

Introduction and Objectives: The microbial communities' control is crucial to maintaining homeostasis of gut-liver axis; clinical evidence demonstrates disruptions of microbiota-gut-liver in individuals with Metabolic-associated fatty liver disease (MAFLD). Foods rich in fiber and polyphenols have been associated with an improvement in microbiota diversity, index and miRNAs expression. The aim of this study was to evaluate the effect of a supplementation with a mixture of Mexican foods (MexMix): *Opuntia ficus indica* (nopal), *Theobroma cacao* (cocoa) and *Acheta domesticus* (crickets) on gut-liver axis in a MAFLD mice model.

Materials and Patients: Thirty C57BL/6J mice were divided into three groups: 1) control: normal diet. 2) HF: high fat diet (60%) and fructose/sucrose water 3) MexMix: HF diet up to week 10, followed by HF diet supplemented with 6.7% nopal, 8.7% cocoa, and 8.7% cricket for 8 weeks.

Results: The MexMix animals showed a significantly decreased in body weight, visceral and epididymal fat, adipocyte size, triglycerides, insulin, leptin, and PAI-1; while adiponectin levels increased. Using 16S rRNA gene sequencing, MexMix increased phylogenetic diversity, Firmicutes abundance, and enrichment of 10 beneficial genera, including *Lachnospiraceae*, *Ruminococcaceae*, *Akkermansia*, and *Eubacterium_coprostanoligenes_group*. In the gut, MexMix supplementation significantly increased SCFAs concentration, intestinal crypts depth, *Ocln* and *Cldn1* expression, and decreased *Il6* and *Tnf-α* expression. In liver, MexMix significantly reduced steatosis and *Tnf-α* expression. Besides, MexMix increased nuclear translocation of NFR2 and, in consequence, a higher hepatic expression of *Cat* and *Sod*. MexMix also decreased hepatic expression of miRNA-34a, miRNA-103, and miRNA-33a.

Conclusions: Synchronous supplementation with three nutraceuticals, nopal, cacao, and cricket, produced better results compared to previous studies where foods were administered individually. MexMix demonstrated its efficacy as a prebiotic, promoting the growth of beneficial genera and improving intestinal health. These findings indicate that MexMix has the potential to serve as a therapeutic approach for treating MAFLD in patients, as well as other conditions associated with excessive consumption of fats and sugars.

Ethical statement

The protocol was registered and approved by the Ethics Committee.

Declaration of interests

None

Funding

None

<https://doi.org/10.1016/j.aohep.2024.101465>

Effect of methyl donor supplementation on gut microbiota and hepatic expression of key miRNAs in a murine model of MAFLD

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Introduction and Objectives: Metabolism-associated fatty liver disease (MAFLD) is the most common liver disease worldwide, and intestinal dysbiosis is associated with its development. Methyl donor

supplementation has shown beneficial effects for MAFLD treatment; however, its role on the intestinal microbiota and miRNAs hepatic expression has been poorly studied. The aim of this study was to evaluate the effect of methyl group donor supplementation on gut microbiota and hepatic expression of key miRNAs in a murine model of MAFLD.

Materials and Patients: Twenty-four male C57BL/6J mice were divided into three groups: 1) Control: Conventional diet. 2) HF/FS: Diet rich in fats and sugars for 18 weeks. 3) HFMS: HF/FS diet for the first 10 weeks, followed by a HF/FS diet plus orogastric supplementation with methyl group donors for the last 8 weeks.

Results: The intestinal microbiota was characterized by 16S rRNA gene sequencing; supplementation with methyl donors modified microbial composition analyzed by beta diversity. In addition, HFMS group strongly tended to increase alpha diversity and induced enrichment of six genus: *Acinetobacter*, *Anaeroplasm*, *Pseudomonas*, *Stenotrophomonas*, *Tuzzerella*, and *Moraxellaceae* family. HFMS group significantly increased SCFAs fecal concentration and restored intestinal permeability dysfunction by increasing *Ocln* and *Cldn1* expression; consequently, a decrease in liver inflammation was observed due to a decrease in *Tnf-α* expression. On the other hand, HFMS group significantly increased hepatic expression of miR-122 and decreased miR-33a expression.

Conclusions: This study offers valuable insights into the role of methyl donors as microbiota modifiers, highlighting their ability to promote restoration of intestinal health and liver metabolism. These findings contribute to the proposition that methyl donors could be a promising strategy for treating MAFLD and hepatic related conditions.

Ethical statement

The protocol was registered and approved by the Ethics Committee.

Declaration of interests

None

Funding

None

<https://doi.org/10.1016/j.aohep.2024.101466>

Exploring the metabolic and molecular benefits of methyl donor supplementation in a model of metabolic and fatty liver disease

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Introduction and Objectives: Metabolic fatty liver disease (MAFLD) is currently the most common cause of chronic liver damage worldwide. Differential methylation in genes and histones has been correlated with metabolic alterations present in the disease. Supplementation with methyl group donor molecules could work as a therapeutic strategy to reverse the progression of the disease.

Materials and patients: Male C57BL/6J mice of 20-25g of initial weight were fed with a conventional diet (ND n=8); or a diet high in