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Research Article

A New Pyrrolidone Alkaloid and Other Constituents from *Rourea oligophlebia* Stems

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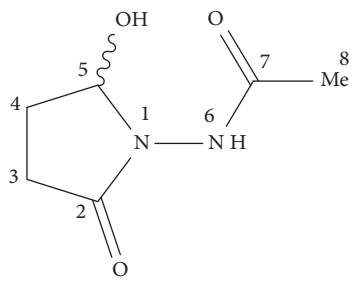
Phytochemical study of *Rourea oligophlebia* stems led to the isolation of a new 2-pyrrolidone alkaloid (*R*,*S*)-*N*-(5-hydroxyl-pyrrolidin-2-one-1-yl)acetamide (**1**), together with 14 known compounds including friedelin (**2**), friedanol (**3**), taraxerol (**4**), vanillin (**5**), coniferyl aldehyde (**6**), apigenin (**7**), 7α-hydroxy-3β-sitosterol (**8**), coniferyl alcohol (**9**), scopoletin (**10**), emodin (**11**), protocatechuic acid (**12**), catechin (**13**), procyanidin A1 (**14**), and (*E*)-2,3,5,4'-tetrahydroxystilbene-2-β-D-glucoside (**15**). Several isolated compounds were evaluated for cytotoxicity and antimicrobial activity. Compound **11** exhibited good antimicrobial activity on Gram (+) strains and moderate cytotoxicity against KB, Hep-G2, and LU cancer cell lines. Compounds **6** and **8**–**10** showed selective activity on HepG-2 and MCF-7 over KB and LU cancer cell lines, while compound **7** exhibited similar effects on KB, HepG-2, and MCF-7 cell lines with IC_{50} values of 36.46 ± 0.81, 32.00 ± 0.58, and 32.03 ± 0.61 μg/mL, respectively.

1. Introduction

The genus of *Rourea* is a group of climbing shrubs belonging to the family of Connaraceae which are widely distributed in the Amazon, Pacific region, Africa, and Asia [1]. Chemical investigations have revealed that *Rourea* species contain a substantial number of biologically active constituents, including flavonoids, phytosteroids, triterpenes, lipids, phenolic acids, and coumarins [1–6]. The *Rourea* plant extracts and their active components exhibited interesting biological activities such as hypoglycemic activity [1, 5, 7], antibacterial activity [1, 8], antinociceptive activity [9], antiplasmodial activity [3, 10], and antioxidant activity [1, 4, 8]. *Rourea oligophlebia* Merr. is a species found on mountains of central provinces of Vietnam. According to folk medicine, *R. oligophlebia* stems have been used for the treatment of bleeding and bone fractures [11]. A preliminary study of *R. oligophlebia* revealed the presence of triterpene, sterol, and phenolic constituents [12]. In this study, we described the isolation and identification of a new pyrrolidone alkaloid (*R*,*S*)-*N*-(5-hydroxyl-pyrrolidin-2-one-1-yl)acetamide (**1**) (Figure 1) and fourteen known compounds including friedelin (**2**), friedanol (**3**), taraxerol (**4**), vanillin (**5**), coniferyl aldehyde (**6**), apigenin (**7**), 7α-hydroxy-3β-sitosterol (**8**), coniferyl alcohol (**9**), scopoletin (**10**), emodin (**11**), protocatechuic acid (**12**), catechin (**13**), procyanidin A1 (**14**), and (*E*)-2,3,5,4'-tetrahydroxystilbene-2-β-D-glucoside (**15**) from the stems of *R. oligophlebia* (Figure S1). The isolated compounds were evaluated for antimicrobial activity and cytotoxicity.

2. Materials and Methods

2.1. General Experimental Procedures. The NMR data including ^{1}H-NMR, ^{13}C-NMR, ^{15}N-NMR, HSQC, and HMBC spectra were recorded by a Bruker AM500 FT-NMR



N- (5-Hydroxy-pyrrolidin-2-one-1-yl)acetamide(1)

Figure 1: Structure of new compound isolated from *R. oligophlebia*.

spectrometer using TMS as an internal standard. The HR-ESI-MS was obtained using an Agilent 6530 Accurate Mass Q-TOF LC/MS system. Column chromatography (CC) was performed on silica gel (Merck, 230–400 mesh) or Sephadex LH-20 (Sigma Aldrich). Thin layer chromatography used precoated silica gel plates (Merck 60 F_{254}). Compounds were visualized by spraying with 10% aqueous H_2SO_4.

