Research Article

HMG-CoA Reductase Inhibitors from *Monascus*-Fermented Rice

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Seven compounds were isolated from *Monascus*-fermented rice by column chromatography with silica gel and semiprep HPLC. Their structures were elucidated by extensive spectroscopic methods. All compounds displayed HMG-CoA reductase inhibitory potential, among them compound 7 exhibited strong inhibition with IC_{50} value comparable with lovastatin. In this study, two compounds (1 and 2) were obtained from natural source for the first time.

1. Introduction

Monascus-fermented rice, also called red yeast rice, red Koji or “Hongqu”, is commonly used in Asian food and medicine for centuries. Its pharmaceutical function was stated that “Hongqu” promotes “digestion and blood circulation, can strengthen the spleen and dry the stomach.” by Li Shizhen, the great pharmacologist of the Ming Dynasty [1].

Since monacolin K was first isolated from *Monascus ruber* by Endo in 1979, a series of monacolins, such as monacolin J, monacolin L, monacolin X and monacolin M, have been found and disclosed to be potent 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA reductase) inhibitors [2–5]. After that dihydromonacolin-MV and dehydromonacolin-MV2 isolated from *Monascus* sp. have been characterized for their antioxidant action [6, 7]. Non-monacolin secondary metabolites have also been identified so far [8], but it is still unclear whether the cholesterol-lowering effect of *Monascus*-fermented rice is due solely to the monacolin K content or if other monacolins, sterols, and isoflavones contribute to its cholesterol-lowering effect.

In our search for HMG-CoA reductase inhibitory compounds from *Monascus*-fermented rice, we carried out the chemical investigation on *Monascus purpureus* (*M. purpureus*, CGMCC No. 0272)-fermented rice, resulting in the isolation of seven HMG-CoA reductase inhibitory compounds including (4*R*, 6*R*)-6-(2-((1*S*, 2*S*)-2,6-dimethyl-1,2-dihydro naphthalene-1-yl)-ethyl)-4-hydroxy-tetrahydropyran-2-one (1), (4*R*, 6*R*)-6-(2-(2,6-dimethylnaphthalene-

1-yl)ethyl-4-hydroxy-tetrahydropyran-2-one (2), 1-monolinolein (3), (9*Z*, 12*Z*)-octadeca-9,12-dienoic acid (4), Monascinol (5), Pulchellalactam (6), and Lunatinin (7). Their structures were determined based on spectroscopic data. In our study compounds 1 and 2 were obtained from natural source for the first time, and compounds 3 and 4 were isolated from the genus for the first time. Details of the isolation, structure elucidation, and HMG-CoA reductase inhibitory activities of these compounds are reported here.

2. Materials and Methods

2.1. General. NMR spectra were run on a Bruker Avance III 600 MHz spectrometer. EI-MS and HR-ESI-MS were measured on Agilent 5973N and Bruker micrOTOF-QII mass spectrometers. IR spectra were recorded on Nicolet Nexus-670 and Nicolet 380 FT-IR spectrometers. UV spectra were measured on a Shimadzu UV2401PC UV/vis spectrophotometer. Column chromatography (CC) was performed with silica gel (200–300 mesh) and thin-layer chromatography (TLC) was performed on silica gel GF₂₅₄ from Qingdao Marine Chemical Inc., China. RP-C18 silica gel (YMC) was purchased from Greenherbs Science & Technology Development Co., Ltd., China. Sephadex LH-20 (Pharmacia) was purchased from H&E Co., Ltd., China. MPLC separation was performed with Combiflash (ISCO) and HPLC was performed on Agilent 1260 apparatus using 5C18-MS-II column (ODS, 250 mm × 10 mm) and monitored with a

DAD detector. NADPH and HMG-CoA were purchased from Merck and Sigma respectively; Cholestyramine was obtained from Nanjing Lifecare Pharmaceutical; Lovstatin was purchased from China National Institutes for Food and Drug Control. All other chemicals were obtained from Beijing Chemical Reagent Co., Ltd. All organic solvents were of analytical purity and purchased from Beijing Chemical Reagent Co., Ltd., China.

