

## A Review of *Garcinia indica* - Botanical Features, Phytochemistry and Pharmacology

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**Abstract:** The ancient fruit kokum (*Garcinia indica*), a member of the Clusiaceae family, is frequently eaten as sharbat in the western ghats of India. The fruit tree kokum has uses in nutrition, medicine, and cooking. Benzophenone garcinol, found in high concentrations in fruit rinds, has been associated with a range of potential bioactivities, such as cytotoxic and antioxidant effects. It has been determined that cyanidin-3-glucoside and cyanidin-3-sambubioside are the main red pigments in the fruit rind. This review article aims to provide information primarily on a range of pharmacological activities, including anti-inflammatory, anti-helminthic, anti-ulcer, cardioprotective, UV protection, anti-hyperglycemic, and Parkinson disease protective effects.

**Key words:** *Garcinia indica*, benzophenone, garcinol, cyanidin-3-glucoside, cyanidin-3-sambubioside

### I. Introduction

The stunning evergreen tree known as "Kokum," *G. indica* Choisy (Syn. *G. pupurea*), is

located in the Western Ghats, along the west coast of Karnataka, Goa, Konkan, and north Malabar. The tree is between ten and fifteen metres tall. This thin tree is exceptionally beautiful in a garden or forest because of its pyramidal shape, drooping branches, and dark green foliage. After a typical pre-bearing phase of around 7-8 years, which runs from November to February, the tree blossoms, and the fruits ripen in April and May. The fruit tree has a lovely appearance. The fruits are often pink or deep purple, though they can sometimes infrequently be yellow (known as white kokum). In Ayurvedic medicine, kokum has a long history of use for treating wounds, dermatitis, diarrhoea, dysentery, ear infections, and digestive issues.<sup>1</sup>

The branching of *Garcinia indica* displayed a canopy with a crown form that ended in horizontal branchlets. The leaves are green in colour, simple, opposite, and have an acute apex. They are typically thick, and the petiole is distinguished by the presence of foveola near the base. Leaves have intercostae venation. The purpose of this work is to assess the anatomy of the leaves and petioles because there isn't a lot of information regarding *G. indica*'s anatomical features in the literature.<sup>2</sup>

**Table1: Plant profile**

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

### Vernacular Names

Malayalam: Kokkam, Punampuli

Marathi: Bhirand, Kokam, Kokambi, Amsol, Katambi, Ratamba

Punjabi: Kokam

Sanskrit: Vrikshamla, Amlabija, Amlashaka, Chukraphala, Raktapuraka

Tamil: Murgal Telugu: Puranapuli

French: Brindonnier

German: Cocum, Kokam

Italian: Cocum

Japanese: Garushinia indica

Spanish: Cocum

Tibetan: Da tri ga, Da tri gi.



Figure 1: *Garcinia indica*

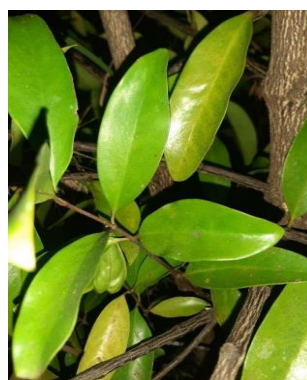


Figure 2: *Garcinia indica* leaves

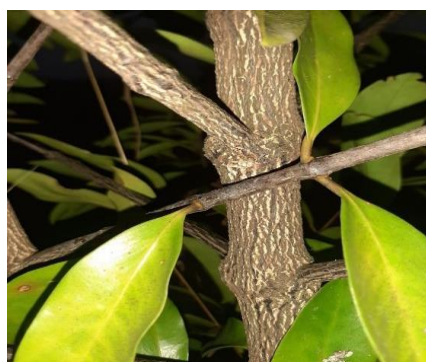


Figure 3: *Garcinia indica* bark



Figure 4 : *Garcinia indica* fruit

### Description of the plant

#### Fruit and Fruit Rinds

- Kokum fruits come in a variety of shapes and sizes, with colours ranging from yellow to purple.
- Kokum rinds are used to make juice, which is used as a cooling, and the dried rinds are used as a condiment.

