Salidroside inhibits insulin resistance and hepatic steatosis by downregulating miR-21 and subsequent activation of AMPK and upregulation of PPARa in the liver and muscles of high fat diet-fed rats

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This study evaluated if salidroside (SAL) alleviates high-fat diet (HFD)-induced non-alcoholic fatty liver disease (NAFLD) by downregulating miR-21. Rats (n¼8/group) were treated for 12 weeks as normal diet (control/ND), NDagmoir negative control (NC) (150 mg/kg), NDSAL (300mg/kg), HFD, HFDSAL, HFDcompound C (an AMPK inhibitor) (200 ng/kg), HFDSALNXT629 (a PPAR-a antagonist) (30mg/kg), and HFDSALmiR-21 agomir (150 mg/kg). SAL improved glucose and insulin tolerance and preserved livers in HFD-fed rats. In ND and HFD-fed rats, SAL reduced levels of serum and hepatic lipids and the hepatic expression of SREBP1, SREBP2, fatty acid (FA) synthase, and HMGCOAR. It also activated hepatic Nrf2 and increased hepatic/muscular activity of AMPK and levels of PPARa. All effects afforded by SAL were prevented by CC, NXT629, and miR-21 agmoir. In conclusion, activation of AMPK and upregulation of PPARa mediate the anti-steatotic effect of SAL.