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佛司可林类成分的光谱特征(三)

许云龙[1]*,金歧端[1],刘 剑[2]

(1.中国科学院昆明植物研究所,植物化学与西部植物资源持续利用国家重点实验室,昆明 650204;
2.云南云河药业有限公司,个旧 661000)

摘 要:二萜佛司可林 E、F、G、H,已从毛喉鞘蕊花分离得到。本文根据一维和二维的核磁共振谱详细描述了它们的光谱特征,改正了原先错误的指定。

关键词:毛喉鞘蕊花;佛司可林 E、F、G、H;光谱特征

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Spectral Characteries of Forskolins(3)

XU Yun-long[1]*, JIN Qi-duan[1], LIU Jian[2]

(1. *State Key Laboratory of Phytochemistry and Plant Resources in West China kunmung Insitute of Botant, CAS*, Kunming 650204, China; 2. *Yunnan Yunhe Pharmaceutical Co., Ltd.*, Gejiu 661000, China)

Abstract: Diterpenoids, forskolin E(**7**, 1α,7β-diacetoxy-6β-hydroxy-8,13-epoxy-labd-14-en-11-one), forskolin F(**8**, 7β-acetoxy-6β,9α-dihydroxy-8, 13-epoxy-labd-14-en-11-one), forskolin G (**9**, 1α-hydroxy-6β, 7β-diacetoxy-8, 13-epoxy-labd-14-en-11-one), forskolin H(**10**, 1α,6β-diacetoxy-8,13-epoxy-labd-14-en-11-one), were isolated from *Coleus forskohlii* (Willd.) Briq. This paper describes detailedly their spectral characteries, including 1D and 2D NMR data.

Key words: *Coleus forskohlii*; forskolinE, F, G, H; spectral characteries

Introduction

Coleus forskohlii (Willd.) Briq was known to contain abundant labdane diterpenoids, which possessed significant bioactivity. As a continuation of our study on *C. forskohlii*, has isolated twenty constituents including eight new labdane diterpenoids[1-9]. In this paper, we report detailedly spectral characteries of forkolin E(**7**), F(**8**), G(**9**) and H(**10**) (including ^{1}H, ROESY, DEPT, ^{1}H-^{1}H COSY, HMQC and HMBC data).

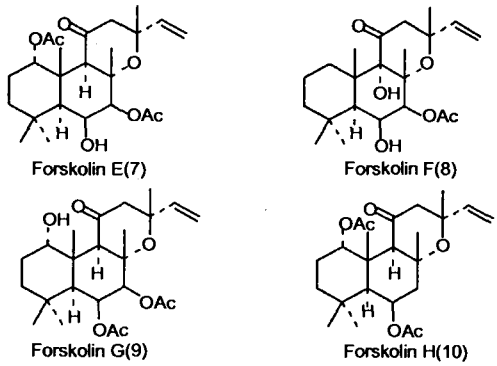

Fig.1 Forskolin E, F, G and H

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* Corresponding author E-mail: xuyl@mail.kib.ac.cn

Results and Discussion

Compound **7** was obtained as colorless needles(MeOH). EI-MS *m/z* 436[M]$^+$, together with ^{13}C and DEPT NMR spectra indicated the molecular formula as $C_{24}H_{36}O_7$. DEPT spectra showed five tertiary methyl groups, four methylene groups, six methine groups, four quaternary carbons, two olefinic carbons, one ketonic carbon and two acetoxy signals. Comparison of the data of **7** with forskolin B[3] suggested that **7** had a typical 8,13-epoxy-labd-14-en-11-one skeleton[1-3]. In its ^{1}H NMR spectrum, the five methyl signals at δ_H 0.94, 0.98, 1.24, 1.66 and 1.78, and the signals of AB coupling system at δ_H 2.83(1H, d, J = 18.2 Hz) and 2.76(1H, d, J = 18.2 Hz), and three olefinic proton signals at δ_H 5.99, 4.99 and 5.40 also confirmed the above assumption. The HMBC spectrum showed cross-peaks of δ_H 4.77(1H, t, 2.6, 1β-H) with δ_C 36.89(C-3), 46.38(C-5), 42.61(C-10), and 170.44(OAc), δ_H 2.04(3H, s, 1-OAc) with δ_C 70.32(C-1); δ_H 6.14(1H, dd, J = 2.2, 4.0 Hz, 6α-H) with δ_C 46.38(C-5), 79.60(C-7), 78.79(C-8), and 42.61(C-10), δ_H 5.59(1H, d, J = 4.0 Hz, 7α-H) with δ_C 46.38(C-5), 70.32(C-6), 78.79(C-8), 58.36(C-9), and 170.44(OAc), δ_H 2.11(3H, s, 7-OAc) with δ_C 79.60(C-7); which revealed the locations of 1-OAc, 6-OH and 7-OAc. The above inferences were also supported by the HMQC

