Trelagliptin

Trelagliptin (trade name Zafatek) is a pharmaceutical drug used for the treatment of type 2 diabetes (diabetes mellitus).

Zang et al. from The First Affiliated Hospital of Jinzhou Medical University, Jinzhou, reported the protective effects of Trelagliptin against blood brain barrier disruption and macrophage infiltration. The results indicate that the infarction volume, the neurological score, and macrophage infiltration staining with CD68 were increased in middle cerebral artery occlusion (MCAO) mice but significantly reversed by treatment with Trelagliptin. Additionally, Trelagliptin reduced the permeability of the BBB by increasing the expression of the tight junction zonula occludens protein-1 (ZO-1) in the cerebral cortex. In an in vitro hypoxia model of endothelial cells, the increased migration of macrophages, enlarged permeability of endothelial monolayer, downregulation of ZO-1, and elevated expression level of CXCL1 by hypoxic conditions were all reversed by treatment with Trelagliptin in a dose-dependent manner. The results demonstrate that Trelagliptin might mitigate macrophage infiltration by preventing the breakdown of the blood-brain barrier in the brains of MCAO mice [1].

Nonalcoholic fatty liver disease (NAFLD) occurs in patients with type 2 diabetes mellitus (T2DM). Trelagliptin is an important member of the Gliptins family, which has been recently licensed for the treatment of T2DM. However, the pharmacological function of trelagliptin in NAFLD has not been previously reported. In this study, we aimed to investigate the roles of trelagliptin in the development of NAFLD in a mouse model. To induce NAFLD disease, C57BL/6 mice were fed a high-fat diet for 10 weeks. Our results indicate that trelagliptin reduced plasma lipid levels in NAFLD mice by reducing triglycerides, total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. Treatment with trelagliptin exhibited an improvement in insulin resistance. More important, trelagliptin improved liver function by reducing alanine transaminase, aspartate transaminase, lactate dehydrogenase, and total bile acid. In addition, trelagliptin ameliorated oxidative stress in the liver of NAFLD mice by reducing malondialdehyde and increasing the levels of reduced glutathione and superoxide dismutase activity. Also, the enzyme-linked immunosorbent assay results indicate that trelagliptin-treated mice displayed anti-inflammatory properties by reducing the levels of interleukin 1β (IL-1β), IL-6, and tumor necrosis factor-α. Hematoxylin and eosin and Oil red O staining show that trelagliptin treatment ameliorates liver tissue damage and hepatic lipid deposition. Mechanistically, we found that the administration of trelagliptin reduced the activity of hepatic nuclear factor-κB but increased the activity of AMP-activated protein kinase. These findings suggest that trelagliptin might become a promising therapeutic agent for the treatment of NAFLD [2].

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Zang L, Yang B, Zhang M, Cui J, Ma X, Wei L. Trelagliptin Mitigates Macrophage Infiltration by Preventing the Breakdown of the Blood-Brain Barrier in the Brain of Middle Cerebral Artery Occlusion Mice. Chem Res Toxicol. 2021 Mar 17. doi: 10.1021/acs.chemrestox.0c00323. Epub ahead of print. PMID: 33728903.
2)
Wang G, Wu B, Zhang L, Jin X, Wang K, Xu W, Zhang B, Wang H. The protective effects of trelagliptin on high-fat diet-induced nonalcoholic fatty liver disease in mice. J Biochem Mol Toxicol. 2021 Jan 9:e22696. doi: 10.1002/jbt.22696. Epub ahead of print. PMID: 33421258.