2.2. Biological Material. *Monascus*-fermented rice was prepared from cooked rice inoculated with *M. purpureus* (CGMCC No. 0272), produced by Beijing Peking University WBL Biotechnology Co., Ltd. The *Monascus*-fermented rice was dried with a drying oven at 80°C, and the dried *Monascus*-fermented rice was pulverized with a pulverizer.

The *Monascus purpureus* was identified by China General Microbiological Culture Collection Center (CGMCC) and deposited in CGMCC.

2.3. Extraction and Isolation. Dried and powdered *Monascus*-fermented rice (4 kg) was successively ultrasonic extracted 3 times with petroleum ether and ethyl acetate to yield petroleum ether crude extract (82 g) and ethyl acetate crude extract (170 g). The petroleum ether crude extract was subjected to silica gel column chromatography eluted with a gradient mixture of petroleum ether-ethyl acetate (50:50 to 0:100) to yield 2 fractions (P1-P2). Fr P1 (54 g) was further subjected to a silica gel column eluted with petroleum ether-ethyl acetate (75:25) to yield 3 fractions (P1A-P1C). Fraction P1C (2.05 g) was chromatographed over a C18 column eluted with 75% MeOH to give 3 fractions (P1C1-P1C3). P1C1 subfraction (1.03 g) was purified by gel chromatography over Sephadex LH-20 eluted with CH₂Cl₂-MeOH (1:1) and further purified by MPLC using 75–85% MeOH to afford compound 5 (54 mg) and compound 6 (50 mg). Fr P2 (20 g) was further subjected to a silica gel column eluted with petroleum ether-ethyl acetate (25:75) to yield 3 fractions (P2A-P2C). P2B subfraction (8.5 g) was purified by gel chromatography over Sephadex LH-20 eluted with CH₂Cl₂-MeOH (1:1) and further purified by HPLC using 90% MeOH to afford compound 3 (14 mg). Ethyl acetate crude extract (170 g) was subjected to silica gel column chromatography eluted with a gradient mixture of petroleum ether-ethyl acetate (50:50 to 0:100) to yield 2 fractions (E1-E2). Fr E2 (48 g) was further subjected to a silica gel column eluted with petroleum ether-ethyl acetate (33:67) to yield 4 fractions (E2A-E2D). Fr E2B (10.8 g) was chromatographed on MPLC eluted with CH₂Cl₂-ethyl acetate-MeOH (30:30:1) to yield 4 fractions (E2B1-E2B4). E2B1 subfraction (3.8 g) was purified by gel chromatography over Sephadex LH-20 eluted with CH₂Cl₂-MeOH (2:1) and further purified by HPLC using 66% acetonitrile-MeOH (1:1) in H₂O to afford compound 1 (48 mg) and compound 2 (18 mg). E2B2 subfraction (4.0 g) was purified by C18 column chromatography eluted with 82% acetonitrile-MeOH (1:1) in H₂O and further purified by gel chromatography over Sephadex LH-20 eluted with CH₂Cl₂-MeOH (2:1) to afford compound 7 (56 mg). Fr E2C (4.7 g) was chromatographed

over a Sephadex LH-20 column (CH₂Cl₂-MeOH 6:4) and afforded five subfractions (E2C1-E2C5). E2C4 subfraction (0.49 g) was purified by C18 column chromatography eluted with 85% MeOH and further purified by HPLC using ACN to afford compound 4 (6.7 mg).

