Review Article

Medicinal Properties of Malabar Tamarind [*Garcinia Cambogia* (Gaertn.) DESR.]

Tharachand, Immanuel Selvaraj*, Mythili avadhani
School of Biosciences and Technology, VIT University, Vellore-632014, Tamilnadu, India.
***Corresponding author's E-mail:** immmer@gmail.com

Accepted on: 20-02-2013; **Finalized on:** 31-03-2013.

ABSTRACT

The parts of the plant *Garcinia cambogia* (Gaertn.) Desr. commonly known as Malabar tamarind, have been used by many Asian countries in traditional medicine for treating intestinal parasites, constipation, cancer, piles, bowel complaints, rheumatism, edema, delayed menstruation, demulcent, bilious affections and other diseases. The root contains the xanthone called garbogiol. The bark of the stem contains benzophenones such as garcinol and isogarcinol. Malabar tamarind is shown to possess antioxidant, antihelmintic, anticattarhal, anti-cancer and antimicrobial activities. The rind of the fruit is the most extensively studied part of the plant. Hydroxycitric acid, the most abundant constituent of the fruit rind apart from the other constituents, has reported to be the active principle for many of its useful properties. The ethanol extract of the leaves and the fruit have been shown to possess *invitro* antihelmintic activity. This review paper describes the chemical compounds present in Malabar tamarind, their therapeutic applications and their occurrence in different parts of the plant.

Keywords: Malabar tamarind, *Garcinia cambogia,* Guttiferones, Hydroxycitric acid, Xanthones.

INTRODUCTION

Malabar tamarind is a tropical tree from India, Sri Lanka, Africa and Malaysia. It is a dicotyledonous tree belonging to the family Guttiferae (Clusiaceae). The genus *Garcinia* comprises around 200 species throughout the world in which most of them are located in the Southeast Asia and African continents. Out of the reported 200 species, 36 species were reported from India. The tree is found in the evergreen forests of Western Ghats at an altitude of 6000 ft which extend in the states of Maharashtra, Goa, Karnataka, Kerala and Tamilnadu. It is a semi-domesticated crop in Kerala state of India[1]. Rural areas of Ernakulam and Kottayam districts of Kerala, Tuticorin and Dindigul districts of Tamilnadu and Uttar Kannad district of Karnataka are the specific pockets for the cultivation and export of *Garcinia cambogia.* Trees grow to a height of 20 m have rounded crown. The branches are thin and soft, drooping or horizontal. Leaves are dark green, shining, ovate in shape, ranging 2½ to 3½ inch in length, 1 to 1½ inch broad. Fruits are ovoid in shape having 1 to 1½ inch in diameter, yellow or red in color with 6-8 grooves. Fruit pulp contains 5 to 8 big seeds which are surrounded by a succulent aril. The tree flowers from December to February and fruits from March to June.

Malabar tamarind has been shown to contain a variety of secondary metabolites such as xanthones[2], flavonoids[3] and benzophenones[4]. Xanthones are oxygenated heterocyclic compounds present in higher plants. Xanthone nucleus is symmetric and is known as xanthen-9H-ones or 9-xanthenone or dibenzo-γ-pyrone. The biological activities of these compounds depend on the different substituent's position and nature[5]. Flavonoids are polyphenolic compounds which are remarkable group of plant metabolites. The antioxidant and free radical scavenging activity of flavonoids depend on the position of hydroxyl groups and other chemical features[7]. It was studied that dietary flavonoids have protective role in coronary heart disease. The mortality due to coronary heart disease is observed to reduce in cases with intake of dietary flavonoids [9]. Benzophenones are organic group of aromatic ketones having the parent compound diarylketone which have wide applications in pharmaceutical industry[8]. Substituted benzophenones such as oxybenzone and dioxybenzone are used in sunscreen lotions. As the plant has a wide range of biologically active compounds showing broader activity range, the evaluation of the medicinal properties of the plant enhances its exploration.

XANTHONES ISOLATED FROM MALABAR TAMARIND

Oxy-guttiferons are a group of xanthones which are tetra cyclic in nature. Masullo *et al* isolated oxy-guttiferone K for the first time from the natural source *G. cambogia* fruits[10]. The same author later discussed the isolation procedure and structure of oxy-guttiferones M, oxy-guttiferone K_2 and oxy-guttiferone I[11]. A new Xanthone, Garbogiol along with the known xanthone, rheediaxanthone A was reported from the root of *Garcinia cambogia*[13]. Different xanthones and their occurrence in different parts of the plant are given in table 1 and the reported biological activities of xanthones for *Garcinia cambogia* and from other *Garcinia* species are also summarized in table 2. In addition to the mode of action of xanthones, with relevance to their biological activity, the present data may help in designing new and efficient structures for the discovery of xanthone based drugs. The chemical structures for the above mentioned xanthones are illustrated in the figures 1-3.