2.2. Plant Materials. The plant stems were collected from the Ben En National Park, Thanh Hoa province, Vietnam, in 2018. The plant was identified by Dr. Do Ngoc Dai, Nghe An University of Economics, as *Rourea oligophlebia* Merr. (Connaraceae). A voucher specimen (MT-202) was deposited at Hong Duc University, Faculty of Natural Sciences.

2.3. Extraction and Isolation. The stem powder (5.3 kg) of *Rourea oligophlebia* was extracted successively with *n*-hexane, ethyl acetate, and methanol (12 L × 3 times, 24 hours/time) at room temperature. The combined extracts were evaporated *in vacuo* to obtain *n*-hexane residue (17.6 g), ethyl acetate residue (10 g), and MeOH residue (300 g), respectively.

The ethyl acetate residue (10 g) was separated on the silica gel CC, eluted with *n*-hexane/ethyl acetate gradient (0–100% ethyl acetate) to afford 15 fractions E1–E15. Compounds **2** (15 mg), **3** (5.5 mg), and **4** (4.5 mg) were obtained from E1 fraction (0.2 g), E3 fraction (0.12 g), and E4 fraction (0.15 g), respectively, by crystallization in *n*-hexane. Fraction E10 (0.5 g) was fractionated by Sephadex CC, eluted with CH_2Cl_2/MeOH (1/9, v/v) to afford 4 subfractions E10.1–E10.4. Subfraction E10.2 (17 mg) was purified by preparative TLC using CH_2Cl_2/MeOH (95/5, v/v) as eluent to yield **5** (2 mg) and **6** (2.5 mg). Fraction E10.3 (25 mg) was purified by silica gel CC, eluted with CH_2Cl_2/MeOH (95/5, v/v) to obtain compound **7** (15 mg). Fraction E12 (0.9 g) was fractionated by Sephadex CC, eluted with CH_2Cl_2/MeOH (1/9, v/v) to give 3 subfractions E12.1–12.3. Compound **8** (6.1 mg) was obtained from E12.1 fraction (85 mg) by crystallization in *n*-hexane. Fraction E12.2 (30 mg) was chromatographed by silica gel CC, eluted with CH_2Cl_2/MeOH (95/5, v/v) to yield **9** (15 mg). Fraction E13 (0.7 g) was purified by Sephadex CC, eluted with CH_2Cl_2/MeOH (1/9), to give two subfractions E13.1–E13.2. Subfraction E13.2 (20 mg) was purified by preparative TLC using CH_2Cl_2/MeOH (95/5, v/v) as an eluant to afford compound **10** (3 mg). The MeOH extract (300 g) was chromatographed on a silica gel CC and eluted with a gradient solvent system of *n*-hexane-ethyl acetate (100 : 1–0 : 1, v/v) to afford 14 fractions M1–M14, respectively. Fraction M6 (0.8 g) was separated by Sephadex LH-20 CC eluting with CH_2Cl_2/MeOH (1/9, v/v) to yield compound **11** (7 mg). Fraction M12 (0.6 g) was purified by Sephadex LH-20 CC and eluted with CH_2Cl_2/MeOH (1/9, v/v) to afford compound **12** (6 mg). Compound **13** (12 mg) was obtained from M13 fraction (1.1 g) by purification on Sephadex LH-20 CC, eluted with CH_2Cl_2/MeOH (1/9, v/v). Fraction M14 was purified by silica gel CC and eluted with CH_2Cl_2/acetone (9 : 1, v/v) to give 3 fractions M14.1–M14.3. Fraction M14.1 (0.5 g) was subjected to a Sephadex LH-20 CC and eluted with CH_2Cl_2/MeOH (1/9, v/v) to yield **14** (5.7 mg). Fraction M14.2 (2 g) was separated by Sephadex LH-20 CC and eluted with CH_2Cl_2/MeOH (1/9, v/v) to give 3 fractions M14.2.1–M14.2.3. Fraction M14.2.1 (0.45 g) was purified by Sephadex LH-20 CC, followed by separation with silica gel CC, eluted with CH_2Cl_2/MeOH (9/1, v/v) to yield compound **1** (20 mg). Fraction M14.2 (0.28 g) was subjected to silica gel CC eluted with CH_2Cl_2/MeOH (9/1, v/v) to yield 2 subfractions M14.2.2.1-M14.2.2.2. Fraction M14.2.2.2 (84 mg) was purified by Sephadex LH-20 CC, eluting with CH_2Cl_2/MeOH (1/9, v/v) to yield compound **15** (7 mg).

