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XANTHONES OF *GARCINIA MANGOSTANA* LINN.*

T. R. GOVINDACHARI†, P. S. KALYANARAMAN, N. MUTHUKUMARASWAMY and B. R. PAI

Department of Chemistry, Presidency College, Madras 5.

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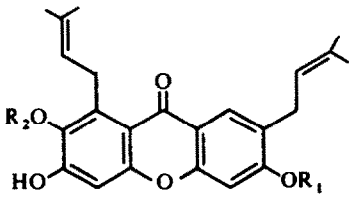
Abstract—Two new xanthones, gartanin and 8-desoxygartanin, have been isolated from very ripe fruits of *Garcinia mangostana* and their structures have been shown to be VIIa and X respectively. Partially ripe fruits contain only mangostin and β-mangostin. The structural similarity of 8-desoxygartanin to the acridone alkaloid atalaphylline is discussed.

MANGOSTIN and β-mangostin, the two xanthones isolated[1,2] from the fruit hulls, bark and dried latex of *Garcinia mangostana* Linn. (Family: Guttiferae) have been assigned structures Ia[3] and Ib[4] respectively. On reinvestigation of the fruit hulls, we isolated three additional xanthones, which we designated gartanin, 8-desoxygartanin and normangostin. Normangostin (Ic) has been found to be identical with the recently reported *v*-mangostin.[5] The present paper deals with the structure elucidation of gartanin and 8-desoxygartanin.



Ia: $R_1 = H$; $R_2 = Me$
b: $R_1 = R_2 = Me$
c: $R_1 = R_2 = H$

Extraction of very ripe fruits with hexane yielded a yellow crude material. Mangostin was removed from this by column chromatography and a second yellow product was obtained which was shown by TLC to be a mixture of two compounds with close R_f Repeated extensive chromatography of this over silica gel resulted in the separation of the two pure components. The compound with lower R_f was named gartanin (VIIa) and that with higher R_f was found to be 8-desoxygartanin (X). 8-Desoxygartanin was present only in minor quantities. Further extraction of the crude material with acetone gave only mangostin and normangostin (Ic).

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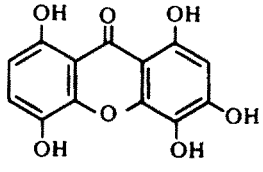
† Present address: CIBA Research Centre, Goregaon, Bombay 63.

Gartanin crystallized from benzene as yellow needles, m.p. 167°, and analysed for $C_{23}H_{24}O_6$ (M^+ at *m/e* 396). The mass spectrum showed major fragments at 341 ($M^+ - 55$) and 285 (341–56) due to cleavage of two prenyl groups. The presence of these groups was confirmed by catalytic hydrogenation to give tetrahydrogartanin whose mass spectrum showed molecular ion peak at *m/e* 400 and significant peaks at *m/e* 343 ($M^+ - 57$) and *m/e* 287 (343–56).

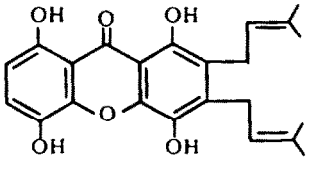
The IR spectrum of gartanin showed a highly chelated CO at 1630 cm^{-1} and OH's at 3200 cm^{-1}. The presence of phenolic hydroxyls was also indicated by the green ferric reaction. Acetylation gave a tetraacetate, $C_{31}H_{32}O_{10}$, and methylation with methyl iodide and potassium carbonate under forcing conditions gave a tetra-O-methyl ether, $C_{27}H_{32}O_6$. Thus gartanin must possess four phenolic hydroxyls. An alcoholic solution of gartanin gave an immediate red colour with *p*-benzoquinone pointing out the presence of a quinol moiety in the molecule (gossypetone reaction[6]). The UV spectrum was reminiscent of 1,3,5,8-tetraoxygenated xanthones obtained from Gentianaceae.[7]

