

# The efficacy of a Chinese herbal formula GQD on type 2 diabetes and its mechanism

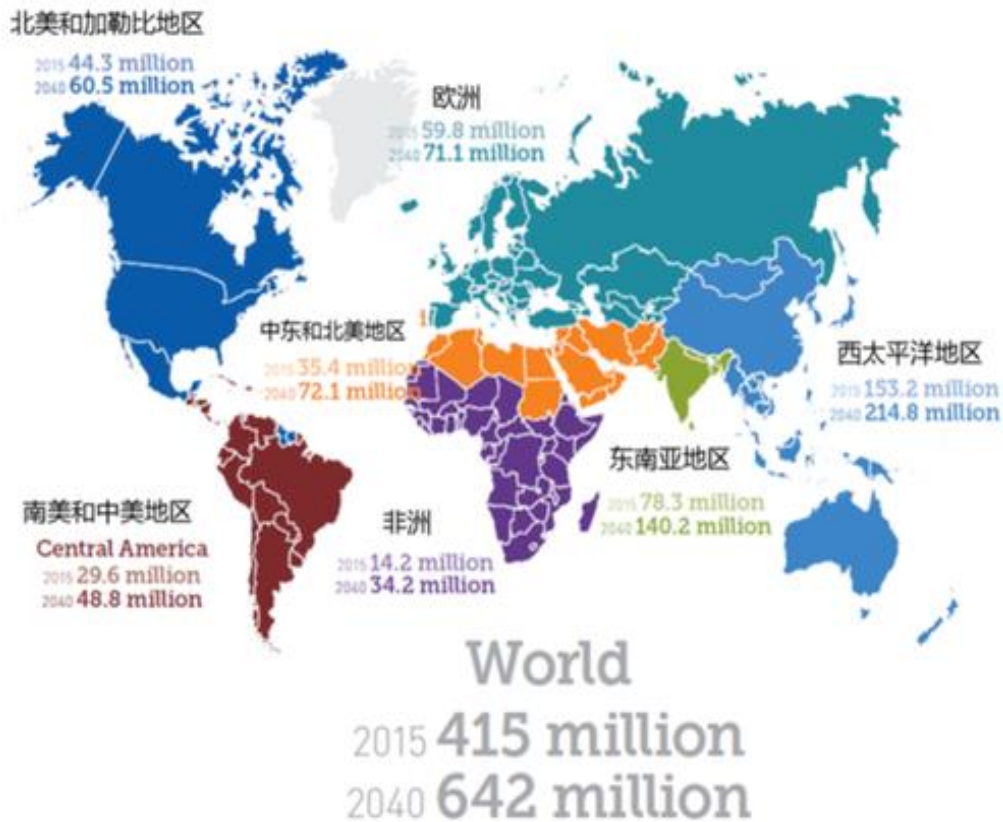
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Beijing, China

# Melonzhao (Dr. Linhua Zhao)

- Doctor of traditional Chinese Medicine in Endocrinology department
- Researcher of Molecular Biology Research Laboratory
- Dose-response relationship study of Chinese Medicine Committee of World Federation of Chinese Medicine Societies (Secretary)
- Dose-response relationship study of Chinese Medicine Branch of Chinese Association of Chinese Medicine (Secretary)
- Chinese medicine research and Promotion Association of diabetes mellitus (permanent member)

The main research area is the clinical and basic research of diabetes mellitus and diabetic complications. As the project leader and backbone · I hosted and participated 14 national and city level scientific research projects.

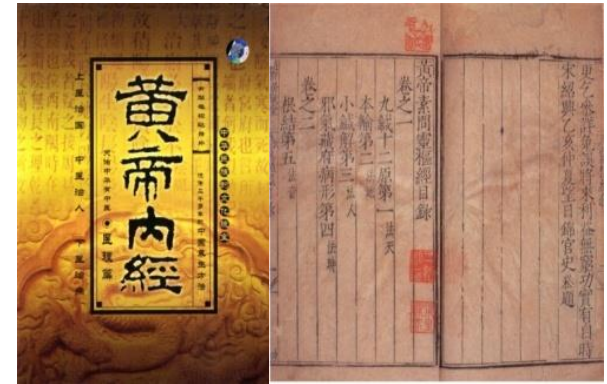
A total of 45 academic papers were published and 16 of them were included by SCI, and 8 papers were as co-author of first or correspondence author. The highest impact factor of one of the papers is 9.302, which is the first international clinical trial about the intestinal flora structure changes and the dose-response relations of traditional Chinese medicine on type 2 diabetes.



Diabetes mellitus is one of the most important chronic diseases that threaten the health of human beings in the world. According to the International Diabetes Federation (IDF) of the latest statistics in 2015, the prevalence of diabetes in adults aged 20-79 years old is 8.8%, the number of patients has reached 415 million.

# Traditional Chinese medicine has a long history in the treatment of diabetes, and the effect is exact.

There are many reports of diabetes treatment recorded in the ancient classic medical books.



