

Rutaecarpine Analogues Reduce Lipid Accumulation in Adipocytes via Inhibiting Adipogenesis/Lipogenesis with AMPK Activation and UPR Suppression

Ying-Chun Chen, Xiao-Yi Zeng, Yan He, Hong Liu, Bin Wang, Han Zhou, Jian-Wen Chen, Pei-Qing Liu, Lian-Quan Gu, Ji-Ming Ye,* and Zhi-Shu Huang*

ACS Chem. Biol. 2013, 8, 2301–2311. DOI: 10.1021/cb4003893

S Supporting Information

This correction is issued with respect to the chemical structures of **R17** and **R18** in our original article. Specifically, on page 2301 in the abstract and table of contents graphics and page 2302 in Figure 1, the chemical structures of **R17** and **R18** are incorrect. The correct abstract and table of contents graphics and Figure 1 should read as follows.

The published structures and the corrected ones are isomers, which present similar spectra data. We failed to

interpret some of ^1H NMR data when determining their structures before. However, the correct structures for **R17** and **R18** were recently confirmed (Figure 1, Figures S1 and S2) by analyzing the differences between the NMR and mass spectrum data of **R17** (Figure S3) and that of the reducing form of **R17** (**R17-r**, Figure S4) and the 2D NMR (H–H COSY, HSQC, and HMBC, see Figure S5) experimental data of **R17**.

