Institute of Chemistry[1], Vietnamese Academy of Science and Technology, Hanoi, Viet Nam, and Department of Bioorganic Chemistry[2], Leibniz-Institute of Plant Biochemistry, Halle/Saale, Germany

# Isoquinolone and protoberberine alkaloids from *Stephania rotunda*

T. T. Thuy[1], A. Porzel[2], K. Franke[2], L. Wessjohann[2], T. V. Sung[1]

*Received August 3, 2004, accepted November 25, 2004*

*Prof. Dr. Tran Van Sung, Institute of Chemistry, Vietnamese Academy of Science and Technology, 18-Hoang Quoc Viet Road, Cau Giay, Hanoi, Viet Nam*
*tvs@ich.ncst.ac.vn*

*Pharmazie 60: 701–704 (2005)*

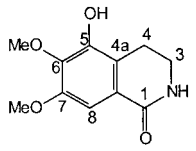
Chemical investigation of *Stephania rotunda* Lour. growing in Viet Nam led to the isolation and structural elucidation of three new alkaloids, 5-hydroxy-6,7-dimethoxy-3,4-dihydroisoquinolin-1(2*H*)-one (**1**), thaicanine 4-O-β-D-glucoside (**6**), as well as (−)-thaicanine N-oxide (4-hydroxycorynoxidine) (**8**), along with 23 known alkaloids. These structures were determined on the basis of MS and NMR spectroscopic data.

## 1. Introduction

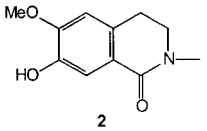
*Stephania rotunda* Lour. (Menispermaceae) is a climber tree growing wild in the mountainous areas of North Viet Nam. The tuber of this plant is used in Viet Nam under the local name "Binh voi" for treating a range of disorders, such as fever, abdominal complaints, as well as urinary, diarrhea, and intestinal diseases (Loi 1991). It has also regulative action on sleep, sedation, and respiration (Perry 1980). Chemical investigations of *Stephania* species from other countries have been reported, and a wide variety of alkaloids was described including members of the tetrahydroprotoberberine, protoberberine, benzyltetrahydroisoquinoline, aporphine, oxoaporphine, protoaporphine, hasubanane, and benzylisoquinoline classes (Kashiwaba et al. 1997; Blanchfield et al. 2003). However, no detailed study exists on the chemical constituents of *S. rotunda* growing in Viet Nam. In a previous paper, we have reported the isolation and structural determination of (*S*)-isocorydine and (*S*)-corydalmine (Sung et al. 2002) from the tubers of *S. rotunda* Lour. growing in Viet Nam. In a continued investigation of the alkaloid constituents, we have obtained a new isoquinolone alkaloid, 5-hydroxy-6,7-dimethoxy-3,4-dihydroisoquinolin-1(2*H*)-one (**1**); two novel tetrahydroprotoberberine alkaloids, thaicanine 4-*O*-β-D-glucoside (**6**), as well as (−)-thaicanine *N*-oxide (**8**, 4-hydroxycorynoxidine), together with 23 known alkaloids. This paper describes the isolation and structural determination of three new as well as a number of known protoberberine alkaloids with a substituent at the 4-position. These structures were elucidated by MS and various NMR techniques, including HSQC, HMBC, NOESY, and 1D NOE experiments.

## 2. Investigations, results and discussion

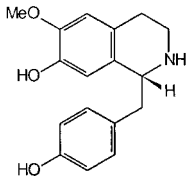
The residue of an ethanol extract of the tubers of *S. rotunda* was partitioned successively with *n*-hexane, ethyl acetate, and *n*-butanol. The EtOAc and *n*-butanol extracts, after evaporation of the solvents, were subjected to crystallization from EtOAc/EtOH to remove most of the tetrahydropalmatine, which represents approximately 65% of the alkaloid content of *Stephania sp*. The residual mother liquid was further purified by column chromatography, re-