and ^{1}H-^{1}H COSY. Additionally, the relative configurations of 1-OAc, 6-OH and 7-OAc were determined respectively as α, β and β orientation due to ROESY correlations of 1-H with 2β-H and 20β-Me, 6-H with 5α-H and 18α-Me; 7-H with 5α-H, 6α-H and 9α-H respectively. Thus, **7** was determined as 1α, 7β-diacetoxy-6β-hydroxy-8, 13-epoxy-labd-14-en-11-one, named 9-dehydroxyforskolin B[3], or forskolin E.

Compound **8**, colorless prisms(MeOH), was assigned $C_{22}H_{34}O_6$ by EI-MS: *m/z* 394 $[M]^+$, ^{1}H and ^{13}C spectra. The NMR data of **8** were very similar to those of **7**. Further comparison of ^{13}C NMR of **8** with that of **7** showed that **8** also possessed the same typical 8, 13-epoxy-labd-14-en-11-one skeleton[1-3]. Moreover, the correlations of HMBC between δ_H 6.15(1H, dd, *J* = 2.2, 4.0 Hz, 6α-H) with δ_C 46.24(C-5), 80.13(C-7), 78.48(C-8), 42.52(C-10); δ_H 5.57(1H, d, *J* = 4.0 Hz, 7α-H) with δ_C 70.78 δ_C-6), 78.48(C-8) and 169.49(OAc), δ_H 2.12(3H, s, 7-OAc) with δ_C 80.13(C-7); indicated the presence of 6-OH, 7-OAc, and 9-OH substitution and located at 6β, 7β, and 9α position respectively in compound **8**, which were confirmed by the ROESY correlations of 6-H with 5α-H and 18α-Me; 7-H with 5α-H, 6α-H and 9α-OH respectively. Therefore, **8** was deduced as 7β-acetoxy-6β, 9α-dihydroxy-8, 13-epoxy-labd-14-en-11-one, named 1-deacetoxy-forskolin B[3], or forskolin F.

Compound **9**, $C_{24}H_{36}O_7$, was obtained as colorless needles. Its IR, MS, ^{1}H and ^{13}C NMR were very similar to those of **7**, suggesting that **9** had a typical 8, 13-epoxy-labd-14-ene-11-one skeleton[1-3]. In addition, the HMBC showed the cross peaks between δ_H 5.75(1H, dd, *J* = 4.0, 2.2 Hz, 6α-H) to δ_C 33.86(C-4), 41.89(C-10), 46.22(C-5), 77.98(C-8), 78.66(C-7) and 170.11(OAc), δ_H 5.10(1H, d, *J* = 4.0 Hz, 7α-H) to δ_C 23.92(C-17), 57.85(C-9), 69.92(C-6), 77.98(C-8) and 169.84(OAc), and δ_H 4.38(1H, brs, 1α-H) to δ_C 36.30(C-3) and 46.22(C-5), indicating that **9** has 6β-OAc, 7β-OAc and 1α-OH. Its HMBC, HMQC and ^{1}H-^{1}H COSY also supported the above deduces. Therefore, **9** was elucidated as 1α-hydroxy-6β, 7β-diacetoxy-8, 13-epoxy-labd-14-en-11-one, and named 1-deacetyl-9-dehydroxyforskolin A[3], 1-deacetyl-6-acetyl forskolin E, or Forskolin G.

