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Dong Sheng Ming<sup>a</sup>; De Quan Yu; Shi Shan Yu<sup>a</sup>; Jian Liu<sup>a</sup>; Cun Heng He<sup>a</sup>

<sup>a</sup> Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

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## A NEW FUROFURAN MONO-LACTONE FROM *FORSYTHIA SUSPENS*A

DONG SHENG MING, DE QUAN YU\*, SHI SHAN YU,  
JIAN LIU and CUN HENG HE

*Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking  
Union Medical College, Beijing 100050, China*

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A new furofuran mono-lactone, named forsythenin, was isolated from the fruits of *Forsythia suspensa*, together with the known compounds, ocotillone, ocotillol monoacetate, (6'-O-palmitoyl)-sitosterol-3-O- $\beta$ -D-glucoside and palmitic acid. The structure of the new compound was elucidated on the basis of spectroscopic means and X-ray crystallography.

*Keywords:* *Forsythia suspensa*; Furofuran mono-lactone; Forsythenin

### INTRODUCTION

The fruit of *Forsythia suspensa* Vahl. (Oleaceae) is an important Chinese traditional drug "Lian Qiao" which has been used for antiinflammatory, antibacterial, diuretic, and antidotal purposes. Previously, we have reported the isolation and structure characterization of three new quinoid compounds from the fruits of *F. suspensa* [1]. Further phytochemical analysis of this plant has resulted in the isolation of a new compound, forsythenin (**1**), along with four known compounds, all of which were obtained from this species for the first time. This paper deals with the isolation, identification and structure elucidation of these compounds.

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\* Corresponding author. Tel.: 63165224. Fax: 63017757. E-mail: dquanyu@public.bta.net.cn.

## RESULTS AND DISCUSSION

The EtOAc soluble part of the 70% EtOH extract of the fruits of *F. suspensa* was separated by silica gel column chromatography into 30 fractions. Compound **1** was isolated from the medium polar fractions (fr. 10–15) after a series of chromatographic separations.

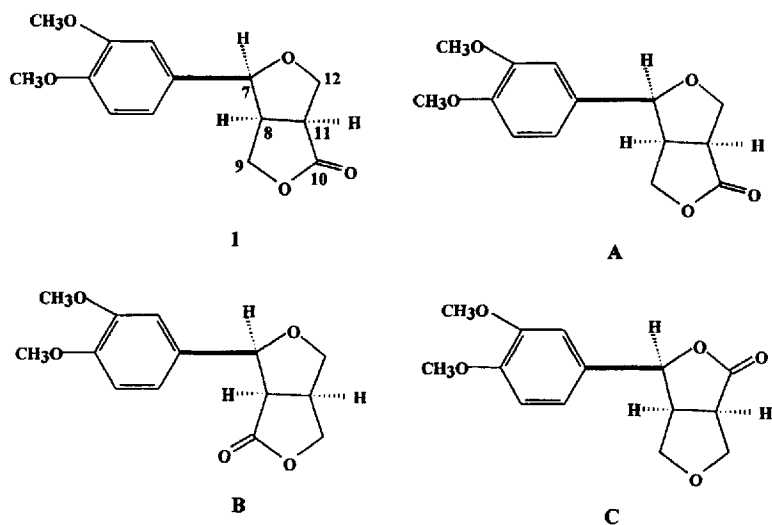
A molecular formula of  $C_{14}H_{16}O_5$  ( $m/z$  264) was assigned for compound **1** by EIMS and elemental analysis. Its IR spectrum revealed the existence of a five membered lactone ring ( $1774\text{ cm}^{-1}$ ) and benzene ring ( $1518$  and  $1468\text{ cm}^{-1}$ ). The low-field part of the  $^1\text{H-NMR}$  (Table I) spectrum of **1** showed three proton resonances at  $\delta$  6.80 (1H, d,  $J = 1.6$  Hz), 6.78 (1H, dd,  $J = 8.2, 1.6$  Hz) and 6.87 (1H, d,  $J = 8.2$  Hz). On the basis of their chemical shifts and coupling-patterns a 1,3,4-trisubstituted phenyl ring was suggested to be present in the molecule.  $^{13}\text{C-NMR}$  (Table I) spectrum and DEPT experiments of **1** showed 14 signals: two methoxyls, two oxymethylenes, six methines (one of them bearing an oxygen atom) and four quaternary carbons, of which the signals at  $\delta$  129.0, 109.0, 149.2, 148.6, 111.2, 118.1, and  $55.9 \times 2$  demonstrated the presence of a veratryl (3,4-dimethoxyphenyl) moiety.