- The fruit itself possesses antihelmintic and cardiotoxic qualities, and the rinds are used to manufacture medicines for gastrointestinal problems, rheumatic symptoms, and inflammatory disorders.
- The rind of kokum, when combined with yoghurt and salt, is a natural antacid that is used to cure stomach ulcers and a burning sensation.

- Kokum rinds are utilised in the commercial industry to generate concentrated syrups that, when correctly diluted, result in chilled health drinks that are ready to drink, especially in the off-season.
- In the Goan community, the rinds are frequently used to produce wine.
- Dried rinds are powdered and sold as an acidulant in traditional curries.
- The aqueous extract of this species' fruits is often used to alleviate anxiety. The fruits are soaked in sugar syrup to prepare amrutkokum, a drink used to treat sunstroke .

#### Leaves

- The fruits and leaves are commonly known for their astringent and sour taste, as well as their digestive, constipating, and thermogenic qualities.
- The leaf's midrib has a thick cuticle, a uniseriate epidermis, a parenchymatous hypodermis that is one to several layers thick, and polygon-shaped cells.
- The cells have a lot of chlorophyll. Sclerenchyma covers the arched vascular zone. The mesophyll reveals the presence of secretory cavities, starch grains, and druses outside the vascular zone.
- The epidermal cells of the leaf are highly pigmented and have an irregular, polygonal shape.
- The stomata, which have an elongated stomatal pore, have two subsidiary cells that are positioned parallel to the guard cells. The nature of the stomata is rubiaceous.
- The epidermis and hypodermis are uniseriate, the cells are spherical, and the petiole has thick cuticle.
- The ground tissue is prominently dispersed with numerous starch grains and druses . The siphonous curved vascular tissue present in the petiole consist of interfascicular parenchyma towards the upper side with narrow gap.<sup>2</sup>

#### Seeds

- The confectionery, pharmaceutical, and cosmetic industries have a strong demand for kokum butter, which is derived from the seeds.
- When creating chocolates, kokum butter is used in place of cocoa butter because it has similar solidification properties, tolerance to milk fat, and compositions of fatty acids and triacylglycerol.

- Furthermore, research indicates that the addition of kokum butter to cocoa butter improves the heat-resistance properties of both chocolate and cocoa butter, preventing heat-induced softening and consistency loss in chocolate products.
- The treatment of diarrhoea, phthisis pulmonalis, dysentery, and scorbutic disorders can be aided by kokum butter.
- It is well known that applying kokum butter to the skin can help heal wounds and is helpful in treating inflammatory sores, lip and hand fissures, chapped skin, and ulcerations.
- The seed butter is a remedy for mucous diarrhoea and dysentery. The root, bark, fruit, and seed oil are used to treat worm infestations, piles, stomach ailments, and oral ailments. It can be applied topically to skin conditions like allergic rashes or used as an infusion. An emollient called kokum butter can be used to soothe burns, scalds, and chapped skin.<sup>3</sup>

#### Phytochemical Properties

The most notable chemical compounds found in *Garcinia indica*, which is widely accessible in India, are poly-isoprenylated benzophenone derivatives, which include isogarcinol, the structural isomer of Garcinol, and Garcinol itself. Iso-garcinol is colourless, while garcinol is a yellow fat-soluble pigment.

#### Fruit

- In addition, the fruit includes hydroxycitric acid lactones, citric acid, and oxalic acid. It also has a higher concentration of malic acid, as well as trace levels of tartaric and citric acids, which give the fruit a delightful tangy flavour.
- Fruit composition of *Garcinia indica* has a high concentration of active chemicals such as garcinol, xanthochymol, isoxanthochymol, and hydroxy citric acid.
- Flavonoids, benzophenones, xanthenes, lactones, and phenolic acids are examples. Garcinol, hydroxycitric acid, citric acid, acetic acid, malic acid, and ascorbic acid are all found in the fruits.
- Garcinol C38H50O6, a polyisoprenylated benzophenone, isogarcinol, and camboginol are the main components of kokum rind.
- Garcinol's main components are macurin, mangostin, isogarcinol, gambogic acid, clusianone, oblongifolin (A, B, C), and guttiferone (I, J, K, M, N).
- The pH of the Kokum fruit ranges from 1.5 to 2.0, naturally imparting the greater acidity.