The NMR spectrum showed the presence of two 3,3-dimethylallyl side-chains with the protons belonging to the *gem*-dimethyls at δ 1·70, 1·80 (12H), two methylenes at δ 3·35–3·65 (4H, broad) and two vinylic protons at δ 5·25 (broad). The fact that both methylenes merged near δ 3·50 and that neither of them was at a downfield region near δ 4·10, showed that, unlike mangostin,[8] neither of the iso-pentenyl side-chains occupied the 8-position. The aromatic region consisted of two *ortho*-coupled aromatic protons at δ 6·52 (J = 9 cs) and δ 7·22 (J = 9 cs), showing that C-6 and C-7

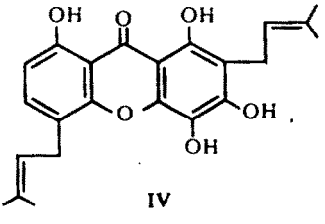


II

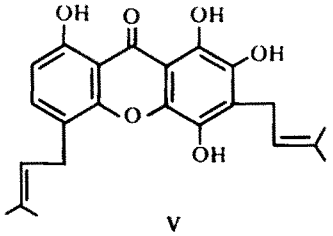
were free as in the case of corymbin (II).[9] Thus, the four hydroxyls and two 3,3-dimethylallyl side-chains must occupy the remaining six positions necessitating the complete substitution of ring A. The low field region in the NMR spectrum exhibited singlets due to the hydroxyls, of which two were at δ 11·33 and δ 12·16 characteristic of two chelated hydroxyls at C-1 and C-8.[7] Allowing for the quinol-type substitution, gartanin could then be assigned five possible structures, III to VIIa.



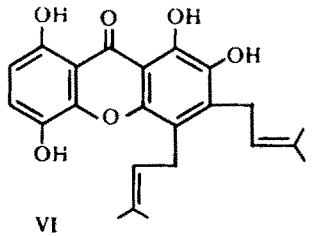
III



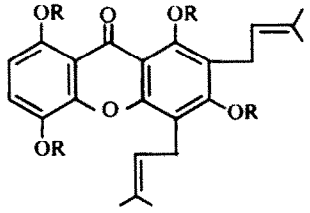
IV



V



VI

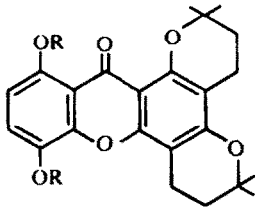


VIIa : R = H
b : R = Me
c : R = COMe

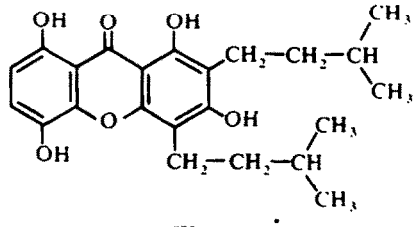
The long wavelength band in the UV spectrum of gartanin in 95% EtOH was shifted by 29 mμ on addition of sodium acetate indicating the presence of 3-hydroxyl group.[9] However no shift was observed with sodium acetate–boric acid[9] showing the absence of two *ortho*-hydroxyls. These facts could satisfactorily be represented only by structure VIIa. Structures III. V and VI were rejected on biogenetic considerations also. since all naturally occurring polyhydroxyxanthones are only oxygenated at C-3 and not alkylated.[10]

When gartanin was refluxed in benzene with *p*-toluenesulphonic acid, only one product could be obtained. It contained two hydroxyl groups, as shown by the formation of di-O-methyl ether and its NMR spectrum showed clearly that it was bicyclogartanin. The vinylic protons had disappeared and the C-Me groups appeared upfield at δ 1·38 and 1·45 (12H). The two methylene signals appeared separately, one as a triplet at δ 1·82 (4H) and the other as a broad signal at δ 2·70 (4H), the former due to the newly-formed aliphatic methylenes and the latter due to the benzylic methylenes. This is characteristic of 2,2-dimethylchromans.[14] Therefore, in gartanin, both the prenyl side-chains must have adjacent hydroxyls. Of the two hydroxyls in bicyclogartanin, only one was chelated as shown by the appearance of a singlet at a much downfield region (δ 12·67) in the NMR spectrum as well as by positive bathochromic shifts in the UV spectrum in the presence of aluminium chloride. This could be only at C-8, the 1-OH having got involved in the cyclisation process. The other OH could therefore be either at C-5, C-6 or C-7. Since the NMR spectrum still showed two *ortho*-coupled aromatic protons, the OH could not be placed at C-6. Its location at C-7 was also ruled out, since bicyclogartanin could not be methylenated with methylene iodide and potassium carbonate, whereas similar xanthones have been methylenated under the same conditions[11]. Therefore the second OH could be placed only at C-5, which was supported by a positive gossypetone reaction and negative Gibbs test[12] given by bicyclogartanin. Thus the most probable structural representation

for bicyclogartanin is VIIIa, its di-O-methyl ether VIIIb, gartanin VIIa and tetrahydrogartanin IX.