Table 1: Xanthones isolated from *Garcinia cambogia*

Xanthone	Part of the plant xanthone is isolated	Ref
Oxy-guttiferone M	Fruit	11
Oxy-guttiferone K	Fruit	10, 11
Rheediaxanthone A	Roots	13
Oxy-Guttiferone K_2 and I	Fruit	11

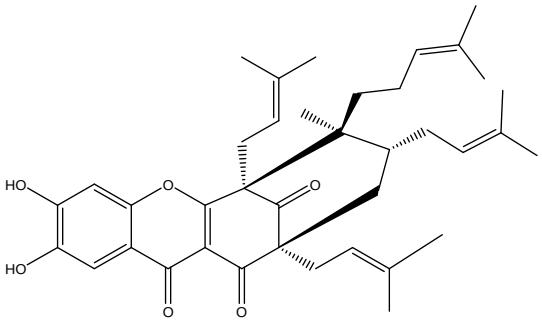

Figure 1: Chemical structure of Oxy-guttiferone K

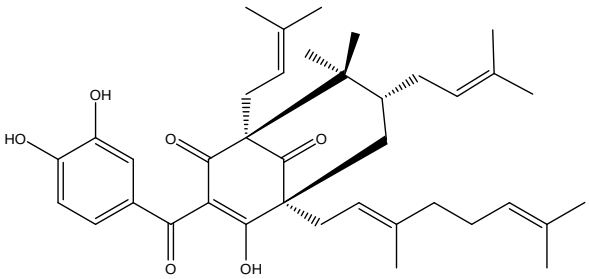

Figure 2: Chemical structure of Oxy-guttiferone M

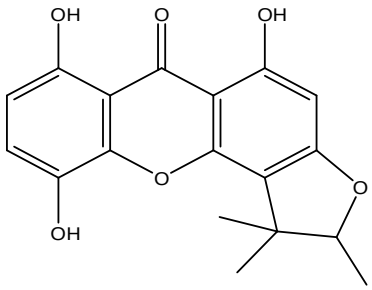

Figure 3: Chemical structure of Rheediaxanthone A

BENZOPHENONES ISOLATED FROM MALABAR TAMARIND

Benzophenones garcinol and isogarcinol were isolated from the bark of *G.cambogia*[13]. The compound garcinol is also termed as camboginol, as it is for the first time reported from *Garcinia cambogia.* The occurrence of benzophenones in various parts of the plant is reported in table 3. The strong antioxidant activity of garcinol is attributed to the presence of both phenolic hydroxyl groups and β-diketone moiety[14]. The summarization of anticancer activity of garcinol and observation recorded is in table 4. The chemical structure for garcinol is illustrated in figure 4.

Table 2: Summary of reported biological activities of xanthones

Activity	Experimental details	Ref
Vasodilatory	Vaso-active in coronary artery	27
Antimalarial	Moderate activity on chloroquino-resistant strain of *Plasmodium falciparum*	28
Antiviral activity	Inhibitory effect on Epstein-Barr virus early antigen	29
Human Leukemia	Showed inhibitory activity against HL-60 cell line	30
Cytotoxic activity	Reported mangostin as a potential anti melanoma agent	31
	Cytotoxic potency is higher in xanthones with greater number of prenyl substitutes	35
α-glucosidase activity	Inhibited α-glucosidase, α-chymotrypsin properties	32
CNS pharmacological activity	Inhibited rat microsomal MAO A	33
Platelet activating factor (PAF)	PAF receptor binding was inhibited in rabbit platelets	34
Anti oxidant activity	Antioxidant activity is due to the formation of prooxidant-derived antioxidant	36
Anti-proliferative activity	Active against *Drosophila* S2 cells	37
Colon cancer	Induced cell cycle arrest and apoptosis in human colon cancer DLD-1 cells	38

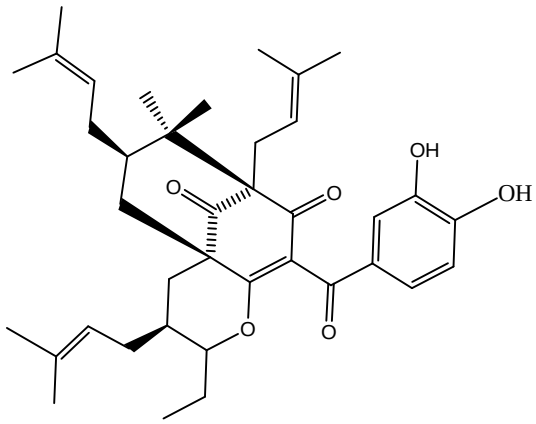

Figure 4: Chemical structure of Garcinol

Table 3: Benzophenones isolated from various parts of the plant

Benzophenone	Part of the plant used	Ref
Guttiferone I, J and N	Fruit	10
Guttiferone M	Fruit	10, 11
Guttiferone K	Fruit	10, 12
Garcinol/camboginol	Root	13
Isogarcinol	Root	13