2.4. HMG-CoA Reductase Inhibitory Assay

2.4.1. Preparation of Microsomes. Male Sprague-Dawley rats (100–200 g) were killed by cervical dislocation at or near the peak of the daily circadian rhythm in reductase activity. In most experiments rats were fed a diet containing 5% cholestyramine for 4 days prior to the preparation of microsomes. Livers were excised, rinsed in ice-cold buffer A (KESD buffer) containing 10 mM potassium phosphate, 2 mM EDTA, 250 mM sucrose, and 1 mM DTT (pH 6.8). The livers were then minced through a tissue press and homogenized in three volumes of buffer A per g of liver by four strokes with the loose pestle of a Dounce homogenizer and one stroke with the tight pestle. Mitochondria and cell debris were sedimented by centrifugation two times at 12,000 g for 15 min at 4°C. Crude microsomes were prepared from the two 12,000 g supernatants by sedimentation at 105,000 g for 90 min at 4°C. The pellet was resuspended in buffer A (1 mL/g liver) and resedimented at 105,000 g for 90 min at 4°C [9]. The washed microsomal pellets were quickly-frozen in an acetone-dry ice bath and stored at –80°C prior to use.

2.4.2. Solubilization of HMG-CoA Reductase. For optimal solubilization of the reductase, the frozen microsomes were allowed to thaw at room temperature before addition of an equal volume of 50% glycerol in buffer B, containing 0.2 M sucrose, 0.1 M KCl, 0.08 M potassium phosphate, 2 mM potassium EDTA, and 10 mM DTT (pH 7.2), preheated to 37°C. The suspension was rehomogenized with 10 downward passes of a hand-driven, all-glass Potter-Elvehjem homogenizer and then incubated at 37°C for 60 min. The suspension was diluted threefold with buffer B preheated to 37°C to a final glycerol concentration of 8.3%, rehomogenized with 10 downward passes of the glass homogenizer pestle, and centrifuged at 105,000 g for 60 min at 25°C. The supernatant containing solubilized HMG-CoA reductase was removed and used immediately for enzyme purification [10].

2.4.3. Purification of HMG-CoA Reductase. The solubilized enzyme was fractionated with saturated ammonium sulfate solution and the protein precipitating between 35% and 50% ammonium sulfate was dissolved in buffer B [11].

2.4.4. Assay of HMG-CoA Reductase. The activity of HMG-CoA reductase was determined at 37°C in total volume of 200 µL. HMG-CoA reductase 10 µL was preincubated with buffer C (KCl 200 mM, potassium phosphate 160 mM, EDTA 4 mM, DTT 10 mM, pH 6.8) for 5 min at 37°C, and the reaction was initiated by adding 15 µL of cofactor-substrate solution (200 µM NADPH and 50 µM HMG-CoA in buffer C) and 5 µL of sample solution (dissolved in 50% DMSO) or 5 µL of 50% DMSO (negative control) [12]. The dynamic change of

FIGURE 1: Structures of compounds 1-7 and monacolin L.

OD₃₄₀ was detected with VerSamax ELISA microplate reader, and the rate of the change within 5 min was used to evaluate the activity of HMG-CoA reductase, and then to evaluate the inhibition activity of each sample.

3. Results and Discussion

Repeated column chromatography of the petroleum ether extract and ethyl acetate extract of *Monascus*-fermented rice afforded seven known compounds (1-7, see Figure 1). The compounds were identified as (4*R*, 6*R*)-6-(2-((1*S*, 2*S*)-2,6-dimethyl-1,2-dihydro naphthalene-1-yl)-ethyl)-4-hydroxy- tetrahydropyran-2-one (1) [13, 14], (4*R*, 6*R*)-6-(2-(2,6-dimethylnaphthalene-1-yl)ethyl)-4-hydroxytetrahydropyran-2-one (2) [15], 1-monolinolein (3) [16], (9*Z*,12*Z*)-octadeca-9,12-dienoic acid (4) [17], Monascinol (5) [18], Pulchellalactam (6) [19], and Lunatinin (7) [20, 21] on the basis of comparison of their NMR data and HR-ESI-MS or EI-MS data with those reported in the literature. It is worthwhile to point out that compounds 1 and 2 were isolated from natural source for the first time, and compounds 3 and 4 were isolated from the genus for the first time. All isolated compounds were evaluated for their ability to inhibit HMG-CoA reductase.