- > The primary components of ripe Kokum fruit rind are hydroxyacetic acid and hydroxycitric acid. It also includes 2.4% pigment in the form of a 4:1 combination of two anthocyanins, cyanidin-3-sambubioside and cyanidin-3-glucoside.

Seed

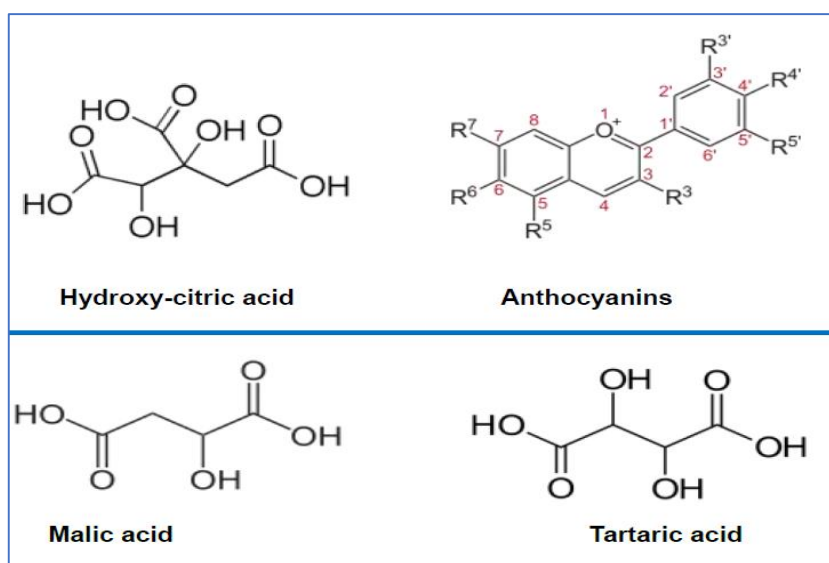
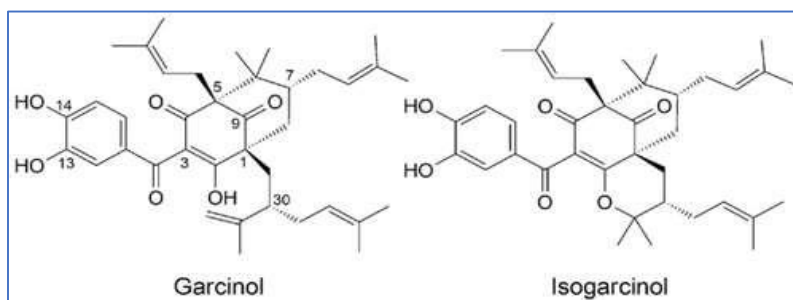
- > Glycerides of stearic acid (55%), oleic acid (40%), palmitic acid (3%), linoleic acid (1.5%), hydroxyl capric acid (10%), and myristic acid (0.5%) are abundant in kokum seeds.
- > Kokum seed contains around 25% edible fat, which is frequently referred to as Kokum butter. It is usually extracted by crushing the seeds, boiling them in water, and then extracting the fat from the top, or by churning the seeds in water or solvent extraction.

- > The yellowish crude kokum butter is utilised as a ghee adulterant or edible fat. High-quality hydrogenated fats are equal to white-colored refined Kokum butter. Free fatty acids make up to 7.2% of total Kokum butter.