Table 4: Anti-Cancer Activity of Garcinol

Cancer type	Cell lines used for the study	Observations recorded	Ref
Leukemia	KBM5	Garcinol induced the expression of death receptors in these cell lines	15
	U937, K562, NB4, HL60	Showed significantly growth suppression due to activation of caspase-3 mediated apoptosis	16
Prostate cancer	LNCaP, C4-2B, PC-3	Down regulation of NF–kappa B signal pathway	17
Pancreatic cancer	BxPC3	Down regulation of NF–kappa B signal pathway	17
Lung cancer	A549	Potent inhibition of PGE2 and LT formation without marked inhibition of COX isoenzymes.	18
Breast cancer	MDA, MB231, MCF7	Garcinol induced the expression of death receptors in these cell lines.	15
	MCF7, MDA-MB231	Down regulation of NF–kappa B signal pathway.	17
Colon cancer	HT-29, HCT-116, ICE-6	Inhibitory effect on intestinal cells based on Caspase-3 activation.	19
	Male F344 rats	Induction of liver GST and QR, inhibition of O_2^- and NO generation.	20
HeLa cells	HeLa core Histones-P^{300} HAT inhibition	By non-specific inhibition	21
	HeLa Histones	By inhibiting HAT-activity dependent chromatin transcription factor	22
Tongue cancer	Male F344 rats	Inhibits 4-NQO-induced tongue carcinogenesis	23
Kidney cancer	A293 (Human embryonic kidney carcinoma)	Induction of trail receptors and death receptors	15
Hepatocellular carcinoma	MH1C1-HEP G2	Genes regulated by Nob are involved in the growth suppression	24
	Hep3B	Activated the ER stress modulator GADD 153	25
	Carcinogen induced liver cancer F344 rats	Carcinogenesis can be predicted from gene expression pattern	26

Anti-bacterial activity of garcinol, a benzophenone derivative showed inhibitory property against methicillin resistant bacteria species *Staphylococcus aureus* more than that of the antibiotic, vancomycin[40]. *Helicobacter pylori* showed more susceptibility to antioxidants when combined with garcinol rather than using them individually. The result showed was 90% when compared to controls[39]. The other compounds belonging to the same class of benzophenones were also reported from Malabar tamarind which includes guttiferone I, guttiferone J, guttiferone N[10], guttiferone K[12, 10] and guttiferone M[10, 11]. The structure for the guttiferone A and guttiferone F are mentioned in figures 5 and 6 respectively.

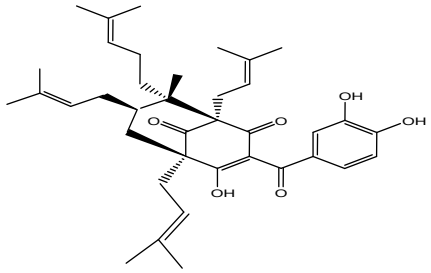

Figure 5: Chemical structure of guttiferone A

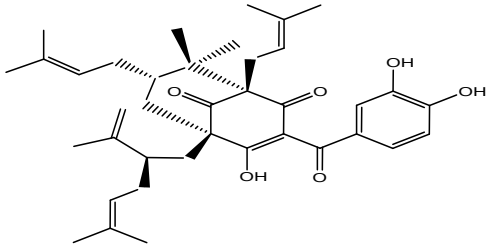

Figure 6: Chemical structure of guttiferone F

Table 5: Summary of the reported biological activities of guttiferones

Compound	Activity	Experimental details	Ref
Guttiferone A	Leishmanicidal activity	showed significant activity on *Leishmania* (L.) *amazonensis*	41
Guttiferone A	Anticancer activity	Permeabilizes mitochondrial membrane	42
Guttiferone A	Antifungal activity	Against pathogenic fungi *Candida* species	43
Guttiferone A	Antiproteolytic activity	Inhibits cysteine and serine proteases	44
Guttiferone Q	Cytotoxicity assay	Guttiferone Q showed potent cytotoxicity against MCF-7, Hela and NCI -H460 cancer cell lines	45
Guttiferone R			
Guttiferone S			
Guttiferone E	Antioxidant activity	-	46
Guttiferone K	Oxidative/nitrative protein damage in human blood platelets	Protective effects against lipid and protein oxidation	47
Guttiferone K	Antitumor effect on colon cancer	Caspase-3 mediated apoptosis	48
Guttiferone K	Antiproliferative activity	Human ovarian cancer cell line A2780 showed sensitivity to guttiferone K	49
Guttiferone E	Apoptotic effect	Showed strong apoptotic effect against HeLa-C3 cells	50
Guttiferone F			
32-hydroxy-*ent*-guttiferone M	Antioxidant activity	Showed antioxidant activity in both DPPH and ABTS free radical scavenging assays	51
Guttiferone I	Agonist against Liver X Receptors	-	52
6-epi-guttiferone J	Antioxidant activity	Inactive against antioxidant activity	51
Guttiferone I and J	Cytotoxic acivity	Weakly cytotoxic on KB cell line	53
Guttiferone O and P	Inhibition of enzyme	Inhibited the phosphorylation of the synthetic biotinylated peptide substrate	54

Flavonoids are generally found in human diet in a variety of fruits and vegetables. They have different roles in anti-inflammatory, anti-carcinogenic, antiviral and antioxidant properties. *Garcinia kola* a different species belonging to the same family *Guttiferae* is reported as a rich source of flavonoids. Apigenin- 5, 7, 4' –trimethylether, apigenin-4'methylether and fisetin (3', 4', 7-trihydroxyflavonol) were the simple flavonoids reported from *Garcinia kola*[56]. The lipid level lowering effect of flavonoids, when administered to hypercholesterol rats was reported along with the reduction of activities of glucose-6-phosphate dehydrogenase and isocitrate dehydrogenase. They also reported the higher rate of degradation of cholesterol in hepatic and fecal samples[55].