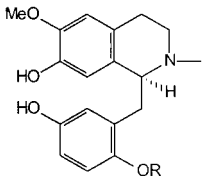
1



2

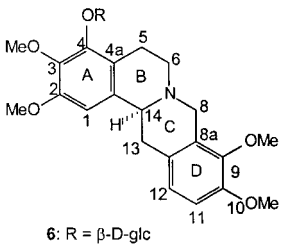


3



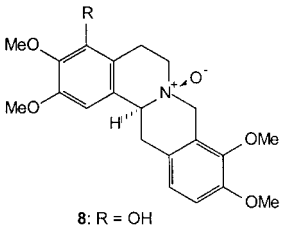
4: R = H

5: R = Me



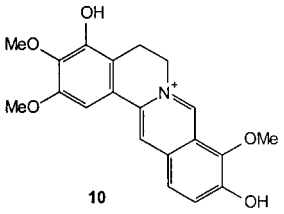
6: R = β-D-glc

7: R = H



8: R = OH

9: R = H



10

**Table 1: $^{13}C$ and $^{1}H$ NMR data of compound 1 at 125/ 500 MHz**

| | $\delta_C$, $CDCl_3$ | $\delta_H$ multiplicity (J in Hz), DMSO-$d_6$ | HMBC correlation (w = weak) |
|---|---|---|---|
| 1 | 165.9 | – | $H_2$-3, H-8 |
| 3 | 40.4 | 3.31 td (6.7, 2.8) | $H_2$-4, N–H |
| 4 | 21.4 | 2.71 t (6.7) | $H_2$-3, N–H |
| 4a | 118.5 | – | $H_2$-3, $H_2$-4, H-8 |
| 5 | 145.3 | – | $H_2$-4, H-8 (w) |
| 6 | 138.2 | – | H-8, 6-$OCH_3$ |
| 7 | 150.6 | – | H-8, 7-$OCH_3$ |
| 8 | 103.2 | 7.01 s | |
| 8a | 124.0 | – | $H_2$-4, H-8, N–H |
| NH | – | 7.78 br s | |
| 6-OMe | 61.1 | 3.72 s | |
| 7-OMe | 56.0 | 3.79 s | |
| 5-OH | – | 9.15 br s | |

crystallization, and preparative TLC to give **1**, **6**, and **8**, together with 23 known alkaloids.

The HR-ESI-MS of compound **1** gave the $[M + Na]^+$ peak at m/z 246.07355 leading to the molecular formula $C_{11}H_{13}NO_4$ (M = 233). The $^1H$ NMR spectrum of **1** was relatively simple, it revealed two methoxy groups resonating at δ 3.72 and 3.79, only one aromatic proton at δ 7.01 and a broad singlet of a hydroxy group at δ 9.15. The coupling pattern of the remaining three sets of signals was analyzed and assigned. The N–H proton occurred as a broad singlet at δ 7.78 and two methylene groups coupled to each other were at δ 3.31 and 2.71 (t, J = 6.7 Hz). The $^1H$, $^{13}C$ NMR and HMBC assignments of **1** are depicted in Table 1. The connection of substituents were deduced from the correlation of H-8 (δ 7.01) with C-1, C-4a, C-5, C-6, C-7, C-8a from the HMBC experiment. Further proof was gained from the NOE-difference spectrum. The aromatic proton at δ 7.01 gave an NOE interaction to 7-OMe (δ 3.79) but no effect to the methylene protons at C-3. On the basis of the above observations, the structure of **1** was elucidated as 5-hydroxy-6,7-dimethoxy-3,4-dihydroisoquinolin-1(2*H*)-one. In addition, we have also found thalifoline (7-hydroxy-6-methoxy-2-methyl-3,4-dihydroisoquinolin-1(2*H*)-one, **2**), which was isolated for the first time from *Thalictrum minus* L. var. *adiantifolium* Hort. (Doskotch et al. 1969). The new isoquinolones **1** and **2** may be originated from the oxidative degradation (Doskotch et al. 1969; Chou et al. 1994) of the benzyltetrahydroisoquinoline alkaloids coclaurine (**3**), **4** and dehassiline (**5**), respectively, which are known constituents of *S. rotunda*.