Leaves

- > Per 100g, kokum leaves include L-leucine, 75% hydration, 2.3g protein, 0.5g fat, 1.24g fibre, 17.2g carbs, iron 15.14mg, calcium 250mg, ascorbic acid 10mg, and oxalic acid 18.10mg.
- > Minor amounts of hydroxycitric acid, lactone, and citric acid may be found in the leaves and rinds.
- > D-Leucine isogarcinol, xanthochymol, isoxanthochymol, HCA and HCA lactone, Cambogic acid, mangostin, garcinol, fukugicide, GB-1, GB-2, and amentoflavone are also reported in leaves.<sup>3</sup>

**Table 2 :The Molecular structures of the important chemical constituents of *Garcinia indica*<sup>4</sup>**



**Table 3 :** Active constituents of different parts of *Garcinia indica*

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

### Pharmacological activity

#### Antioxidant activity

##### • Ferric ion reducing antioxidant power (FRAP) assay

FRAP assay was used to determine the total antioxidant power of the extracts. Aqueous leaf extract of *Garcinia indica* in varied concentrations ranging from 100 µg to 500 µg/ml were mixed with 2.5 mL of 0.2 mM phosphate buffer (pH 7.4) and 2.5 mL of potassium ferricyanide [1% weight/volume (W/V)]. Temperature was set to 50°C and the resulting solution was incubated for 20 minutes. Later 2.5 mL of TCA (10% W/V) was added and centrifuged for 10 minutes (3000 rpm). Then, 2.5 mL of deionised water was added followed by 0.5 mL of ferrous chloride (0.1% W/V). Finally, the optical density was measured at 700 nm. A positive reference standard, ascorbic acid, was used to compare the antioxidant property of GI extracts.

##### • 2,2-Diphenyl-1-picrylhydrazyl radical scavenging ability (DPPH) assay

Free radical scavenging effect of aqueous leaf extract was determined using the 2-diphenyl 1 picrylhydrazyl (DPPH) with slight modifications. In brief, the concentrations (100-500 µg/ml) of extracts were prepared. 1 mL of DPPH solution (0.004% prepared in ethanol) was treated with 1 mL of aqueous leaf extracts and standard ascorbic acid solution separately. The mixture was left for incubation in the dark under room temperature for 30 minutes and the optical density was measured at 517 nm. The extent of DPPH-purple decolorization to DPPH yellow confirmed the scavenging efficiency of the extract. Higher antioxidant activity was observed as the optical density of the reaction mixture was decreased. Scavenging activity was calculated using the following formula:

$$\text{DPPH scavenging activity (\%)} = \frac{AC - AT}{AC} \times 100$$

AC-the absorbance of the control reaction (1 ml of ethanol with 1 ml of DPPH solution)

AT-the absorbance of the test sample.

The results were analyzed in triplicates. The IC<sub>50</sub> value indicates the required sample concentration to inhibit 50% of the DPPH free radical.<sup>14</sup>

#### Antimicrobial activity

The antimicrobial activity of the all extracts (leaf, fruit) was performed according to the standard agar-cup diffusion method. 100 µl of 6 different concentrations of both the extract [100 µg, 50, 25, 12.5, 6.25, 3.12 µg/ml] were used to detect qualitative antibacterial activity against *Escherichia coli* (*E. coli*), *Klebsiella spp.* and *salmonella spp.* Each assay was carried out in triplicate and DMSO was used as a negative control for the entire antibacterial assay.<sup>5</sup>

#### The Minimum Inhibitory Concentration (MIC):

A loop full of bacterial and fungal cultures from the slant was inoculated into nutrient broth and potato dextrose broth respectively and incubated at

37°C for 24 h for bacteria and at room temperature for 4-5 days for fungi. The fresh broth (20 ml) was seeded with 0.25 ml of 24 h bacterial broth culture or 4-5 day's fungal broth culture. Then 0.2 ml of the extract was added to 1.8 ml of seeded broth which was the 1st dilution. 1 ml of the solution was diluted further with 1 ml of the seeded broth to produce 2<sup>nd</sup> dilution and the procedure was repeated until six dilutions were obtained. A set of tubes containing only seeded broth were kept as control. After incubation for 24 h at 37°C for bacteria and after 4-5 days at room temperature for fungi, the last tube with no visible growth of bacteria or fungi was taken to represent MIC of test samples which was expressed in mg/ml. The broth dilution assay was also carried

out with streptomycin for bacteria and nystatin for fungi in the same way as the extracts and MIC values of streptomycin and nystatin were determined.<sup>6</sup>

### Thrombolytic activity

#### • Sample preparation :

The leaf extract was used to prepare sample solution of concentration (10mg/mL) using sterile distilled water & mixed properly by vortexing.

