SHORT REPORT

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Scopariaine A: a New Alkaloid from *Scoparia dulcis* with Protective effect on Cardiomyocytes Injury *in Vitro*

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Abstract: A new alkaloid, termed scopariaine A (**1**), was obtained from the whole plant of *Scoparia dulcis L*. The new structure was established by applying various spectroscopic methods including 1D (^{1}H-, ^{13}C-NMR), 2D-NMR (HMBC, HSQC) and high resolution electrospray ionization mass spectrometry (HR-ESI-MS). Scopariaine A (**1**) was tested for its protective effect on attenuating palmitate-induced viability at 5, 10 and 25 μM. The results showed that the cell viability was significantly increased in palmitic acid combined with scopariaine A treated H9C2 cells.

Keywords: *Scoparia dulcis* L.; scopariaine A; alkaloid; H9C2 cells.

1. Plant Source

The alkaloids in *Scoparia dulcis* L. have attracted much attention from chemists and pharmacologists worldwide. These alkaloids, mainly coixol and its derivatives, have various biological activities. In the course of finding new alkaloids from *Scoparia dulcis* L, a new alkaloid scopariaine A (**1**) was obtained. Herein, we report the isolation, structural elucidation, and its protective effect on the model of cardiomyocytes injury induced by high concentration of palmitic acid in H9C2 cells (Figure 1).

The whole plants of *S. dulcis* were collected from Wuzhi Mountain of Hainan Province in 2018. The plant was authenticated by Prof. Yuguang Fan, and a voucher specimen (No.SD201807) with a FMHU code (FHMU6255) was deposited at the herbarium of Hainan Medical University.

2. Previous Studies

The stems and leaves of *S. dulcis* are sweet when chewing. Therefore, it was called sweet broomwort herb. Interestingly, *S. dulcis* is a medicinal plant to treat diabetes and gastric ulcer, etc [1,2]. Many pharmacological studies revealed that this plant had the ability in anti-diabetic, anti-inflammatory,

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and the anti-gastric ulcer [3,4]. In chemical investigations, alkaloids such as coixol, 6-metoxibenzoxazolinone, diterpenes, and others were obtained from *S. dulcis* [5-7].

3. Present Study

The whole plants of *S. dulcis* (10.0 kg) were dried in shade and cut into small pieces. Then the plants were extracted under reflux by ethanol for three times. The ethanol extract was concentrated under reduced pressure to give a residue (1.20 kg). The residue was dissolved in water and extracted by petroleum. The residue was then partitioned by dichloromethane for three times. The dichloromethane extract was isolated by silica gel column chromatography using a gradient ratio of petroleum-dichloromethane-acetone as the eluent to give six fractions (Fra.1-Fra.6). Fra.5 was subjected to a Sephadex LH-20 using methanol as the eluent and then purified by HPLC using a mixture of methanol-water (40:60) to afford **1** (5.0 mg).

*Scopariaine A (**1**)*: colorless crystal (MeOH), m.p. 238-240 °C, UV (MeOH) λ_{max} (log ε) 248 (3.86), 286 (2.24) nm. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) = 3.44 (2H, t, *J* = 7.2 Hz, H-9), 3.80 (3H,s, 6-OCH_3), 4.23 (2H, t, *J* = 7.2 Hz, H-8), 6.76 (1H, dd, *J* = 8.4, 2.4 Hz, H-5), 6.82 (1H, d, *J* = 2.4 Hz, H-7), 6.86 (2H, d, *J* = 8.4 Hz, H-12, 16), 7.01 (1H, d, *J* = 8.4 Hz, H-13, 15), 7.87 (2H, d, *J* = 8.4 Hz, H-12, 16). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm) = 35.9 (C-8), 37.7 (C-9), 56.0 (6-OCH_3), 97.6 (C-7), 109.2 (C-4), 109.4 (C-5), 115.5 (C-13, 15), 124.7 (C-3a), 129.7 (C-11), 130.7 (C-12, 16), 130.7 (C-11), 143.3 (C-7a), 155.0 (C-2), 156.1 (C-6), 160.3 (C-14), 195.5 (C-10). HR-ESI-MS: *m/z* 336.0846 ([M + Na]$^+$, calcd. $C_{17}H_{15}NO_5$ for 336.0848).

Bioactivity Test-Cell Viability Assay: Cell viability was assessed by the MTT assay as previous report [8]. Cells were incubated with 5, 10 and 25 μM of scopariaine A and palmitic acid. Then the cell viability was measured.

The whole plant of *S. dulcis* was dried, cut into pieces, and extracted with ethanol. The extract was concentrated under reduced pressure to give a residue. The residue was subjected to conventional purification procedures and resulting in the isolation of scopariaine A (Figure 1).

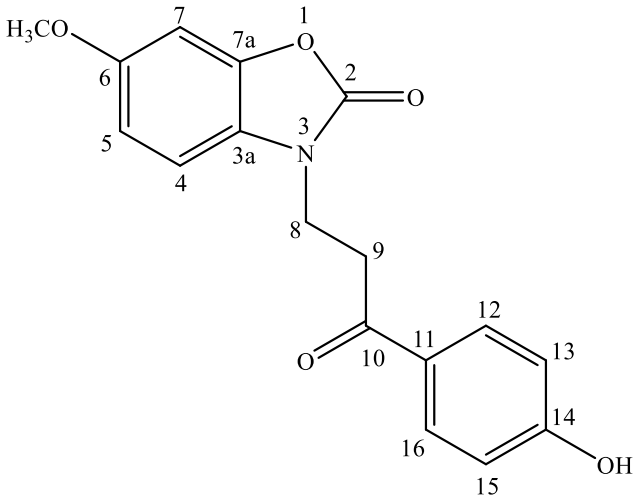

Figure 1. Structure of scopariaine A (**1**) isolated from *Scoparia dulcis*

Compound **1,** scopariaine A, was obtained as a colorless crystal. Its molecular formula $C_{17}H_{15}NO_5$ was determined by analyzing the HR-ESI-MS at *m/z* 336.0846 ([M + Na]$^+$ (calcd 336.0848). The ^{1}H