3.1. Chemistry. Compound 1 was obtained as a colorless gum. The HR-ESI-MS gave a pseudo molecular ion peak at m/z 323.1492 $[M + Na]^+$, consistent with a molecular formula of $C_{19}H_{24}O_3$. The UV spectrum showed maximum absorption at 229.0 and 265.8 nm. Its IR spectrum revealed absorption bands at 3380 (hydroxyl), and 1712 cm^{-1} (carbonyl). The ^1H and ^{13}C NMR data of 1 were similar to those of monacolin L previous reported [22]. Comparing the molecular formula and NMR data of 1 with those of monacolin L, it was found that 1 absent four hydrogens and had two more aromatic double bond signals at δ 127.3/6.93 (1H, d, $J = 7.8$ Hz, H-7) with 136.2 (C-6) and 127.6/6.96 (1H, d, $J = 7.8$ Hz, H-8) with 135.7 (C-8a). In addition, the chemical shift of 6-Me at δ 2.29 (3H, s) was moved obviously downfield. The two aromatic double bonds were located between C-5 and C-4a based on the HMBC correlations of H-7/C5, C-8a and 6-Me, H-8/C-4a, C-8a, C-1, and C-7 (see Figure 2). Additionally, the optical rotation at $[\alpha]_D^{25} + 31.5$ (c 0.111, CH_2Cl_2) is similar to that of monacolin L, whose optical rotation at $[\alpha]_D^{25} + 164.16$ (c 0.6, $CH_2Cl_2/MeOH = 2:1$), suggesting that the chiral carbons C-1, C-2, C-3' and C-5' of compound 1 also had S, S, R, R-configurations. It is further confirmed by the NOESY correlations (see Figure 2) observed between H-1 (δ_H 2.58) with H-2 (δ_H 2.72), H-3'

FIGURE 2: Key HMBC ($\rightarrow$), and NOESY ($\leftrightarrow$) correlations in compound **1**.

with H-1 (δ_{H} 2.58), and H-3' with H-2 (δ_{H} 2.72). Similarly, NOESY cross peaks between 2-Me (δ_{H} 1.06) with H-7' (δ_{H} 1.58 and 1.76), H-7' (δ_{H} 1.58 and 1.76) with H-5' (δ_{H} 4.56). Thus the structure of **1** was identified as (4*R*, 6*R*)-6-(2-((1*S*, 2*S*)-2,6-dimethyl-1,2-dihydro-naphthalene-1-yl)-ethyl)-4-hydroxy-tetrahydropyran-2-one. This compound was reported by Greenspan et al. and Stokker [13, 14]. The ^1H and ^{13}C NMR data was assigned unambiguously by HSQC and HMBC experiments (see Tables 1 and 2). Compound **1** was obtained from natural source for the first time.

Compound **2** was obtained as a colorless gum. The HR-ESI-MS gave a pseudo molecular ion peak at m/z 321.1484 $[\text{M} + \text{Na}]^+$, consistent with a molecular formula of $\text{C}_{19}\text{H}_{22}\text{O}_3$. The UV spectrum showed maximum absorption at 231.8 and 281.6 nm. Its IR spectrum revealed absorption bands at 3434 (hydroxyl), and 1712 cm^{-1} (carbonyl). The UV and NMR data of **2** were similar to those of **1** but showed one more double bond signals at δ 134.2 (C-1) and 132.2 (C-2) and absent two hydrogens (H-1 and H-2), and the downfield chemical shift of 2-Me at δ 2.49 (3H, s), indicating that **2** was 1,2-two dehydrogenated **1**. Additionally, the optical rotation at $[\alpha]_{\text{D}}^{25} + 11.2$ (c 0.06, CH_2Cl_2) is similar to that of monacolin L, suggesting that the chiral carbons C-3' and C-5' of compound **2** also had *R*, *R*-configurations. Thus, the structure of **2** was determined as (4*R*, 6*R*)-6-(2-(2,6-dimethylnaphthalene-1-yl)ethyl)-4-hydroxy-tetrahydropyran-2-one. This compound was reported by Oka et al. [15]. The ^1H and ^{13}C NMR data was assigned unambiguously by HSQC and HMBC experiments (see Tables 1 and 2). Compound **2** was also obtained from natural source for the first time.

