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Chemical constituents and biological activities of Garcinia cowa Roxb

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Abstract

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Keywords

biological, chemical, roxb, cowa, garcinia, activities, constituents, CMMB

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Review

Chemical constituents and biological activities of *Garcinia cowa* Roxb.

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Abstract: *Garcinia cowa* is an abundant source of bioactive phytochemicals. Phytochemical investigations of the plant parts indicated that the fruit, twig and stem are the best source of secondary metabolites, providing flavonoids, phloroglucinols and xanthones respectively. Seventy-eight of these compounds have been identified from the plant and several have interesting pharmacological activities.

Keywords: *Garcinia cowa*, flavonoids, xanthones, phloroglucinols

INTRODUCTION

Many pharmaceutical drug discoveries originated from traditional folk medicine and its associated plant materials and bioactive secondary metabolites. The Genus *Garcinia*, belonging to the Family Clusiaceae which comprises about 300 species, have been widely investigated in terms of their bioactive ingredients. Native to Asia, Africa, South America and Polynesia, the plants are small to medium sized evergreen trees which may grow up to 30 m in height and are widely distributed in the tropical and temperate regions of the world [1]. Twenty-nine species have been observed in Thailand, with 20, 13, 12, 7, 6 and 3 species found in the south, middle, north, east, north-east and west of the country respectively (Figure 1).

Garcinia is a rich source of secondary metabolites, especially triterpenes [1], flavonoids [5], xanthones [6] and phloroglucinols [7]. The latter two groups are well recognised as cheomotaxonomic markers for this genus [8a-e]. Many of the isolated compounds have a wide range

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of pharmacological activities including anticancer, anti-inflammatory, antibacterial, antiviral, antifungal, anti-HIV, antidepressant and antioxidant [1, 9-13].

Figure 1. Species of *Garcinia* found in different parts of Thailand [2-4]

Garcinia cowa (Figure 2a), commonly known as Cha-muang in Thai, is widely distributed throughout Malaysia, Thailand and Myanmar. The fruits and young leaves are edible with a sour taste. The bark is dark brown with a yellow latex (Figure 2b). The plant has unisex flowers: yellow orange female flowers found at the end of branches and male flowers found along the branches as clusters (Figure 2c). The leaves are glossy, deep green, oblong and up to 6-15 cm in length and 2.5-6.0 cm in width (Figure 2d). The fruits are globose (2.5-6.0 cm in size), green when young and dull

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orange or yellow at maturity with 5-8 shallow grooves, at least near the top, and contain 6-8 large 3-angled seeds (Figure 2e) [14].

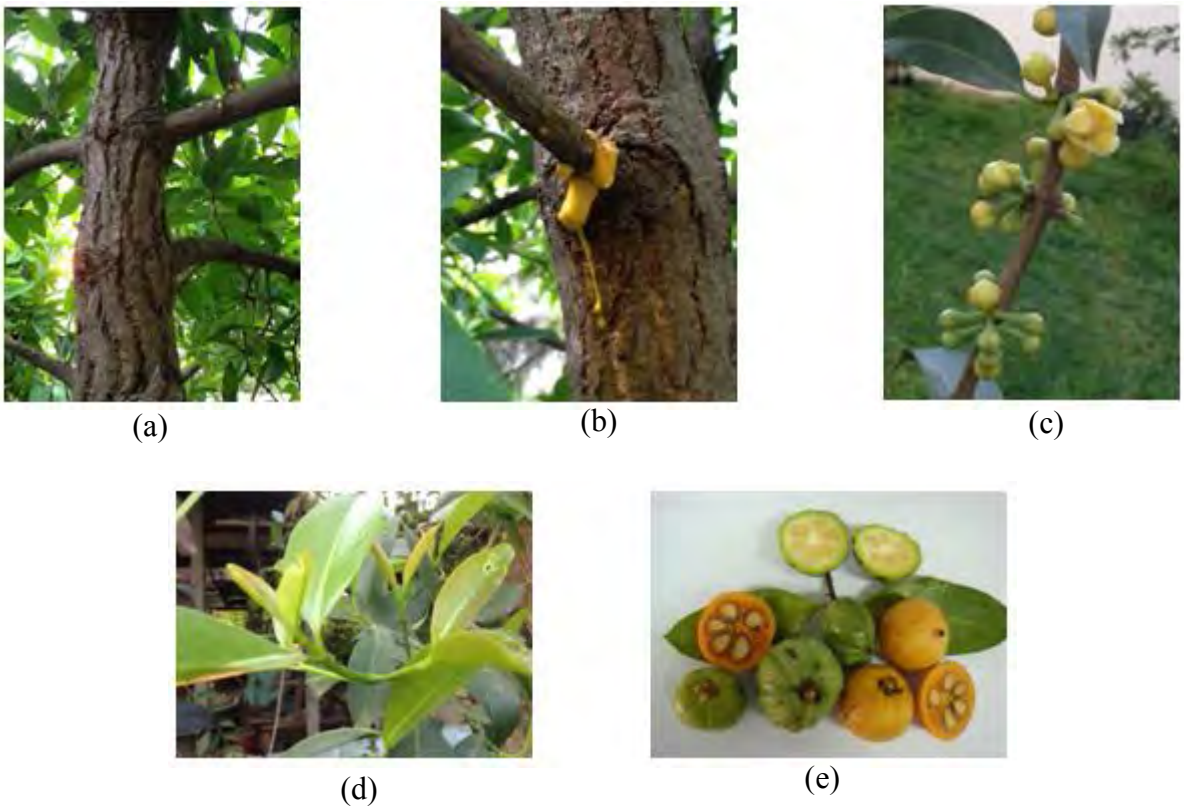

Figure 2. Parts of *G. cowa*: (a) branch, (b) bark and latex, (c) inflorescences, (d) leaves and (e) ripe and immature fruits (Photos taken by S. Laphookhieo, 2011)

Many parts of *G. cowa* have been used in traditional folk medicine. For example, the bark, latex and root have been used as an antifever agent [15, 16] while the fruit and leaves have been used for indigestion and improvement of blood circulation, and as an expectorant [16]. The chemical composition and biological activities of various parts of *G. cowa* have been investigated. The major compounds found were xanthones and phloroglucinols. However, minor compounds, including depsidones, terpenoids, steroids and flavonoids, were also observed. Currently, 78 compounds have been isolated from the twig [17], stem [18], fruit [19, 20] and latex [15]. This review mainly focuses on the chemical structures and biological activities of the phytochemicals isolated from *G. cowa* and covers the literature up to April 2012.

