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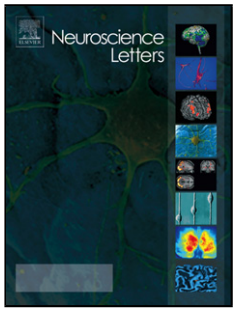

Title: Geniposide improves repeated restraint stress-induced depression-like behavior in mice by ameliorating neuronal apoptosis via regulating GLP-1R/AKT signaling pathway

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ACCEPTED MANUSCRIPT

Geniposide improves repeated restraint stress-induced depression-like behavior in mice by ameliorating neuronal apoptosis via regulating GLP-1R/AKT signaling pathway

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Highlights

- •Geniposide improves depression-like behaviors induced by RRS.
- •Geniposide suppresses hippocampal apoptosis and inflammatory responses by upregulating GLP-1R/AKT signaling pathway.
- •Exendin(9-39) blocked the effects of geniposide.

Abstract

Geniposide (GP), a bioactive iridoid glycoside isolated from *Gardenia jasminoides* Ellis, as well as an agonist of Glucagon-like peptide-1 receptor (GLP-1R), has been reported to exhibit antidepressant-like effects in several rodent models. However, the underlying mechanisms remain obscure. In this study, we mainly investigated the antidepressant-like effects of GP and explored the possible mechanisms associated with GLP-1R signaling by using the repeated restraint stress (RRS)-induced depression model of mice. We found that GP treatment significantly ameliorated

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