The structure of the remaining part of the molecule was derived by analysis of 2D-NMR spectrum. In the  $^1\text{H-}^1\text{H}$  COSY spectrum the doublet at  $\delta$  4.98 (H-7) showed a cross peak with  $\delta$  3.37 (m) attributed to the H-8 proton. The latter was coupled with a double doublet at  $\delta$  3.95 and a multiplet at

TABLE I NMR data for forsythenin (in  $\text{CDCl}_3$ )

Position	$\delta_{\text{C}}$	$\delta_{\text{H}}$
1	129.0	
2	109.0	6.80d (1.6)
3	149.2	
4	148.6	
5	111.2	6.87d (8.2)
6	118.1	6.78dd (8.2, 1.6)
7	84.0	4.98d (5.4)
8	43.6	3.37m
9	70.9	4.51dd (9.5) 3.95dd (9.5, 6.8)
10	178.6	
11	46.0	3.36m
12	68.3	4.08dd (8.2, 9.9) 3.83dd (9.9, 4.0)
OCH <sub>3</sub>	55.9	3.88s
	55.9	3.88s

$\delta$  3.36, assigned to H-9a and H-11, respectively. The H-11 proton was further correlated with two double doublets at  $\delta$  4.08, 3.83 assigned as the two protons (H-12) of a methylene. The above correlation revealed the connectivities of CH(7)–CH(8)–CH<sub>2</sub>(9) and CH(8)–CH(11)–CH<sub>2</sub>(12). The corresponding carbon signals in the <sup>13</sup>C–<sup>1</sup>H COSY spectrum were  $\delta$  84.0, 43.6, 70.9, 46.0 and 68.3, respectively, these together with the presence of an ester carbonyl signal at  $\delta$  178.6 indicated that the unidentified moiety was a furofuran mono-lactone ring. Further analysis of the COSY spectrum allowed the assignment of all proton and carbon resonances of the structures. The above information suggested that the alternative structures of compound **1** are as follows:



It was very difficult to determine precisely the position of the carbonyl group in the structure from the above spectral data. The ambiguity in the structure was resolved by X-ray single crystal diffraction analysis, which confirmed the structure of forsythenin to be A and showed its relative configuration (see Fig. 1). Compound **1** showed a positive Cotton effect at 280 nm ( $\Delta\epsilon + 0.3$ ) in its CD spectrum. This band could be assigned to the  $n \rightarrow \pi$  transition of the carbonyl group of **1**. Application of the sector rule suggested the absolute configuration shown in structure **1** for this compound.

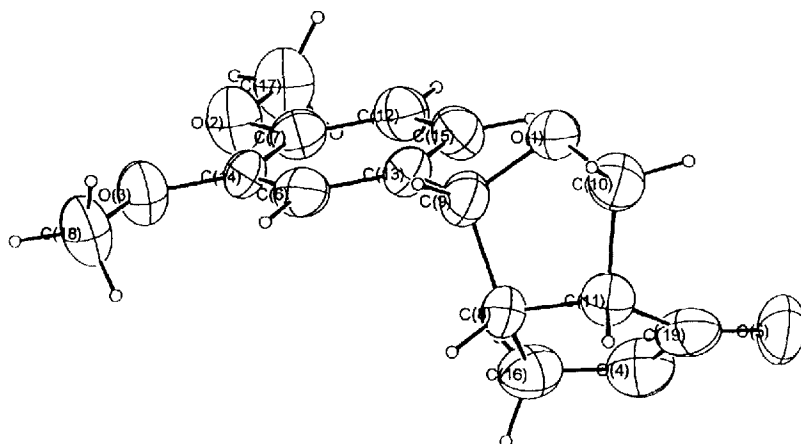


FIGURE 1 X-ray crystallographic structure of forsythenin.