DISTRIBUTION AND BIOLOGICAL ACTIVITY

The biological activities of the extracts from various parts of *G. cowa* have been investigated, including the hexane and chloroform extracts of the fruit rind and methanol extract of the leaves and twigs [21-23].The hexane and chloroform extracts from the fruit rind of *G. cowa* were tested against four Gram-positive bacteria (*Bacillus cereus, B. coagulans, B. subtilis* and *Staphylococcus aureus*) and one Gram-negative bacterium (*Escherichia coli*). Both extracts significantly inhibited bacterial

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growth of the Gram-positive bacteria (IC_{50}s 15-30 μg/mL) but not *E. coli* (IC_{50}s 250-500 μg/mL) [21]. The extracts were also found to inhibit the growth of *Aspergillus flavus* ATCC 46283, a common fungal food contaminant which produces aflatoxin B_1. The degree of inhibition of aflatoxin B_1 production (100% at a concentration of 2000 ppm) was found to be much higher than the inhibition of fungal growth (*ca* 40-60% at the same concentration) [22]. The methanol extracts of the leaves and twigs of *G. cowa* were evaluated for their ability to inhibit low-density lipoprotein peroxidation induced by copper ions. The twig extract had an IC_{50} value of 20.5 μg/mL and was more potent (higher % inhibition at 1000 μg/mL) than the leaf extract (IC_{50} not measured). The twig extract was more potent than the leaf extract on platelet aggregation of human whole blood induced by arachidonic acid, adenosine diphosphate and collagen. These activities may be due to the total phenolic content of these extracts, which were 19 and 61 mg of gallic acid equivalent per g of extract for the leaf and twig extracts respectively [23]. The structural types, chemical structures and biological activities of the natural products isolated from different parts of *G. cowa* were summarised in Table 1. A summary of the number of natural product compounds first discovered in each structural class is shown in Figure 3 and from different parts of the plant is shown in Figure 4.

Table 1. Structure, distribution and biological activity of phytochemicals isolated from different parts of *G. cowa*

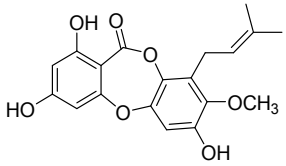
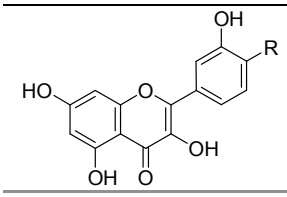
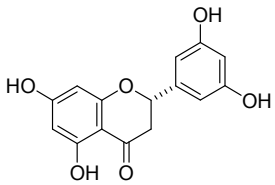
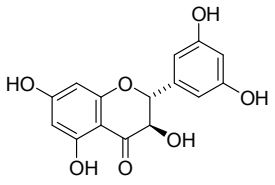
Category and structure	Name (code), source and reference	Biological activity
Depsidone		
	Cowadepsidone (**1**); twig [17]*	Cytotoxicity [17] NCI-H187 IC_{50} 31.47 μg/mL MFC-7 IC_{50} 36.03 μg/mL
Flavonoid		
	R = H Kaempferol (**2**); branch [24]	
	R = OH Quercetin (**3**); stem [18]	
	2-(3,5-Dihydroxyphenyl)-2,3-dihy-dro-5,7-dihydroxy-3′,5,5′,7-tetrahydroxyflavanone (**4**); stem [18]	
	2-(3,5-Dihydroxy-phenyl)-2,3-dihy-dro-3,5,7-trihydroxy-(2*R*,3*R*)-3,3′,5,5′,7-pentahydroxy flavanone (**5**); stem [18]	

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Table 1. (continued)

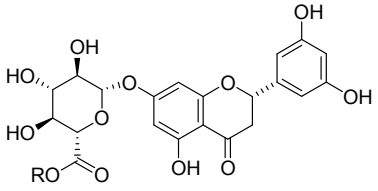
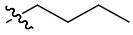
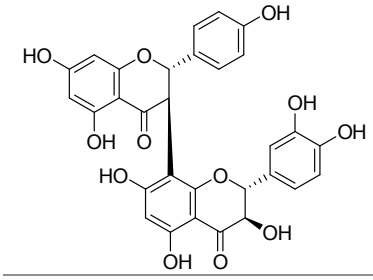
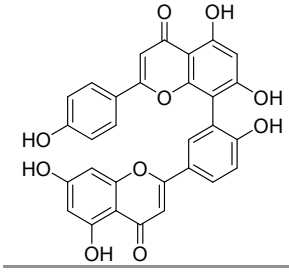
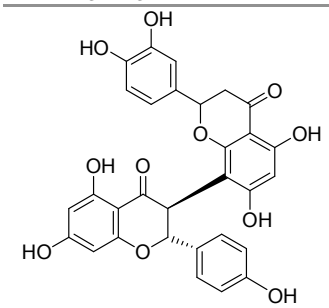
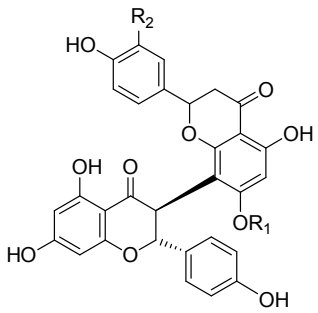
Category and structure	Name (code), source and reference	Biological activity
Flavonoid		
	R =  Garccowaside A (**6**); stem [18]* R =  Garccowaside B (**7**); stem [18]* R = CH_3 Garccowaside C (**8**); stem [18]*	
	GB-2 (**9**); branch [24]	
	Amentoflavone (**10**); fruit [19]	
	Morelloflavone (**11**); fruit [19] twig [16]	Antioxidant activity [16] DPPH assay IC_{50} 10.01 µg/mL Hydroxyl radical scavenging assay IC_{50} $3.11x10^{-4}$ µg/mL Superoxide anion scavenging assay IC_{50} $1.50x10^{-4}$ µg/mL
	$R_1 = R_2 = H$ Volkensiflavone (**12**); twig [16]	
	R_1 = β-glucoside; R_2 = OH Morelloflavone-7′-*O*-glucoside or fukugiside (**13**); twig [16]	Antioxidant activity [16] DPPH assay IC_{50} 12.92 µg/mL Hydroxyl radical scavenging assay IC_{50} $5.31x10^{-4}$ µg/mL Superoxide anion scavenging assay IC_{50} $6.39x10^{-4}$µg/mL

