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Bergamot polyphenol fraction prevents nonalcoholic fatty liver disease via stimulation of lipophagy in cafeteria diet-induced rat model of metabolic syndrome.

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Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease in industrialized countries. Defective autophagy of lipid droplets (LDs) in hepatocytes, also known as lipophagy, has recently been identified as a possible pathophysiological mechanism of NAFLD. Experimental and epidemiological evidence suggests that dietary polyphenols may prevent NAFLD. To address this hypothesis and analyze the underlying mechanisms, we supplemented bergamot polyphenol fraction (BPF) to cafeteria (CAF) diet-fed rats, a good model for pediatric metabolic syndrome and NAFLD. BPF treatment (50 mg/kg/day supplemented with drinking water, 3 months) potently counteracted the pathogenic increase of serum triglycerides and had moderate effects on blood glucose and obesity in this animal model. Importantly, BPF strongly reduced hepatic steatosis as documented by a significant decrease in total lipid content (-41.3%±12% S.E.M.), ultrasound examination and histological analysis of liver sections. The morphometric analysis of oil-red stained sections confirmed a dramatic reduction in LDs parameters such as total LD area (48.5%±15% S.E.M.) in hepatocytes from CAF+BPF rats. BPF-treated livers showed increased levels of LC3 and Beclin 1 and reduction of SQSTM1/p62, suggesting autophagy stimulation. Consistent with BPF stimulation of lipophagy, higher levels of LC3II were found in the LD subcellular fractions of BPF-expose livers. This study demonstrates that the liver and its lipid metabolism are the main targets of bergamot flavonoids, supporting the concept that supplementation of BPF is an effective strategy to prevent NAFLD.

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