HYDROXYCITRIC ACID (1,2 DIHYDROXYPROPANE-1,2,3-TRICARBOXYLIC ACID)

Hydroxycitric acid (HCA) is reported only from *Garcinia* and *Hibiscus* species. *Garcinia cambogia, Garcnia indica* and *Garcinia astroviridis* are the species containing hydroxycitric acid. Hydroxycitric acid is also enriched in the calyx of the flowers of *Hibiscus subdariffa* and *H. rosa-sinensis* [58]. Hydroxycitric acid for the first time in nature is encountered in *Garcinia cambogia* fruit[57]. Lewis and Neelakantan for the first time extracted this hydroxycitric acid from the fruit rinds of *Garcinia cambogia* based on spectroscopic and chemical studies[60]. Microbial strains producing HCA in trace amounts were also reported [58]. Among 2,000 microbial strains isolated from different locations, *Streptomyces* sp. U121 and *Bacillus megaterium* G45C showed HCA content similar to that of standard[58]. Malabar tamarind is used commercially for "Colombo curing" of fish. Bacteriostatic effect with respect to *Staphylococcus* in the cured product of fish pickling is due to the presence of acids which lowers the pH [59]. The absolute configuration can be found out by measurement of optical rotation.

For the first time the spectroscopic data regarding naturally available diastereomic, optically active γ-lactones of 2-hydroxycitric acid, namely garcinia acid [(2S, 3S)-tetrahydro-3-hydroxy-5-oxo-2,3-furandicarboxylic acid] [62]. The structure of Hydroxycitric acid is represented in the below figure 7.

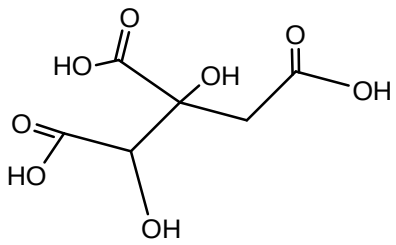

Figure 7: Chemical structure of Hydroxycitric acid

The structure of – (-) Hydroxycitric acid was determined by the IR peaks at 3200, 1760 and 1680 cm^{-1} and ^1H NMR data[63]. The estimation of Hydroxycitric acid from the fruits by using conventional acid-base titration methods is inaccurate because of the presence of other acids like malic acid, citric acid and tartaric acid gives the total acid content of the fruit. The extraction and estimation method by HPLC analysis for Hydroxycitric acid from *Garcinia cambogia* fruit rind was explained. The method explains HCA absorption at 203 nm wavelength with retention time of 20 minutes using 0.01N H_2SO_4 as the mobile phase[64]. The other method was also explained for the determination of HCA spectrophotometrically. The color complex formation between HCA and sodium meta vanadate is the basic principle involved in HCA estimation by this method. The reddish orange color complex formed between sodium meta vanadate and HCA is specific and unique[65]. The improved liquid chromatographic method for HCA determination along with other minor organic acids was elaborated[66].

The biological effect of HCA is mainly in the inhibition of extra mitochondrial cleavage of citrate to oxaloacetate and acetyl-CoA. As acetyl-CoA that is formed in the mitochondria is the source for carbon atoms in the fatty acid synthesis[70]. Once acetyl-CoA formation is inhibited, synthesis of fatty acids is reduced drastically. The inhibition of citrate cleavage is due to HCA has greater affinity to citrate, the natural substrate than the citrate cleavage enzyme ATP citrate lyase[69]. The mode of action of HCA appears to be competitive inhibitor for the enzyme ATP citrate lyase[75]. ATP citrate lyase has been suggested to play an important role in gluconeogenesis and in lipogenesis[68]. Hydroxycitric acid shows its anti-obesity activity by inhibiting the cleavage of citrate to oxaloacetate and acetyl-CoA, a key molecule, which plays an important role in energy storage as fat. Now, instead of using energy to synthesize fat, the energy is diverted to the production of liver and muscle glycogen. This process slows down the production of cholesterol, fatty acids and triglycerides with the net effect of reduced fat production and storage. In a pilot study conducted on human population, Hydroxycitric acid combined with niacin bound chromium reduced body weight and BMI by 7.8% and 7.9% respectively. Also it enhanced the excretion of urinary fat metabolites by 146-281% [71].

Some possible concerns about HCA

The concern about HCA is with respect to dosage and time of administration for its efficiency. The effect of HCA in animals is maximum when administered 30-60 minutes prior to feeding[73]. Hydroxycitric acid reportedly does not have any known adverse effects in healthy adults. But for pregnant and lactating women and those diagnosed with *diabetes mellitus* are suggested not to take HCA[72]. Researchers suggested malonyl-CoA has an important role in transmitting insulin signals in the cells. As it is discussed that HCA prevents the formation of Acetyl CoA from which malonyl CoA is produced subsequently, HCA may have adverse side effects on insulin sensitivity [74]. As contradictory to the above said concerns, the combination of HCA with niacin bound chromium can serve as a safe weight management solution which is supported in their study as there were no drop outs because of adverse side effects [71].