Compound **3** colorless oil, HR-ESI-MS m/z 377.2698 $[\text{M} + \text{Na}]^+$. ^1H NMR (600 MHz, CDCl_3) δ : 5.34 (4H, m, H-9, 10, 12 and 13), 4.17 (1H, dd, $J = 11.4, 3.6$ Hz, H-1'b), 4.13 (1H, dd, $J = 11.4, 6.0$ Hz, H-1'a), 3.91 (1H, m, H-2'), 3.69 (1H, dd, $J = 11.4, 3.6$ Hz, H-3'b), 3.59 (1H, dd, $J = 11.4, 6.0$ Hz, H-3'a), 2.76 (2H, m, H-11), 2.33 (2H, t, $J = 7.8$ Hz, H-2), 2.04 (4H, m, H-8 and H-14), 1.62 (2H, m, H-3), 1.31 (14H, m, H-4 to H-7 and H-15 to H-17), 0.88 (3H, t, $J = 7.2$ Hz, H-18); ^{13}C NMR (150 MHz, CDCl_3) δ : 174.5 (C-1), 130.4 (C-10), 130.2 (C-9), 128.2 (C-13), 128.0 (C-12), 70.4 (C-2'), 65.3 (C-1'), 63.5 (C-3'), 34.3 (C-2), 31.7 (C-16), 29.7 (C-7), 29.5 (C-6), 29.3 (C-5), 29.2

TABLE 1: ^1H NMR (600 MHz) data for **1**, **2**, and monacolin L (δ in ppm, J in Hz).

No.	1 ^a	2 ^a	Monacolin L ^b
1	2.58 (m)	—	1.40 (m)
2	2.72 (m)	—	2.31 (m)
3	5.74 (dd, 9.6, 3.0)	7.27 (d, 8.4)	5.72 (m)
4	6.35 (dd, 9.6, 2.4)	7.56 (d, 8.4)	5.87 (m)
4a	—	—	—
5	6.86 (brs)	7.58 (brs)	5.39 (m)
6	—	—	2.32 (m)
7	6.93 (d, 7.8)	7.34 (dd, 9.0, 1.2)	1.46 (m), 1.53 (m)
8	6.96 (d, 7.8)	7.94 (d, 9.0)	1.20 (m), 1.81 (m)
8a	—	—	2.05 (m)
1'	—	—	—
2'	2.55 (m)	2.68 (ddd, 17.4, 3.6, 1.8)	2.44 (dd, 15.0, 8.4)
	2.66 (dd, 18.0, 5.4)	2.77 (dd, 17.4, 4.8)	2.55 (dd, 15.0, 4.8)
3'	4.28 (m)	4.40 (m)	4.20 (m)
4'	1.63 (m), 1.86 (m)	1.82 (m), 2.00 (m)	1.62 (m), 1.78 (m)
5'	4.56 (m)	4.86 (m)	3.76 (m)
6'	1.42 (m), 1.66 (m)	1.92 (m), 1.98 (m)	1.60 (m), 1.65 (m)
7'	1.58 (m), 1.76 (m)	3.16 (m), 3.37 (m)	1.30 (m), 1.73 (m)
2-Me	1.06 (d, 7.8)	2.49 (brs)	0.99 (dd, 7.2, 1.8)
6-Me	2.29 (s)	2.50 (brs)	0.90 (dd, 7.2, 3.0)

^a CDCl_3 .

^b CD_3OD .

(C-4 and C-15), 27.4 (C-8), 27.3 (C-14), 25.8 (C-11), 25.0 (C-3), 22.7 (C-17), and 14.2 (C-18). Compound **3** was characterized as 1-monolinolein by comparison with the literature [16] and was isolated from the genus for the first time.

