Supporting Information

Correction to Rutaecarpine analogues reduce lipid accumulation in adipocytes via inhibiting adipogenesis/lipogenesis with AMPK activation and UPR suppression

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The procedure of reduction of R17

To a solution of R17 (50 mg, 0.13 mmol) in 8 mL absolute ethanol, was added NaBH₄ (24.6 mg, 0.65 mmol) in 0°C. The reaction was achieved after two hours, 10 mL 0.1 N HCl water solution was added to quench the reaction. 20 mL×2 CH₂Cl₂ was added to extract the product, the organic phase was combined, dried with MgSO₄, and then concentrated to crude product. It was purified by silica gel column with CH₂Cl₂ to MeOH in 20:1, and gave 38 mg pale yellow product, yield to 76%.

Pharmacokinetics Analysis. Pharmacokinetic properties of **R17** were analyzed by Medicilon Company, Shanghai, China. Six male SD rats with body weight of 230–260 g were purchased from Shanghai SIPPR-BK LAB Animal Ltd., Shanghai, China, and used for the pharmacokinetic analysis of **R17**. Compound **R17** were formulated in methanol for the po and iv administrations. A final dosage of 5 mg/kg mouse/rat of the formulated compounds was administrated, and the blood samples were taken at various time points in 24 h. The concentration of the compounds in blood was analyzed by LC–MS/MS (Shimadzu liquid chromatographic system and API4000 mass spectrometer, Applied Biosystems, Ontario, Canada).

Table S1. Full ^1H and ^{13}C NMR spectral assignments for **R17** and reference data for reported natural product bouchardatine^{1,2}.

Position	R17 (in CDCl_3)		Bouchardatine (in pyridine- d_5) ^a	
	^1H	^{13}C	^1H	^{13}C
1	7.74 (1H, d, 8.0)	128.0	7.65 (dd, 8.1, 0.7)	128.3
2	7.63 (1H, t, 8.0)	132.4	7.71 (ddd, 8.2, 7.1, 1.6)	135.1
3	7.37 (1H, t, 8.0)	126.1	7.47 (overlap)	127.7
4	7.55 (1H, d, 8.0)	121.2	8.57 (dd, 7, 9, 1.5)	127.3
4a		114.5		123.4
5		159.5		162.3
6				
8	11.44 (1H, s)	191.2	10.69 (s)	187.5
8a		117.5		117.0
8b		126.8		129.9
9	8.50 (1H, d, 8.2)	123.1	8.38 (brd, 7.3)	120.3
10	7.25 (1H, t, 8.2)	122.8	7.47 (overlap)	124.2
11	7.27 (1H, t, 8.2)	124.9	7.50 (ddd, 8.4, 7.2, 1.3)	126.4
12	7.34 (1H, d, 8.2,)	111.3	7.80 (brd, 7.3)	113.9
12a		135.1		137.3
13	10.62 (1H, brs)		14.60 (brs)	
13a		143.2		137.0
13b		154.7		^b
14				
14a		149.3		149.6
1'	8.94 (1H, brs)			^b
2'	3.69 (2H, t, 4.3)	42.7		^b
3'	1.85 – 1.79 (2H, m)	24.0		^b
4'	2.56 (2H, t, 4.3)	59.5		^b
5'				
6'	2.35 (3H, s)	45.3		^b
7'	2.35 (3H, s)	45.3		^b

^a Some data from literature [1].

^b No data given in literature.

Table S2. Pharmacokinetic parameters in plasma after a single administration of R17 citrate in SD mice

Index	AUC _(0-t)	AUC _(0-∞)	MRT _(0-∞)	t _{1/2z}	V _z	V _{ss}	CL _z	C ₀
	µg/L*hr	µg/L*hr	Hr	hr	L/kg	L/kg	L/hr/kg	µg/L
<u>IV (5 mg/kg)</u>								
101	631.42	664.05	3.58	2.84	30.87	26.99	7.53	430.50
102	655.72	681.42	3.23	2.85	30.17	23.69	7.34	437.14
103	616.82	666.98	3.86	3.73	40.30	28.93	7.50	556.90
AV	634.65	670.82	3.56	3.14	33.78	26.53	7.45	474.84
SD	19.65	9.30	0.32	0.51	5.66	2.65	0.10	71.14
	AUC _(0-t)	AUC _(0-∞)	MRT _(0-∞)	t _{1/2z}	T _{max}	C _{max}	F	
	µg/L*hr	µg/L*hr	Hr	hr	Hr	µg/L	%	
<u>PO (5 mg/kg)</u>								
201	151.02	169.07	6.52	2.97	4.00	17.97	25.20	
202	387.01	484.69	15.44	9.50	6.00	27.38	72.25	
203	202.57	228.01	6.91	2.96	4.00	25.90	33.99	
AV	246.86	293.93	9.62	5.14	4.67	23.75	43.82	
SD	124.07	167.81	5.04	3.77	1.15	5.06	25.02

Figure S1. The correct structure of **R17** and the known structures of natural products rutaecarpine and bouchardatine.

Figure S2. Key correlations of H-H COSY and HMBC of **R17**

Figure S3. ^1H (600 MHz, in CDCl_3), ^{13}C NMR, and LC-MS spectrum of **R17**

Figure S4. ^1H NMR (400 MHz, in $\text{DMSO}-d_6$) and LC-MS spectrum of **R17-r**

H-H COSY

HSQC

Figure S5 H-H COSY, HSQC, and HMBC spectrum of **R17** (600 MHz, in CDCl_3)

Figure S6. Does-Time curve in plasma after a single administration of **R17** citrate treated in SD mice

Figure S7. Individual time curve in plasma after a single administration of **R17** citrate in SD mice

Reference

- [1] Wattanapiromsakul, C., Forster, P. I., Waterman, P. G. (2003) Alkaloids and limonoids from *Bouchardatia neurococca*: systematic significance, *Phytochemistry*, *64*, 609–615.
- [2] Naik, N. H., Urmode, T.D., Sikder, A. K., Kusurkar, R. S. (2013) Total Synthesis of Bouchardatine, *Aust. J. Chem.* *66*, 1112.