CONCLUSION

Discovery of medicinal properties in components of *Garcinia cambogia* such as xanthones, benzophenones, guttiferones and Hydroxycitric acid suggests the application of Malabar tamarind in therapeutic applications. The potential beneficial effects include its anti-oxidant property, anti-helmenthic, antimicrobial and anti-obesity and weight reducing agent. Although many studies have been published on the roles of compounds from malabar tamarind, many functions and interactions are yet to be investigated fully. Even though positive results were reported from Malabar tamarind in *invitro* conditions further studies need to be done extensively on human population.

REFERENCES

1. Abraham Z, Malik S.K, Rao G.E, Narayanan S.L and Biju S.L, Collection and characterization of Malabar tamarind [*Garcinia cambogia* (Gaertn.) Desr.], Genetic Resources and Crop Evolution, 53, 2006, 401-406.
2. Iinuma M, Ito T, Miyake R, Tanaka T and Chelladurai V, A xanthone from *Garcinia cambogia*, Phytochemistry, 47(6), 1169-1170.
3. Koshy A. S, Anila L and Vijayalakshmi N. R, Flavonoids from Garcinia cambogia lower lipid levels in hypercholesteromic rats, Food chemistry, 72(3), 2001, 289-294.
4. Masullo M, Bassarello C, Suzuki H, Pizza C and Piacente S, Polyisoprenylated Benzophenones and an unusual Polyisoprenylated Tetracyclic Xanthone from the Fruits of *Garcinia cambogia,* Journal of Agricultural and Food chemistry, 56, 2008, 5205-5210.
5. Peres V, Nagem T. J, Oliveira F. F, Tetraoxygenated naturally occurring xanthones, Phytochemistry, 55(7), 2000, 683-710.
6. Andersen O. M and Markham K. R, Flavonoids Chemsitry, Biochemistry and Applications, CRC press, Taylor & Francis group, 2006, 37-142.
7. Koshy A. S, Anila L and Vijayalakshmi N. R, Flavonoids from Garcinia cambogia lower lipid levels in hypercholesterolemic rats, Food chemistry, 72, 2001, 289-294.
8. Vinaya K, Kavitha C. V, Prasanna D. S, Chandrappa S, Ranganatha S. R, Raghavan S. C, Rangappa K. S, Synthesis and antileukemic activity of Novel 2-(4-(2,4-dimethoxybenzoyl)phenoxy)-1-(4-(3-(piperidin-4-yl)propyl)piperidin-1-yl)ethanone derivatives, Chemical biology and drud design, 79(3), 2012, 360-367.
9. Knekt P, Kumpulainen J, Ritva J, Rissanen H, Heliovaara M, Reunanen A, Hakulinen T and Aromaa A, Flavonoid intake and risk of chronic diseases, Am J Clin Nutr, 76, 2002, 560-568.
10. Iinuma M, Ito T, Miyake R, Tanaka T and Chelladurai V, A xanthone from *Garcinia cambogia*, Phytochemistry, 47(6), 1169-1170.
11. Masullo M, Bassarello C, Bifulco G and Piacente S, Polyisoprenylated benzophenone derivatives from the fruits of Garcinia cambogia and their absolute configuration by quantum chemical circular dichroism calculations, Tetrahedron, 66, 2010, 139-145.
12. Kolodziejczyk J, Masullo M, Olas B, Piacente S and Wachowicz B, Effects of Garcinol and Guttiferone K isolated from *Garcinia cambogia* on oxidative/nitrative modifications in blood platelets and plasma, Platelets, 20(7), 2009, 487-492.
13. Iinuma M, Ito T, Miyake R, Tanaka T and Chelladurai V, A xanthone from *Garcinia cambogia*, Phytochemistry, 47(6), 1169-1170.
14. Padhye S, Ahmad A, Oswal N, Sarkar F H, Emerging role of Garcinol, the antioxidant chalcone from *Garcinia indica* Choisy and its synthetic analogs, Journal of Hematology and Oncology, 2(38), 2009
15. Prasad S, Ravindran J, Sung B, Pandey M. K and Agarwal B. B, Garcinol potentiates TRAIL-Induced Apoptosis through Modulation of death receptors and antiapoptotic proteins, Mol Cancer Ther, 9(4), 2010, 856-868.
16. Matsumoto K, Akao Y, Kobayashi E, Ito T, Ohguchi K, Tanaka T, Iinuma M and Nozawa Y, Cytotoxic benzophenone derivatives from *Garcinia* species display a strong apoptosis-inducing effect against Human Leukemia Cell lines, Biol. Pharm. Bull, 26(4), 2003, 569-571.
17. Ahmad A, Wang Z, Wojewoda C, Ali R, Kong D, Maitah M. Y, Banerjee S, Bao B, Pandhye S and Sarkar F H, Garcinol induced apoptosis in prostate and pancreatic cancer cells is mediated by NF Kappa B signaling, Frontiers in Bioscience, 3, 2011, 1483-1492.
18. Koeberle A, Northoff H and Werz O, identification of 5-lipoxygenase and microsomal prostaglandin E_2 Synthase-1 as functional targets of the anti-inflammatory and anti-carcinogenic garcinol, Biochemical pharmacology, 77, 2009, 1513-1521.
19. Hong J, Kwon S. K, Sang S, Ju J, Zhou J, Ho C, Huang M and Yang C. S, Effects of garcinol and its derivatives on intestinal cell growth: Inhibitory effects and autoxidation-dependent growth-stimulatory effects, Free radical biology & medicine, 42, 2007, 1211-1221.
20. Tanaka T, Kohno H, Shimada R, Kagami S, Yamaguchi F, Kataoka S, Ariga T, Murakami A, Koshimizu K and Ohigashi H, prevention of colonic aberrant crypt foci by dietary feeding of garcinol in male F344 rats, Carcinogenesis, 21(6), 2000, 1183-1189.
21. Arif M, Pradhan S. K, Thanuja G. R, Vedamurthy B. M, Agarwal S, Dasgupta D and Kundu T. K, Mechanism of p300 Specific Histone Acetyltransferase Inhibition by Small Molecules, J. Med. Chem, 52(2), 267-277.
22. Balasubramanyam K, Altaf M, Varier R. A, Swaminathan V, Ravindran A, Sadhale P. P, Kundu T. K, Polyisoprenylated Benzophenone, Garcinol, a Natural Histone Acetyltransferase Inhibitor, Represses Chromatin Transcription and Alters Global Gene Expression, 279(32), 2004, 33716-33726.
23. Yoshida K, Tanaka T, Hirose Y, Yamaguchi F, Kohno H, Toida M, Hara A, Sugie S, Shibata T and Mori H, Dietary garcinol inhibits 4-nitroquinoline 1-oxide-induced tongue carcinogenesis in rats, 221, 2005, 29-39.
24. Ohnishi H, Asamoto M, Tujimura K, Hokaiwado N, Takahashi S, Ogawa K, Kuribayashi M, Okuyama H and Shirai T, Inhibition of cell proliferation by nobiletin, a dietary phytochemical, associated with apoptosis and characteristic gene expression, but lack of effect on early rat hepatocarcinogenesis in vivo, 95(12), 2004, 936-942.
25. Cheng A, Tsai M, Liu C, Lee M, Nagabhushanam K, Ho C and Pan M, Garcinol inhibits cell growth in hepatocellular carcinoma Hep3B cells through induction of ROS-dependent apoptosis, 1, 2010, 301-307.
26. Hokaiwado N, Asamoto M, Tsujimura K, Hirota T, Ichihara T, Satoh T and Shirai T, Rapid analysis of gene expression changes caused by liver carcinogens and chemopreventive agents using a newly developed three-dimensional microarray system, Cancer Sci, 95(2), 2004, 123-130.
27. Wang Y, Shi J, Wang M, Che C and Yeung J, Vasodilatory actions of xanthones isolated from a Tibetan herb, *Halenia elliptica,* Phytomedicine, 16(12), 2009, 1144-1150.
28. Hay A, Heles beux J, Duval O, Medhi L, Grellier P and Richomme P, Antimalarial xanthones from *Calophyllum caledonicum* and *Garcinia vieillardii,* Life Sciences, 75(25), 2004, 3077-3085.
29. Ito C, Itoigawa M, Furukawa H, Rao K. S, Enjo F, Bu P, Takayasu J, Tokuda H and Nishino H, Xanthones as inhibitors of Epstein-Barr virus activation, Cancer Letters, 132(1-2), 1998, 113-117.
30. Niu S, Li Z, Ji F, Liu G, Zhao N, Liu X, Jing Y and Hua H, Xanthones from the stem bark of *Garcinia bracteata* with growth inhibitory effects against HL-60 cells, Phytochemistry, 77, 2012, 280-286.
31. Wang J, Sanderson B and Zhang W, Cytotoxic effect of xanthones from pericarp of the tropical fruit mangosteen (*Garcinia*