(*R*,*S*)-*N*-(5-Hydroxyl-pyrrolidin-2-one-1-yl)acetamide (**1**): colorless oil; $[\alpha]_D^{25}$~0 (*c* 0.4, MeOH); IR ν_{max} (KBr) 3239, 3022, 1706, 1664, 1211 cm^{-1}; HR-ESI-MS (positive-ion mode) *m/z* 141.0673 $[(M\text{-}H_2O) + H]^+$ (calcd. for $C_6H_9N_2O_2^+$, 141.0659); ^1H and ^{13}C-NMR data (Table 1).

2.4. Cytotoxicity Assay. The cytotoxicity assays were carried out in triplicate against KB, HepG-2, LU, and MCF-7 cell lines (American Type and Culture Collection, ATCC). Cells were maintained in Dulbecco's D-MEM medium, supplemented with 10% fetal calf serum, L-glutamine (2 mM), penicillin G (100 UI/mL), streptomycin (100 μg/mL), and gentamicin (10 μg/mL). Stock solutions of compounds were prepared in DMSO/H_2O (1/9), and the cytotoxicity assays were carried out against cancer cell lines (3×10^3 cells/mL) using a modification of the published method [13]. After 72 h of incubation at 37°C in air/CO_2 (95 : 5) with or without test compounds, cell growth was estimated by colorimetric measurement at 540 nm with a Titertek Multiskan photometer. Ellipticine was used as a positive compound.

2.5. Antimicrobial Assay. The antimicrobial activity was evaluated by the microdilution method previously described by Hadacek [14] and expressed as IC_{50} (50% inhibitory concentration) values. Six bacterial strains and a fungus were used for the test: 3 strains of Gram (+) bacteria: *Staphylococcus aureus* ATCC 13709, *Bacillus subtilis* ATCC 6633, and *Lactobacillus fermentum* N4; 3 strains of Gram (−) bacteria: *Salmonella enterica* ATCC12228, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 15442; fungus: *Candida albicans* ATCC 10231. Bacterial solutions with a concentration of 5×10^5 CFU/ml and a fungal solution with a concentration of 1×10^3 CFU/ml were prepared. The isolated compounds were diluted in DMSO at the following dilution concentrations: 128, 64, 32, 16, 8, and 4 μg/mL. The positive controls were ampicillin for Gram (+) bacterial strains,

Table 1: ^{1}H and ^{13}C NMR data of **1**.

C	1 (acetone-d_6)		1 (MeOH-d_4)	
	δ_C [a]	δ_H [b] (m, *J*, Hz)	δ_C [a]	δ_H [b] (m, *J*, Hz)
2	172.4	—	175.0	—
3	27.3	2.46–2.39 (m, H-3a) 2.38–2.32 (m, H-3b)	27.8	2.59–2.50 (m, H-3a) 2.38–2.32 (m, H-3b)
4	27.1	2.27–2.21 (m, H-4a) 1.88–1.81 (m, H-4b)	27.1	2.27–2.21 (m, H4a) 1.88–1.81 (m, H4b)
5	83.4	5.22 (br s)	84.2	5.22 (dd, J = 3.5 Hz, 6.5 Hz)
7	169.6	—	172.1	—
8	20.6	1.96 (s)	20.5	2.06 (s)
OH	—	5.47 (br d, J = 5.5)	—	—
NH	—	9.16 (br s)	—	—

cefotaxime for Gram (−) bacterial strains, and nystatin for fungus. IC_{50} values were determined based on the measured turbidity by optical Biotech spectra and raw data software.