Column chromatography of the n-butanol extract provided compound **6** as a white solid, positive to Dragendorff and Mayer reagent. The HR-ESI-MS of compound **6** gave the $[M + H]^+$ peak at m/z 534.23459 leading to the molecular formula $C_{27}H_{35}NO_{10}$ (M = 533). The sugar moiety was easily identified as β-D-glucopyranose from its characteristic signals in the $^1H$ and $^{13}C$ NMR spectra (Tables 2, 3) and EIMS (m/z 371, $[M\text{-}Glu]^+$), thus giving $C_{21}H_{25}NO_5$ as aglycone. The EIMS spectra of compound **6** exhibited characteristic fragments due to an Retro Diels Alder cleavage of a tetrahydroprotoberberine skeleton possessing two methoxy groups in the D ring (m/z 164) as well as, two methoxy and one hydroxy group in the A ring (m/z 206) (Ruangrunsi et al. 1986; Chia et al. 1998). The $^1H$ and $^{13}C$ NMR spectra indicated the presence of two aromatic rings, four methoxy groups and five methylene groups (one $CH_2$ of glucose). The aromatic region of the $^1H$ NMR spectrum displayed one proton singlet, which suggested that this proton can be located at the position 1 or 4 and thus two methoxy groups are at C-2 and C-3. Placement of two methoxy groups in ring D at C-9 and C-10 have been confirmed by a pair of doublets with AB-system and *ortho* coupling (J = 8.4 Hz) between H-11 and H-12 in the $^1H$ NMR spectrum and 2D NMR experiments. Full analysis of all HMBC correlations resulted in the structure of thaicanine for the aglycone moiety (Ruan-

**Table 2: $^{1}H$ NMR data of compounds 6 and 8 at 500 MHz (δ multiplicity, J in Hz)**

| H | **6**, $CD_3OD$ | **8**, $CDCl_3$ |
|---|---|---|
| 1 | 6.76 br s | 6.27 s |
| 5 A | 3.16[a] | 3.56[a] |
| 5 B | 2.81 ddd (16.9, 11.2, 5.1) | 2.91 br d (12.9) |
| 6 A | 3.20[a] | 3.97 m |
| 6 B | 2.59 ddd (11.6, 11.6, 3.8) | 3.57[a] |
| 8 A | 4.21 d (15.8) | 4.78 br d (15.3) |
| 8 B | 3.53 d (15.8) | 4.56 br d (15.3) |
| 11 | 6.89 d (8.5) | 6.86 d (8.4) |
| 12 | 6.93 d (8.5) | 6.99 d (8.4) |
| 13 α | 3.43 dd (16.2, 3.9)[b] | 3.32 dd (16.4, 4.1) |
| β | 2.76 dd (16.2, 11.5) | 3.67 m |
| 14 α | 3.61 dd (11.5, 3.9) | 4.53 br d (11.7) |
| 2-OMe | 3.85 s | 3.85 s |
| 3-OMe | 3.82 s | 3.80 s |
| 9-OMe | 3.82 s | 3.83 s |
| 10-OMe | 3.83 s | 3.85 s |
| 1′ | 5.04[c] | |
| 2′ | 3.43[a, c] | |
| 3′ | 3.43[a, c] | |
| 4′ | 3.42[c] | |
| 5′ | 3.19 ddd (9.5, 5.2, 2.3)[b] | |
| 6′ | 3.76 dd (12.0, 2.3) | |
| | 3.64 dd (12.0, 5.3) | |

[a] Chemical shift of HSQC correlation peak; [b] From 1D DPFG NOE spectrum; [c] Part of strong ABCX system