Besides the new compound **1**, the other isolated compounds from this plant were identified as ocotillone [2], ocotillol monoacetate [3], (6'-O-palmitoyl)-sitosterol-3-O- $\beta$ -D-glucoside [4] and palmitic acid on the basis of the spectral evidence and comparison of physical data with those of literature values.

## EXPERIMENTAL SECTION

**General** Melting points were determined with a XT4-100X micromelting point apparatus and are uncorrected.  $[\alpha]_D$  was measured with a Perkin-Elmer 241 polarimeter. IR spectra were recorded on Perkin-Elmer 683 spectrophotometer. NMR spectra were run on a Bruker AM-500 spectrometer. EIMS and FABMS were recorded on a ZAB-2F instrument. Elemental analysis was performed on a MOD 1106 elemental analyzer.

**Plant Material** The fruits of *F. suspensa* were collected in Beijing, China, in July 1995. The plant material was identified by Wan Zhi Song, and a Voucher specimen has been deposited in the Herbarium of Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College.

**Extraction and Isolation** The fruits of *F. suspensa* (10 kg) were extracted with hot 70% EtOH (30l) three times, and the solutions were combined and concentrated *in vacuo*. A suspension of the EtOH extract in H<sub>2</sub>O was

extracted with EtOAc. The combined EtOAc extracts (180 g) were chromatographed over Si gel (180–200 mesh) column eluted with a petroleum ether–Me<sub>2</sub>CO gradient solvent system. Fractions with similar *R<sub>f</sub>* values by TLC were evaporated and combined to give 30 fractions. Fractions 10–15 (obtained from petroleum ether: Me<sub>2</sub>CO = 25: 75) were repeatedly subjected to column chromatography over Si gel eluted with petroleum ether: Me<sub>2</sub>CO gradient to afford ocotillone (12 mg), ocotillol monoacetate (48 mg), (6'-O-palmitoyl)-sitosterol-3-O-β-D-glucoside (15 mg), palmitic acid (8 mg), and forsythenin (**1**, 18 mg).

*Forsythenin* Colorless crystals (Me<sub>2</sub>CO), mp 196–198°C;  $[\alpha]_D^{20} + 197.0^\circ$  (*c* 0.1335, CHCl<sub>3</sub>); IR(KBr)  $\nu_{\max}$  1774, 1518, 1468, 1258, 1142, 1028, 760 cm<sup>-1</sup>. <sup>13</sup>C-NMR and <sup>1</sup>H-NMR data see Table I; EIMS 264 [M]<sup>+</sup>(100), 249 (8), 233 (24), 179 (12), 166 (82), 151 (78), 135 (10), 107 (10), 95 (20), 77 (24), 65 (15), 51 (20), 43 (10). Anal. C 63.41, H 6.14, calcd. for C<sub>14</sub>H<sub>16</sub>O<sub>5</sub>, C 63.64, H 6.06.

### X-ray Crystallographic Analysis

Compound **1** crystallized in the orthorhombic space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub> with one molecule of composition C<sub>14</sub>H<sub>16</sub>O<sub>5</sub> (*Z* = 4) forming the asymmetric unit, accurate cell constants of *a* = 6.663 (2) Å, *b* = 9.522 (3) Å, *c* = 19.759 (6) Å,  $\alpha = \beta = \gamma = 90^\circ$ ,  $v = 1253.61$  (8) Å<sup>3</sup> [3]. All reflections were collected on the MAC Science DIP-2000 Imaging Plate using graphite monochromated MoK $\alpha$  radiation (0.71073 Å). To reduced data by the programs DENZO and SCALEPACK, a total of 912 reflections was measured within maximum with  $2\theta < 50^\circ$  (*R*<sub>merge</sub> = 0.032). After correction for Lorentz, polarization and background effects, 906 of the 912 unique reflections were judged observed [*I* > 3σ(*I*)]. The structure was solved by MAC science crys-tanG. Hydrogen atoms were located in a difference electron density synthesis after full least-squares refinement of the non-hydrogen atoms. The final conventional crystallographic residual *R* = 0.0508 and *R<sub>w</sub>* = 0.0491 for 906 observed reflections. The final X-ray model is shown in Fig. 1. The final atomic parameters, bond lengths and angles will be deposited with the Cambridge crystallographic data center.

### Acknowledgment

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