灵枢（中研院）

original article

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## The safety and effectiveness of TM81, a Chinese herbal medicine, in the treatment of type 2 diabetes: a randomized double-blind placebo-controlled trial

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ORIGINAL ARTICLE  
Endocrine Research

### Chinese Herbal Medicine Tianqi Reduces Progression From Impaired Glucose Tolerance to Diabetes: A Double-Blind, Randomized, Placebo-Controlled, Multicenter Trial

Fengmei Lian, Guangwei Li, Xinyan Chen, Xiuzhi Wang, Chunli Piao, Jingfei Wang, Yuzhi Hong, Zhuoma Ba, Shentao Wu, Xiaoyan Zhou, Jiangming Lang, Yajun Liu, Rongfang Zhang, Jianjun Hao, Zhangzhi Zhu, Huilin Li, Hong Fang Liu, Aimei Cao, Zhu Yan, Yali An, Yujing Bai, Qiang Wang, Zhong Zhen, Chunhao Yu, Chong-Zhi Wang, Chun-Su Yuan,\* and Xiaolin Tong\*\*†



**Primary  
prevention**

**Prediabetes**

**Secondary  
prevention**

**Diabetes  
mellitus**

**Tertiary  
prevention**

**Complications**

**1. Reduce the conversion of DM**

**2. Lower glucose independently  
Delay the development of complications**

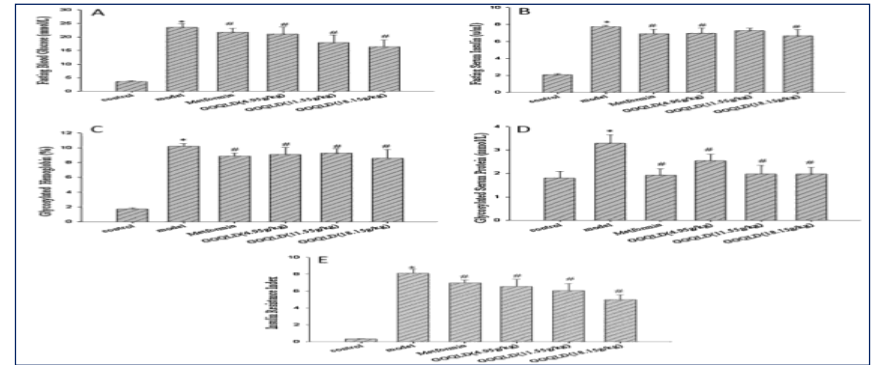
**3. Treat the complications  
Decrease the disability and fatality**

## What's GQD? Diarrhea → →Diabetes

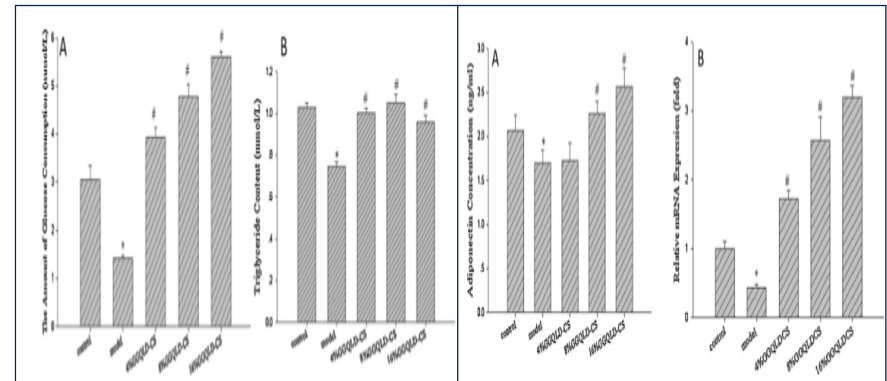
A standardized berberine-containing Chinese herbal formula, Gegen Qinlian Decoction (GQD) has been a treatment for diarrhea in *Shang Han Lun since the East Han Dynasty. Its use was recorded by the prestigious physician Zhongjing Zhang (150-219 AD).*

Subsequently, GQD has been reported to have potentially beneficial effects in the treatment of diabetes in animal trials, as well as in some clinical observations.

First, researchers found GQD significantly reduced fasting blood glucose (FBG) and glycated hemoglobin (HbA1c) in streptozotocin (STZ) and high fat diet-induced diabetic SD rats, and the serum of SD rats that received GQD enhanced glucose consumption in 3T3-L1 adipocytes.



T2D patients treated with a high dose of modified GQD twice daily for 3 months showed a reduction in HbA1c of 1.79% from the initial level of 9.2%. This decrease was significantly different from that of patients receiving a low dose treatment



Tong *et al.*, 2011.

Zhan C H. *et al.* *Phytomedicine*, 2013.