**Table 3: $^{13}C$ NMR data of compounds 6 and 8**

| C | **6**, 100 MHz, $CD_3OD$ | **8**, 125 MHz, $CDCl_3$ |
|---|---|---|
| 1 | 106.7 | 100.6 |
| 2 | 153.2 | 151.2 |
| 3 | 141.3 | 135.4 |
| 4 | 148.3 | 147.0 |
| 4a | 122.8 | 113.4 |
| 5 | 24.6 | 19.0 |
| 6 | 52.0 | 64.3 |
| 8 | 54.7 | 67.2 |
| 8a | 128.4[a] | 122.6 |
| 9 | 146.0 | 145.6 |
| 10 | 151.6 | 150.6 |
| 11 | 112.5 | 112.0 |
| 12 | 125.1 | 123.6 |
| 12a | 128.3[a] | 125.3 |
| 13 | 36.2 | 29.4 |
| 14 | 60.8 | 68.1 |
| 14a | 134.1 | 126.8 |
| 2-OMe | 56.6 | 55.9 |
| 3-OMe | 61.5[b] | 60.6 |
| 9-OMe | 60.5[b] | 60.3 |
| 10-OMe | 56.3 | 55.9 |
| 1′ | 104.7 | |
| 2′ | 75.5 | |
| 3′ | 77.8 | |
| 4′ | 71.4 | |
| 5′ | 78.1 | |
| 6′ | 62.5 | |

[a, b] Exchangeable

grungsi et al. 1986). The connection of the glucose at C-4 was deduced from the HMBC correlation of C-4 (δ 148.3) with the anomeric proton H-1′ (δ 5.04). Further proof was gained from the NOESY spectrum. The aromatic proton (δ 6.76) gave NOE interactions to H-$13_{eq}$ (δ 3.43), H-14 (δ 3.61), 2-OMe (δ 3.85) and no effect to the methylene protons at C-5 and C-6, whereas the correlations of the anomeric proton (δ 5.04) to 3-OMe (δ 3.82) confirmed the glycosylation site at C-4 in the A ring. The aglycone of **6** is known as (−)-thaicanine (**7**) from the leaves of *Parabaena sagittata* Miers (Ruangrungsi et al. 1986), whereas its 4-*O*-glucoside is a novel natural product and belongs to the rare protoberberine glycosides.

The HR-ESI-MS of compound **8** gave the $[M + Na]^+$ peak at m/z 410.15741 and $[M + H]^+$ at m/z 388.17681 leading to the molecular formula $C_{21}H_{25}NO_6$ (M = 387) with one oxygen more than the aglycon moiety of **6**. The EIMS indicated fragments for a tetrahydroprotoberberine skeleton with the same substitution pattern as for **7**. The complete assignment of the substituent groups was made based on the 2D NMR spectra. There are strong CH long-range correlations in the HMBC spectrum between H-1 (δ 6.27) with C-2, C-3, C-4a and C-14. The NOESY spectrum showed a significant correlation between H-1/2-OMe, H-$13_{eq}$, H-14; H-6A/H-8 A; H-8 A /9-OMe; 10-OMe/H-11; H-12/H-$13_{eq}$ and H-$13_{eq}$/H-14. These results confirmed that the hydroxy group in the A ring was positioned at C-4. However, comparison of the $^1H$ and $^{13}C$ NMR data showed significant differences between data from **6**, **7**, and **8**, especially at 5, 6, 8, 13, and 14 position (Table 2 and 3). This suggested that **8** possesses an additional *N*-oxide group. The EI-MS spectral analysis of **8** indicated a close structural relationship to thaicanine, but displayed a mass peak at m/z 371 $[M-O]^+$, characteristic for the *N*-oxide group. Combination of the NMR and MS spectral data confirmed the structure of (−)-thaicanine *N*-oxide (4-hydroxycorynoxidine) for **8**. A similar compound corynoxidine (L-tetrahydropalmatine *N*-oxide, **9**) (Tani et al. 1975), was also isolated from this plant. The B/C ring junction in the new compound **8** according to the data should be the same as in **9**, also based on the assumption of a similar biosynthetic pathway. This was confirmed by the closely related laevorotatory ($[\alpha]_D^{22}$ −43°) and by the comparison $^{13}C$ NMR with those of corynoxidine (**9**). In the $^{13}C$ NMR spectra of **8** the chemical shifts of the B and C ring carbons are identical with those of corynoxidine (**9**) (Tani et al. 1975). That means, (−)-thaicanine *N*-oxide (**8**) likely has 14*S* configuration and a *trans* B/C ring juncture as **9**.