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Table 1. (continued)

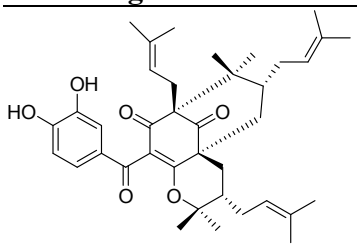
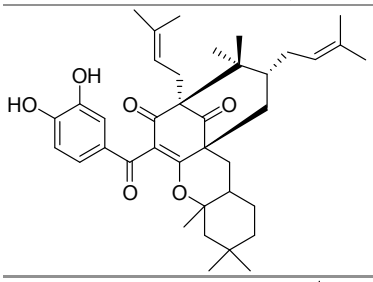
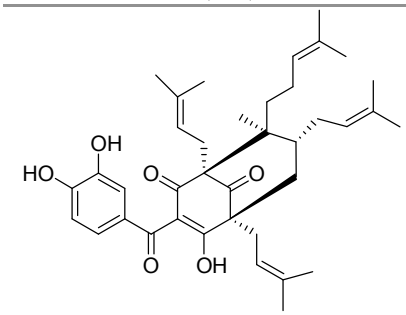
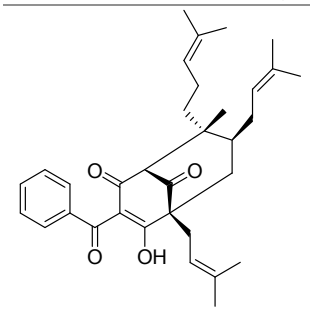
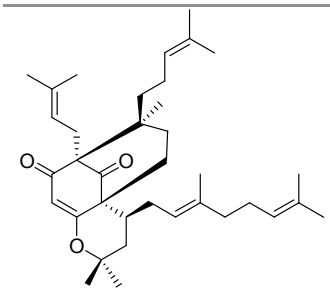
Category and structure	Name (code), source and reference	Biological activity
Phloroglucinol		
	Cambogin (**14**); fruit [25, 26], twig [7], stem [26]	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co
	Guttiferone K (**15a**)[#]; fruit [26]*, stem [26]	
	Guttiferone K (**15b**)[#]; twig [7]	Cytotoxicity [7] against HT-29 IC_{50} 3.25±0.12 µg/mL HCT-116 CCD-18Co
	Chamuangone (**16**); leaf [27]*	Antibacterial activity [27] *S. pyogenes* MIC 7.8 µg/mL *S. viridans* MIC 15.6 µg/mL *H. pylori* MIC 15.6 µg/mL *B. subtilis, Enterococcus sp.* and *S. aureus* MIC 31.2µg/mL
	Garcicowin A (**17**); twig [7]*	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co

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Table 1. (continued)

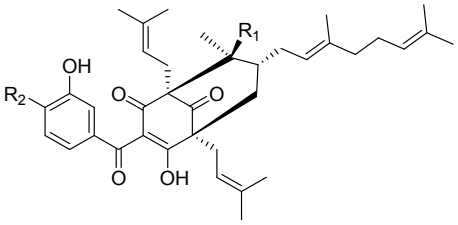
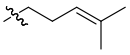
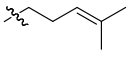
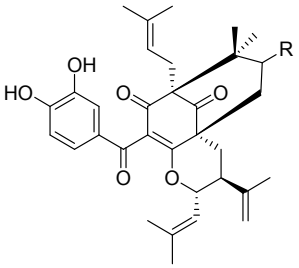
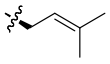
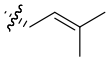
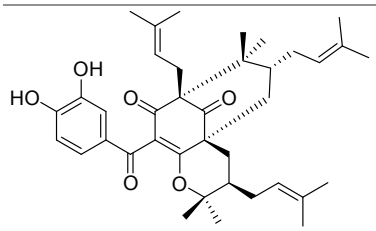
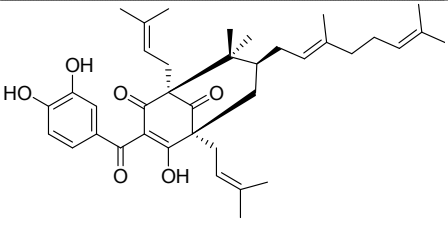
Category and structure	Name (code), source and reference	Biological activity
Phloroglucinol		
	R_1 =  ; R_2 = H Garcicowin B (**18**); twig [7]*	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co
	R_1 = CH_3; R_2 = OH Oblongifolin B (**19**); twig [7]	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co
	R_1 =  ; R_2 = OH Oblongifolin C (**20**); twig [7]	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co
	R =  Garcicowin C (**21**); twig [7]*	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co
	R =  Garcicowin D (**22**); twig [7]*	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co
	30-Epicambogin (**23**); twig [7]	Cytotoxicity [7] against HT-29 IC_{50} 3.07±0.06 µg/mL HCT-116 CCD-18Co
	Oblongifolin A (**24**); twig [7]	

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Table 1. (continued)

