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# Goniothalamusin, a linear acetogenin from *Goniothalamus gardneri*

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**Abstract**

A new acetogenin, trivial name goniothalamusin, has been isolated from the aerial parts of *Goniothalamus gardneri* (Annonaceae). Goniothalamusin is a linear acetylenic and olefinic acetogenin with a C25 skeleton, lacking oxygenated substituents on its alkyl chain and with a new type of saturated γ-hydroxymethyl-γ-lactone terminal ring. Its structure and relative stereochemistry established as *rel*-24α-hydroxymethyl-2β-eicosa-21-en-13-yn-tetrahydrofuran-1-one has been elucidated by spectroscopic analysis. 

*Keywords:* *Goniothalamus gardneri*; Annonaceae; Linear acetogenin; Goniothalamusin

## 1. Introduction

A total of ca 250 bioactive acetogenins have been isolated so far from the Annonaceae, predominantly from the genera *Annona, Asimina, Rollinia, Uvaria* and *Goniothalamus* (see for example, Cavé, Figadère, Laurens & Cortes, 1997). Other major secondary metabolites isolated from the genus *Goniothalamus* Hook. f. & Thoms. include styryl-lactones (Dictionary of Natural Products, 1999) and isoquinoline-derived alkaloids (Din, Colegate & Razak, 1990). In a continuation of our phytochemical study on the Annonaceae, we describe herein the isolation and structural determination of a new linear acetogenin, goniothalamusin (**1**), obtained from the petrol extract of the aerial parts of *G. gardneri* Hook. f. & Thoms., a shrub widely distributed in the mid-altitude rain forests of Sri-Lanka (Dassanayake & Fosberg, 1985).

## 2. Results and Discussion

Goniothalamusin (**1**) was isolated as an amorphous solid. The IR spectrum showed absorption typical of a lactone carbonyl function (1754 $cm^{-1}$), hydroxyl (3459 $cm^{-1}$) and exomethylene groups (3077, 1643, 948 $cm^{-1}$). The molecular formula of $C_{25}H_{42}0_3$ was determined by HREIMS which revealed a molecular ion fragment at $m/z$ 390. The $^1H$ NMR spectrum (Table 1) exhibited an olefinic methine at δ 5.79 coupled to an $sp^2$ methylene and an $sp^3$ methylene (—$CH_2$—CH=$CH_2$), an oxymethine proton at δ 4.58, two non equivalent oxymethylene protons at δ 3.86 and 3.63, a methine next to a carbonyl (δ 2.70), a broad singlet (δ 2.50) attributable to one hydroxyl group, two methylenes adjacent to another centre of unsaturation (δ 2.13) and a series of further signals at δ 2.30 (1H), δ 1.98 (1H), δ 1.83 (1H) and δ 1.45–1.26 (25H).

The *J*-modulated $^{13}C$ NMR spectrum (Table 1), assigned by $^1H$–$^{13}C$ HC–COBI, revealed 25 carbons. It confirmed the presence of the carbonyl function, $sp^2$ methine and methylene of the vinylic group, the oxymethine and oxymethylene, the methine next to the carbonyl (δ 39.7) and the methylene adjacent to the

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Table 1
$^{1}H$ NMR and $^{13}C$ NMR chemical shift data for **1**[a]

| C/H | $^{1}H$ | $^{13}C$ |
|---|---|---|
| 1 | | 180.3 |
| 2 | 2.70 *m* | 39.7 |
| 23 | 2.30/1.98 | 29.7 |
| 24 | 4.58 *m* | 78.9 |
| 3 | 1.45/1.83 | 31.3 |
| 4 | 1.37 *m* | 27.3 |
| 5–11 | 1.26–1.46 *m* | 28.7–29.6 |
| 12 | 2.13 *t* (6.2) | 18.8 |
| 13–14 | | 80.3 |
| 15 | 2.13 *t* (6.2) | 18.8 |
| 16–19 | 1.26–1.46 *m* | 28.7–29.6 |
| 20 | 2.00 *t* (6.6) | 33.8 |
| 21 | 5.79 *ddt* (17.0, 10.0, 6.6) | 139.1 |
| 22 | 4.98 *dd* (17.0, 2.1) | 114.3 |
| 22 | 4.92 *dd* (10.0, 2.1) | |
| 25–$CH_2$–O | 3.86 *dd* (12.3, 2.9) | 64.4 |
| | 3.63 *dd* (12.3, 4.8) | |
| OH | 2.50 *brs* | |

[a] All data obtained in $CDCl_3$.

vinylic group (δ 33.8). It further showed two equivalent quaternary carbons at δ 80.3 and 16 methylenes of which two were shielded at δ 18.8. These data were in agreement with the presence of one acetylenic bond symmetrically substituted by two methylenes (Morris, 1983).