Compound **10**, $C_{24}H_{36}O_6$, Comparing the ^{13}C NMR data of **10** with those of **9** showed that they possessed the same 8, 13-epoxylabd-14-ene-11-one skeleton[1-3]. In addition, the HMBC showed the correlation between δ_C 69.47(C-6) to δ_H 2.24(1H, dd, *J* = 14.6, 2.6 Hz, 7-Ha), 2.03(3H, s, OAc) and 1.45(1H, d, *J* = 2.1 Hz, 5(-H), δ_C 75.07(C-1) to δ_H 3.21(1H, brs, 9α-H), 1.94(3H, s, OAc), 1.45(1H, d, *J* = 2.1 Hz, 5α-H) and 1.40(3H, s, 20-Me), and signals of δ_H 5.55(1H, t, *J* = 2.6 Hz, 6α-H) and 5.51 (1H, brs, 1β-H) in ^{1}H NMR, indicating that **10** has 1(-OAc and 6β-OAc. Its HMBC, HMQC and ^{1}H-^{1}H COSY also supported the above deduces. Accordingly, **10** was identified as 1α, 6β-diacetoxy-8, 13-epoxy-labd-14-en-11-one, and named as 7-deacetoxy-9-dehydroxyforskolin A[3], or Forskolin H.

Table 1 ^{13}C NMR data of **7** and **8**(in C_5D_5N), **9** and **10**(in $CDCl_3$)

Carbon	7	8	9	10
1	70.32 d	36.42 t	71.01 d	75.07 d
2	26.02 t	18.51 t	25.50 t	21.72 t
3	36.89 t	36.23 t	36.30 t	36.90 t
4	34.16 s	35.42 s	33.86 s	33.73 s
5	46.38 d	46.24 d	46.22 d	49.06 d
6	70.32 d	70.78 d	69.92 d	69.47 d
7	79.60 d	80.13 d	78.66 d	46.21 t
8	78.79 s	78.48 s	77.98 s	75.72 s
9	58.36 d	80.24 s	57.85 d	58.22 d
10	42.61 s	42.52 s	41.89 s	40.46 s
11	206.32 s	207.09 s	207.00 s	206.19 s
12	50.24 t	50.13 t	49.73 t	49.06 t
13	75.50 s	76.08 s	74.84 s	74.55 s
14	146.52 d	147.02 d	145.78 d	146.71 d
15	112.86 t	111.83 t	112.72 t	112.33 t
16	31.65 q	31.43 q	31.48 q	31.68 q
17	24.25 q	25.08 q	23.92 q	29.47 q
18	32.85 q	33.03 q	32.63 q	32.86 q
19	23.33 q	23.51 q	22.81 q	22.88 q
20	18.09 q	18.51 q	17.76 q	17.37 q
OAc	170.44 s	169.49 s	170.11 s	169.81 s
	21.23 q	21.50 q	21.28 q	21.72 q
OAc	170.44 s	–	169.84 s	169.50 s
	20.95 q	–	20.83 q	21.68 q

Table 2 ^{1}H NMR data of **7** and **8**(in C_5D_5N), **9** and **10**(in $CDCl_3$)

H	7	8	9	10
1β-H	4.77 t,2.6	1.75 m	4.38 brs	5.51 brs
1α-H	–	1.68 m	–	–
2β-H	2.13 m	2.13 m	2.11 m	2.17 m
2α-H	1.66 m	1.67 m	1.41 m	1.70 m
3α-H	2.01 m	2.04 m	1.73 m	1.38 m
3β-H	1.05 m	1.05 m	1.08 m	1.07 m
5α-H	2.07 d,2.2	2.07 d,2.2	1.63 d,2.2	1.45 d,2.1
6α-H	6.14 dd, 4.0,2.2	6.15 dd, 4.0,2.2	5.75 dd, 4.0,2.2	5.55 t, 2.6
7α-H	5.59 d,4.0	5.57 d,4.0	5.10 d,4.0	2.24 dd, 14.6,2.6
7β-H	–	–	–	1.88 dd, 14.6,2.6
9α-H	4.17 brs	–	3.60 brs	3.21 brs
12α-H	2.83 d,18.2	2.85 d,18.2	2.71 d,18.2	2.64 d,18.6
12β-H	2.76 d,18.2	2.77 d,18.2	2.58 d,18.2	2.58 d,18.6