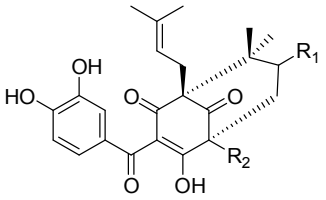
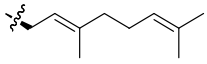
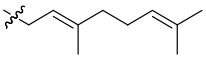
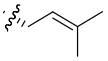
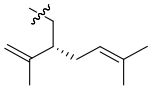
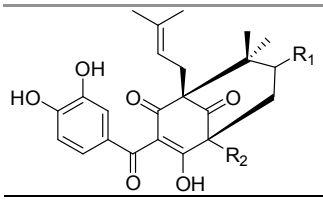
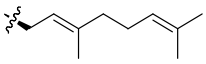
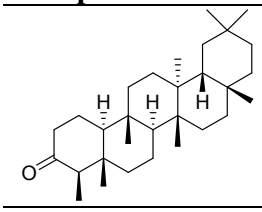
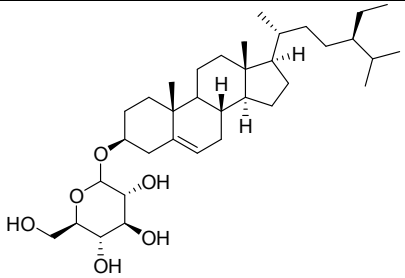
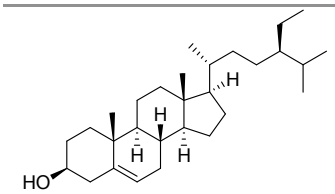
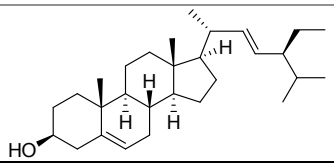
Category and structure	Name (code), source and reference	Biological activity
Phloroglucinol		
	R_1 =  R_2 =  Guttiferone B (**25**); twig [7]	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co
	R_1 =  R_2 =  Guttiferone F (**26**); twig [7]	
	$R_1 = R_2$ =  Oblongifolin D (**27**); twig [7]	Cytotoxicity [7] against HT-29 HCT-116 CCD-18Co
Terpene and Steroid		
	Friedelin (**28**); branch [24]	
	Daucosterol (**29**); branch [24], fruit [19]	
	*β*-Sitosterol (**30**); branch [24], fruit [19]	
	Stigmasterol (**31**); branch [24]	

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Table 1. (continued)

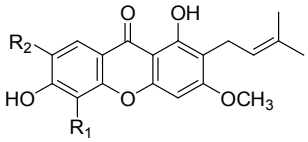
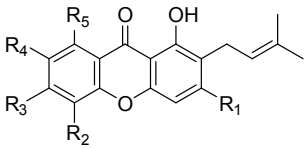
Category and structure	Name (code), source and reference	Biological activity
Xanthone		
	$R_1 = OCH_3$; $R_2 = H$ Cowaxanthone A (**32**); fruit [20] or cowagarcinone C; latex [15]*	Anti-inflammatory activity [16]
	$R_1 = H$; $R_2 = OCH_3$ 1,6-Dihydroxy-3,7-dimethoxy-2-(3-methyl-2-butenyl)xanthone (**33**); fruit [20]	
	$R_1 = OH$; $R_2 = H$; $R_3 = R_4 = OCH_3$; R_5 = prenyl Cowaxanthone B (**34**); fruit [20]*	Antibacterial activity [20] *S. aureus* MIC 128 µg/mL MRSA MIC 128 µg/mL Anti-inflammatory activity [16]
	$R_1 = R_3 = R_4 = OCH_3$; $R_2 = H$; R_5 = prenyl Fuscaxanthone C (**35**); fruit [20]	
	$R_1 = R_3$= OH; $R_2 = R_5$ = prenyl; $R_4 = OCH_3$ 7-*O*-Methylgarcinone E (**36**); stem [28]*, bark [29], fruit [20]	Antibacterial activity [20] *S. aureus* MIC 128 µg/mL MRSA MIC 64 µg/mL Antimalarial activity [29] *Plasmodium falciparum* IC_{50} 1.5-3.0 µg/mL Antimalarial activity [29] *Plasmodium falciparum* IC_{50} 1.5-3.0 µg/mL
	$R_1 = R_3 = OH$; $R_2 = H$; $R_4 = OCH_3$; R_5 = prenyl α-Mangostin (**37**); fruits [20], bark [29]	Antibacterial activity [20] *S.aureus* MIC 8 µg/mL MRSA MIC 8 µg/mL Anti-inflammatory activity [16] Antimalarial activity [29] *Plasmodium falciparum* IC_{50} 1.5-3.0 µg/mL
	$R_1 = R_4 = OCH_3$; $R_2 = H$; $R_3 = OH$; R_5 = prenyl β-Mangostin (**38**); fruit [20], twig [17]	Antibacterial activity [20] *S. aureus* MIC 128 µg/mL MRSA MIC 64 µg/mL

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Table 1. (continued)

