Gypenosides Improve Lipid Homeostasis by Regulating Fatty Acid Metabolism in the Liver

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Background Information

- If the lipid balance caused by the synthesis, metabolism, and transport of triglycerides in the liver is compromised, then excessive accumulation of triglycerides in liver cells will occur leading to fatty liver disease
- Gypenosides (GPs), triterpenoid saponins found in legumes, have the effect of lowering blood lipids. They are the main chemical constituents and the major pharmacological substances of *G. pentaphyllum*, a herbaceous climbing vine that is widely used in traditional Chinese medicine.
- No serious adverse reactions have been observed with long-term use of *G. pentaphyllum* products.

Figure 1. *G. pentaphyllum*

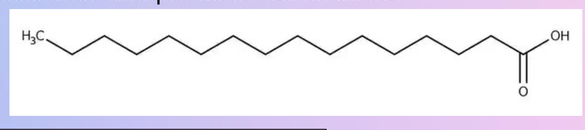
Aim & Hypothesis

Aim: To examine the effect of gypenosides on hepatic lipid metabolism in hyperlipidemic mice. Male mice were placed on a high-fat diet and then administered gypenosides.
Hypothesis: That the gypenosides found in *G. pentaphyllum* will lower the liver index, total cholesterol, and low-density lipoprotein cholesterol in the serum of male mice.

Scientific Theory

- This poster relates back to the scientific theory we learned in class about fatty acid transport and metabolism, and the oxidation of fats.
- It also talks about palmitic acid (16:0, PA); the most common saturated fatty acid found in the human body that can be provided in the diet or synthesized from other fatty acids, carbohydrates and amino acids.
- However, abnormally elevated levels of palmitic acid in tissues can cause lipotoxicity. When it occurs in the liver, it will induce lipid metabolism disorders and insulin resistance and promote inflammation.

Figure 2.
Palmitic acid



Safety/Ethical Considerations

Since this experiment dealt with live male mice, precautions and permissions were taken to safely use them in the experiment, making sure that the mice were not harmed during the process.

- Mice were housed in the specific pathogen-free level animal rooms (temperatures 21–22°C, humidity of 56–65%, and a 12-hour light/dark cycle) with free access to food and water.
- All procedures and operations involving the use of laboratory animals followed the regulations of the Animal Experimentation Ethics Committee of Zunyi Medical University.

Methodology

The mice were divided into 3 groups:

a) Normal diet fed group (ND)
b) High-fat diet fed group (HFD)
c) Gypenosides treated high-fat diet fed group (GPs)

Methodology (contd.)

1. *Liver Index:* The mice were anesthetized to collect blood and liver sample. Liver tissues were harvested, and the liver index was calculated using the formula: Liver index = liver weight/body weight
2. *Histological Biochemical Evaluations:* Tissues were stained with hematoxylin. Sections were incubated with eosin. The histological morphology was observed under an optical microscope.
3. *TC and LDL Measurements:* The collected liver tissues were embedded in paraffin and stained with hematoxylin and eosin (HE) for microscopic examination. The serum levels of total cholesterol (TC) and LDL-C were measured by colorimetry and ELISA.
4. *Palmitic Acid Measurement:* The UPLC-MS/MS system was used for the quantitative analysis of palmitic acid.