Based on the obtained negative optical rotations of isolated compounds **6**–**9** and the biogenetic information known (Blanchfield et al. 2003; Chia et al. 1988; Ruangrungsi et al. 1986; Tani et al. 1975), we propose the 14*S* configuration also for the new compound **6**. A known 4-substituted quaternary protoberberine, fissisaine (**10**) was also isolated and identified by comparison of its spectral data (MS, NMR) with literature values (Chia et al. 1998). The new isoquinolinone **1** and the rare protoberberines **6**–**8** and **10** show an identical substitution pattern with oxidation at C-5 (isoquinolinone) and C-4 (protoberberine), respectively. This is likely caused by either a common metabolic origin or a later oxidation by a nonspecific but regioselective oxidase.

The known isolated alkaloids were the isoquinoline thalifoline, the tetrahydroprotoberberines (−)-tetrahydropalmatine, (−)-corydalmine, corynoxidine and stefolidine (Sung et al. 2003), the quaternary protoberberines jatrorrhizine, columbamine, dehydrocorydalmine, stepharanine, palmatine, and fissisaine, the benzyltetrahydroisochinolines coclaurine, dehassiline, and polycarpine; the aporphines roemerine, (−)-stephanine, (*S*)-isocorydine, and dehydroroemerine, the oxoaporphines oxoxylopine, oxostephanine, and lanuginosine, the protoaporphine (−)-stepharine as well as the morphinane (−)-salutaridine (Sung et al. 2002; Blanchfield et al. 2003; Thuy et al. in prep.).

## 3. Experimental

### 3.1. General

Optical rotation $[\alpha]_D$: Digital Polarimeter Jasco DIP 1000. EIMS: ADM 402, 70 eV, Finigan TSQ 700. HR-ESI-MS: BRUKER BIOAPEX 70e Fourier transform ion cyclotron resonance mass spectrometer equipped with an Infinity™ cell, a 7.0 Tesla supraconducting magnet, a RF-only hexapole ion guide and an external electrospray ion source (Apollo™). NMR: Varian Mercury 400 MHz, Unity 500 spectrometer at 499.83 MHz ($^1H$) and 100, 125 MHz ($^{13}C$, $^{13}C$ APT). Chemical shifts were referenced to internal TMS (δ = 0, $^1H$) and $CDCl_3$ (δ = 77.0, $^{13}C$) or $CD_3OD$ (δ = 49.0, $^{13}C$). $^1H$, 1D, NOE difference and 2D spectra: Varian unity 500 spectrometer at 499.83 MHz. CC: Silica gel 60, 0.06–0.2 mm (Merck) for the first column, silica gel 60, 40–63 μm (Merck) for the following columns. TLC: Silica gel 60 F-254 (Merck); reversed phase (LiChroprep RP-18) (Merck).

### 3.2. Plant material

Tubera of *S. rotunda* Lour. were collected in Hoa Binh, North Viet Nam, in 1999. The species was identified by Dr. Vu Xuan Phuong, Institute of Ecology and Natural Resouces, Vietnamese Academy of Science and Technology, Hanoi. A voucher specimen Nr. 5111 (19/08/2001) is deposited in the Herbarium at the same Institute.