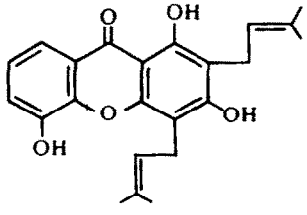


VIIIa : R = H
b : R = Me

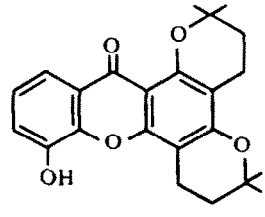


IX

8-*Desoxygartanin*. The minor compound, m.p. 165·5°, analysed for $C_{23}H_{24}O_5$ (M^+ at *m/e* 380). The fragmentation pattern in the mass spectrum was exactly similar to that in the case of gartanin excepting that the peaks were shifted to lower mass by 16 units indicating a similar substitution. The compound gave a green colour with ferric chloride, but no red colour in the gossypetone reaction showing the absence of quinol moiety. The UV spectrum was typical of a 1,3,5-trioxygenated xanthone nucleus.[13] In the NMR spectrum, there was only one chelated OH at δ 13·16 and the upfield region was similar to that in the spectrum of gartanin suggesting the presence of two 3,3-dimethylallyl side-chains under identical environments. The aromatic region showed a clear ABX pattern characteristic of 6,7 and 8 protons, the 8-proton appearing as a quartet at δ 7·58 and the 6 and 7 protons as a complex multiplet at δ 7·05–7·30. These data suggested structure X for this minor compound, which was only the 8-desoxyderivative of gartanin. This was converted into the bicycloderivative by refluxing in benzene with *p*-toluenesulphonic acid. Bicyclo-8-desoxygartanin gave a positive Gibbs test with maximum intensity at 733 mμ and negative gossypetone test, in conformity with structure XI*. XI showed NMR signals at δ 1·42 and 1·45 (two s's, 12H), 1·85 (t, 4H), 2·50–3·00 (broad, 4H), 7·05–7·30 (m. 2H), 7·68 (q, 1H) and 9·27 (s, 1H).



X

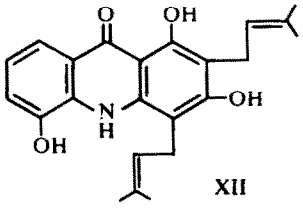


XI

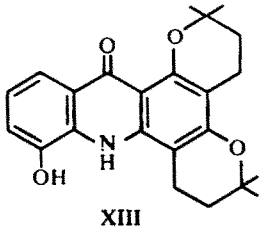
The structures of gartanin and 8-desoxygartanin show a strong similarity to the acridone alkaloid atalaphylline (XII), recently reported from these laboratories.[14] Indeed 8-desoxygartanin is only the xanthone analogue of atalaphylline. This is

* Prof. A. C. Jain has recently synthesised compound XI and reported its identity with bicyclo-8-desoxygartanin (personal communication).

clearly shown by the similarity in the fragmentations in the mass spectra of atalaphylline, 8-desoxygartanin and gartanin (Table). The base peak is at M^+-111 in the spectra of all the three compounds, corresponding to the loss of the two isoprenyl linkages. This then undergoes further successive losses of CO and H to yield the



XII



XIII

TABLE 1.

