(-)-CORYDECUMBINE, A NOVEL PHTHALIDEISOQUINOLINE ALKALOID FROM *CORYDALIS DECUMBENS*

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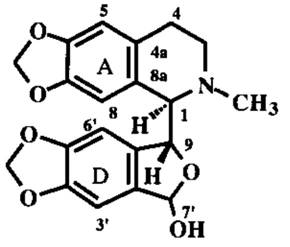
Abstract ---- A novel alkaloid, (-)-corydecumbine (**1**) was isolated from the cultivated tuber of *Corydalis decumbens* (Thunb.) Pers. (Papaveraceae) and the structure was determined by the use of 2D NMR.

Quirion *et al.* reported two alkaloids; (+)-decumbensine and (+)-*epi*-α-decumbensine from *Corydalis decumbens*[1] and their structures were proposed as **2** and **3**, respectively. In 1989, Rozwadoska *et al.* synthesized α-hydroxybenzyltetrahydroisoquinolines (**2**) and (**3**) but the spectral data of (+)-decumbensine and (+)-*epi*-α-decumbensine were found to be quite different[2] than those of **2** and **3**, so they pointed out that (+)-decumbensine and (+)-*epi*-α-decumbensine were not the α-hydroxybenzyltetrahydroisoquinolines (**2**) and (**3**). In addition, they also suggested that (+)-*epi*-α-decumbensine was probably the (+)-corytensine (**4**)[3] based on the ^{1}H-NMR data,[4] in spite of different molecular formula. Also in 1990, Gawley *et al*. synthesized (-)-egenine (**5**) and (-)-corytensine[5,6] while the (+)-egenine (**6**) was previously isolated from *Fumaria vailantii*[7] and the spectral data of egenine and (+)-decumbensine were found to be the same.[8] Therefore it was concluded that (+)-decumbensine and (+)-egenine (**6**) were same compounds, so (+)-decumbensine was not a new alkaloid. Latter, Quirion *et al.* also realized that their proposed structures for (+)-decumbensine and (+)-*epi*-α-decumbensine were not correct.[9] On this series of the alkaloids, Wu *et al*.[3] also incorrectly suggested that (+)-corytensine is the $C_{7'}$ epimer of (+)-egenine (**6**).[10]

As we were comparing the alkaloidal constituents of wild and cultivated *C. decumbens* tubers in order to evaluate the quality of the crude drugs by hplc method,[11] we came across one of the alkaloidal constituents showing a close similarity with compounds discussed above. We studied the structure of **1** by 2D nmr experiments such as ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY, ^{1}H-^{13}C long-range COSY in detail and other spectroscopic methods, which revealed that compound (**1**) is a new and the first type in this series of alkaloids due to presence of methylenedioxy group at 4' and 5' positions instead of common positions at 3' and 4'. We wish to report the structure elucidation of **1** in the present communication.



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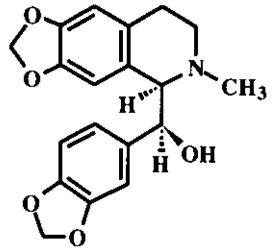

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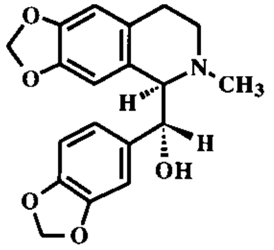

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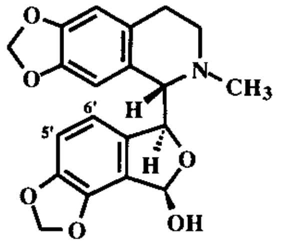

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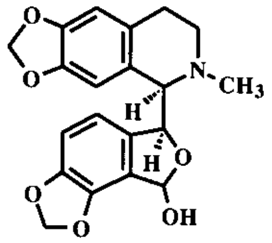

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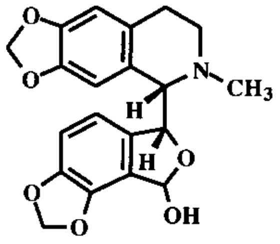

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(-)-Corydecumbine (**1**) was a creamy white crystalline solid, mp 214 °C, found to be optically active $[\alpha]_D$ -142.3° (c = 0.62, $CHCl_3$). The positive ion fast atomic bombardment mass spectrum (FAB-ms) exhibited the quasi-molecular ion peak at *m/z* 370 $(M+H)^+$ and its molecular formula was determined to be $\{(C_{20}H_{19}NO_6+H)^+$; Found, 370.1274; Calcd for $C_{20}H_{20}NO_6$, 370.1319$\}$ by high-resolution FAB-ms, which is also supported by ^{13}C-nmr spectrum. The uv and ir absorptions were found to be the similar pattern to that of the (+)-corytensine (**4**), (+)- and (-)-egenine (**5** and **6**).[7] The chemical shifts of the ^1H- and ^{13}C-nmr were very similar to that of (+)-corytensine (**4**) and egenine[12] but the characteristic differences were observed due to the ^1H-nmr signals. There was a singlet signal of two protons at δ 6.84 for **1** in our experiment but it had been reported that two doublet signals at δ 6.85 and 6.83 (each 1H, J = 8.0 Hz) were assigned for $C_{5'}$-H and $C_{6'}$-H, in **4**, **5** and **6**[3,5,6] respectively. This differences clearly suggests that there was no *ortho*-coupling protons in **1** as they were found in **4**, **5** and **6**. There is no possible structure having two aromatic protons in the *ortho*-position on the ring D, so the structure for corydecumbine was suggested to be as **1** and to assign all the ^1H- and ^{13}C-signals, 2D nmr experiments were performed (Tables I and II).