### 3.3. Extraction and isolation

The dried and powdered tubera of *S. rotunda* (2.4 kg) were extracted with 85% aq. EtOH at room temperature. EtOH was evaporated *in vacuo* at 45 °C and the aq. solution (200 g) was partitioned with *n*-hexane followed by EtOAc and *n*-BuOH. The organic solvents were evaporated *in vacuo* to afford 9.5, 70 and 30 g extracts, respectively. The EtOAc extract was crystallised from EtOAc/MeOH to remove (−)-tetrahydropalmatine. The residue of the mother liquid, containing various minor alkaloids, was chromatographed over silica gel with gradient $CHCl_3$–MeOH (98 : 2 → 85 : 15) to give 30 fractions (F-1 → F-30) (200 ml/fraction). Fraction 5 [$CHCl_3$–MeOH (98 : 2)] was further purified by silica gel CC (80 g) and finally by prep. TLC over silica gel with $CHCl_3$–EtOAc–MeOH (80 : 20 : 1) to afford **1** (4 mg, 0.00017%) and **2** (8 mg, 0.00033%). The crude compound **8** was isolated from fraction 18 and further purified by chromatography on silica gel (60 g) with EtOAc–MeOH–$H_2O$ (80 : 20 : 1) to yield **8** (7 mg, 0.00031%). The *n*-BuOH extract was separated on silica gel using $CHCl_3$–MeOH (65 : 35) and then $CHCl_3$–MeOH–$H_2O$ (65 : 35 : 5) to afford 58 fractions (F-1 → F-58) (200 ml/fraction). The crude compound **6** was isolated from fraction 8 and further purified by chromatography on silica gel (120 g) to yield **6** (56 mg, 0.00233%). Other fractions from the above column containing various alkaloids as well as (−)-tetrahydropalmatine were separated by CC, prep. TLC and crystallization to provide in total 23 known alkaloids.

#### 3.3.1. 5-Hydroxy-6,7-dimethoxy-3,4-dihydroisoquinolin-1(2H)-one (1)

The compound was purified by prep. TLC [silica gel, $CHCl_3$/MeOH 95 : 5); Rf 0.60 [silica gel, $CHCl_3$–MeOH (19 : 1)]; Powder from MeOH; HR-ESI-MS (m/z): 246.07355 $[M + Na]^+$ ($C_{11}H_{13}NO_4Na$ calc. 246.07368); $^1H$ and $^{13}C$ NMR data see Table 1.

#### 3.3.2. Thaicanine-4-O-β-D-glucopyranoside (6, 2,3,9,10-tetramethoxy-4-O-β-D-glucopyranosyl-tetrahydroprotoberberine)

The compound was purified by CC [silica gel, $CHCl_3$/MeOH/$H_2O$ 65 : 35 : 5); Rf 0.74 [silica gel, $CHCl_3$–MeOH–$H_2O$ (13 : 7 : 1)]; Powder from MeOH; $[\alpha]_D^{22}$ −147° (MeOH, c 0.5); HR-ESI-MS (m/z): 534.23459 $[M + H]^+$ ($C_{27}H_{36}NO_{10}$ calc. 534.23337); EIMS 70 eV, m/z (rel. int.): 533 $[M]^+$ (18), 502 $[M-31]^+$, 371 $[M\text{-glc}]^+$(38), 370 (62), 369 (100), 354 (57), 340 (22), 324 (16), 206 (18), 163 (51), 149 (23), 108 (8), 60 (51); $^1H$ and $^{13}C$ NMR data see Tables 2 and 3.