Compound	Masses	
	M^+	Other major fragments
Atalaphylline (XII)	379	364. 362. 336. 324. 308. 280. 268
8-Desoxygartanin (X)	380	365. 363. 337. 325. 309. 281. 269
Gartanin (VIIa)	396	381. 379. 353. 341. 325. 297. 285
Bicycloatalaphylline (XIII)	379	324. 323. 308. 268. 267
Bicyclo-8-desoxy-gartanin (XI)	380	325. 324. 309. 269. 268
Bicyclogartanin (VIIIa)	396	341. 340. 325. 285. 284

stable dibenzofuran in the case of the xanthones and carbazole in the case of atalaphylline. The mass spectra of mangostin and β-mangostin were distinctly different from these. Also the mass spectra of bicyclo-atalaphylline, bicyclo-8-desoxygartanin and bicyclogartanin were similar in the fragmentation pattern. Although similarity in the oxygenation patterns among a few xanthones and acridones has been cited previously,[15] this is the first instance wherein an exact identity in the nature and positions of substituents has been observed. This would suggest that perhaps there may be a common biogenetic pathway for acridones and xanthones. A similar view has recently been expressed by Bowen *et al.*[16]

Even though the 1,3,5-oxygenation of 8-desoxygartanin is common, the 1,3,5,8-oxygenation observed in gartanin has not so far been reported from plants of Guttiferae. The literature on xanthones mentions only three members with two isopentenyl residues.[17] Gartanin and 8-desoxygartanin are additions to that list. However, these two are strikingly different from others in that these are the first members with two 3,3-dimethylallyl side-chains occurring in the same ring.

In contrast with the very ripe fruits, the less ripe fruits yielded only mangostin and β-mangostin, identified by comparison with authentic samples.

EXPERIMENTAL

M.ps are uncorrected. UV spectra were determined in Beckmann model DK2A and IR spectra in Perkin–Elmer 421 instruments. NMR spectra were determined at 60 Mc. in $CDCl_3$. a few drops of CD_3SOCD_3 being added wherever necessary.

Isolation

(i) The hulls of one hundred fruits collected in Madras in 1968 were dried. powdered (1 kg) and extracted with hexane (3 × 3 l). Concentration of the extract and cooling in a refrigerator yielded a yellow solid (4 g). TLC examination (silica-benzene: MeOH—25:0·5) showed two spots. A portion of the crude material (2 g) was chromatographed over silica gel (100 g) and eluted with benzene. 25 ml fractions were collected. Fractions 10–12 yielded a yellow compound. crystallizing from benzene as yellow flakes (70 mg). m.p. 150–165°. NMR showed it to be a mixture. Fractions 13–25 were combined and evaporated to give mangostin (700 mg). m.p. 181° (benzene). Further extractions of the fruit hulls with acetone gave only mangostin.

(ii) Partially ripe fruits (500) were collected from Courtallam in 1969 and were processed as before to yield a yellow powder (15 g). A portion of this (5 g) was chromatographed over silica gel (500 g) and eluted with benzene. First 200 ml of the eluate gave no material. The next 250 ml gave β-mangostin (500 mg). m.p. 175° (benzene). The later 300 ml gave mangostin (2·5 g).

(iii) Well-ripened fruits (500) collected in Madras in 1970 were dried. powdered (5 kg) and extracted with hexane (5 × 4 l). Solvent removal gave an oily residue solidifying to a yellow powder (12 g) on cooling. This showed two spots in TLC (silica-benzene: methanol—25:0·5). The top spot resolved into a two-coloured oval-shaped spot on repeating the TLC in chloroform:hexane (90:10) and exposing the plate to iodine vapours.

The crude material (2 g) was chromatographed over silica gel (250 g) and eluted with chloroform:hexane (60:40). 10 ml fractions were collected. Fractions 11–15 were mixed and evaporated to give 8-desoxygartanin (15 mg). Fractions 16–24 gave a mixture of 8-desoxygartanin and gartanin (200 mg). Fractions 25–30 gave pure gartanin (80 mg). Elution with chloroform gave mangostin (600 mg). The mixture of 8-desoxygartanin and gartanin (200 mg) was rechromatographed over silica gel (50 g) to give pure 8-desoxygartanin (15 mg) and gartanin (150 mg).

Further extraction of the fruit hulls with acetone (3 × 5 l.) gave a yellow solid (150 g) showing two spots in TLC (silica–benzene; EtOAc—75:25). Part of this (6 g) was chromatographed over silica gel (120 g). Benzene elution (1 l.) gave mangostin (4·5 g). Elution with benzene:EtOAc (85:15) gave normangostin. crystallizing from benzene-EtOAc as a yellow amorphous powder (0·5 g). m.p. 198–200°.