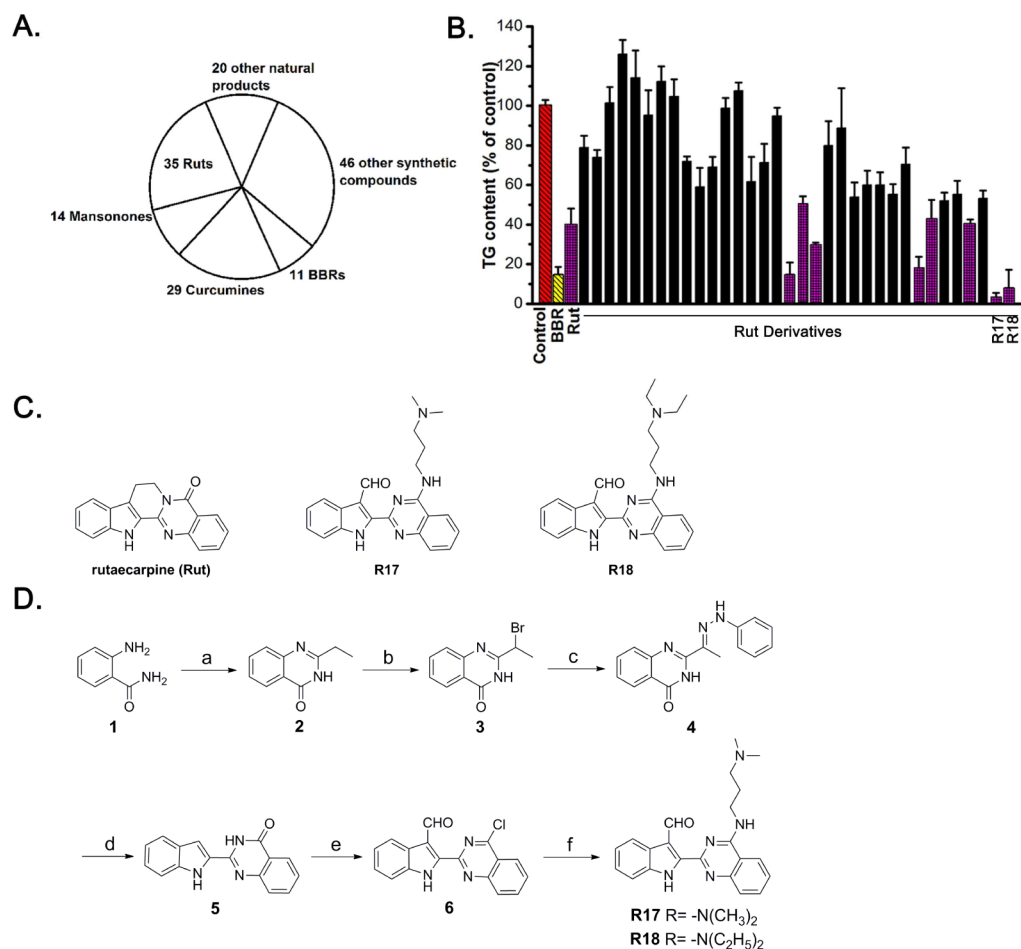


Figure 1.

Published: April 23, 2015

First, the ^1H and ^{13}C NMR spectra show the existence of an aldehyde group (a proton signal at δ 11.44 and a carbon signal at δ 191.2). After reducing, the molecular weight of **R17-r** is increased by 2 relative to **R17** (Figure S4), and the disappearance of the ^1H NMR signal at δ 11.44 (1H, CHO) and the generation of signal at δ 5.14 (2H, CH_2OH) showed the reduction of the aldehyde group. Analysis of the HMBC correlations associated with the indole moiety (Table S1 and Figure S5) indicated an indole type substructure with the aldehyde substituted at C-3 of the indole.

Second, analysis of the H–H COSY experiment (Figure S5) indicated the correlation between the amino proton resonating at δ 8.94 (H-1') and the signal of two protons at δ 3.67 (H-2'). The HMBC experiment showed the correlations between the amino proton at δ 8.94 (H-1') and ^{13}C resonances at δ 24.0 (C-3') and δ 159.6 (C-5), the proton signal at δ 3.69 (H-2') and carbon signal at δ 159.6 (C-5), and the proton signal at δ 7.55 (H-4) and carbon signal at δ 159.6 (C-5), confirming the existence of an alkyl amino side chain at C-5 of the quinazoline ring.

In addition, comparing the NMR data of **R17** with known natural product bouchardatine¹ (Table S1) showed that both compounds had the same structure of the β -indoloquinazoline moiety, also supporting our determination again. For the same reasons, the chemical structure of **R18** is revised.

To address the specificity of **R17** and its stability in plasma, we have performed an additional study to examine the metabolism of compound **R17** in SD mice. As shown in Table S2, the pharmacokinetic parameters including AUC, MRT, $t_{1/2}$, and CL_z demonstrate very good bioavailability (~44%) and stability *in vivo* even after 24 h of single administration of **R17** citrate (IV/PO). Furthermore, the results in Figure S6 and Figure S7 also demonstrate that compound **R17** exerts beneficial absorbance and metabolic features in SD mice after a single administration of **R17** citrate via PO and IV.

This correction does not change any other aspects in the interpretation of data, analysis, or the article's conclusions. The authors apologize for this unintended error.

■ ASSOCIATED CONTENT

● Supporting Information

The procedure of reduction of **R17**; pharmacokinetics analysis; full ^1H and ^{13}C NMR spectral assignments for **R17**; pharmacokinetic parameters in plasma after a single administration of **R17** citrate in SD mice; correct structure of **R17**; key correlations of H–H COSY and HMBC of **R17**; ^1H (600 MHz, in CDCl_3), ^{13}C NMR, and LC-MS spectrum of **R17**; ^1H NMR (400 MHz, in $\text{DMSO}-d_6$) and LC-MS spectrum of **R17-r**; H–H COSY, HSQC, and HMBC spectrum of **R17**; dose–time curve in plasma after a single administration of **R17** citrate treated in SD mice; and individual time curve in plasma after a single administration of **R17** citrate in SD mice. This material is available free of charge via the Internet.

■ REFERENCES

- (1) Wattanapiromsakul, C., Forster, P. I., and Waterman, P. G. (2003) Alkaloids and limonoids from *Bouchardatia neurococca*: systematic significance. *Phytochemistry* 64, 609–615.