impact via inhibiting digestive enzymes. [63]

The anti-obesity activity of *Garcinia indica* extract standardized for 20% Garcinol (GIE) was used in this study. In vitro, the effects on adipogenesis were investigated using 3T3L1 cells, and the anti-obesity activity was investigated using C57/BL6 mice fed a high-fat diet. The mechanism of action was investigated using ELISA, western blot, histochemical analysis, and real-time quantitative polymerase chain reaction. In both in vitro and obese animals, GIE containing 20% garcinol decreases adipogenesis by improving the ER stress response in adipocytes. [64]

In vitro, the anti-adipogenic properties of a supercritical ethanolic extract of *Garcinia indica* dried fruits were assessed. In 3T3-L1 preadipocytes, the high-pressure ethanolic (HPE) extract significantly reduced adipocyte development in a dose-dependent manner as extract concentration increased. These findings demonstrate that the primary mechanism by which *G. indica* HPE extract reduces obesity is through signaling pathways that influence the expression of genes linked to fat metabolism and weight regulation. [65]

### **Anti-depressant and anxiolytic activity**

The aqueous extract of *Garcinia indica* fruit exhibited dose-dependent antidepressant efficacy; the maximum concentration utilized in this investigation, 50 mg/kg, was highly successful in lowering the immobility period in comparison to the control in the forced swim test and tail suspension test. [66]

*Garcinia indica* fruit rind was found to significantly decrease immobility and despair behavior in various tests, including forced swim, tail suspension, and reserpine-induced hypothermia. It also altered hypothermia to normal temperature. *Garcinia indica*'s anti-anxiety effects were observed, increasing time spent in the light-dark model, the number of entries in the elevated plus maze, and head dipping in the hole board. The fruit rind also showed neuroprotective potential by lowering monoamine oxidase and malondialdehyde levels. The rind had a strong anxiolytic and antidepressant effect, but no psychostimulation or influence on locomotor activity. [67]

*Garcinia indica* (3.5 g/kg) demonstrated significant anxiolytic activity, comparable to Diazepam, in Wistar albino rats tested using the elevated plus maze. [68]

The ethanolic extract of *Garcinia indica* fruit rind has significant antidepressant activity in animal models (Wistar albino rats) of depression and compared with the control and standard drugs, imipramine, and fluoxetine. This study shows that its phytochemical constituent, hydroxy citric acid can increase serotonin levels in the brain. [69]

### **Human peripheral blood cells**

The modulatory action of *G. indica* extract against the damage caused by 3 Gray (Gy) gamma radiation in human peripheral blood cells was observed. As per standard protocol, different quantities of *G. indica* extract, ranging from 1 to 25 µg/mL, were given to the blood after irradiation at 0 hours on Chromosomal Aberration (CA) and Cytochalasin B blocked Micronuclei Cytome (CBMN) Assay. This study found that *Garcinia indica* fruit rind extract (GIFRE) had a radio-modulatory effect on the development of CA and MN. [70]

### **Immunomodulatory activity**

Swiss albino mice were used to test the immunomodulatory effects of *Garcinia indica* L. (Guttiferae) against the sheep red blood cell (SRBC) antigen. Hexane extract (HE) administered orally increased phagocytosis, delayed-type hypersensitivity response, and Haemagglutination antibody (HA) titers in a

dose-dependent manner. HE showed more immunostimulatory activities at the chosen maximum dose as compared to the control and positive standard (levamisole). [71]

### **Anti -arthritic activity**

A Garcinol garcinol-enriched fraction (GEF) derived from the fruit rind of *Garcinia indica*, containing 89.4% w/w garcinol, was studied for its anti-inflammatory and anti-arthritic potential. Administered at 10 mg/kg, GEF was tested in Wistar albino rats with Complete Freund's Adjuvant (CFA)-induced arthritis. Measurements of paw swelling, arthritis index, body weight, motility, and stair-climbing ability were recorded at various intervals. Results showed that GEF significantly reduced paw swelling and arthritis index, while also improving motility and reducing hyperalgesia. [72]

### **Analgesic activity**

The fruit rind extract of *Garcinia indica* choisy at a dose level of 250 and 500mg/kg showed a significant increase in the response latency in a dose-dependent manner when compared with the standard drug tramadol at 180min in the hot plate and tail clip test. [73]