8-Desoxygartanin crystallized from benzene:hexane as yellow fluffy needles. m.p. 165·5°. It gave a green colour with alcoholic ferric chloride and no red colour in the gossypetone reaction. The developed spot in a TLC plate assumed a yellow colour when exposed to iodine vapours; λ_{max}^{EtOH} 244. 260. 324. 375 mμ (log ε 4·47. 4·37. 4·17. 3·55). ν_{max}^{Nu} 3540. 3190. 1650. 1620, 138 . 850 cm^{-1}. (Found: C. 72·38; H. 6·34. $C_{23}H_{24}O_5$ requires: C. 72·61; H. 6·36%); NMR: δ 13·16 (1H. s). 9·75 (1H. s) 9·05 (1H. s). 7·58 (1H. q). 7·30–7·05 (2H. m). 5·24 (2H. br). 3·60–3·40 (4H. br). 1·82 and 1·66 (12H. singlets) ppm. Mass spectrum: *m/e* 380 (M^+). 365. 363. 337. 325. 309. 281. 269 (100%).

Gartanin crystallized from benzene as yellow needles, m.p. 167. It gave a green colour with alcoholic $FeCl_3$ and a red colour in the gossypetone reaction. The developed spot in TLC plate assumed an immediate green colour on exposing to I_2 vapours; λ_{max}^{EtOH} 259. 284. 325 (sh). 351 mμ (log ε 4·30. 4·38. 3·87. 4·05); $\lambda_{max}^{EtOH-NaOAc}$ 240. 284. 380 mμ (log ε 4·48. 4·40. 4·34); $\lambda_{max}^{EtOH-AlCl_3}$ 269. 299. 330 (sh). 388 mμ (log ε 4·36. 4·42. 3·94. 4·07); ν_{max}^{Nu} 3420. 3200. 1630. 1585. 810 cm^{-1} (Found: C. 69·58; H. 6·40; $C_{23}H_{24}O_6$ requires: C. 69·68; H. 6·10%); NMR: δ 12·16 (1H. s). 11·33 (1H, s). 9·33 (1H, s). 7·22 (1H. d. J = 9 cs). 6·52 (1H. d. J = 9 cs). 5·25 (2H. br). 3·65–3·35 (4H. br). 1·80 and 1·70 (12H. s's). Mass spectrum: *m/e* 396 (M^+). 381. 379. 353. 341. 325. 297. 285 (100%).

Tetrahydrogartanin (IX). Gartanin (20 mg) in MeOH (20 ml) was hydrogenated in a Parr apparatus with Adams catalyst at 15 lbs/in^2. for 1½ hr. the soln filtered and the solvent removed *in vacuo* to yield a yellow residue which crystallized from benzene:hexane as needles (9 mg), m.p. 180–181°. Mass spectrum: *m/e* 400 (M^+). 384. 343. 327. 287. 271. $C_{23}H_{28}O_6$ requires molecular weight 400.

Tetra-O-acetylgartanin (VIIc). Acetylation of gartanin (100 mg) with pyridine (2 ml) and Ac_2O (2 ml) on steam-bath for 8 hr. gave tetra-O-acetylgartanin mixed with some starting material. The mixture was separated by preparative TLC over silica gel (benzene:EtOAc—88:12) to give pure *tetra-O-acetylgartanin* which crystallized from MeOH as white fluffy needles (40 mg). m.p. 149°. λ_{max}^{EtOH} 246. 277. 345 mμ (log ε 4·64. 4·00. 3·82). (Found: C. 66·12; H. 5·61; $C_{31}H_{32}O_{10}$ requires: C. 65·95; H. 5·71%); NMR: δ 7·42

(1H. d. $J = 9$ cs). 6·90 (1H. d. $J = 9$ cs). 5·18 (2H. br). 3·32 (4H. br). 2·41. 2·35. 2·33 (12H. s's) and 1·75 (12H. br).