#### 3.3.3. (−)-Thaicanine N-oxide (8, 2,3,9,10-tetramethoxy-4-hydroxy-tetrahydroprotoberberine N-oxide)

The compound was purified by CC [silica gel, EtOAc/MeOH/$H_2O$ 40 : 10 : 1) and prep. TLC [silica gel, $CHCl_3$/MeOH/$H_2O$ 65 : 35 : 5 × 2

time); Rf 0.80 [silica gel, $CHCl_3-CH_3OH-H_2O$ (13 : 7 : 1)]; Powder from MeOH/EtOAc; ($[\alpha]_D^{22}$ −43° (MeOH, c 0.2) ($[\alpha]_D^{22}$ −81° in $CHCl_3$/MeOH for **9**, reported for the corynoxidine $[\alpha]_D^{22}$ −57° (Tani et al. 1975) and reported for the (−)-thaicanine $[\alpha]_D^{22}$ −243° in $CHCl_3$ (Ruangrungsi et al. 1986)); HR-ESI-MS (m/z): 388.17681 $[M+H]^+$ ($C_{21}H_{26}NO_6$, calc. 388.17546), 410.15839 $[M+Na]^+$ ($C_{21}H_{26}NO_6Na$, calc. 410.15741); EI-MS 70 eV, m/z (rel. int.): 371 $[M-O]^+$ (44), 369 $[M-18]^+$ (100), 354 $[M-CH_3-H_2O]^+$ (63), 338 (32), 324 (32), 206 (14), 178 (16), 164 (35), 149 (32), 135 (8), 121 (5); $^1H$ and $^{13}C$ NMR data see Table 2 and 3.

Acknowledgements: We are indebted to BMBF, Germany, for financial support in form of a project. We thank Dr. Juergen Schmidt (Institute of Plant Biochemistry, Halle/(Saale), Germany) for the mass spectra.

**References**

Blanchfield JT, Sands DPA, Kennard CHL, Byriel KA, Kitching W (2003) Characterisation of alkaloids from some Australian *Stephania* (Menispermaceae) species. Phytochemistry 63: 711–7120.

Chia YC, Chang FR, Li CM, Wu YC (1998) Protoberberine alkaloids from *Fissistigma balansae*. Phytochemistry 48: 367–369.

Chou CJ, Lin LC, Chen KKT, Chen CF (1994) Northalifoline, a new isoquinolone alkaloid from the pedicels of *Lindera megaphylla*. J Nat Prod 57: 689–694.

Doskotch RW, Schiff PL, Beal J, Beal JL (1969) Alkaloids of *Thalictrum*-X, two new alkaloids from *T. minus* var. *adiantifolium*: noroxyhydrastinine and thalifoline. Tetrahedron 25: 469–475.

Kashiwara N, Morooka S, Kimura M, Murakoshi Y, Ono M, Toda J, Suzuki H, Sano T (1997) Alkaloidal constituents of the tubers of *Stephania cepharantha* cultivated in Japan: structure of 3,4-dehydrocycleanine, a new bisbenzylisoquinoline alkaloid. Chem Pharm Bull 45: 470–475.

Loi DT (1991) Nhung cay thuoc va vi thuoc Viet Nam (Glossary of Vietnamese Medicinal Plants and Drugs). Hanoi Publishing House for Science and Technics, p. 859–862.

Perry LM (1980) Medicinal Plants of East and Southeast Asia, attributed properties and uses. Cambridge, the M. I. T. Press, p. 268.

Ruangrungsi N, Lange GL, Lee M (1986) Constituents of *Parabaena sagitata*, two new tetrahydroprotoberberine alkaloids. J Nat Prod 49: 253–258.

Sung TV, Thuy TT, Dan TT (2002) Isolation and structural elucidation of (*S*)-isocorydine and (*S*)-corydalmine from *Stephania* sp. Lour. Tap chi Hoa hoc (Journal of Chemistry, Viet Nam) 40 (2): 35–40.

Tani C, Nagakura N, Hattori S, Masaki N (1975) Structures of corynoxidine and epicorynoxidine, new alkaloids from *Corydalis koidzumiana*. Chem Lett, 1081–1084.

Thuy TT, Sung TV, Katrin F, Wessjohann L (2004) Characterisation of alkaloids from *Stephania rotunda*. Tap chi hoa hoc (Journal of Chemistry, Viet Nam) in preparation.