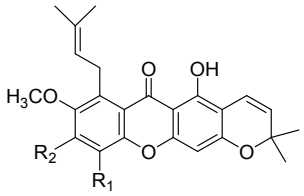
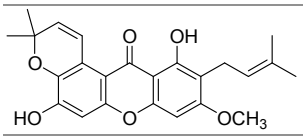
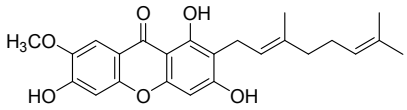
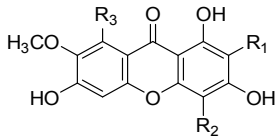
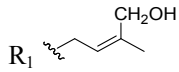
Category and structure	Name (code), source and reference	Biological activity
Xanthone		
	R_1 = prenyl; R_2 = OH Cowaxanthone C (**39**); fruit [20]*	Antibacterial activity [20] *S. aureus* MIC 128 µg/mL MRSA MIC 128 µg/mL Anti-inflammatory activity [16]
	R_1 = H; R_2 = OH Mangostanin (**40**); fruit [20]	Antibacterial activity [20] *S. aureus* MIC 4 µg/mL MRSA MIC 4 µg/mL Anti-inflammatory activity [16]
	R_1 = H; R_2 = OCH_3 6-*O*-Methylmangostanin (**41**); fruit [20]	
	Cowaxanthone D (**42**); fruit [20]*	Anti-inflammatory activity [16]
	Cowaxanthone (**43**); fruit [20], latex [15, 30*], twig [17], bark [29]	Antimalarial activity [29] *Plasmodium falciparum* IC_{50} 1.5-3.0 µg/mL Cytotoxicity [17] NCI-H187 IC_{50} 3.87 µg/mL KB IC_{50} 15.43 µg/mL MFC-7 IC_{50} 15.45 µg/mL
	R_1 = R_3 = prenyl; R_2 = CHO Cowaxanthone E (**44**); fruit [20]*	
	 ; R_2 = H; R_3 = geranyl Cowanol (**45**); fruit [20], latex [15, 30*], twig [17], bark [29]	Antibacterial activity [20] *S. aureus* MIC >128 µg/mL MRSA MIC >128 µg/mL Anti-inflammatory activity [16] Antimalarial activity [29] *Plasmodium falciparum* IC_{50} 1.5-3.0 µg/mL Cytotoxicity [17] NCI-H187 IC_{50} 37.26 µg/mL KB IC_{50} 32.34 µg/mL MFC-7 IC_{50} 34.62 µg/mL

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Table 1. (continued)

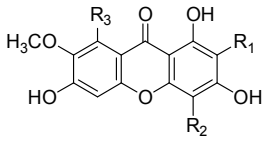
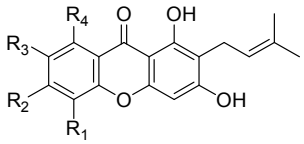
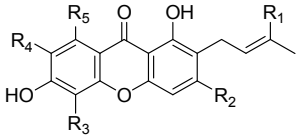
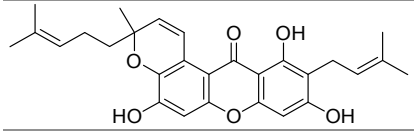
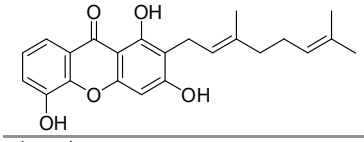
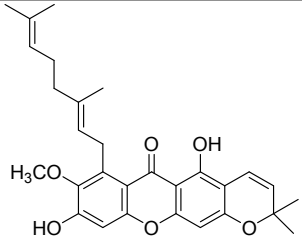
Category and structure	Name (code), source and reference	Biological activity
Xanthone		
	R_1 = prenyl; R_2 = H; R_3 = geranyl Cowanin (**46**); fruit [20], latex [15, 30*], twig [17], bark [29]	Antibacterial activity [20] *S .aureus* MIC >128 µg/mL MRSA MIC >128 µg/mL Anti-inflammatory activity [16] Antimalarial activity [29] *Plasmodium falciparum* IC_{50} 1.5-3.0 µg/mL
	R_1 = prenyl; R_2 = OH; R_3 = OCH_3; R_4= H 1,3,6-Trihydroxy-7-methoxy-2,5-bis(3-methyl-2-butenyl)xanthone (**47**); latex [15, 30*]	
	R_1 = H; R_2 = R_3 = OH; R_4 = geranyl Norcowanin (**48**); latex [30]*, twig [17]	Cytotoxicity [17] NCI-H187 IC_{50} 5.92 µg/mL KB IC_{50} 6.43 µg/mL MFC-7 IC_{50} 18.85 µg/mL
	R_1 = CH_3; R_2 = OH; R_3 = prenyl; R_4 = OCH_3; R_5 = geranyl Cowagarcinone A (**49**); latex [15]*	
	R_1 = CH_3; R_2 = R_3 = OCH_3; R_4 = R_5 = H Cowagarcinone B (**50**); latex [15]*	
	R_1 = CH_2OAc; R_2 = OH; R_3 = H; R_4 = OCH_3; R_5 = geranyl Cowagarcinone E (**51**); latex [15]*	
	Cowagarcinone D (**52**); latex [15]*	
	Mangostinone (**53**); latex [15]	
	Fuscaxanthone A (**54**); latex [15]	

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Table 1. (continued)

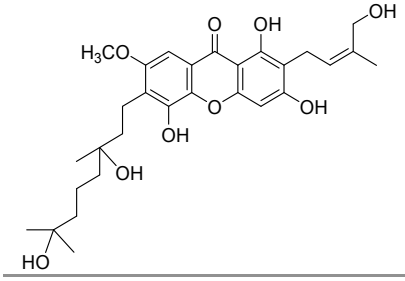
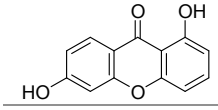
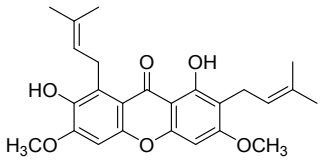
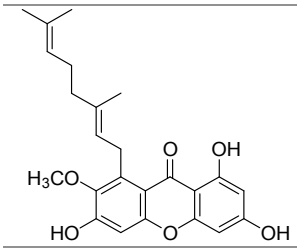
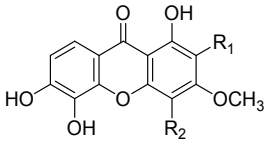
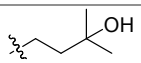
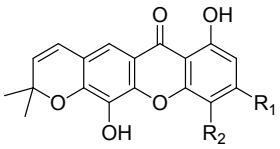
Category and structure	Name (code), source and reference	Biological activity
Xanthone		
	Cowaxanthone F (**55**); twig [16]*	
	1,6-Dihydroxyxanthone (**56**); twig [16]	
	3,6-Di-*O*-methyl-γ-mangostin (**57**); twig [17]	Cytotoxicity [17] NCI-H187 IC_{50} 8.58 μg/mL KB IC_{50} 6.64 μg/mL MFC-7 IC_{50} 10.59 μg/mL
	Rubraxanthone (**58**); stem [31, 32]	
	R_1 = H; R_2 =  1,5,6-Trihydroxy-3-methoxy-4-(3-hydroxyl-3-methylbutyl)xanthone (**59**) or nigrolineaxanthone T; stem [18, 33*]	
	R_1 = H; R_2 = prenyl Dulxanthone A (**60**); stem [18, 33, 34]	Cytotoxicity [34] HepG2
	R_1 = prenyl; R_2 =  4-(1,1-Dimethyl-prop-2-enyl)-1,5,6-trihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthen-9-(9*H*)-one (**61**); stem [32]*	
	R_1 = OCH_3; R_2 = prenyl 1,5-Dihydroxy-3-methoxy-4-(3-methylbut-2-enyl)-6′,6′-dimethyl-2*H*-pyrano(2′,3′:6,7) xanthone (**62**); stem [18, 33*]	

