

**The Hypoglycemic Effect of Berberine and Berberrubine Involves Modulation of
Intestinal FXR Signaling Pathway and Inhibition of Hepatic Gluconeogenesis**

Runbin Sun¹, Bo Kong², Na Yang⁴, Bei Cao⁴, Dong Feng¹, Xiaoyi Yu¹, Chun Ge¹, Siqi Feng¹,
Fei Fei⁴, Jingqiu Huang¹, Zhenyao Lu¹, Yuan Xie¹, Chung S. Yang³, Grace L. Guo², Guangji
Wang^{1,*} and Jiye Aa^{1,*}

¹Jiangsu Province Key Laboratory of Drug Metabolism and Pharmacokinetics, State Key
Laboratory of Natural Medicines, China Pharmaceutical University, Nanjing, China, 210009

²Department of Pharmacology and Toxicology, Ernest Mario School of Pharmacy, Rutgers,
The State University of New Jersey, Piscataway, New Jersey, United States of America,
08854

³Department of Chemical Biology, Ernest Mario School of Pharmacy, Rutgers, The State
University of New Jersey, Piscataway, New Jersey, United States of America, 08854

⁴Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School,
Nanjing, China, 210008

Animal treatment

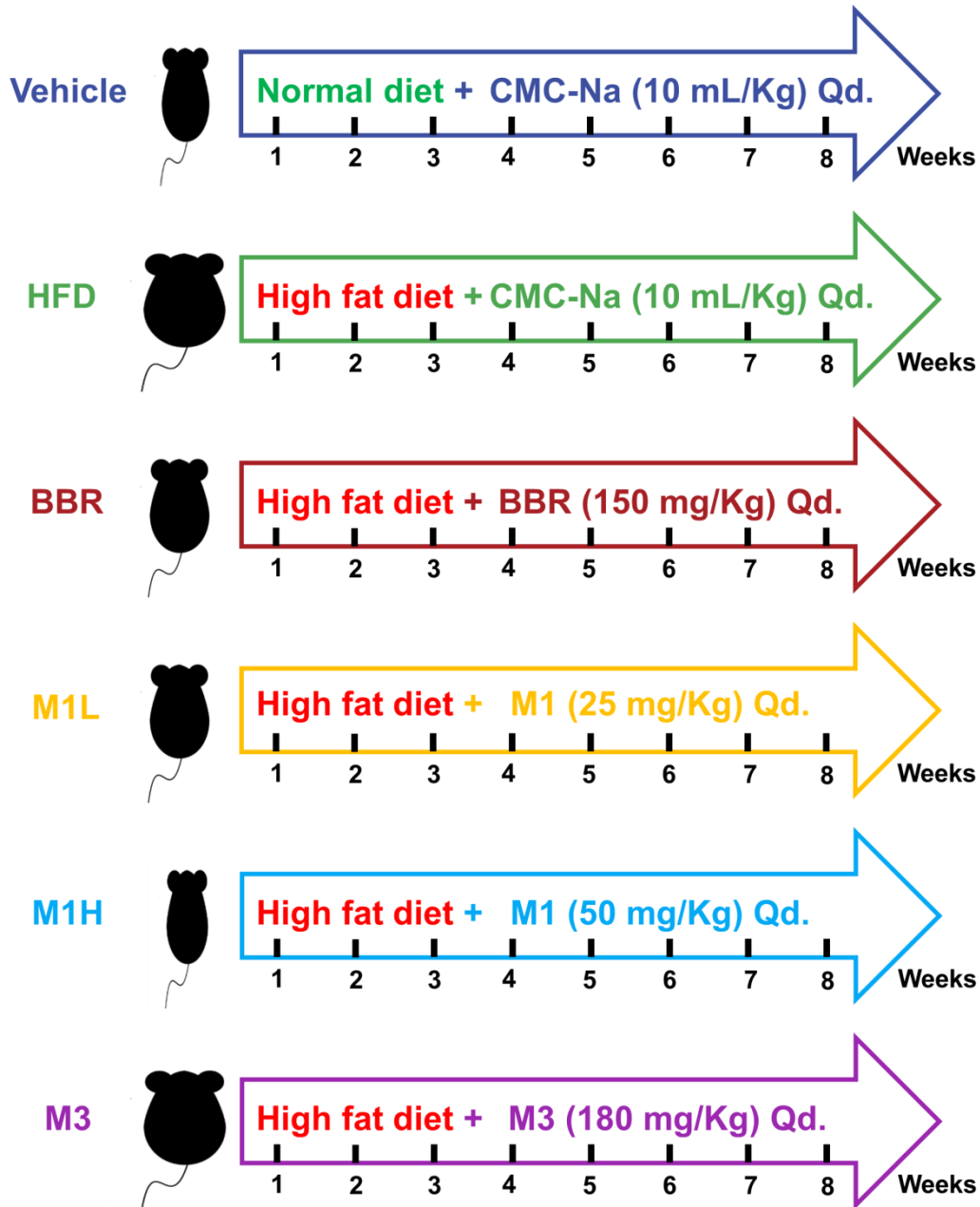


Figure S1. An overview of the schedule of animal experiments.

