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The Gut-Liver Axis in NAFLD Progression: Insights into Pathogenesis and Therapeutic Opportunities

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Abstract: *Non-alcoholic fatty liver disease (NAFLD) represents a complex disorder characterized by hepatic lipid accumulation and inflammation, ranging from simple steatosis to non-alcoholic steatohepatitis (NASH) and fibrosis. Emerging evidence suggests that dysregulation of the gut-liver axis plays a pivotal role in the pathogenesis and progression of NAFLD. This review comprehensively examines the bidirectional communication between the gut and liver, encompassing intestinal barrier dysfunction, gut microbiota dysbiosis, bile acid metabolism, and immune-mediated responses. We explore the mechanisms by which gut-derived factors, including microbial metabolites, lipopolysaccharides (LPS), and bile acids, influence hepatic lipid metabolism, inflammation, and fibrosis in NAFLD. Furthermore, we discuss therapeutic strategies targeting the gut-liver axis, including prebiotics, probiotics, bile acid modulators, andgut barrier enhancers, with the potential to attenuate NAFLD progression. Understanding the intricate interplay between the gut and liver in NAFLD pathogenesis offers novel insights into disease mechanisms and therapeutic opportunities for the effective management of this increasingly prevalent liver disorder. Non-alcoholic fatty liver disease (NAFLD) is a complexdisorder that is characterized by the accumulation of fat and inflammation in the liver. This canrange from simple steatosis to more severe conditions such as non-alcoholic steatohepatitis (NASH) and fibrosis. Research has shown that the gut-liver axis, which includes the communication between the gut and liver, plays a significant role in the development and progression of NAFLD. This comprehensive review examines the two-way communication between the gut and liver, including intestinal barrier dysfunction, gut microbiota dysbiosis, bile acid metabolism, and immune-mediated responses. We explore how gut-derived factors such as microbial metabolites, lipopolysaccharides (LPS), and bile acids can affect hepatic lipidmetabolism, inflammation, and fibrosis in NAFLD. Additionally, we discuss various therapeutic strategies, such as prebiotics, probiotics, bile acid modulators, and gut barrier enhancers, that target the gut-liver axis and potentially reduce the progression ofNAFLD. Understanding the complex relationship between the gut and liver in NAFLD pathogenesis can provide new insights into the disease's mechanisms and offer therapeutic opportunities for managing this increasingly prevalent liver disorder.*

Keywords: Non-alcoholic fatty liver disease