8th to the end of protocol. Weight was recorded on weekly basis. Insulin tolerance test was performed at the end of treatment. Dual channel microarrays were hybridized to the Mus musculus genome version with 22,000 genes using hepatic mRNAs. Liver and fat histological analyses were carried out, and liver proteins were analyzed by western blot and Chromatin immunoprecipitation (ChIP). Molecular docking was used to validate binding of PFD to JMJD2BBBBB.

Results: Compared with HF group, mice treated with PFD reduced weight gain, hepatic fat accumulation, and epididymal fat. In addition, treatment drastically decreased cholesterol, triglycerides and VLDL, ALT and AST. Inflammatory nodules, fibrosis, and steatosis in liver tissue were also reduced. Besides, PFD modified expression of genes, such as, Jmjd2b, Pparg, Fasn and Srebp1. Likewise, PFD restored the repressive marks in H3k9, suggesting its capacity as an epigenetic regulator by decreasing Jmjd2b protein activity and interacting with its catalytic site (JmjC).

Conclusions: PFD played an important role as an epigenetic regulator modifying Jmjd2b activity and improving NASH features.

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P-3 PIRFENIDONE PREVENTS OBESITY-ASSOCIATED NONALCOHOLIC STEATOHEPATITIS AND CARDIAC FIBROSIS THROUGH HORMONAL REPROGRAMMING

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Introduction and Objectives: Obesity is now a worldwide epidemic, associated with insulin resistance, nonalcoholic steatohepatitis (NASH), and cardiovascular diseases (CVDs), being the latter main cause of global death. NASH is common among Hispanics, characterized by fatty infiltration, inflammation, with or without hepatic fibrosis, and shows hormonal dysregulation. Pirfenidone (PFD) is an anti-inflammatory, and anti-fibrotic drug. Previously, we reported that PFD has anti-steatosis effects on hepatic and cardiac tissues in mice with NASH, but its mechanisms involved are not completely known. The aim of this study was to investigate the effects of PFD on hormonal regulation in high-fat/high-carbohydrate (HFHC)- diet-induced obese male C57BL/6J mice.

Materials and Methods: At the age of 19-20 weeks, mice were fed with normal diet (ND, 6.2% lipids, 44.2 carbohydrates, 18.6% proteins, n=7) and normal water. Other mice were fed with HFHC (60.3% lipids, 21.4% carbohydrates, 18.3% proteins, n=14) and water with carbohydrates (2.31% fructose and 1.89% sucrose) diet for 16 weeks; at 8 weeks of feeding, seven mice with HFHC diet were administered PFD (300 mg/kg/day) by gavage. Experiments were performed according to the ARRIVE guidelines. Insulin tolerance test (4 h of fasting), ELISA, Hematoxylin-Eosin and Masson staining, and morphometric analysis were performed. Data analysis were evaluated using one-way ANOVA with Tukey post hoc test.

Results: HFHC mice showed NASH with an increase in resistin and aspartate aminotransferase (P0.05). Parameters significantly elevated in HFHC were prevented by PFD such as weight (body, liver, and heart), tibia length, epididymal fat, hepatic steatosis, insulin resistance, hormones (insulin, glucagon, leptin, plasminogen activator inhibitor 1) (Table), triglycerides, total cholesterol, LDL, and VLDL, including inflammatory foci and fibrosis in hepatic and cardiac tissue (P0.05). PFD decreased alanine aminotransferase (P0.05).

Conclusions: PFD decreases metabolic hormones and could be a promising drug for the prevention of obesity-induced NASH and CVDs.

Male C57BL/6J			
Hormones (pg/mL)	ND	HFHC	HFHC+PFD
Adiponectin	11,094.2 ± 718.8	9,308.3 ± 1603.7*	12,752.6 ± 335.5
Glucagon	2,368.1 ± 592.7	5,184.4 ± 584.8*	1,601.3 ± 624##
GIP	135.5 ± 14.3	193.2 ± 54.6	135.3 ± 15.5##
GLP-1	136.9 ± 13.1	207.4 ± 18.8	179.2 ± 48.6
Insulin	5,753.9 ± 449.1	18,029.7 ± 2,749.3***	9,191.9 ± 968.7##
Leptin	1,470 ± 192.5	14,678.8 ± 2,094***	4,475.7 ± 846.4###
Resistin	55,051.6 ± 4,168.4	89,032.2 ± 10,975.5*	85,795.1 ± 5,184.5
PAI-1	715.3 ± 111.3	2,424 ± 301.8***	1,058.4 ± 152.9##
Ghrelin	18,293.9 ± 2,347.1	20,636.8 ± 3120.7	16,557.8 ± 2,428.6

Table. Serum hormones levels. Data are expressed as mean ± SEM. *P < 0.05, ***P < 0.001 vs. ND; ##P < 0.01, ###P < 0.001 vs. HFHC. Abbreviations: GIP, Glucose-dependent insulinotropic peptide; GLP-1, Glucagon-like peptide-1; PAI-1, Plasminogen activator inhibitor-1.

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P-4 HETEROGENEITY OF PRE-LIVER TRANSPLANT EVALUATION PRACTICES IN LATIN AMERICA COUNTRIES: THE LIVER TRANSPLANT ALEH SPECIAL INTEREST GROUP, INTERNATIONAL SURVEY 2023

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