Data

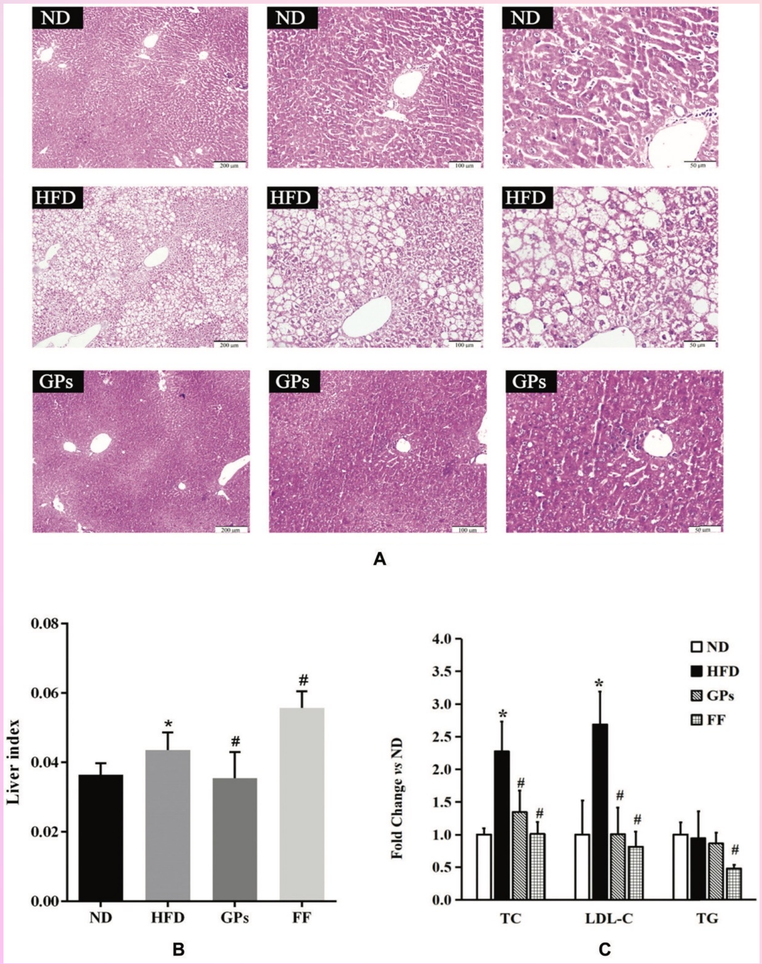


Figure 3. The effects of gypenosides on fat accumulation in liver. (A) The effect of gypenosides on the pathological changes of liver in mice. (B) The effect of gypenosides on the liver index of mice. (C) The effect of gypenosides on Triglyceride (TG), Total cholesterol (TC), and LDL-C in mice.

Data (contd.)

- Histopathological data show the presence of many lipid droplets in the livers of the rats in the HFD group. However, no significant lipid droplet aggregation was seen in the livers of the GPs group, suggesting that fat accumulation was significantly diminished (Fig. 3a).
- Compared with the ND group, the liver index of the HFD group was significantly increased, while it was significantly decreased by GPs (Fig. 3b).
- Also, compared with the ND group, the levels of LDL-C and TC in the serum of the HFD group were significantly increased. The results showed that GPs significantly reduced serum TC and LDL-C to near-normal levels (Fig. 3c).
- UPLC-MS/MS was used to measure the palmitic acid content in the liver. The data presented in Figure 3 show that the content of palmitic acid increased in the HFD group liver compared to the ND group, while it decreased in the HFD group liver after GP administration.

Evidence-based Conclusions

- As a long-chain fatty acid containing 16 carbons, palmitic acid is the most common saturated fatty acid in the body and the most abundant in the blood. It is also the basis for the body to synthesize other fatty acids.
- When the palmitic acid level is in the normal range, it mainly undergoes oxidative decomposition to supply energy and perform its physiological functions.
- However, as discussed, abnormally elevated levels of palmitic acid in tissues can cause lipotoxicity and, in the liver, can induce lipid metabolism disorders, insulin resistance, and promote inflammation.
- In the present study, the level of palmitic acid in the liver, as shown by the results, the HFD group had an increased palmitic acid content compared with the ND group, while the palmitic acid content decreased after the treatment of GPs.
- It indicated that GPs could reduce the level of palmitic acid in the liver and suggested that GPs could regulate the metabolism of fatty acids.

Summary

GPs could significantly reduce the serum total cholesterol and LDL-cholesterol levels, diminish hepatic fat accumulation, and decrease hepatic palmitic acid content. These findings suggested that the role of GPs in regulating lipid homeostasis was closely related to their influence on fatty acid metabolism.

When comparing to what we learn in class, this experiment can help us learn more about the possible effects of fatty acid metabolism and how certain intermediates of the process (ex: palmitic acid) can help us learn more about diseases. Additionally, it also provides us with a novel approach to combat fatty liver disease.