

## GALANGUSTIN, A NEW FLAVONE FROM GALEOPSIS ANGUSTIFOLIA

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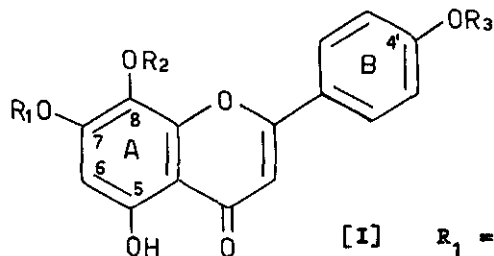
**Abstract** - Galangustin has the structure of 5,7-dihydroxy-8,4'-dimethoxyflavone.

During the examination<sup>1</sup> of the acetone extract of the aerial part of a sample of *Galeopsis angustifolia* Ehrh. ex Hoffm. (family Labiatae) collected in Northern Italy, we isolated a flavone amongst other products. As the substance seems to be new, we discuss its structure here and propose for it the name galangustin.

Galangustin has m.p. 225°C (from MeOH) and formula  $C_{17}H_{14}O_6$  (MS,  $M^+$  314). Its MS shows peaks at  $m/z$  314 (68%), 299 (100), 271 (22), 167 (10), 139 (18), 135 (7), 133 (6), 132 (18), 121 (4), 118 (20), 111 (11). The NMR spectrum (60 MHz, DMSO- $d_6$ ) has a singlet at  $\delta$  3.81 for two  $OCH_3$  groups, a singlet at 6.28 (one proton), a singlet at 6.83 (one proton), an  $A_2B_2$  quartet at 7.12 and 8.01 with  $J$  9 Hz, and a singlet at 12.59 for a phenolic chelated OH.

The above data indicate that: ring B is substituted only at position 4' and probably with an  $OCH_3$  group (NMR:  $A_2B_2$  system; MS: peaks 135, 132, 121, 118); the chelated OH group is on position 5; the second  $OCH_3$  group and the second OH group should be on ring A (NMR: singlets at  $\delta$  6.28 and 6.83, no coupling; MS: peaks 167, 139, 111). The base peak at 299 is consistent<sup>2</sup> with the very easy loss of  $CH_3$  from an  $OCH_3$  group at positions 6 or 8.

The UV spectrum (abs. EtOH) shows maxima at nm 275 (log  $\epsilon$  4.09), 297 (4.04), 315 (sh, 4.00); addition of NaOAc promotes a small bathochromic shift from nm 275 to 280 (4.12), whereas the maximum at 297 changes into a sh and the sh at 315 shifts at 350 (3.66); addition of  $EtO^-$  gives a shift from 275 to 285 (4.30) and from 315 to 385 (3.64), whereas the maximum at nm 297 disappears. This behaviour rules out<sup>3</sup> the possibility of a 4'-OH substituent and favours position 7 as the site of the second OH group; the strong decreasing of the absorbance of the sh at 315 after addition of NaOAc is typical<sup>4</sup> of a 7-OH group when no other OH occurs



- [I]  $R_1 = \text{CH}_3$   $R_2 = \text{CH}_3$   $R_3 = \text{CH}_3$   
 [II]  $R_1 = \text{H}$   $R_2 = \text{CH}_3$   $R_3 = \text{CH}_3$   
 [III]  $R_1 = \text{CH}_3$   $R_2 = \text{H}$   $R_3 = \text{CH}_3$   
 [IV]  $R_1 = \text{CH}_3$   $R_2 = \text{CH}_3$   $R_3 = \text{H}$

on ring B.

Acetylation of galangustin with  $\text{Ac}_2\text{O}$ -pyridine yields a diacetate  $\text{C}_{21}\text{H}_{18}\text{O}_8$  (MS,  $\text{M}^+$  398), m.p.  $217^\circ\text{C}$  (from EtOAc). Its MS has peaks at  $m/z$  398, 356, 314, 299, 285, 271, 234, 167, 153, 139, 135, 133, 132. The NMR spectrum (60 MHz,  $\text{CDCl}_3$ ) shows signals at  $\delta$  2.28 and 2.33 (s, 2  $\text{OCOCH}_3$ ), 3.81 and 3.97 (s, 2  $\text{OCH}_3$ ), 6.56 (s, 1 H), 6.76 (s, 1 H), 7.00 and 7.84 ( $\text{A}_2\text{B}_2$  quartet  $J$  9 Hz, 4 H).

Methylation of galangustin with ethereal diazomethane gives a  $\text{C}_{18}\text{H}_{16}\text{O}_6$  derivative (MS,  $\text{M}^+$  328), m.p.  $223\text{--}224^\circ\text{C}$ , identified (m.p., MS, NMR, UV) as 5-hydroxy-7,8,4'-trimethoxyflavone [I], already known as both a synthetic<sup>5</sup> and a natural<sup>6</sup> product. MS: peaks at  $m/z$  328 (36%), 313 (100), 285 (12), 181 (23), 153 (87), 135 (19), 133 (32), 132 (19), 125 (48), 121 (5), 118 (15). NMR (60 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.83 (s, 1  $\text{OCH}_3$ ), 3.86 (s, 2  $\text{OCH}_3$ ), 6.38 (s, H-6), 6.56 (s, H-3), 7.01 and 7.93 ( $\text{A}_2\text{B}_2$  quartet,  $J$  9 Hz, 2',3',5',6'-H), 12.65 (s, chelated phenolic OH).

The identification of [I] thus proves that position 6 is not substituted in galangustin; positions 7,8 and 4' must be therefore the sites of two methoxy and one hydroxy groups. In theory, galangustin could have the structures [II] or [III] or [IV]. But its mass spectrum, when compared with the spectrum of [I], proves beyond any doubt that the hydroxy group rests on ring A at positions 7 or 8. So structure [IV] can be ruled out definitively; moreover, the flavone [IV] had been described previously<sup>6</sup> as a natural and synthetic product, and its physical and spectroscopic data are quite different from those of galangustin. Also the flavone [III] had been synthesized<sup>5,7</sup> and its data are not in agreement with those of our product.

Only the structure [II] can account for the evidence given here. Therefore, galangustin is 5,7-dihydroxy-8,4'-dimethoxyflavone. The behaviour of the UV spectrum is consistent<sup>3,4,8,9</sup> with structure [II]. The fragmentations in the mass spectra of galangustin and [I], as depicted in the schema, are in agreement with previous reports<sup>10,11,12</sup>.



It can be remarked that a product, named cirsitakaogenin, was reported recently<sup>13</sup> as an extractive from Cirsium japonicum D.C. var. takaoense Kitamura (family Compositae) and claimed to have structure [II]. However, the physical and spectroscopic data quoted in the above paper<sup>13</sup> do not agree at all<sup>14</sup> with those found on our product. Therefore we believe that the two products are clearly different; cirsitakaogenin has not structure [II] but an isomeric one, and it is worthy of further investigation.

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14. Reported<sup>13</sup> cirsitakaogenin, m.p. 259-260°C; diacetate, m.p. 186-187°C.

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