mangostana Linn.) on human melanoma cells, Food and Chemical Toxicology, 49(9), 2011, 2385-2391.

32. FouotsaH, Lannang A, Mbazoa C, Rasheed S, Marasini B, Ali Z, Devkota K. P, Kengfack A. E, Shaheen F, Choudhary M I and Sewald N, Xanthones inhibitors of α-glucosidase and glycation from *Garcinia nobilis*, Phytochemistry letters, 5(2), 2012, 236-239.
33. Tomic M, Tovilovic G, Butorovic B, Krstic D, Jankovic T, Aljancic I and Menkovic N, Neuropharmacological evaluation of diethylether extract and xanthones of *Gentiana kochiana,* Pharmacology Biochemistry and Behavior, 81(3), 2005, 535-542.
34. Jantan I, Juriyati J and Warif N. A, Inhibitory effects of xanthones on platelet activating factor receptor binding *in vitro*, Journal of Ethnopharmacology, 75(2-3), 2001, 287-290.
35. Han Q, Yang N, Tian H, Qiao C, Song J, Chang D. C, Chen S, Luo K. Q and Xu H,Xanthones with growth inhibition against HeLa cells from *Garcinia xipshuanbannaensis*, Phytochemistry, 69(11), 2008, 2187-2192.
36. Lee B. W, Lee J. H, Lee S. T, Lee H. S, Lee W. S, Jeong T. S and Park K. H, Antioxidant and cytotoxic activities of xanthones from *Cudrania tricuspidata*, Bioorganic & Medicinal chemistry letters, 15(24), 2005, 5548-5552.
37. Wabo H. K, Kikuchi H, Katou Y, Tane P and Oshima Y, Xanthones and a benzophenone from the roots of *Pentadesma butyracea* and their antiproliferative activity, Phytochemistry letters, 3, 2010, 104-107.
38. Matsumoto K, Akao Y, Ohguchi K, Ito T, Tanaka T, Iinuma M and Nozawa Y, Xanthones induce cell-cycle arrest and apoptosis in human colon cancer DLD-1 cells, Bioorganic and Medicinal chemistry, 13(21), 2005, 6064-6069.
39. Chatterjee A, Bagchi D, Yasmin T and Stohs S. J, Antimicrobial effects of antioxidants with and without clarithromycin on *Helicobacter pylori*, Mol Cell Biochem, 270(1-2), 2005, 125-130.
40. Iinuma M, Tosa H, Tanaka T, Kanamaru S, Asai F, Kobayashi Y, Miyauchi K and Shimano R, Antibacterial activity of some *Garcinia* benzophenone derivatives against methicillin-resistant *Staphylococcus aureus*, Biol Pharm Bull, 19 (2), 1996, 311-314.
41. Pereira I. O, Marques M. J, Pavan A. L. R, Codonho B. S, Barbieri C. L, Beijo L. A, Doriguetto A. C, D Martin E. C and Santos M. H, Leishmanicidal activity of benzophenones and extracts from *Garcinia brasiliensis* Mart. Fruits, Phytomedicine, 17(5), 2010, 339-345.
42. Pardo-Andreu G. L, Figueredo Y. N, Tudella V. G, Cuesta-Rubio O, Rodrigues F. P, Pestana C. R, Uyemura S. A, Leopoldino A. M, Albercici L. C and Curti C, The anti-cancer agent guttiferone –A permeabilizes mitochondrial membrane: Ensuing energetic and oxidative stress implications, Toxicology and Applied Pharmacology, 253(3), 2011, 282-289.
43. Dias K. S. T, Januario J. P, Dego J. L. D, Dias A. L.T, Santos M. H, Camps I, Coelho L. F. L and Viegas Jr C, Semisynthesis and antimicrobial activity of novel guttiferone-A derivatives, Bioorganic & Medicinal Chemistry, 20(8), 2012, 2713-2720.
44. Martins F. T, Assis D. M, Santos M. H, Camps I, Veloso M, Juliano M. A, Alves L. C, Doriguetto A. C, Natural polyprenylated benzophenones inhibiting cysteine and serine proteases, European Journal of Medicinal Chemistry, 44, 2009, 1230-1239.
45. Nguyen H. D, Trinh B. T. D and Nguyen L. D, Guttiferones Q-S, cytotoxic polyisoprenylated benzophenones from the pericarp of *Garcinia cochinchinensis*, Phytochemistry letters, 4(2), 2011, 129-133.
46. Acuna U. M, Dastmalchi K, Basile M. J and Kennelly E. J, Quantitative high-performance liquid chromatography photo-diode array (HPLC-PDA) analysis of benzophenones and biflavonoids in eight *Garcinia* species, Journal of Food Composition and Analysis, 25(2), 2012, 215-220.