#### • Streptokinase solution preparation :

Icikinase vial (15,00,000 IU) bought from Vijay Life Care [Bhandup (W)] was used as positive control. 5mL distilled water was added in this vial & mixed properly to prepare stock solution.

#### • Thrombolytic assay :

1.5mL of blood sample was collected from healthy individual & 500  $\mu$ L blood was transferred in a clean pre-weighed Eppendorf tubes & incubated at 37°C for 45 min.

2. After clot formation, the tubes were centrifuged using cooling centrifuge at 2000 RPM for 5 mins.

3. The serum was removed completely & the tubes were weighed to determine clot weight.

4. 100  $\mu$ L of plant extract was added to each tube, 100  $\mu$ L of streptokinase & distilled water were used as positive & negative control respectively.

5. All the tubes were incubated at 37°C for 90 mins.

6. After incubation, the excess fluid was decanted & all the tubes were again weighed to determine the difference in weight.

Formula: % clot lysis = (Weight of lysis clot/Weight of clot before lysis) x 100

*G. indica* exhibited comparatively good thrombolytic activity i.e. 53.67%.

### Anthelmintic activity

*In vitro* anthelmintic activity of all the extracts (leaf, fruit) was evaluated. The earthworms were divided into individual groups (each group containing five organisms) for each treatment at two different concentrations. The standard drug albendazole at two different concentrations of 25 and 50 mg/mL was used for comparing the activity of the extracts with saline (0.89% NaCl w/v) as a control. Similarly, all the extracts were prepared at concentrations of 25 and 50 mg/mL as test. A volume of 10mL of each extract of both the concentrations were taken in Petri dishes. Five earthworms were added to each Petri dish. Earthworms were observed for their movements. The time taken for the worm to

lose its movement (except when external stimulus was given) was considered for paralysis time and the time taken to lose its motility even in the presence of external stimulus (when dipped in warm water at 55°C) and faded body colour was considered for death time. Paralysis time and death time of each earthworm in the group was recorded.<sup>7</sup>

### Anti-ulcer

Agent Phytochemicals found in *Garcinia indica* have been shown to have pharmacological activities, hence it was chosen for research to assess its anti-ulcer efficacy. *Garcinia indica* fruit rind water and ethanol extract were shown to have strong anti-ulcer effects in research. In rats, gastric lesion was produced with HCl or ethanol, whereas ulcer genesis was generated with indomethacin. Aqueous *Garcinia indica* fruit rind extracts reduced mortality by 52.94% in the former rats and 36.80% in the later rats. Ethanolic extracts reduced mortality by 34.45% in the former rats and by 61.62% in the later animals. The molecule responsible for this effect is unknown and must be isolated and tested pharmacologically.<sup>3</sup>

### Cardioprotective Activity

*Garcinia indica* fruit rinds were used to test cardiac preventive effects due to its phyto-constituents and established traditional medicinal usage. Research found that *Garcinia indica* extract at doses of 250 mg/kg by weight and 500 mg/kg by weight reduced the activities of biochemical parameters such as LDH, AST, ALT, CK-MB, and CPK when compared to isoprenaline hydrochloride induced cardiotoxicity in rats and control rats. Similarly, the examination of membrane bound enzymes, i.e., ATPase, revealed a decrease in Ca<sup>2+</sup> ATPase and Mg<sup>2+</sup>ATPase activity and a substantial increase in Na<sup>+</sup> K<sup>+</sup> ATPase activity at the same dose. When compared to the control and isoprenaline-treated groups. The cardio protective action of *Garcinia indica* may be attributed to its membrane stabilizing characteristics as well as its capacity to suppress the generation of free radicals. The precise mechanism is yet unknown.<sup>8</sup>