Tetra-O-*methylgartanin* (VIIb): A soln of gartanin (100 mg) in acetone (50 ml) was refluxed with MeI (7 ml) and anhyd K_2CO_3 (500 mg) over steam-bath for 20 hr. Usual work-up led to a yellow solid (80 mg) containing some starting material. Separation by preparative TLC over silica gel (benzene:EtOAc—75:25) gave pure *tetra*-O-*methylgartanin*, crystallizing from hexane as white leaflets (40 mg). m.p. 85°; λ_{max}^{EtOH} 243. 312. 365 mμ (log ε 4·59. 3·91. 3·74). (Found: C. 71·56; H. 6·92. $C_{27}H_{32}O_6$ requires: C. 71·66; H. 7·13%); NMR: δ 7·10 (1H. d. $J = 9$ cs). 6·62 (1H. d. $J = 9$ cs). 5·25 (2H. br). 3·90. 3·80 (12H. s's). 3·52 (4H. br). 1·82 and 1·68 (12H. s's).

Bicyclogartanin (VIIIa). Gartanin (300 mg) was dissolved in dry benzene (80 ml) and refluxed with *p*-toluenesulphonic acid (150 mg) on steam-bath for 8 hr. cooled and diluted with EtOAc (50 ml). The soln was washed well with water, dried (Na_2SO_4) and solvent removed to give a yellow solid (300 mg) containing some starting material. Separation by preparative TLC over silica gel (benzene:EtOAc—75:25) and crystallization from MeOH gave shiny yellow prisms (180 mg). m.p. 215–216°. It gave a green colour with alcoholic $FeCl_3$ and a red colour in the gossypetone reaction. However it gave a negative Gibbs test. λ_{max}^{EtOH} 241. 258. 281. 335 mμ (log ε 4·30. 4·40. 4·28. 4·12); $\lambda_{max}^{EtOH-AlCl_3}$ 267. 296. 370 mμ (log ε 4·38. 4·40. 4·10); ν_{max}^{KBr} 1650. 1605. 1580 cm^{-1}. (Found: C. 67·56; 67·60; H. 6·63; 6·67. $C_{23}H_{24}O_6 \cdot CH_3OH$ requires: C. 67·28; H. 6.59%); NMR: δ 12·67 (1H. s). 7·08 (1H. d. $J = 9$ cs). 6·50 (1H. d. $J = 9$ cs). 2·70 (4H. br). 1·82 (4H. br). 1·45 and 1·38 (12H. s's). Mass spectrum: *m/e* 396 (M^+). 341. 340. 325. 285. 284. Refluxing with CH_2I_2 and anhyd K_2CO_3 in acetone for 20 hr did not give the methylene ether. but gave back the starting material.

Di-O-*methylbicyclogartanin* (VIIIb). Bicyclogartanin (100 mg) was dissolved in acetone (30 ml) and refluxed with MeI (60 ml) and anhyd K_2CO_3 (500 mg) over steam-bath for 40 hr. Usual work-up yielded *di*-O-*methylbicyclogartanin* as a white solid crystallizing from MeOH as colourless needles (70 mg). m.p. 218·5° λ_{max}^{EtoH} 243. 275. 322 mμ (log ε 4·40. 4·15. 4·15); ν_{max}^{KBr} 1655. 1590. 1490 cm^{-1}. (Found: C. 70·85; H. 7·10. $C_{25}H_{28}O_6$ requires: C. 70·74; H. 6·65%); NMR: δ 7·05 (1H. d. $J = 9$ cs). 6·60 (1H. d. $J = 9$ cs). 3·90 (6H. s). 2·92–2·62 (4H. m). 1·80 (4H. m). 1·41 and 1·38 (12H. s's).

Bicyclo-8-*desoxygartanin* (XI). 8-Desoxygartanin (100 mg) in benzene (39 ml) was refluxed with *p*-toluenesulphonic acid (50 mg) on steam-bath for 8 hr and worked up as in the case of gartanin to give *bicyclo*-8-*desoxygartanin* crystallizing from MeOH as yellow prisms (30 mg). m.p. 259–262°. With Gibbs reagent it developed an intense green colour and a sharp maximum at 733 mμ (log ε 3·92) was obtained: NMR: δ 9·27 (1H. s). 7·68 (1H. q). 7·05–7·30 (2H. m). 2·50–3·00 (4H. br). 1·85 (4H. t). 1·45 and 1·42 (12H. s's). Mass spectrum: *m/e* 380 (M^+). 325. 324. 309. 269. 268. $C_{23}H_{24}O_5$ requires molecular weight 380.

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