C57BL/6J mice were treated with BBR (150 mg/kg, i.g.), M1 (M1-25 group, gavaged with 25 mg/Kg of M1), M1 (M1-50 group, gavaged with 50 mg/Kg of M1) and M3 (M3-180 group, gavaged with 180 mg/Kg of M3) for 8 weeks.

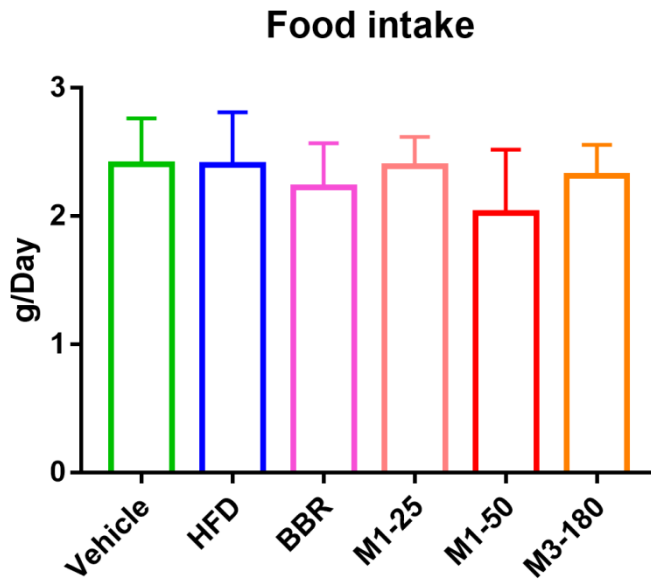


Figure S2. The food intake of each group.

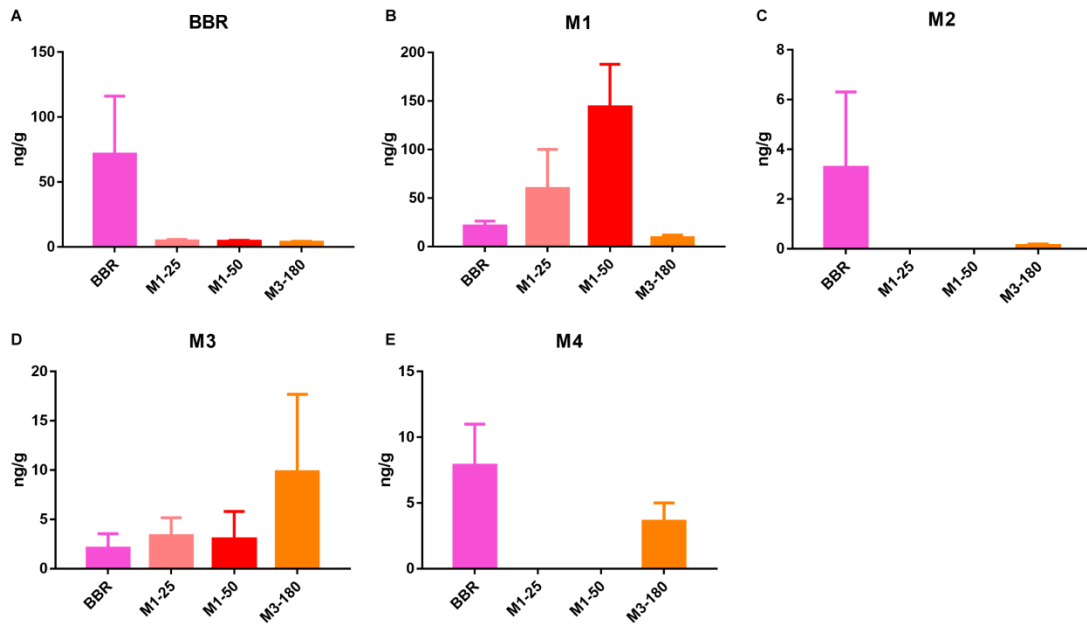


Figure S3. The concentrations of BBR and its metabolites in the liver of mice treated with BBR, M1 and M3.