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ON THE STRUCTURES OF GARCINOL, ISOGARCINOL AND CAMBOGINOL

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Summary: A new polyisoprenylated phenolic pigment, garcinol, and its colourless isomer, isogarcinol, have been isolated from *Garcinia indica* and their structures proposed on the basis of chemical and spectral data. A modification is suggested for the recently proposed structure of camboginol.

The genus *Garcinia* (Family: Guttiferae) is known to produce a variety of polyisoprenylated polyphenols; e.g., morellin from *G. morella*[1], xanthochymol (I) and isoxanthochymol from *G. xanthochymus*[2,3], and, more recently, cambogin (II, the enantiaomer of isoxanthochymol) and camboginol (III) from *G. cambogia*[4]. We now wish to report the isolation and structures of two new compounds, garcinol and isogarcinol from *Garcinia indica*.

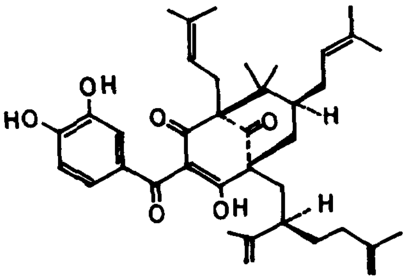
Garcinol, $C_{38}H_{50}O_6$ (M^+ 602.39252), m.p. 122°, $[\alpha]_D^{22}$ -143° (1% $CHCl_3$), crystallised out from the hexane extract of the fruit rind of *G. indica* as yellow needles (1.5%). The molecular formula and the absorption spectral data [λ_{max}^{EtOH} 255 and 365 nm (ϵ 12740 and 9380); ν_{max} 3450-3300 (broad), 1720 and 1660-1630 (broad) cm^{-1}] indicated that the compound is possibly related to the isomeric xanthochymol (I) and, more appropriately in view of the sign of rotation[5], to cambogin (II) etc. The presence of an enolisable 1,3-diketone system in the molecule was confirmed by the formation of two isomeric trimethyl ethers, hydrolysable to a single dimethyl ether with dilute alkali. Alkali degradation of the methyl ether under stronger conditions (20% ethanolic KOH, reflux) yielded veratric acid indicating the presence of a 3,4-dihydroxybenzoyl unit (see below). The UV spectrum of garcinol suggested that the 1,3-diketone system is conjugated to the 3,4-dihydroxybenzoyl moiety. The IR spectrum of the trimethyl ether showed the presence of a saturated carbonyl group (1727 cm^{-1}) and two α,β-unsaturated carbonyl groups (1668 and 1642 cm^{-1}), thus accounting for all the oxygen atoms.

The PMR spectrum of garcinol in $CDCl_3$ showed the presence of two saturated tertiary methyls (singlets at δ 1.01 and 1.17) and seven $=\overset{|}{C}-CH_3$ groups (signals at δ 1.54 for two methyls and at 1.60, 1.67, 1.70, 1.74 and 1.84 for one methyl each). It also showed signals for a vinylic methylene (δ 4.38, 2H, broad singlet) and three other olefinic protons (δ 5.0m) in addition to three aromatic protons (ABX pattern around δ 6.60 and 6.95) and a hydrogen bonded phenolic hydroxyl at δ 18.0. The mass spectrum of garcinol, which was very similar to that of xanthochymol[6] showed major peaks at m/e 602(M^+), 465($M^+-C_{10}H_{17}$, base peak), 341 (465-C_9H_{16}) and 137 (dihydroxybenzoyl). These data clearly indicate a structure of type III for garcinol, biogenetically derivable from maclurin (2,4,6,3',4'-pentahydroxybenzophenone) and five isoprenyl units[4].