Compound **4** colorless oil, EI-MS m/z 280 $[\text{M}]^+$. ^1H NMR (600 MHz, CD_3OD) δ : 5.37 (2H, m, H-9 and H-10), 5.31 (2H, m, H-12 and H-13), 2.78 (2H, brt, $J = 7.2$ Hz, H-11), 2.27 (2H, t, $J = 7.2$ Hz, H-2), 2.07 (4H, m, H-8 and H-14), 1.60 (2H, m, H-3), 1.35 (14H, m, H-4 to H-7, and H-15 to H-17), 0.91 (3H, t, $J = 7.2$ Hz, H-18); ^{13}C NMR (150 MHz, CD_3OD) δ : 177.9 (C-1), 131.1 (C-9 and C-10), 129.3 (C-13), 129.2 (C-12), 35.2 (C-2), 32.9 (C-16), 30.9 (C-7), 30.7 (C-6), 30.5 (C-5), 30.4 (C-4 and C-15), 28.4 (C-8 and C-14), 26.8 (C-11), 26.3 (C-3), 23.8 (C-17), and 14.6 (C-18). Compound **4** was identified as (9*Z*,12*Z*)-octadeca-9,12-dienoic acid. This compound was reported by Luo et al. [17]. The ^1H and ^{13}C NMR data was assigned by 2D NMR data. Compound **4** was also isolated from the genus for the first time.

Compound **5** yellow oil, HR-ESI-MS m/z 383.1875 $[\text{M} + \text{Na}]^+$; UV (MeOH) λ_{max} : 230.5 and 388.5 nm; IR ν_{max} cm^{-1} (KBr): 3461, 3018, 2955, 2931, 2859, 1780, 1716, 1673, 1522, 1065, 756. ^1H NMR (600 MHz, CDCl_3) δ : 6.47 (1H, dt, $J = 15.0, 6.6$ Hz, H-2), 5.88 (1H, dd, $J = 15.0, 1.2$ Hz, H-3), 5.28 (1H, d, $J = 3.6$ Hz, H-5), 5.01 (1H, dd, $J = 12.6, 1.2$ Hz, H-12b), 4.69 (1H, d, $J = 12.0$ Hz, H-12a), 4.16 (1H, dt, $J = 9.0, 3.6$ Hz, H-16), 3.00 (1H, td, $J = 12.0, 4.2$ Hz, H-8), 2.73 (1H, dd, $J = 13.2, 3.0$ Hz, H-15), 2.72 (1H, dd, $J = 18.0, 3.6$ Hz, H-7b), 2.56 (1H, dd, $J = 18.0,$

TABLE 2: ^{13}C NMR (150 MHz) data for **1**, **2**, and monacolin L.

No.	1 ^a	2 ^a	Monacolin L ^b
1	42.2	134.2	43.7
2	32.8	132.2	30.2
3	134.5	129.4	134.2
4	126.9	125.9	129.7
4a	133.4	133.0	138.4
5	127.0	127.8	131.0
6	136.2	134.2	32.8
7	127.3	128.5	35.9
8	127.6	123.4	23.8
8a	135.7	130.4	36.5
1'	171.1	170.9	174.0
2'	38.7	38.8	43.2
3'	62.7	62.8	68.2
4'	36.1	36.2	30.7
5'	76.7	75.9	71.2
6'	33.8	35.8	44.9
7'	22.6	24.2	26.0
2-Me	15.3	20.1	14.4
6-Me	21.1	21.5	21.8

^aCDCl₃.^bCD₃OD.

12.0 Hz, H-7a), 1.85 (3H, dd, $J = 6.6, 1.2$ Hz, H-1), 1.54 (2H, m, H-17), 1.54 (1H, m, H-18b), 1.40 (3H, s, H-13), 1.31 (2H, m, H-19), 1.31 (2H, m, H-20), 1.31 (1H, m, H-18a), 0.89 (3H, t, $J = 6.6$ Hz, H-21); ^{13}C NMR (150 MHz, CDCl₃) δ : 18.6 (C-1), 135.3 (C-2), 124.6 (C-3), 160.4 (C-4), 103.5 (C-5), 114.2 (C-6), 31.0 (C-7), 41.5 (C-8), 83.2 (C-9), 190.9 (C-10), 151.2 (C-11), 63.9 (C-12), 17.7 (C-13), 175.3 (C-14), 49.1 (C-15), 69.6 (C-16), 35.2 (C-17), 26.0 (C-18), 31.7 (C-19), 22.7 (C-20), and 14.1 (C-21). Those data were identical to the literature data for monascinol [18]. Thus, compound **5** was determined as monascinol.