14-H	5.99dd, 17.4,10.8	5.97dd, 17.4,10.8	5.97dd, 17.4,10.7	5.90dd, 17.3,10.7
15-Hc	4.99 d,10.8	4.97 d,10.8	5.05 d,10.7	5.02 d,10.7
15-Ht	5.40 d,17.4	5.41 d,17.4	5.21 d,17.4	5.17 d,17.3
16-Me	1.24 s	1.35 s	1.24 s	1.24 s
17-Me	1.78 s	1.64 s	1.51 s	1.44 s
18-Me	0.98 s	1.02 s	0.98 s	0.95 s
19-Me	0.94	0.97 s	0.93 s	0.97 s
20-Me	1.66 s	1.55 s	1.40 s	1.40 s
OAc	2.11 s	2.12 s	2.08 s	2.03 s
OAc	2.04 s	–	2.07 s	1.94 s

Experimental Section

General experimental procedures

Melting points were measured on an XRC-1 micromelting apparatus and were uncorrected. IR were obtained on a Bio-Rad FTS-135 infrared spectrometer with KBr pellets. The MS spectra were performed on a VG Autospec-3000 spectrometer with 70 eV. ^{1}H NMR, ^{13}C NMR and 2D NMR were recorded on a Bruker AM-400 and DRX-500 spectrometer with TMS as internal standard. The silica gel for TLC and column chromatography was obtained from Qingdao Marine Chemical Inc., China.

Plant material

The roots of *Coleus forskohlii* (Willd.) Briq. were collected in Yunnan Province, China, in September 2001, which were identified by Professor H. W. Li, botanist of Kunming Institute of Botany. The voucher specimen has been deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and isolation

10 kg dried ground roots of *Coleus forskohlii* were extracted with 50 L × 3 of 95% ethanol for 15 days at room temperature. The extract was decoloured with 400 g × 3 active charcoal and the solvent was removed in vacuum. The residues(525 g)were dissolved in H_2O. The aqueous solution was partitioned with petroleum ether, chloroform and n-butanol. The chloroform extract was evaporated to afford 120 g of residues. The residues were subjected to CC silica gel, eluted with petroleum ether-acetone (from petroleum ether to petroleum ether-acetone 1: 1) and $CHCl_3$-acetone. The fractions were combined by monitoring with TLC to obtain fractions B 1-B 22. Then the fractions B **7** ~ **10** were chromatographied repeatedly on silica gel and recrystallized from MeOH to afford compound **7** ~ **10**.

Forskolin E(7) $C_{24}H_{36}O_7$, M 436, colorless needles (MeOH), mp. 156 ~ 158 ℃; $[\alpha]_D^{26}$-26.25 (*c* 0.42, MeOH), $IR\upsilon_{max}^{KBr}$: 3509, 3004, 1738, 1723, 1707, 1448, 1395, 1371, 1260, 1204, 1175, 1101, 1070, 1052, 1021, 975, 951, 927 cm^{-1}; ^{13}C NMR data see Table 1; ^{1}H NMR data see Table 2; EI-MS: (70 eV, rel %) *m/z*: 436(16, M^+), 421(75, M^+-CH_3), 403(39, M^+-H_2O-CH_3), 376(5, M^+-HOAc), 361(37, 376-CH_3), 343(35, 361-H_2O), 325(77, 361-2H_2O), 316(10, M^+-2HOAc), 301(41, 316-CH_3), 283(36), 273(27), 246(30), 231(54), 203(68), 189(39), 175(50), 153(94), 139(60), 123(59), 109(68), 99(79), 81(78), 69(88), 55(100).