47. Kolodziejczyk J, Masullo M, Olas B, Piacente S and Wachowicz B, Effects of Garcinol and Guttiferone K isolated from *Garcinia cambogia* on oxidative/nitrative modifications in blood platelets and plasma, Platelets, 20(7), 2009, 487-492.
48. Kan W. L, Yin C, Xu H. X, To K. K, Cho C. H, Rudd J. A and Lin G, Antitumor effects of novel compound, guttiferone K, on colon cancer by p21Waf1/Cip1-mediated G(0)/G(1) cell cycle arrest and apoptosis, Int J Cancer, 132(3), 2013, 707-716.
49. Cao S, Brodie P. J, Miller J. S, Ratovoson F, Brikinshaw C, Randrianasolo S, Rakotobe E, Rasamison V. E and David G. I, Guttiferones K and L, Antiproliferative compounds of *Rheedia calcicola* from the Madagascar rain forest, J Nat Prod, 70(4), 2007, 686-688.
50. Liu X, Yu T, Gao X. M, Zhou Y, Qiao C. F, Peng Y, Chen S. L, Luo K. Q and Xu H. X, Apoptotic effects of polyprenylated benzoylphloroglucinol derivatives from the twigs of Garcinia multiflora, J Nat Prod, 73(8), 2010, 1355-1359.
51. Acuna U. M, Figueroa M, Kavalier A, Jancovski N, Basile M. J and Kennelly E. J, Benzophenones and biflavonoids from from *Rheedia edulis*, J Nat Prod, 73(11), 2010, 1775-1779.
52. Herath K, Jayasuriya H, Ondeyka, J. G, Guan Z, Borris R. P, Stijfhoorn E, Stevenson D, Wang J, Sharma N, MacNaul K, menke J. G, Ali A, Schulman M. J and Singh S. B, Guttiferone I, a new prenylated benzophenone from Garcinia humilis as a liver X receptor ligand, J Nat Prod, 68(4), 2005, 617-619.
53. Merza J, Mallet S, Litaudon M, Dumontet V, Seraphin D and Richomme P, New cytotoxic guttiferone analogues from *Garcinia virgata* from New Caledonia, Planta med, 72(1), 2006, 87-89.
54. Carroll A. R, Suraweera L, King G, Rali T and Qunn R. J, Guttiferones O and P, Prenylated Benzophenone MAPKAPK-2 Inhibitors from *Garcinia solomonensis,* J Nat Prod, XXXX, xxx, 2009, 000.
55. Koshy A. S, Anila L and Vijayalakshmi N. R, Flavonoids from Garcinia cambogia lower lipid levels in hypercholesterolemic rats, Food Chemistry, 72, 2001, 289-294.
56. Iwu M and Igboko O, Flavonoids of *Garcinia kola* seeds, J Nat Prod, 45(5), 1982, 650-651.
57. Jena B. S, Jayaprakasha G. K and Sakariah K. K, Organic acids from leaves, fruits, and rinds of *Garcinia cowa*, J Agric Food Chem, 50(12), 2002, 3431-3434.
58. Yamada T, Hida H and Yamada Y, Chemistry, physiological properties and microbial production of Hydroxycitric acid, Appl Microbiol Biotechnol, 75, 2007, 977-982.
59. Sreenivasan A and Venkataraman R, Chromatographic detection of the organic acid constituents of Gorikapuli (*Garcinia cambogia* Desr.) used in pickling fish, Current Science, 1958, 151-152.
60. Lewis Y. S and Neelakantan, (-)- Hydroxycitric acid – the principal acid in the fruits of *Garcinia cambogia* desr., Phytochemistry, 4(4), 1965, 619-625.
61. Mofett S. A, Bhandari A. K, Ravindranath B and Balasubramanyam K, Hydroxycitric acid concentrate and food products prepared therefrom, U.S. Patent, 5656314, aug.12, 1997.
62. Ibnsaud I, Thomas P. T, Rani R. N, Sasi P. V, Beena T and Hisham A, Chiral γ-butyrolactones related to optically active 2-hydroxycitric acids, Tetrahedron, 58(24), 2002, 4887-4892.
63. Jayaprakasha G. K and Sakariah K. K, Determination of (-) Hydroxycitric acid in commercial samples of Garcinia cambogia extract by liquid chromatography with ultraviolet detection, Journal of liquid chromatography and related technologies, 23(6), 2000, 915-923.
64. Antony B, Varghese W and Elias M, Preparation and evaluation of hydroxycitric acid from *Garcinia cambogia* extract using RP-amide HPLC, Indian J. Pharm. Sci, 66(2), 2004, 208-211.