Compound **6** Colorless solid, HR-ESI-MS m/z 152.1056 $[\text{M} + 1]^+$; UV (MeOH) λ_{max} : 275.50 nm. ^1H NMR (600 MHz, CDCl₃) δ : 9.53 (1H, brs, NH), 5.86 (1H, s, H-3), 5.12 (1H, d, $J = 9.6$ Hz, H-1'), 2.74 (1H, m, H-2'), 2.06 (3H, s, 4-Me), 1.09 (6H, d, $J = 6.6$ Hz, 2'-Me $\times$ 2); ^{13}C NMR (150 MHz, CDCl₃) δ : 173.0 (C-2), 120.8 (C-3), 148.8 (C-4), 137.8 (C-5), 120.9 (C-1'), 27.6 (C-2'), 23.0 (2'-Me $\times$ 2), and 12.0 (4-Me). Compound **6** was elucidated as pulchellalactam by comparing with the reference data [19].

Compound **7** Off-white amorphous powder, HR-ESI-MS m/z 273.0753 $[\text{M} + \text{Na}]^+$; UV (MeOH) λ_{max} : 240.5sh, 247.0, 280.5, and 330.0 nm; IR ν_{max} cm⁻¹ (KBr): 3342, 3124, 2969, 1676, 1624, 1584, 1515, 1455, 1152, 1117, 833. ^1H NMR (600 MHz, CDCl₃) δ : 11.30 (1H, s, 8-OH), 10.77 (1H, s, 6-OH), 6.46 (1H, s, H-5), 6.42 (1H, s, H-4), 3.97 (1H, m, H-2'), 2.50 (2H, m, H-1'), 2.00 (3H, s, 7-Me), 1.12 (3H, d, $J = 6.0$ Hz, H-3'); ^{13}C NMR (150 MHz, CDCl₃) δ : 166.2 (C-1), 154.4 (C-3), 101.5 (C-4), 136.3 (C-4a), 105.2 (C-5), 159.9 (C-6), 109.6 (C-7), 163.5 (C-8), 97.8 (C-8a), 42.5 (C-1'), 63.9 (C-2'), 23.3 (C-3'), and 7.9 (7-Me). The structure of compound **7** was elucidated by extensive 1D and

2D NMR spectroscopy and confirmed by comparison of its ^1H and ^{13}C NMR data with those of Lunatinin [20, 21].

3.2. HMG-CoA Reductase Inhibitory Activity. The compounds **1–7** were tested *in vitro* for their HMG-CoA reductase inhibitory activities by using the method as described in the experimental part. Lovastatin was used as the positive control. Compounds **1–2** (IC₅₀ 272 and 312 $\mu\text{g/mL}$) and **6–7** (IC₅₀ 280 and 128 $\mu\text{g/mL}$) demonstrated strong HMG-CoA reductase inhibitory activity comparable with the standard drug lovastatin (IC₅₀ 160 $\mu\text{g/mL}$). Compounds **3–5** caused moderate activity at the highest concentration (400 $\mu\text{g/mL}$). It indicates that no statin compounds in *Monascus*-fermented rice also have strong HMG-CoA reductase inhibitory activity.

4. Conclusions

In conclusion, we isolated seven compounds from *Monascus*-fermented rice and evaluated their HMG-CoA reductase inhibitory activities *in vitro*. All compounds showed good HMG-CoA reductase inhibitory activity, among them compound **7** exhibited strong inhibition with IC₅₀ value comparable with that of the standard drug lovastatin. Thus, no statin compounds in *Monascus*-fermented rice also have strong HMG-CoA reductase inhibitory activity.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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