PO1.020

DA-1241, a GPR119 agonist, ameliorates fatty liver through the upregulation of TFEB-mediated autophagy

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G protein-coupled receptor 119 (GPR119) is predominantly expressed in pancreatic β-cells, enteroendocrine cells, and the liver. It is a novel therapeutic for dyslipidemia and type 2 diabetes. DA1241, a GPR119 agonist, improves glucose tolerance by inhibiting gluconeogenesis and enhancing insulin secretion. It mitigates hepatic inflammation by inhibiting NFκB signaling. However, the mechanism by which DA1241 ameliorates nonalcoholic fatty liver disease (NAFLD) remains unknown. We hypothesized that DA1241 improves liver steatosis by inducing autophagy in a TFEB-dependent manner. It induced autophagy and TFEB nuclear translocation, and decreased lipid content in liver cell lines. Lysotracker staining and DQ-Red BSA assay revealed it increased lysosomal activity. Furthermore, DA1241 increased the colocalization of RFP-LC3 and lipid droplets, which were completely abolished by GPR119 knockdown. DA1241 treatment improved glucose tolerance and insulin sensitivity, and decreased liver enzymes activity and hepatic triglyceride levels, and the NAFLD activity score with increased number of autophagosomes and lysosomes in high-fat diet-fed mice. These effects persisted despite GLP-1 signaling suppression by EX9-39 cotreatment. Despite DA1241 treatment, lysosomal activity and subsequent lipid content reduction were not induced in TFEB knockout HeLa cells. DA1241 treatment failed to produce favorable metabolic effects, including reduced hepatic triglyceride levels, in liver-specific TFEB knockout mice. Thus, DA1241 attenuates hepatic steatosis through TFEB-mediated autophagy induction.

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MASLD and HFpEF: the upcoming worldwide tsunami

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Introduction: Hepatic steatosis, particularly in the presence of obesity, lipid, and glucose metabolism abnormalities, is not only a cardiometabolic risk, but also progressing to liver cirrhosis and hepatocellular carcinoma. It's now considered part of metabolic syndrome, named metabolic dysfunction associated steatotic liver disease "MASLD", and HF "heart failure" is a common endpoint for many diseases processes
Main core: The prevalence of MASLD in HF-preserved left ventricular ejection fraction (HFpEF) patients can reach 50%, they share a common pathophysiology, which are the elements of the multiple hits' theory; insulin resistance, systemic inflammation, oxidative stress, impaired adiponectin, increased visceral fat, and increased systemic organ fibrosis.[1] Fibrogenesis, collagen turnover, and systemic fibrosis may be the links between HFpEF and MASLD. In any systemic disease (e.g., chronic liver diseases and HF), the synthesis and degradation of collagen, occur not only in the myocardium but also in the arterial wall, liver, and kidneys.[2] The connection between ectopic fat deposition and HFpEF is a burgeoning field within cardiovascular research, and it has been shown that visceral adipose tissue (VAT) and epicardial adipose tissue (EAT) are predictive of HFpEF, but not heart failure with a reduced ejection fraction. HFpEF is described as a multisystem disease characterized by Impaired left ventricular diastolic function, myocardial stiffness, and reduced relaxation capacity which linked to obesity and ectopic fat accumulation in the heart through the production of excess systemic FFA-mediated lipotoxicity and microinflammation within cardiomyocytes.[3] Currently GLP1RAs are safe to use in MASH (including compensated cirrhosis) and should be used for their respective indications, namely, type 2 diabetes, and obesity, as their use improves cardiometabolic outcomes, and proper blood pressure control among hypertensive MASLD patients can decrease the risk for deterioration of cardiac function. Studies including HFpEF and MASLD patients are ongoing regarding pathophysiology, and use of pharmacotherapy.
Conclusion: Identifying MASLD patients is critically important, has proposing them for management focused on symptoms and comorbidities is mandatory for early diagnosis of HFpEF and proper assessment of the cardiac condition; thus, identifying stage A or B patients (at risk for HF, pre HF) according to the American College of Cardiology and American Heart Association (ACC/AHA) before progressing to advanced stages of HF, and providing care is challenging and mandatory given the dramatic rise in obesity and diabetes worldwide and because the vast overlap of screening for liver disease in CV patients as well as screening for liver steatosis in CV patients seems reasonable. A multidisciplinary team should support each other in the treatment of their patients, aiming for reduce the morbidity and mortality of patients with MASLD which is mainly from cardiac related complications, is crucial.

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Culinary Uses and Health Benefits of Nettle in Türkiye

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Introduction: Turkish cuisine has been influenced by many cultures throughout history and has developed and diversified through them. The ingredients used in the kitchen stand out not only for their taste but also for their health benefits and nutrition. Among these foods, there are herbs that have high nutritional value and are prominent with their health benefits. Among these, nettle (Urtica dioica) is a frequently used herb in Turkish cuisine; it stands out in terms of taste and nutritional value. Nettle, which is usually freshly collected in the spring months, is frequently preferred in many dishes.
Methods: In this study, systematic review method was used. Studies on the use of nettle as food in Türkiye in the existing literature were examined. Its place in Turkish cuisine, areas of use, and health benefits parameters were discussed.
Results: Nettle is a plant known for its high nutritional value and health benefits. In traditional medicine, it is used in the treatment of various diseases such as rheumatism, arthritis, and allergic reactions. Its rich vitamin and mineral content are emphasized. Especially rich in vitamins A, C and K and minerals such as iron, calcium, magnesium and phosphorus, nettle can have many positive effects on health. Nettle is used in traditional medicine in the treatment of diseases such as rheumatism, arthritis, allergic reactions, and urinary tract infections. It attracts attention with its anti-inflammatory, antioxidant, and diuretic properties. In addition, it is emphasized in various studies that it can be beneficial for diabetics, heart patients and people with high blood pressure. The use of nettle in traditional recipes in different regions of Türkiye reflects the cultural diversity and the nutritional habits of the local people. In Turkish cuisine, the tender leaves and branches of nettle are used in many dishes such as soup, pastry, gözleme, kavurma, omelet, meatballs, pilaf, and salad. Its seeds are usually consumed for therapeutic purposes by brewing or eating directly.
Conclusion: Studies can be conducted to protect and promote the gastronomic potential of nettle. In addition, in future studies, the effects of nettle on health and the effects of different cooking methods on nutritional values can be tested. Comparative culinary culture field studies can be conducted in the geographies where this plant grows.

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