### UV Protection

*Garcinia indica* fruit extracts were made with acidified methanol, ethanol, and ethyl acetate, whereas kokum butter extracts were made with ethyl acetate. A spectrophotometric analysis of the UV protection activities of both the fruit rinds and the kokum butter found that the ethyl acetate fraction of the fruit rinds exhibited good UV-A and UV-B absorbance at a concentration of 0.4 mg/ml. In the

UVA area, kokum butter had lower UV absorption than in the UVB zone. Additionally, SPF was evaluated by making several sunscreen formulas. The sunscreen formulation had a Sun Protection Factor (SPF) of 2.02 at 105% ethyl acetate concentration, which was fairly good. Because the findings of these extracts outperformed TiO<sub>2</sub>, which was used as a benchmark, it shows that this might be a suitable and effective choice for sunscreen goods.<sup>9</sup>

#### Anti-hyperglycemic Agent

The rinds of kokum are used to cure diabetes. Kokum restores the number of erythrocytes, an intracellular antioxidant, and studies have shown that it is effective in lowering the chance of developing secondary problems; this reflects the potential properties of kokum in treating both hyperglycemia and other complications.<sup>10</sup> *Garcinia indica* has long been recognized as an antioxidant and free radical scavenger. These are the characteristics that distinguish this plant as an antihyperglycemic agent. The blood glucose level was shown to be considerably lower following administration of 400mg/kg of aqueous whole fruit extract to euglycemic and streptozotocin (STZ) induced hyperglycemic Wistar rats of either sex in a study (Khatib & Patil, 2011). The primary cause of type 2 diabetes is oxidative stress, which is regulated by the thiol Glutathione (GSH). GSH deficiency causes a variety of consequences, including neurodegeneration, myocardial infarction, and other cardiovascular disorders. Another study discovered that aqueous extracts of *Garcinia indica* fruit dramatically improved body weight, lowered blood glucose levels, and boosted erythrocyte GSH levels in streptozotocin-induced type 2 diabetic rats.<sup>11</sup>

#### Protective effect against Parkinsons Disease

Garcinol is a potent MAO-B inhibitor, as it shows docking scores more than Zonisamide as well as L-deprenyl, and interacts with both the active sites of the enzyme. This higher free energy of binding is attributed to more number of weak (hydrophobic) interactions formed by Garcinol, owing to its larger size and more number of interacting groups (Fig. 2C). The free energy of binding of Garcinol with the active sites of chain A and chain B of MAO-B have been found. Garcinol, a phytoconstituent of the plants belonging to the genera *Garcinia*, has potential as an anti-parkinsonian drug candidate to enhance the level of dopamine in brain through inhibition of its catabolism by MAO-B, similar to L-deprenyl. This treatment approach may be exploited to reduce the effective dose of L-DOPA. It is further speculated

that Garcinol may prevent MAO-B – mediated production of toxic metabolites and generation of reactive oxygen.<sup>12</sup>

#### 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, prostate and pancreatic cancer cells. 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.<sup>13</sup>

## II. CONCLUSION

*Garcinia* species are a significant group economically and as members of the Western Ghats flora. According to field surveys, the Western Ghats are home to 9 native species and 2 varieties, of which 7 are endemic to the area. Antioxidant, anti-neoplastic, anti-Parkinson, anti-diabetic, antibacterial, hepatoprotective, cardioprotective, anti-depressant, and anti-anxiety effects are just a few of the pharmacological properties of *G. indica*. These features align with the previously documented functions of numerous phytochemical constituents, including cyanidin-3-glucoside, cyanidin-3-sambubioside, and garcinol, which were isolated from *G. indica*. The purported health benefits of kokum have led to a significant increase in its consumption in various processed forms. Kokum and its derivatives, including butter from seed, sarbat,

solkadhi, and powdered dried rind, are abundant in various high-value compounds that may have advantageous physiological effects. The abundant bioactive composition of kokum renders it an exceptionally nourishing and coveted fruit crop. To determine the effectiveness and safety of *G. indica* in humans, more research at the clinical level is necessary, as the majority of trials have been carried out either in vitro or in vivo.

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