The structure of *rel*-24α-hydroxymethyl-2β-eicosa-21-en-13-yn-tetrahydrofuran-1-one was unambiguously established by a combination of COSY, TOCSY and HMBC experiments in combination with HREIMS data. The COSY and TOCSY linked the oxymethylene, oxymethine, a non-equivalent methylene, the methine adjacent to the carbonyl and another methylene in a spin system O—$CH_2$—CH(O)—$CH_2$—CH(C═O)—$CH_2$—. This suggested the presence of a 3-substituted tetrahydrofuran-2-one ring and this was supported by the presence of a base peak at *m*/*z* 129 in the EIMS (Fig. 1).

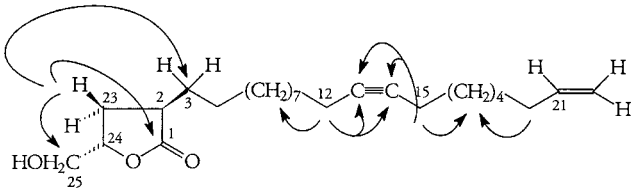


Fig. 2. Some significant correlations in the HMBC spectrum of **1**.

The HMBC spectrum displayed a number of important correlations (Fig. 2):

1. $^{3}J$ couplings between the methylene at δ 2.30/1.98 and the oxymethylene carbon (δ 64.4), the carbonyl group (δ 180.3) and the methylene at δ 31.3, thus confirming the presence of the tetrahydrofuran-2-one ring with its alkyl side chain and hydroxymethyl substituent at C-2 and C-24, respectively.
2. $^{2}J$ and $^{3}J$ couplings between the two methylenes at δ 2.13 and the quaternary carbons at δ 80.3, thus confirming the presence of the acetylenic bond with α-positions substituted by two methylenes.
3. $^{2}J$ and $^{3}J$ couplings between the methylenes adjacent to centres of unsaturation at δ 2.00 (2H, adjacent to vinyl group), δ 2.13 (4H, adjacent to acetylenic bond) and aliphatic methylene carbons at δ 29.6–28.7, thus indicating an acetylenic alkyl chain with a terminal vinyl group.

The length of the alkyl chain and the position of the acetylenic bond were rationalised from the HREIMS mass fragmentation pattern (Fig. 1). The relative

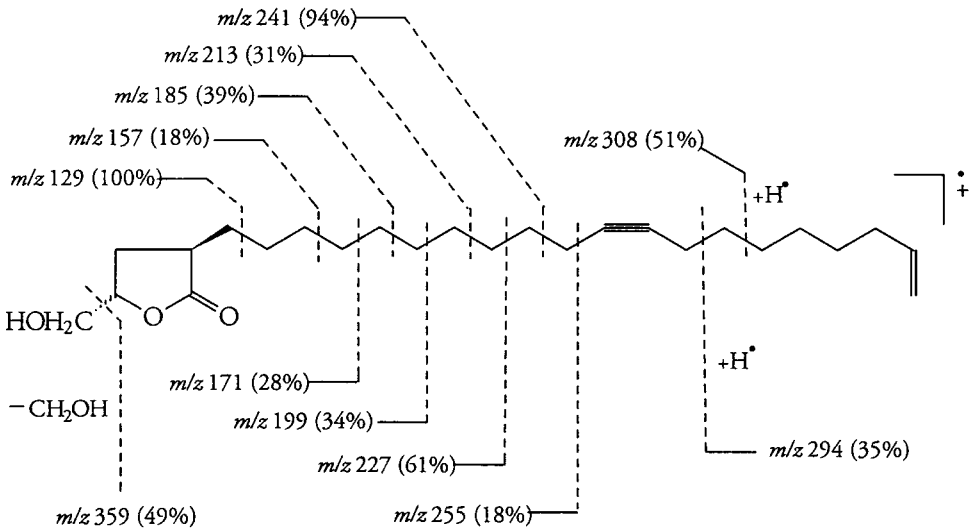


Fig. 1. Fragment ions observed in the EI mass spectrum of **1**.