3. Results and Discussion

3.1. Structure Elucidation. Compound **1** was isolated as colorless oil. Its molecular formula of **1** was deduced as $C_6H_{10}N_2O_3$ from the $[(M\text{-}H_2O)+H]^+$ peak at *m/z* 141.0673 ($C_6H_9N_2O_2$, calcd. for 141.0659) in the positive-ion HR-ESI-MS spectrum (Figure S2). The molecular formula of $C_6H_{10}N_2O_3$ was further confirmed by combined ^{1}H, ^{13}C, and ^{15}N-NMR spectra as ten protons, six carbons, and two signals of nitrogen (δ_N 199.99 and 165.86) were observed (Figure S3). The IR spectrum suggested that **1** contained carbonyl amide groups (1706, 1664 cm^{-1}) and hydroxyl and amine groups (3239 cm^{-1}) (Figure S4), which appeared in the ^{1}H-NMR spectrum (in acetone-d_6) at δ_H 5.47 (br d, J = 5.5 Hz) and 9.16 (br s), respectively (Figure S5). The ^{1}H-NMR spectrum (in MeOH-d_4) showed signals of an oxymethine group at δ_H 5.22 (1H, dd, J = 3.5, 6.5 Hz, H-5), two methylene groups (H-3, H-4), and a methyl singlet of an acetyl group at δ_H 2.06 (3H, s, H-8) (Figure S6). The ^{13}C-NMR spectrum of **1** displayed six carbon signals including two signals of carbonyl group at δ_C 175.0 (C-2) and 172.1 (C-7), an oxymethine group at δ_C 84.2 (C-5), two methylene groups at δ_C 27.1 (C-3) and 27.8 (C-4), and a methyl signal at δ_C 20.5 (C-8) (Figures S7–S10). The HMBC cross-peaks (in acetone-d_6) of the hydroxyl group (δ_H 5.47) to C-5 (δ_C 84.2) confirmed the free hydroxyl group was placed at C-5 position. In the HMBC spectrum (in MeOH-d_4), the correlations of H-3 (δ_H 2.59–2.50 and 2.38–2.32), H-4 (δ_H 2.27–2.21 and 1.88–1.81), and H-5 (δ_H 5.47) to C-2 (δ_C 175.0) suggested a 5-hydroxy-pyrrolidin-2-one moiety in the structure of **1**(Figures S11 and S12). In addition, methyl protons H-8 (δ_H 2.06) have only correlated with the carbonyl carbon C-7 (δ_C 172.1) (Figure 2). Based on the optical rotation value of nearly zero and the CD spectrum (Figure S13), compound **1** may be regarded as a racemate. Therefore, the structure of **1** was assigned as (*R, S*)-*N*-(5-hydroxyl-pyrrolidin-2-one-1-yl)acetamide. It is noted that alkaloids containing 5-hydroxy-2-pyrrolidone fragment were rarely found in nature. To our knowledge, only few examples are brachystemidine D isolated from *Brachystemma calycinum* [15], longistrobin and isolongistrobin from *Macrorungia longistrabus* [16], and lepiota

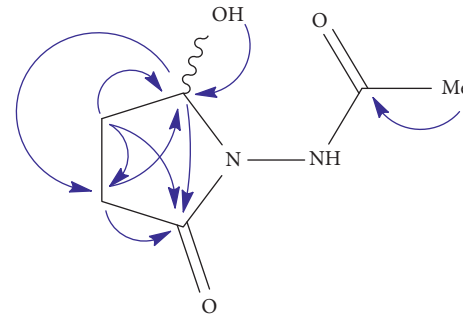


Figure 2: Key HMBC correlations of the new compound **1**.

and (*R*)-5-hydroxypyrrolidin-2-one from the mushroom *Macrolepiota neomastoidea* [17].

The known compounds were elucidated as friedelin (**2**), friedanol (**3**) [12], taraxerol (**4**) [18], vanillin (**5**), coniferyl aldehyde (**6**) [19], apigenin (**7**) [20], 7α-hydroxy-3β-sitosterol (**8**) [21], coniferyl alcohol (**9**) [22], scopoletin (**10**) [23], emodin (**11**) [24], protocatechuic acid (**12**), catechin (**13**) [25], procyanidin A1 (**14**) [26], and (*E*)-2,3,5,4'-tetrahydroxystilbene-2-β-D-glucoside (**15**) [27]. Compounds **2**-**3**, **6**–**9**, **11**-**12,** and **15** were reported for the first time from *Rourea* genus.