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Table 1. (continued)

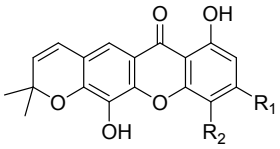
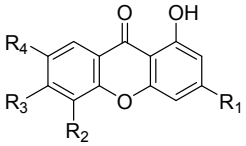
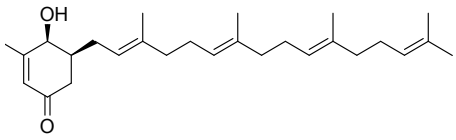
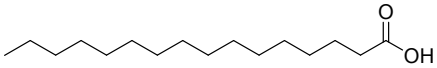
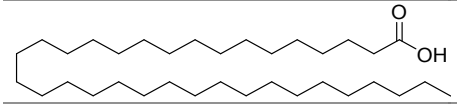
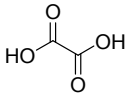
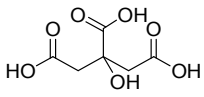
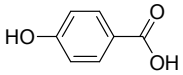
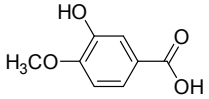
Category and structure	Name (code), source and reference	Biological activity
Xanthone		
	R_1 = OH; R_2 = H 1,3,5-Trihydroxy-6′,6′-dimethyl-2*H*-pyrano(2′,3′:6,7)xanthone (**63**); stem [18, 33]	
	R_1 = R_3 = R_4 = OH; R_2 = H 1,3,6,7-Tetrahydroxyxanthone (**64**) or norathyriol; stem [18, 33]	
	R_1 = R_2 = OH; R_3 = OCH_3; R_4 = H 1,3,5-Trihydroxy-6-methoxy-xanthone (**65**); stem [33]	
	R_1 = R_4 = OCH_3; R_2 = R_3 = OH 1,5,6-Trihydroxy-3,7-dimethoxyxanthone (**66**); stem [18, 33]	
	R_1 = R_2 = R_3 = H; R_4 = OH 1,7-Dihydroxyxanthone (**67**); stem [33]	
Miscellaneous compound		
	(2*E*,6*E*,10*E*)-(+)-4β-Hydroxy-3-methyl-5β-(3,7,11,15-tetramethyl-hexadeca-2,6,10,14-tetraenyl)cyclo-hex-2-en-1-one (**68**); stem [32]*	
	Palmitic acid (**69**); branch [24]	
	Tetratriacontanoic acid (**70**); branch [24]	
	Oxalic acid (**71**); fruit [35], fresh leaf [35], bark [35]	
	Citric acid (**72**); fruit [35], fresh leaf [35], bark [35]	
	4-Hydroxybenzoic acid (**73**); branch [24]	
	Isovanillic acid (**74**); branch [24]	

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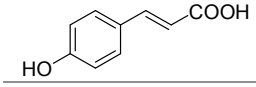
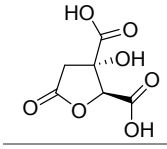
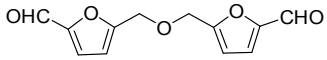
Table 1. (continued)

Category and structure	Name (code), source and reference	Biological activity
Miscellaneous compound		
	*p*-Coumaric acid (**75**); fruit [19]	
	(-)-Hydroxycitric acid lactone (**76**); fruit [35], fresh leaf [35], bark [35]	
	Cirsiumaldehyde (**77**); fruit [19]	

Note: Biological activity: MRSA (Methicillin resistant *Staphylococcus aureus*), NCI-H187 (Human small cell lung cancer), KB (Oral cavity cancer cell), MCF-7 (Breast cancer cell), HT-29 and HCT-116 (Human colon cancer cell), CCD-18Co (Normal human colon cell), HepG2 (Human hepatocellular liver carcinoma cell)

* Firstly discovered compound (new compound)

[#] Guttiferone K (**15a, 15b**) has been given two different structures in the literature [7, 26].