Table I. ^{1}H-Nmr (400 MHz) Data for (-)-Corydecumbine (**1**), Corytensine (**4**) and *epi-α*-Decumbensine in $CDCl_3$

Proton	(-)-Corydecumbine (**1**)	(+)-Corytensine (**4**)	*epi-α*-Decumbensine
1	3.68, br s	3.68, s	3.66, s
3-ax	2.54, ddd (13, 10, 2.5)	2.54, ddd (13, 10.5, 3.0)	2.99, ddd (12.4, 3.8, 2)
3-eq	3.00, dt (10, 3.5)	3.00, dt (10.5, 3)	3.18, ddd (15.3, 12.4, 3.1)
4-eq	2.46, dt (15, 2.5)	2.47, dt (15.5, 3)	2.45, ddd (15.3, 3.1, 2)
4-ax	3.20, ddd (15, 13, 3.5)	3.20, ddd (15.5, 13, 3)	2.53, dt (15.3, 3.8)
5	6.61, br s	6.60, s	6.59, s
8	6.72, br s	6.71, s	6.07, s
9	5.29, br s	5.29, s	5.27, s
2'	-----	-----	6.23, s
3'	6.84, s	-----	-----
4'	-----	-----	-----
5'	-----	6.85, d (8)	6.82, s
6'	6.84, s	6.83, d (8)	6.82, s
7'	6.25, s	6.25, s	-----
NCH_3	1.95, s	1.96, s	1.95, s
OCH_2O (ring A)	5.90, d (1.5) 5.94, d (1.5)	5.90, d (1.7) 5.94, d (1.7)	5.91, m
OCH_2O (ring D)	6.04, d (1.5) 6.08, d (1.5)	6.04, d (1.5) 6.08, d (1.5)	6.04, m

Chemical shift is expressed in δ- ppm taking TMS as an internal standard and the coupling constant (*J*) is expressed in Hz in parenthesis.

Table II. ^{13}C-Nmr (100 MHz) Data for (-)-Corydecumbine (**1**) in $CDCl_3$

Carbon		Carbon		Carbon	
1	68.59 (s)	8	106.90 (d)	5'	141.66 (s)
3	53.87 (t)	8a	130.55 (s)	6'	108.94 (d)
4	29.28 (t)	9	89.81 (d)	7'	97.73 (d)
4a	128.64 (s)	1'	135.23 (s)	NCH_3	46.73 (q)
5	108.18 (d)	2'	124.12 (s)	OCH_2O (ring A)	100.92 (t)
6	146.40 (s)	3'	113.83 (d)	OCH_2O (ring D)	101.89 (t)
7	146.16 (s)	4'	148.22 (s)		

Chemical shift is expressed in δ- ppm. All the ^{1}H- and ^{13}C- signls assignment were due to the results of the DEPT, ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY, ^{1}H-^{13}C long-range COSY experiments and the multiplicity of carbon signals were determined by means of DEPT method indidated as s, d, t, and q.

As it had been observed that the phthalideisoquinoline alkaloids with ***S***- and ***R***-configurations at C_1 are dextro- and levorotatory, respectively.[13] The corydecumbine (**1**) was found to be the levorotatory, $[\alpha]_D$ -142.3°, so that the configutration at C_1 was suggested as ***R***. Both of the ^{1}H-nmr signals at δ 3.68 and 5.29 assigned for C_1-H and C_9-H were broad singlet suggesting the *threo-* configuration at C_1 and C_9,[3,10] hence the configuration at C_9 is suggested as ***R***.

From the foregoing evidences, the structure of (-)-corydecumbine was established to be **1** except for the stereochemistry at the $C_{7'}$ position. Our present result provided the first example of a phthalideisoquinoline alkaloid having substitution groups at C_6 and C_7 positions of the ring A and $C_{4'}$ and $C_{5'}$ positions of the ring D and is interesting from the biogenetic point of view. The distribution of this type of phthalideisoquinoline in other plants of Papaveraceae and their biological activities would be worthy of investigation.[14]

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4. The authors (ref. 2) compared (+)-corytensine (ref. 3) with *epi*-α-decumbensine (ref. 1) to show the proposed structure for *epi*-α-decumbensine was not correct but the structure drawing of (+)-corytensine (ref. 2) was also not correct.
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14. It is not sure that both the cultivated and wild *Corydalis* species contains this type of constituent or not , because of the unavailability of enough amount of wild *Corydalis* tubers, we could not isolate the minor constituents.

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