3.2. Biological Activities. Several isolated compounds were evaluated for antimicrobial activity and cytotoxicity. Only emodin (**11**) showed good antimicrobial activity against Gram (+) strains *S. aureus, B. subtilis*, and *L. fermentum* with IC_{50} values of 4.51, 15.83, and 28.94 μg/mL, respectively, but exhibited no activity against Gram (−) strains and fungus at the concentration of 128 μg/mL. Other compounds were also inactive ($IC_{50} > 128$ μg/mL) in antimicrobial activity test. The cytotoxicity of isolated compounds was evaluated against KB, HepG-2, LU, and MCF-7 cancer cell lines (Table S1). Compounds **6** and **8**–**10** showed selective activity on HepG-2 and MCF-7 with IC_{50} ranging from 18.73 ± 0.40 μg/mL to 43.63 ± 0.90 μg/mL over KB and LU cancer cell lines. Compound **7** exhibited similar effect on KB, HepG-2 and MCF-7 cell lines. Among the tested compounds, emodin (**11**) had the best cytotoxicity on LU cancer cell line with IC_{50} values of 21.04±0.52 μg/mL, respectively.

4. Conclusions

In conclusion, fifteen compounds were isolated from the stems of *Rourea oligophlebia*, among which a new alkaloid (*R*,*S*)-*N*-(5-hydroxyl-pyrrolidin-2-one-1-yl)acetamide (**1**) was identified along with fourteen known compounds **2**–**15**. Compound **11** showed good antimicrobial activity on Gram (+) strains and moderate cytotoxicity against KB, Hep-G2, and LU-1 cell lines. Compounds **6** and **8**–**10** showed selective activity on HepG-2 and MCF-7 over KB and LU cancer cell lines, while compound **7** was moderately active on KB, HepG-2, and MCF-7 cell lines.

Data Availability

The data used to support the findings of this study are included within the supplementary materials.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Acknowledgments

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Supplementary Materials

HR-ESI-MS, IR, CD, and NMR spectra of compound **1** associated with this article (). (*Supplementary Materials*)

References

[1] C. P. Osman, Z. Zahari, M. I. Adenan, and R. M. Zohdi, "A review on traditional uses, phytochemistry, and pharmacology of the genus Rourea," *Journal of Applied Pharmaceutical Science*, vol. 9, no. 9, pp. 125–131, 2019.

[2] H. N. Ngoc, S. Löffler, D. T. Nghiem, T. L. G. Pham, H. Stuppner, and M. Ganzera, "Phytochemical study of Rourea minor stems and the analysis of therein contained bergenin and catechin derivatives by capillary electrophoresis," *zJournal*, vol. 149, Article ID 104063, 2019.

[3] Z. D. He, C. Y. Ma, G. T. Tan et al., "Rourinoside and rouremin, antimalarial constituents from *Rourea* minor," *Phytochemistry*, vol. 67, no. 13, pp. 1378–1384, 2006.

[4] M. Kalegari, C. A. B. Gemin, G. A. Silva et al., "Chemical composition, antioxidant activity and hepatoprotective potential of *Rourea induta Planch*. (*Connaraceae*) against CCl4-induced liver injury in female rats," *Nutrition*, vol. 30, no. 6, pp. 713–718, 2014.

[5] M. M. Laikowski, P. R. Santos, D. M. Souza et al., "*Rourea cuspidata*: chemical composition and hypoglycemic activity," *Asian Pacific Journal of Tropical Biomedicine*, vol. 7, no. 8, pp. 712–718, 2017.

[6] P. V. De Oliveira, R. P. L. Lemos, and L. M. Conserva, "Chemical constituents of *Rourea doniana*," *Brazilian Journal of Pharmacognosy*, vol. 22, no. 2, pp. 451–454, 2012.

[7] A. Chaudhary, A. Bhandari, and A. Pandurangan, "Anti-hyperglycemic potential of *Rourea* minor roots in streptozotocin (STZ) induced diabetic rats," *International Journal of Pharmaceutical Research*, vol. 4, no. 1, pp. 59–62, 2012.

[8] M. Kalegari, M. D. Miguel, A. F. Philippsen et al., "Antibacterial, allelopathic and antioxidant activity of extracts and compounds from *Rourea induta Planch*. (*Connaraceae*)," *Journal of Applied Pharmaceutical Science*, vol. 2, no. 9, pp. 61–66, 2012.

[9] M. Kalegari, M. L. Cerutti, S. J. M. Júnior et al., "Chemical composition and antinociceptive effect of aqueous extract from *Rourea induta Planch*. leaves in acute and chronic pain models," *Journal of Ethnopharmacology*, vol. 153, no. 3, pp. 801–809, 2014.

[10] J. Bero, M. Frédérich, and J. Quetin-Leclercq, "Antimalarial compounds isolated from plants used in traditional medicine," *Journal of Pharmacy and Pharmacology*, vol. 61, no. 11, pp. 1401–1433, 2009.