### **Antacid activity**

An investigation showed that, in an artificial stomach model, an aqueous extract of *Garcinia indica* fruit rind at 400 mg/kg and 800 mg/kg showed considerable and consistent acid neutralization when compared to conventional sodium bicarbonate and greater than water. [74]

### **Anti-ulcer activity**

administered garcinol prevented acute ulceration in rats induced by indomethacin and water immersion stress caused by radical formation using electron spin resonance (ESR) spectrometry. [75]

*Garcinia indica* Linn's fruit rind aqueous and ethanol extract used to prevent ulcers against indomethacin-induced ulcerogenesis and HCl/ethanol-induced stomach lesions was examined in the rat models. The gastric lesions caused by HCl/ethanol and indomethacin, oral treatment of 500 mg/kg of *Garcinia indica* fruit rind aqueous and ethanol extracts significantly ( $p < 0.001$ ) decreased the ulcer index. [76]

The antiulcer properties of *Garcinia indica* fruit rind (GIE) aqueous extract against ulcers in rats caused by absolute ethanol, aspirin, and histamine at doses of 400 and 800 mg/kg. GIE treatment resulted in a dose-dependent reduction in the ulcer index. Reducing ulcer-depleted levels of GSH, SOD, CAT, GPx, and GR and reducing ulcer-excess MDA, and GIE, at both doses, produced strong antioxidant activity. [77]

### **Chronic gastritis**

Two groups of sixty individuals with chronic gastritis were randomly assigned. For three weeks, the experimental group ( $n = 30$ ) was given 10 g of kokum rind extract and 18 g of honey twice daily, whereas the control group ( $n = 30$ ) was given 200 ml of warm water twice daily. For 20 days, taking kokum rind extract with honey on an empty stomach can help patients with gastritis symptoms such as heartburn, gastralgia, and postprandial fullness. It can also enhance the patient's quality of life. [78]

### **Anti-cataract activity**

*G. indica* exhibited potent anticataract activity against naphthalene-induced cataractogenesis in rats. Rats were divided into five groups, with varying treatments over 28 days. Naphthalene administration induced cataracts, resulting in increased lipid hydroperoxides (LH), protein carbonyl content, and a decrease in sulfhydryl (SH) content and antioxidant enzymes in the cataract control group compared to the normal control group. Simultaneous administration of Aqueous extract of GI (200 mg/kg/day and 400 mg/kg/day) with naphthalene delayed the onset and maturation of cataracts. [79]

### Anti-aging activity

Due to the presence of phenolic groups, garcinol and cambogiol found in the rinds of *Garcinia indica* fruits have shown strong antioxidant properties. The fraction separated from fruit rind of *Garcinia indica*, crude Methanolic Extract (ME) divided into ethyl acetate and Water Fraction (WF), and those fractions were evaluated for anti-hyaluronidase and anti-elastase activity. Three fractions were examined. Significant hyaluronidase inhibition was demonstrated by the Ethyl Acetate Fraction (EAF) at concentrations as low as 25 µg/ml, but the water fraction demonstrated good elastase and hyaluronidase inhibition at 90 µg/ml. The fractions extracted from *G. indica* fruit rinds contribute to delaying aging. [80]

### DISCUSSION

In recent years, *Vrikshamla* has received increasing attention due to its potential as a natural remedy for various health conditions.

The research studies reviewed in this article indicate that *Vrikshamla* has a wide range of medicinal properties, including anti-hyperlipidemic activity, anti-inflammatory, anti-microbial activity, anti-helminthic activity, anti-oxidative activity, cardioprotective activity, anti-ulcer activity, anti-obesity activity, anti-arthritis activity, anti-depressant, and anti-anxiolytic activity, etc.

*Vrikshamla* has been traditionally used in Ayurveda for the treatment of various health conditions, including diarrhea, dysentery, wound healing, digestive disorders, etc. The results of the reviewed studies support the traditional use of *Vrikshamla* in Ayurveda and provide scientific evidence for its potential as a natural remedy for various health conditions.

### CONCLUSION

*Vrikshamla* is a promising plant species with a wide range of medicinal properties, which has the potential to be developed as a natural remedy for various health conditions. Further research is needed to confirm the results of these studies and to determine the optimal dosages and administration methods for *Vrikshamla*. Additionally, more research is required to understand the mechanisms of action of *Vrikshamla* and to develop safe and effective treatments for various health conditions.

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