Forskolin F(8) $C_{22}H_{34}O_6$, M 394, colorless prisms (MeOH), mp. 165 ~ 167 ℃; $[\alpha]_D^{26}$-35.27 (*c* 0.45, MeOH), $IR\upsilon_{max}^{KBr}$: 3500, 1732, 1705, 1640, 1370, 1256, 1170, 1021, 950 cm^{-1}; ^{13}C NMR data see Table 1; ^{1}H NMR data see Table 2; EIMS(70 eV, rel %) *m/z*: 394(10, M^+), 376(35, M^+-H_2O), 361(17, M^+-H_2O-CH_3), 358(37, M^+-2H_2O), 348(40), 343(13, M^+-2H_2O-CH_3), 334(7, M^+-HOAc), 316(10, M^+-HOAc-H_2O), 301(11, M^+-HOAc-H_2O-CH_3), 123(39), 109(48), 99(39), 81(58), 69(48), 55(100).

Forskolin G(9) $C_{24}H_{36}O_7$, M 436, colorless needles (MeOH), mp. 241 ~ 243 ℃; $IR\upsilon_{max}^{KBr}$: 3510, 2865, 1732, 1448, 1371, 1315, 1261, 1173, 1100, 974, 950, 926, 802, 785, 752, 723 cm^{-1}; ^{13}C NMR data see Table 1; ^{1}H NMR data see Table 2; EI-MS: (70 eV, rel%) *m/z*: 436(26, M^+), 421(90, M^+-CH_3), 403(20, M^+-H_2O-CH_3), 379(4), 376(4, M^+-HOAc), 361(19, M^+-HOAc-CH_3), 343(16, M^+-HOAc-H_2O-CH_3), 325(77), 316(6, M^+-2HOAc), 301(21, M^+-2HOAc-CH_3), 283(16, M^+-2HOAc-H_2O-CH_3), 246(17), 231(29), 203(41), 153(100), 139(37), 123(34), 109(46), 99(100), 81(85), 69(73), 55(88).

Forskolin H(10) $C_{24}H_{36}O_6$, M 420, colorless prisms (MeOH), mp. 231 ~ 234 ℃; $IR\upsilon_{max}^{KBr}$: 3445, 2948, 2867, 1733, 1450, 1393, 1364, 1322, 1238, 1210, 1143, 1106, 1066, 1036, 948, 914, 877, 829 cm^{-1}; ^{13}C NMR data see Table 1; ^{1}H NMR data see Table 2; EI-MS(70 eV, rel %) *m/z*: 420(7, M^+), 405(13, M^+-CH_3), 377(43, M^+-CH_3CO), 360(100, M^+-HOAc), 345(9, M^+-HOAc-CH_3), 310(28), 300(51, M^+-2HOAc), 285(72, M^+-2HOAc-CH^3), 267(12), 247(70), 232(32), 215(77), 190(48), 173(45), 163(26), 147(22), 135(19), 119(25), 109(32), 95(35), 81(33), 69(38), 55(49).

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且中、小剂量组效果优于大剂量组。

山楂和苹果中富含维生素 c(Vc),具有明显的抗氧化作用。是果醋抗脂质过氧化的有效成分之一。葛根中主要有效成分葛根素对实验性脑出血大鼠脑的脂质过氧化有一定改善作用,可以降低 MDA 含量和提高 SOD 活性[6]。红花的水提物及醇提物对超氧阴离子和 DPPH 自由基有良好的清除作用[7],红花注射液还可降低冠心病患者血清 MDA 含量并提高 SOD 活性[8]。因此,果醋降低高脂血症小鼠血清 TC 和 LDL-C 含量,降低肝脏 MDA 含量和提高 SOD 活性的作用是果醋中众多成分综合作用的结果。高脂血症时血清 TC 或(和)TG 含量升高,低密度脂蛋白胆固醇(LDL-C)被自由基等氧化成氧化型沉积于血管壁,形成动脉粥样硬化斑块。高密度脂蛋白胆固醇(HDL-C)则有利于血脂自血液的清除,HDL-C 与 LDL-C 保持一定比例是机体脂代谢正常的基础。肝脏是脂蛋白和胆固醇合成和代谢的场所,脂肪肝及肝脏的脂质过氧化会影响脂蛋白和胆固醇的合成和代谢,加剧体内脂代谢紊乱,形成高脂血症及动脉粥样硬化。果醋能够降低血清 TC、LDL-C 含量,降低肝脏 MDA 含量,升高 SOD 活性,对高脂血症、肝脏脂质过氧化有一定的预防和治疗作用。

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