NMR spectrum exhibited signals for one methoxyl group [δ_H 3.80 (3H, s, 6-OCH_3), a set of benzoyl protons [δ_H 6.76 (1H, dd, J = 8.4, 2.4 Hz, H-5), 6.82 (1H, d, J = 2.4 Hz, H-7), 6.86 (2H, d, J = 8.4 Hz, H-5), 7.01 (1H, d, J = 8.4 Hz, H-13, 15), 7.87 (2H, d, J = 8.4 Hz, H-12, 16)], two methylene groups [3.44 (2H, t, J = 7.2 Hz, H-9), 4.23 (2H, t, J = 7.2 Hz, H-8)]. The ^{13}C NMR spectrum, associated with HSQC experiment, resolved 17 carbon signals of two benzoyl groups [97.6 (C-7), 109.2 (C-4), 109.4 (C-6), 115.5 (C-13, 15), 124.7 (C-3a), 129.7 (C-11), 130.7 (C-12, 16), 130.7 (C-11), 143.3 (C-7a), 155.0 (C-2), 156.1 (C-6), 160.3 (C-14)], one methoxyl [δ_C 56.0], two methylenes [δ_C 35.9 (C-8), 37.7 (C-9)], two carbonyl groups [δ_C 155.0 (C-2), 195.5 (C-10)].

The HMBC spectrum of **1** exhibited correlation from δ_H 6.82 (H-7) to carbons at δ_C 143.3 (C-7a), δ_C 124.7 (C-3a), and correlations from δ_H 6.76 (H-5) to carbons at δ_C 156.1 (C-6), and correlations from δ_H 6.86 (H-4) to carbons at δ_C 124.7 (C-3a), δ_C 109.4 (C-5), 151.6 (C-6) allowed the elucidation of the coixol part [8]. HMBC correlations from the methylene protons δ_H 4.23 (H-8) to carbons at δ_C 37.7 (C-9), 195.5 (C-10), 155.0 (C-2), 124.7 (C-3a), and correlations from proton at δ_H 7.01 (H-12, 16) to δ_C 195.5 (C-10), 130.7 (C-11), 160.3 (C-14) allowed the determination of connection between N3-C8 and the establishment of the structure of **1**. Thus, compound **1** was elucidated with a given name scopariaine A as depicted in Figure 1.

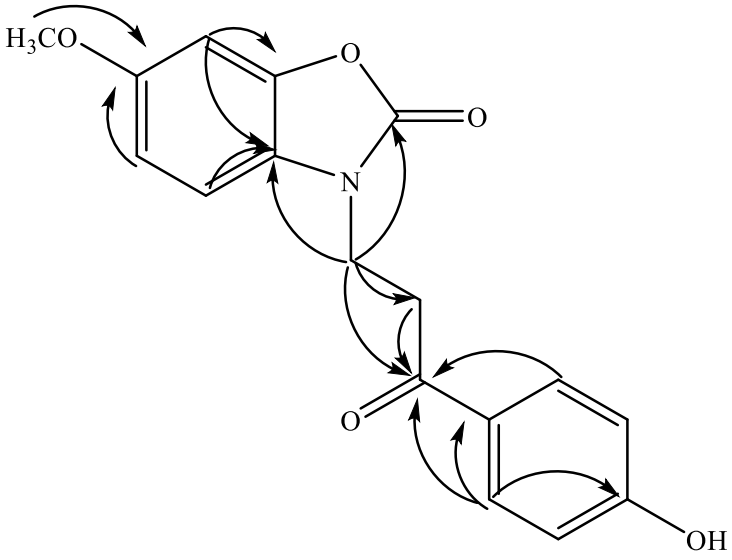

Figure 2. Important HMBC (arrow) correlations for scopariaine A (**1**)

Scopariaine A was tested for its protective effect on the model of cardiomyocytes injury induced by high concentration of palmitic acid in H9C2 cells. The result showed that the new compound relieved cardiomyocyte injury induced by palmitic acid and attenuated the viability by palmitate-induced decrease in H9C2 cells as depicted in Figure 3.

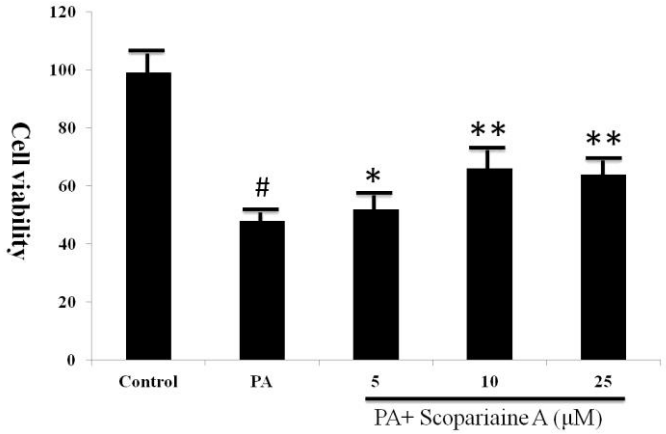

Figure 3. Cell viability treated by scopariaine A (**1**) in H9C2 cells. # p<0.01 compared with control, *p<0.05 compared with PA, **p<0.01 compared with PA

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Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products

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