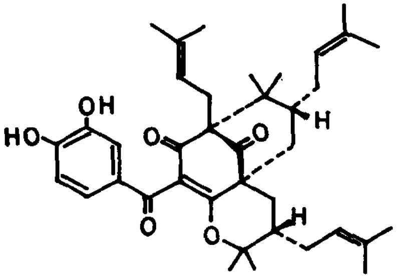
Treatment of garcinol with acid or heating it to about 200° yielded a mixture of products, the major product being a colourless compound which is also present in the hexane extract of G. indica fruits. This compound, which may be called isogarcinol, m.p. 218-9°, $[\alpha]_D^{22}$ -203° (1% EtOH), could be isolated from the mother liquor of garcinol by chromatography on silica gel; its identity with the product from garcinol was established by m.m.p. and by comparison of UV, IR and PMR spectra. The IR spectrum of isogarcinol indicated the presence of a saturated carbonyl group (1715 cm^{-1}), an aroyl group (1670 cm^{-1}) and an α,β-unsaturated carbonyl group (1635 cm^{-1}). The UV spectrum of the compound (λ_{max}^{EtOH} 232 and 278 nm; ϵ 16220 and 17110), which is close to that of 3,4-dihydroxyacetophenone[7], clearly showed that the aroyl and the α,β-unsaturated carbonyl groups are not conjugated. The PMR spectrum of isogarcinol showed signals for four saturated tertiary methyls (δ 0.93, 1.00,1.20and 1.28),six $=\overset{|}{C}-CH_3$ groups[δ 1.63 (9H), 1.70 (6H) and 1.80 (3H)] and three olefinic protons δ4.90 (2H, m) and 5.23 (1H, m) in addition to the expected aromatic, methine and methylene protons; the signal for $=CH_2$ group was absent. On the basis of these data structure IV could be assigned to isogarcinol.

While this work was in progress, Rao et al.[4] reported the isolation of camboginol from the latex of G. cambogia. The structure III was assigned for the compound based mainly on its conversion to cambogin (II) whose structure was earlier determined by X-ray crystallography. However, a closer look at the absorption spectral data indicated that structure III for camboginol is untenable. While garcinol, xanthochymol and isoxanthochymol have similar UV spectra (λ_{max} around 255 and 365 nm)[3] and hence similar chromophore, camboginol reportedly[4] has λ_{max} at 233 and 281 nm, indicating that the 1,3-diketone and the 3,4-dihydroxybenzoyl units are not conjugated. On the other hand a structure of type V (analogous to that of isogarcinol, IV, which has similar UV spectrum) would explain the spectral data as also its conversion to cambogin. We therefore propose structure III for garcinol and V for camboginol. The stereochemical representation (based mainly on the sign of rotation) is essentially conjectural as the probable intermediate VI of the interconversions may cyclise in a number of ways leading to a mixture of products and convertibility to a particular compound does not necessarily define the configurations at carbon atoms α to the carbonyl groups.

The structures of garcinol and isogarcinol are now being studied by X-ray crystallography for determination of absolute configurations.



I



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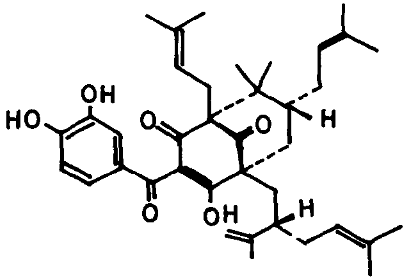

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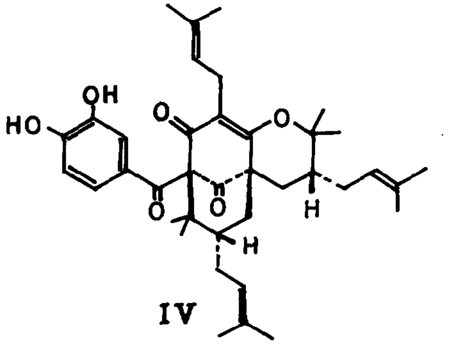
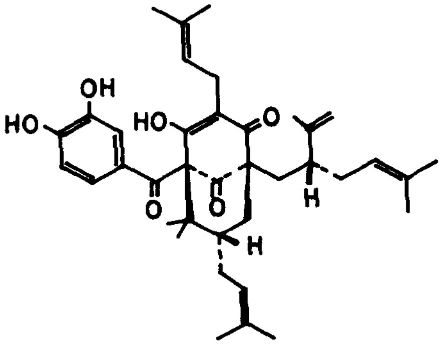
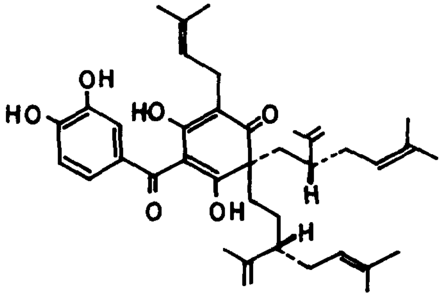


IV



V



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