65. Antony B, Varghese W and Elias M, Spectrophotometric determination of Hydroxycitric acid, Indian J. Pharm. Sci, 1999, 316-317.

66. Jayaprakasha G. K, Jena B. S and Sakariah K. K, Improved liquid chromatographic method for determination of organic acids in leaves, pulp, fruits and rinds of *Garcinia*, Journal of AOAC International, 86(5), 2003, 1063-1068.

67. Watson J. A, Fang M and Lowenstein J. M, Tricarballylate and hydroxycitrate: Substrate and inhibitor of ATP: Citrate oxaloacetate lyase, Archives of Biochemistry and Biophysics, 135, 1969, 209-217.

68. Watson J. A and Lowenstein J. M, Citrate and the conversion of carbohydrate into fat, The Journal of biological chemistry, 245(22), 1970, 5993-6002.

69. Kornacker M. S and Lowenstein J. M, Citrate and the conversion of carbohydrate into fat, Journal of biological chemistry, 95, 1965, 832-837.

70. Spencer A, Corman L and Lowenstein J. M, Citrate and the conversion of carbohydrate into fat, Journal of biological chemistry, 93, 1964, 378-388.

71. Preuss H. G, Bagchi D, Bagchi M, Rao C. V. S, Styanarayana S and Dey D. K, Efficacy of a novel, natural extract of (-)-hydroxycitric acid (HCA-SX) and a combination of HCA-SX, niacin –bound chromium and *Gymnema sylvestre* ectract in weight management in human volunteers: A pilot study, Nutrition research, 24, 2004, 45-58.

72. Sethi A, A review on "*Garcinia cambogia*- a weight controlling agent", Int J. Pharm res and Dev, 3(10), 2011, 13-24.

73. Sullivan A. C, Hamilton J. G, Miller O. N and Wheatley V. R, Inhibition of lipogenesis in rat liver by (-)- hydroxycitrate, Archives of Biochemistry and Biophysics, 150(1), 1972, 183-190.

74. Soni M. G, Burdock G. A, Preuss H. G, Stohs S. J, Ohia S. E and Bagchi D, Safety assessment of (-)-hydroxycitric acid and Super Citrimax, a novel calcium/potassium salt, Food and Chemical toxicology, 42, 2004, 1513-1529.

Source of Support: Nil, **Conflict of Interest:** None.