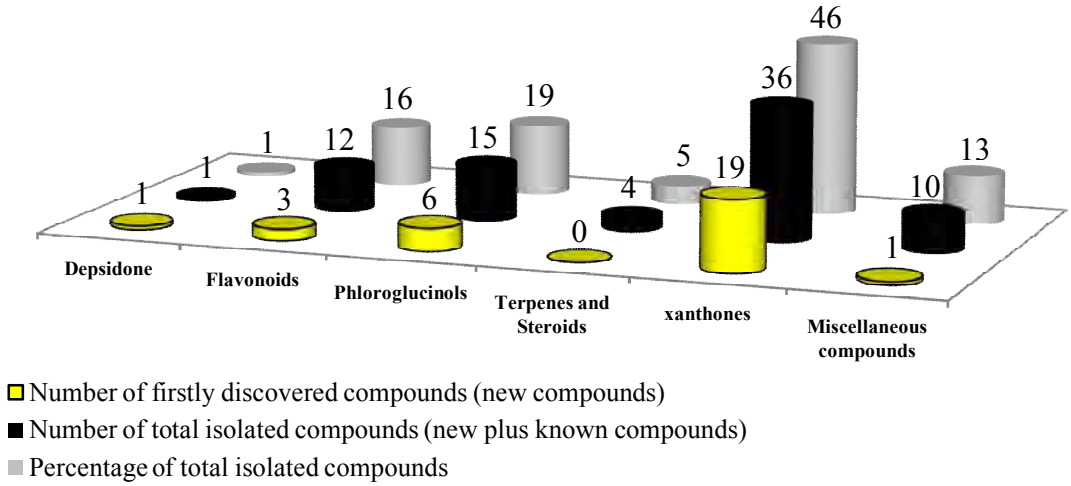


Figure 3. Classes and numbers of natural products isolated from *G. cowa*

CLASSESS OF COMPOUNDS ISOLATED FROM *G. COWA*

Depsidone

Depsidones comprise benzoic acid and phenol skeletons condensed at the *ortho*-positions through ester and ether linkages. This class of natural products is well known in the *Garcinia* species [36, 37]. However, cowadepsidone (**1**) was the first and only known depsidone from *G. cowa*. It was isolated from the twig extract and showed cytotoxicity against NCI-H187 and MFC-7 cancer cell lines [17].

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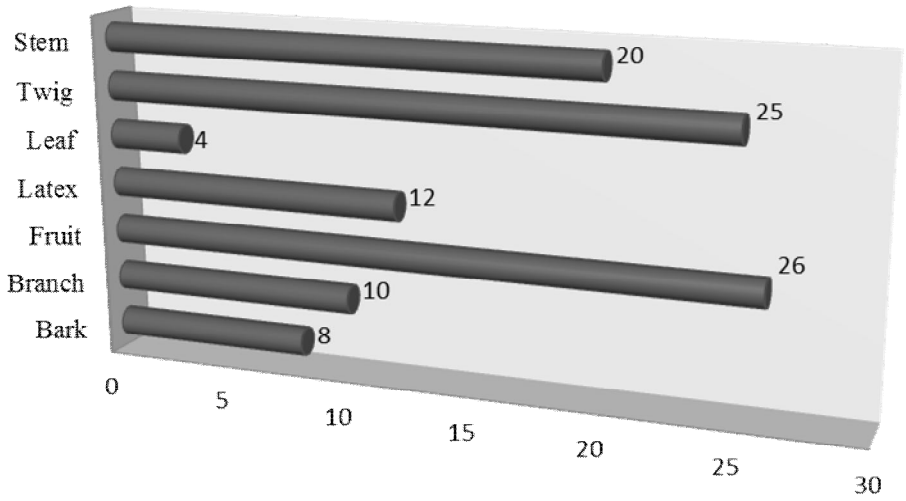

Figure 4. Numbers of natural products from different parts of *G. cowa*

Flavonoids

Twelve flavonoids (compounds **2-13** in Table 1) were isolated from *G. cowa* with garccowasides A (**6**), B (**7**) and C (**8**) being first reported as new compounds [18]. Of these compounds, only morelloflavone (**11**) and morelloflavone-7′′-*O*-glucoside (**13**) showed strong antioxidant activities [16].

Phloroglucinols

Phloroglucinols are based on a phloroglucinol or 1,3,5-benzenetriol core skeleton or its 1,3,5-cyclohexanetrione (phloroglucin) tautomer. The phloroglucinols found in *G. cowa* have a benzoyl group and geranyl and polyprenyl units as substituent groups. So far, fifteen phloroglucinols (compounds **14-27** in Table 1) have been obtained from the twig including six new compounds: guttiferone K (**15a**), chamuangone (**16**), garcicowins A (**17**), B (**18**), C (**21**) and D (**22**) [7, 26, 27], and nine known phloroglucinols: cambogin (**14**), guttiferones K (**15b**), B (**25**) and F(**26**), oblongifolins B (**19**), C (**20**), A (**24**) and D (**27**), and 30-epicambogin (**23**). Some of them showed selective cytotoxicity against two cancer cell lines (HT-29 and HCT-116) and normal colon cells (CCD-18Co). Guttiferone K (**15**) and 30-epicambogin (**23**) exhibited highest cytotoxicity against cancer cell line HT-29 [7]. The name guttiferone K has been given to two different structures in the literature [7, 26] as shown in Table 1. Only one compound, chamuangone (**16**), was tested for its antibacterial activity and was found to be active against *S. pyogenes* (MIC = 7.8 µg/mL), *S. viridans* and *H. pylori* (MICs = 15.6 µg/mL), and *S. aureus*, *B. subtilis* and *Enterococcus* sp. (all of this bacteria shown MICs = 31.2 µg/mL) [27].

Terpenes and Steroids

Terpenes and steroids represent two large classes of natural products, although they are rare in *G. cowa*. Only four of these types of compounds (5% of the total compounds isolated) were present in *G. cowa*, viz. friedelin (**28**), daucosterol (**29**), *β*-sitosterol (**30**) and stigmasterol (**31**) [24]. None of these compounds were further studied for their biological activities. However, these compounds which were isolated from other plants had been investigated for their biological

