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# Reversal of Antidepressant-Like Effects and Cognitive Enhancement of Liuwei Dihuang Decotion by Antagonist of G protein-coupled receptor 30 via CREB-BDNF Signaling Pathway in the Hippocampus

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#### Research

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## Abstract

Backgrounds: Memory impairment is an important factor affecting the prognosis of depression, with unclear mechanism and lack of effective drugs. Our previous study has showed that Liuwei Dihuang decoction (LW) could alleviates depression and memory through upregulation of G protein-coupled receptor 30 (GPR30) - cAMP response element-binding protein (CREB) - brain-derived neurotrophic factor (BDNF). However, further confirmation is needed. In this study, we investigate whether G15, a GPR30 specific antagonist could reverse the effects of LW on depressive mood and spatial memory.

Methods: Chronic unpredictable mild stress (CUMS) rat model was used, divided into normal group, model group, LW(7.81 g/kg/d) group, LW(7.81 g/kg) + 10ug/d G15 group and LW + 40ug/d G15 group. The open field test (OFT) and sucrose preference test (SPT) were used to measure depression in rats, and the morris water maze (MWM) was used to test the learning memory of rats. The serum estrogen level was analysed by Elisa method. The GPR30, CREB and BDNF level of hippocampus were measured by quantitative real-time polymerase chain reaction and western blot analysis.

Results: LW (7.81 g/kg/d) remarkably increased the intake of sugar water, lengthen ed the total distance and rearing times of OFT, shortened mean latency and times crossing the platform and time-spending during the platform quadrant of MWM in CUMS rats. LW also significantly increased serum level of estrogen and upgregulated the mRNA and protein level of GPR30, BDNF and protein level of CREB, while G15 reversed protective effect of LW on all of them.

Conclusion: LW (7.81 g/kg/d) ameliorates depressive behavior and memory deficits associated with CMS-induced in rats. The mechanism may be mediated by hippocampal GPR30 – CREB - BDNF signaling pathway.

## Full Text

This preprint is available for download as a PDF.

## **Figures**



Comparison of body weight in different periods for different groups.



Sucrose preference before and after CUMS procedure.



Open-fieldtests.(A) The total distanced uring the 5 min sessions (B) Number of rearings during the 5 min sessions. (C) Route mappre-administration. (D)Route map after administration.



Morris water maze.(A) times during platform quadrant during the fourth training days. (B) times across platform during the fourth training days. (C, D)Travelled orbit in the place navigation test and spatial probe test (before and after training). (E) The change of latent period of seeking platform after training for 4 days.



Serum estrogen levels.



Hippocampal mRNA expression levels of GPR30, CREB and BDNF.



Hippocampal protein expression levels of GPR30, CREB and BDNF.