

FRUCTOSE AND ADVANCED GLYCATION END-PRODUCTS IN THE HEART-LIVER AXIS: A LITERATURE REVIEW

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RESUMO

INTRODUCTION: Ultra-processed foods are high in added sugars, sodium, and saturated fats, and their consumption is associated with obesity, insulin resistance, and cardiovascular disease. High fructose intake promotes inflammation, oxidative stress, lipid accumulation, formation of advanced glycation end products (AGEs), reduced insulin sensitivity, fatty liver disease, and cardiovascular damage. The environment of oxidative stress, insulin resistance, and the release of pro-inflammatory mediators contribute to the progression of Fatty Liver Disease Associated with Metabolic Dysfunction (MAFLD), a disease that affects not only the liver but the entire organism, impacting various tissues and contributing to an increased risk of cardiovascular disease. **OBJECTIVE:** This review aims to summarize the biochemical mechanisms and clinical evidence linking high consumption of fructose-rich ultra-processed foods to metabolic alterations and the formation of AGEs, which contribute to the development of diseases associated with the heart-liver axis. **METHODOLOGY:** This is a narrative literature review based on a PubMed search using descriptors related to fructose, advanced glycation end products, and the heart-liver axis. Original articles, systematic reviews, and narrative reviews that demonstrated the relationship between high fructose consumption and the generation of AGEs, metabolic alterations, oxidative stress, inflammation, and the development of liver and cardiovascular diseases were included. **RESULTS:** Under physiological conditions, most fructose is metabolized in the intestine; however, excessive intake redirects fructose to the liver through the portal circulation. Fructose absorption occurs mainly via GLUT5 transporters and, to a lesser extent, GLUT2. In the liver, fructose is rapidly phosphorylated by fructokinase C (Kfk-C) into fructose-1-phosphate, initiating its metabolism independently of the regulatory mechanisms that control glycolysis. Hepatic fructose metabolism generates intermediates such as DHAP and glyceraldehyde, which contribute to glycolysis, gluconeogenesis, and especially de novo lipogenesis (DNL). Excess fructose increases acetyl-CoA and malonyl-CoA production, promoting triglyceride accumulation and reducing fatty acid oxidation through carnitine palmitoyltransferase inhibition. Consequently, high fructose intake favors lipid accumulation, hepatic steatosis, and metabolic dysfunction. In addition, a fructose also promotes oxidative stress by increasing reactive oxygen species (ROS) production, impairing antioxidant defenses, and damaging the intestinal barrier. ATP depletion and reduced glutathione (GSH) synthesis enhance ROS accumulation, endoplasmic reticulum stress, enterocyte apoptosis, and intestinal permeability, allowing lipopolysaccharides (LPS) to reach the liver and intensify inflammation. In hepatocytes and Kupffer cells, oxidative stress and endotoxemia activate inflammatory pathways involving TLR-4, NF- κ B, TNF- α , IL-6, and the NLRP3 inflammasome, contributing to lipogenesis, fibrosis, steatosis, and progression of MAFLD. High fructose also contributes to insulin resistance and hyperuricemia by reducing uric acid excretion and enhancing inflammation. Elevated uric acid levels further promote endothelial dysfunction, linking high fructose consumption to cardiovascular damage and an increased risk of cardiac complications. **CONCLUSION:** In summary, reducing dietary fructose intake is an important preventive strategy to minimize liver and cardiovascular damage. Future studies should focus on long-term clinical outcomes and biomarkers related to fructose and AGE accumulation, improving the early identification of diseases affecting the heart-liver axis.

Palavras-chave: Fructose Advanced Glycation End Products Heart-Liver Axis Insulin Resistance Fatty Liver Disease Associated With Metabolic Dysfunction.