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activities. Friedelin (**28**) from the root bark of *Terminalia avicennioides* exhibited antibacterial activity against Bacillus Calmette-Guerin (BCG) with an MIC of 4.9 µg/mL [38]. Friedelin (**28**) and stigmasterol (**31**) isolated from the leaf of *Jatropha tanjorensis* were tested against human pathogenic microorganisms, i.e. Gram-positive bacteria: *Bacillus cereus, B. subtilis, S. aureus* and *S. epidermis*; Gram-negative bacteria: *Aeromonas hydrophila, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis, P. vulgaris, Salmonella paratyphi, S. paratyphi A, Vibrio alcaligenes* and *V. cholera*; and fungi: *Aspergillus fumigatus, Candida albicans, Microsporum gypseum* and *Trichophyton rubrum* using the agar-well diffusion and disk diffusion methods [39]. Friedelin (**28**), at the concentration of 2 µg/mL, showed maximum activity with 37-40, 17-40 and 31-33 mm of clear zone diameter against these three types of microorganisms respectively [39], while stigmasterol (**31**) at the same concentration exhibited maximum activity with 13-15, 8-17 and 7-8 mm of clear zone diameter respectively [39]. Daucosterol (**29**) from the roots of *Astragalus membranaceus* had no growth-inhibitory effect by direct contact but possessed immunomodulatory effect against disseminated candidiasis caused by *Candida albicans* [40]. β-Sitosterol **(30**) and stigmasterol (**31**), isolated from the bark of *Grewia tiliaefolia,* at the same concentration of 1 µg/mL showed antibacterial activity against the Gram-negative bacterium *P. aeruginosa* (ATCC-20852) with 18 and 20 mm of clear zones respectively and against *Klebsiella pneumonia* (MTCC-618) with 15 and 15 mm of clear zones respectively as determined by the agar diffusion method [41].

Xanthones

Xanthones, with two aromatic rings linked via carbonyl and ether linkages, are the major components of the *Garcinia* genus [8c-e]. They are commonly found in several parts of *G. cowa*, especially in the stem, fruit and latex. Thirty six xanthones (46% of the total isolated compounds) have been isolated and nineteen of them were first isolated from *G. cowa*. They are cowagarcinone C (**32**), cowaxanthone (**43**), cowanol (**45**), cowanin (**46**), 1,3,6-trihydroxy-7-methoxy-2,5-bis(3-methyl-2-butenyl)xanthone (**47**), norcowanin (**48**), cowagarcinones A (**49**), B (**50**), E (**51**) and D (**52**) from the latex [15, 30]; cowaxanthones B (**34**), C (**39**), D (**42**) and E (**44**) from the fruit [20]; 7-*O*-methylgarcinone E (**36**), 1,5,6-trihydroxy-3-methoxy-4-(3-hydroxyl-3-methylbutyl)xanthone (**59**), 4-(1,1-dimethyl-prop-2-enyl)-1,5,6-trihydroxy-3-methoxy-2-(3-methylbut-2-enyl)xanthen-9(9*H*)-one (**61**) and 1,5-dihydroxy-3methoxy-6′,6′-dimethyl-2*H*-pyrano(2′,3′:6,7)-4-(3-methylbut-2-enyl) xanthone (**62**) from the stem [18, 33]; and cowaxanthone F (**55**) from the twig [16]. Most of these xanthones showed interesting biological activities.

Antibacterial activity

Eight xanthones from the fruit: cowaxanthones B (**34**) and C (**39**), 7-*O*-methylgarcinone E (**36**), α-mangostin (**37**), β-mangostin (**38**), mangostanin (**40**), cowanol (**45**) and cowanin (**46**) were investigated for their antibacterial activity against *S. aureus* and MRSA. α-Mangostin (**37**) and mangostanin (**40**) showed significant activity against these bacteria. α-Mangostin (**37**) had a MIC value of 8 µg/mL against both *S. aureus* and MRSA while mangostanin (**40**) had an MIC value of 4 µg/mL against both bacteria [20].

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Anti-inflammatory activity

Eight xanthones: cowaxanthones A (**32**), B (**34**), C (**39**) and D (**42**), α-mangostin (**37**), mangostanin (**40**), cowanol (**45**) and cowanin (**46**) were tested for their anti-inflammatory activity using the ethyl phenylpropiolate induced ear edema assay. All xanthones except cowanol were more active than the standard drug, phenylbutazone [16].

Antimalarial activity

Five xanthones isolated from the stem bark: 7-*O*-methylgarcinone E (**36**), α-mangostin (**37**), cowaxanthone (**43**), cowanol (**45**) and cowanin (**46**) had significant in vitro antimalarial activity against *Plasmodium falciparum* with IC_{50} values ranging between 1.5-3.0 µg/mL [29].

Anticancer activity

Six xanthones: cowaxanthone (**43**), cowanol (**45**), cowanin (**46**), norcowanin (**48**), 3,6-di-*O*-methyl-γ-mangostin (**57**) and dulxanthone A (**60**) isolated from twig were evaluated for their cytotoxicity against NCI-H187, KB, MFC-7 and/or HepG2 cell lines. Cowaxanthone (**43**), cowanin (**46**), norcowanin (**48**) and 3,6-di-*O*-methyl-γ-mangostin (**57**) exhibited significant cytotoxicity against the NCI-H187 cell line with IC_{50} values ranging between 3.87-8.58 µg/mL, and moderately inhibited KB and MCF-7 cancer cell lines with IC_{50} values ranging between 6.43-15.43 and 10.59-21.38 µg/mL respectively [17]. Dulxanthone A (**60**) was found to be cytotoxic against the HepG2 cell line [34].

Miscellaneous Compounds

Ten (13% of the total isolated compounds) of the miscellaneous class of compounds have been isolated, including a new discovery: (2*E*,6*E*,10*E*)-(+)-4β-hydroxy-3-methyl-5β-(3,7,11,15-tetramethyl-hexadeca-2,6,10,14-tetraenyl)cyclohex-2-en-1-one (**68**) [32]. None of the isolated compounds from this class were tested for their biological activities.

CONCLUSIONS

G. cowa is an important source of bioactive compounds. Among the parts of this tree, the fruit, twig and stem are the best source of metabolites, thirty of which have been isolated, i.e. one depsidone, one α,β-unsaturated cyclohexenone, three flavonoids, six phloroglucinols and nineteen xanthones. Some of these compounds show interesting pharmacological activities. α-Mangostin (**37**), cowanol (**45**) and cowanin (**46**) are commonly found in all parts of *G. cowa* and they can be used as chemotaxonomic markers of this species. The plant is still under investigation by our research group with the prospect of identifying new bioactive compounds in the near future.

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