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Matrine as a new treatment for hepatosteatosis by suppressing ER stress-associated de novo lipogenesis

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Background & Aim: Hepatosteatosis is the excess lipid deposition within hepatocytes and this is closely associated with type-2 diabetes (T2D). Matrine (Mtr) is a small molecule drug used in humans for the treatment of chronic viral infection in the liver where increased de novo lipogenesis (DNL) often exists. Hepatosteatosis can be induced by DNL promoted by endoplasmic (ER) stress. The aim of this study is to investigate the effect of Mtr on hepatosteatosis induced by DNL and on glycemic control in T2D. We hypothesized that the hepatoprotective drug matrine may be repurposed for the treatment of hepatosteatosis by suppressing ER stress-associated DNL.

Methods: Male C57BL/6J mice were used in the present study. DNL-induced hepatosteatosis was produced by a high fructose (HFru) diet for 8 weeks. Mtr (100 mg/kg/day in diet) was administered in the last 2 weeks. Blood glucose, plasma insulin and glucose tolerance test (2.5 g/kg, ip) were assessed after 5-7 hours of fasting. T2D was generated by a high fat diet (10 weeks) plus five consecutive low doses (40 mg/kg ip) of streptozotocin with or without of Mtr (100 mg/kg/day).

Findings: Matrine attenuates the increased expression of DNL pathway in HFru-fed mice. Also, matrine decreases ER stress and increases HSP72 in the livers of HFru-fed mice. In addition, matrine reduces hepatic lipid accumulation and expression of SREBP-1c in T2D mice.

Summary: In HFru-fed mice, matrine reduces hepatosteatosis by inhibiting ER stress and the DNL pathway. These effects are associated with increased expression of HSP72 in the liver by interaction with HSP90. In T2D mice, matrine reduces both hepatosteatosis and hyperglycemia.

Conclusion: Matrine may have the potential to be repurposed for the treatment of T2D due to its beneficial effects on hepatosteatosis and hyperglycemia. Matrine treatment up-regulates the expression of HSP72 in the liver. HSP72 may decrease the expression of SREBP1c and suppress lipogenesis and ER stress pathways. The overall result is a reduction of lipid accumulation in the liver, thus alleviates the glucose intolerance and fatty liver induced by HFru feeding.

Biography

Ali Mahzari has received his Bachelor of Clinical Laboratory Sciences from College of Applied Medical Sciences of King Saud University in Riyadh, KSA in 2005 and Master's degree of Laboratory Medicine from RMIT University in 2010 and did research in the Cytogenetics and Molecular Cytogenetics Laboratories of the Murdoch Children Research Institute in Melbourne. He has worked as a Medical Technologist 1 in Biochemistry Lab in King Fahad Medical City from 2006-2008 and in 2011. His work involved the testing of quality control of the automated machines, blood sample for clinical chemistry, liver and lipid profile tests. He is currently a PhD student at RMIT University and a Lecturer in the Laboratory Medicine Department at Al-Baha University. His current research interest is in the evaluation of effectiveness and safety of Chinese medicine in the treatment of non-alcoholic fatty liver disease and liver-related disease.

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