lowering effect was associated with higher LDL-receptor (+39%) and lower apolipoprotein B (-17%) hepatic gene expression (both $p<0.01$). Resmetirom reduced hepatic triglycerides content (-25%, $p<0.01$) and significantly reduced NAFLD activity score through lower inflammation score ($p<0.01$), as well as lower IL-6 and IL-1b hepatic gene expression (both $p<0.05$). Resmetirom also showed anti-fibrotic effects as shown by a significantly lower % Sirius Red labelling.
Conclusion: Resmetirom lowers LDL-cholesterol, hepatic inflammation, and fibrosis in the 3-week MASH mouse model. This preclinical model will be useful to expedite preclinical drug development for the treatment of MASH.

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P-0272

Treatment with human placental extract ameliorates metabolic-associated fatty liver disease

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Background: Metabolic-associated fatty liver disease (MAFLD) is characterized by the intense deposition of fat globules in the hepatic parenchyma. Uncontrolled MAFLD may develop into fibrosis, which could potentially progress to liver cirrhosis and hepatocellular carcinoma. We evaluated the effect of human placental extract (HPE) to prevent the progression of MAFLD to hepatic fibrosis and cirrhosis.
Methods: SHRSP5/Dmcr rats (spontaneously hypertensive rats/stroke prone) were fed a high-fat and cholesterol (HFC) diet for 4 weeks and screened for steatosis. A set of animals on HFC diet were treated with HPE (3.6 mg/kg body weight) subcutaneously thrice a week, and another set served as control. The animals were sacrificed at 12 weeks from the beginning of the experiment.
Results: The animals fed with HFC diet depicted well-developed fibrosis with bridging and early cirrhosis. Immunohistochemical staining for α-SMA and 4-hydroxy-2-nonenal (4-HNE) demonstrated activation of hepatic stellate cells and marked increase in lipid peroxidation, respectively. Staining for collagens type I and type III depicted marked deposition of newly formed collagen fibers in the hepatic parenchyma. Animals treated with HPE demonstrated significant reduction in biochemical and histopathological changes compared to the respective control group.
Conclusion: The results of the present study indicated that treatment with HPE could ameliorate MAFLD and might be suitable to use as a therapeutic agent to prevent the progression of steatosis to hepatic fibrosis and cirrhosis. Various cytokines, growth factors, anti-inflammatory agents, and antioxidant molecules present in HPE might contribute towards the amelioration of MAFLD.
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P-0273

Macrophages release miRNA-enriched extracellular vesicles that are taken up by lipotoxic hepatocytes

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Introduction: Lipotoxicity and inflammation in the liver play a critical role in the development of nonalcoholic fatty liver disease (NAFLD). Extracellular vesicles (EVs) carry microRNAs (miRs) to modulate cellular crosstalk. Here, we investigated whether miR-223 can be transported from macrophages to lipotoxic hepatocytes via EVs.
Methods: To demonstrate that macrophages transfer EVs containing miR-223 to hepatocytes, we transfected macrophages with a Cy3-miR-223 mimic. Co-culture between the transfected macrophages and the palmitic acid induced-lipotoxic hepatocytes was performed on a transwell system for 24 hours, and miR-223 and its target genes in the hepatocytes was examined. EV uptake assay was also measured by labelling macrophage-derived EVs with Memglow 488, and incubating them with lipotoxic hepatocytes. Low-density lipoprotein receptor (LDLR) in the lipotoxic hepatocytes was measured.
Results: We found that miR-223 was highly expressed in EV fractions from the transfected macrophages. Upon co-culture, the lipotoxic hepatocytes displayed Cy3 fluorescence and exhibited an increase in miR-223 levels and a decrease in miR-223 target genes, *FOXO3* and *TAZ*, as compared to the control group. Blocking EV secretion from macrophages with GW4869 led to reduced transfer of miR-223 to hepatocyte recipient cells. The MemGlow dye was transferred to lipotoxic hepatocytes when incubated with MemGlow-labeled EVs from macrophages. The results also suggested that LDLR played a partial role in facilitating EV uptake by lipotoxic hepatocytes.
Conclusions: Our results show that macrophages transfer miR-223 to lipotoxic hepatocytes predominantly by EV-dependent manner.

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P-0274

A Systematic Review for Adjusting High-fat/High-fructose Animal Models to Clinical Feature of NAFLD

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Background: The complexities of the etiology and pathophysiology of Non-alcoholic fatty liver disease (NAFLD) lead to difficulty in development of therapeutics. We aim to assess statistically the diet-related factors contributing to NAFLD progression using animal studies, which would inform both physicians and researchers for the management of patients and for their preclinical studies.
Methods: From both PubMed and Cochrane database, we searched NAFLD data through October 2022, focusing on high-fat, high-fructose diet (HFHFD) rodent model. We extracted the details for the compositions of diet and routes of intake, period of induction, and characteristics of rodents. And then, we conducted correlation analysis and multiple linear regression analysis among those variants.
Results: A total 161 data (116 articles) was final selected, which produced 14 independent variables. Unexpectedly, no variant significantly correlated with the progression of Non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH), while three factors were the key contributing factors in fibrosis progression under multiple regression analysis ($r = 0.717$, $p < 0.001$); as a relative portion by 40.2% of inducing period, 33.2% of fructose-derived