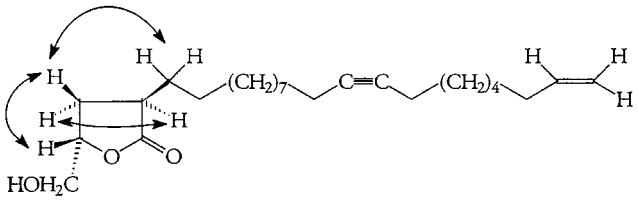

Fig. 3. NOE correlations relating to the stereochemistry of the tetrahydrofuran ring of **1.**

stereochemistry of the lactone ring was established on the basis of NOE interactions (Fig. 3).

The spectral data of **1** showed similarities to butyrolactone-1, a linear acetylenic acetogenin recently isolated from *Porcelia macrocarpa* (Chaves & Roque, 1997). The occurrence of of goniothalamusin (**1**) in *Goniothalamus gardneri* appears to conform with what is already known on the chemistry of the genus. It is the third linear acetogenin isolated from *Goniothalamus* (Fang et al., 1993; Jiang & Yu, 1997). Very few olefinic and/or acetylenic linear acetogenins, lacking hydroxyl groups on the alkyl chain, have been reported in the family (Etse & Waterman, 1986; Zafra-Polo, Figadère, Gallardo, Tormo & Cortes, 1998). Goniothalamusin (**1**) represents the first linear acetylenic/olefinic acetogenin with a C25 skeleton, lacking oxygenated substituents on its alkyl chain, and with a new type of saturated γ-hydroxymethyl–γ-lactone terminal ring. Biogenetically, **1** may be derived from the condensation of pyruvic acid with a $C_{22:1\ (13)}$ fatty acid further unsaturated in C-13 and C-21; this would yield a saturated β-hydroxy–γ-methyl–γ-lactone moiety which would afford **1** after α,β-dehydration and hydroxylation of the methyl group (Chaves & Roque, 1997; Etse & Waterman, 1986).

## 3. Experimental

### 3.1. General

$[\alpha]_D$ was measured on a Bellingham and Stanley model ADP 220 polarimeter. IR, UV and HREIMS were recorded using a Mattson Galaxy 5000 FTIR, Unicam UV 4–100 UV/Visible and JEOL JMS-AX505HA spectrometers, respectively. NMR spectra were recorded at 400 MHz ($^1$H) and 100.56 MHz ($^{13}$C) on a Bruker AMX-400, using the residual solvent peak as int. standard. COSY, TOCSY, NOESY, HC-COBI and HMBC were performed using standard microprograms.

### 3.2. Plant material

Aerial parts of *Goniothalamus gardneri* were purchased from the plantation of Lalani Botanicals (Sri-Lanka) in May 1997. A voucher specimen is kept by Lalani Botanicals.

### 3.3. Extraction and purification

Dried powdered aerial parts (510 g) were Soxhlet extracted successively with petroleum ether (bp 40–60°C), EtOAc and MeOH. The petrol extract (12 g) was concd in vacuo and fractionated by VLC on Si gel 60H, eluting with n-hexane-EtOAc mixts of increasing polarity. The fraction eluted with EtOAc was subjected to gel filtration on Sephadex LH-20. The subfraction obtained on eluting with $CHCl_3$ was then submitted to CC over Si gel 60. Fractions containing **1** on eluting with *n*-hexane–EtOAc (13:7) were pooled, concd in vacuo and further subjected to CC over Si gel 60 eluting with $CHCl_3$–EtOAc (9:1) to afford **1** (93.9 mg).

#### 3.3.1. Goniothalamusin (*1*)

Amorphous solid. $[\alpha]_D$ +14.6° ($CHCl_3$, *c* 0.206). IR (KBr) $\nu_{max}$ cm$^{-1}$: 3459 (OH), 3077, 2931, 2919, 2850, 1754 (C=O), 1643, 1469, 1367, 1272, 1176, 1078, 1047, 948. UV (EtOH) $\lambda_{max}$ nm: 212. Found $[M]^+$ 390.3237 ($C_{25}H_{42}0_3$ requires 390.3134). HREIMS *m/z* (rel. int. %): 390 (15), 359 (49), 341 (16), 308 (51), 294 (35), 255 (18), 241 (94), 227 (61), 213 (31), 199 (34), 185 (39), 171 (28), 157 (18), 129 (100). $^1$H and $^{13}$C NMR — see Table 1.

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