[11] V. V. Chi, *Dictionary of Vietnamese Medicinal Plants*, Medical Publisher, Hanoi, Vietnam, 2012.

[12] D. N. Thuc, V. T. Thuy, V. T. H. Mai, L. N. Thanh, V. V. Quan, Chemical constituents from ethyl acetate extract of the stems of *Rourea oligophlebia* Merr." *Vietnam Journal of Chemistry*, vol. 58, no. 3, pp. 298–301, 2020.

[13] T. Mosmann, "Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays," *Journal of Immunological Methods*, vol. 65, no. 1-2, pp. 59–63, 1983.

[14] F. Hadacek and H. Greger, "Testing of antifungal natural products: methodologies, comparability of results and assay choice," *Phytochemical Analysis*, vol. 11, no. 3, pp. 137–147, 2000.

[15] Y. X. Cheng, J. Zhou, N. H. Tan et al., "Isolation and characterization of brachystemidines A–E, novel alkaloids from *Brachystemma calycinum*," *Journal of Natural Products*, vol. 65, no. 5, pp. 750–752, 2002.

[16] M. A. Wuonola and R. B. Woodward, "Imidazole alkaloids of *Macrorungia longistrobus*: revised structures and total syntheses," *Tetrahedron*, vol. 32, no. 10, pp. 1085–1095, 1976.

[17] K. H. Kim, I. K. Lee, K. M. Park, W. K. Kim, and K. R. Lee, "Isolation of γ-lactam alkaloids from the *Macrolepiota neomastoidea*," *Bulletin of the Korean Chemical Society*, vol. 29, no. 8, pp. 1591–1593, 2008.

[18] Y. C. Koay, K. C. Wong, H. Osman, I. M. S. Eldeen, and M. Z. Asmawi, "Chemical constituents and biological activities of *Strobilanthes crispus* L." *Records of Natural Products*, vol. 7, no. 1, pp. 59–64, 2013.

[19] L. Moujir, A. M. L. Seca, A. M. S. Silva, and M. C. Barreto, "Cytotoxic activity of diterpenes and extracts of *Juniperus brevifolia*," *Planta Medica*, vol. 74, no. 7, p. 751, 2008.

[20] T. Ersöz, Ü. Ş. Harput, I. Saracoğlu, I. Çaliş, and Y. Ogihara, "Phenolic compounds from *Scutellaria pontica*," *Turkish Journal of Chemistry*, vol. 26, no. 4, pp. 581–588, 2002.

[21] C. C. Zhao, J. H. Shao, X. Li, J. Xu, and P. Zhang, "Antimicrobial constituents from fruits of *Ailanthus altissima* Swingle," *Archives of Pharmacal Research*, vol. 28, no. 10, pp. 1147–1151, 2005.

[22] A. B. Aguilar-Guadarrama and M. Y. Rios, "Flavonoids, sterols and lignans from *Cochlospermum vitifolium* and their relationship with its liver activity," *Molecules*, vol. 23, no. 8, p. 1952, 2018.

[23] M. Adfa, T. Yoshimura, K. Komura, and M. Koketsu, "Antitermite activities of coumarin derivatives and scopoletin from *Protium javanicum Burm*. f," *Journal of Chemical Ecology*, vol. 36, no. 7, pp. 720–726, 2010.

[24] J. F. Sanchez, R. Entwistle, J. H. Hung et al., "Genome-based deletion analysis reveals the prenyl xanthone biosynthesis pathway in *Aspergillus nidulans*," *Journal of the American Chemical Society*, vol. 133, no. 11, pp. 4010–4017, 2011.

[25] A. L. Davis, Y. Cai, A. P. Davies, and J. R. Lewis, "^{1}H and ^{13}C NMR assignments of some green tea polyphenols," *Magnetic Resonance in Chemistry*, vol. 34, no. 11, pp. 887–890, 1996.

[26] H. Lou, Y. Yamazaki, T. Sasaki et al., "A-type proanthocyanidins from peanut skins," *Phytochemistry*, vol. 51, no. 2, pp. 297–308, 1999.

[27] H. K. Kim, Y. H. Choi, J. S. Choi et al., "A new stilbene glucoside gallate from the roots of *Polygonum multiflorum*," *Archives of Pharmacal Research*, vol. 31, no. 10, pp. 1225–1229, 2008.