## RCT of GQD on type 2 diabetes

- **Study object** : 224 new diagnosed patients with Type 2 diabetes
- **Study method** : multicentered, randomized, double-blinded, placebo-controlled clinical trial
- **Study design** : high dose, moderate dose, low dose, placebo
- **Primary efficacy outcomes** : HbA1c, the composition of gut microbiota
- **Secondary efficacy outcomes** : FBG, 2h-PBG, TCM symptoms score, lipid levels, body mass index

Supported by the project "Dose-Effect Relationship Study of Chinese Classical Formulas"



# RCT of GQD on type 2 diabetes and its mechanism

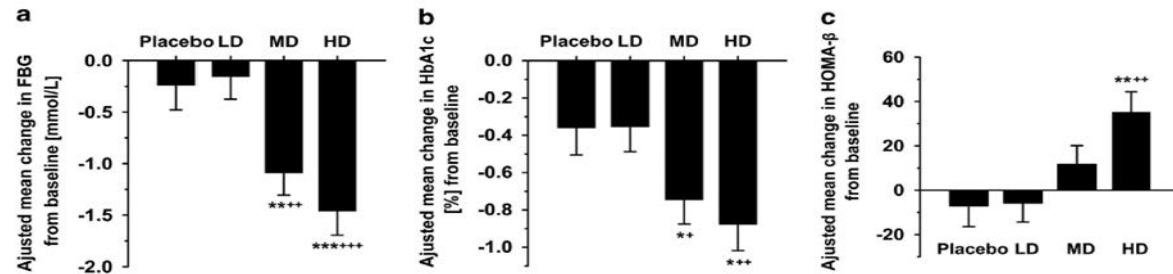
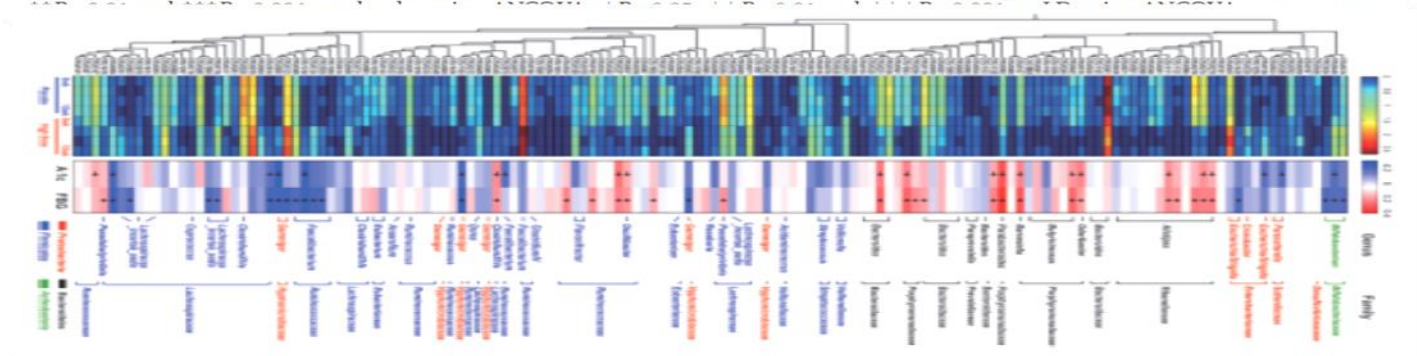
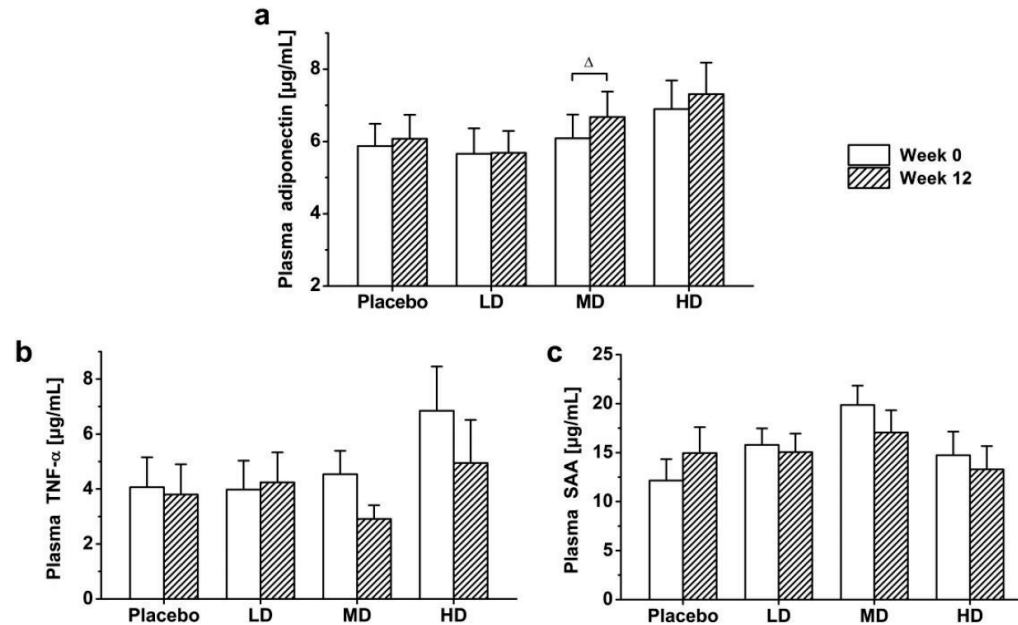


Figure 1 GQD significantly improved glycemic control and HOMA-β in T2D patients. (a) Change in FBG, (b) change in HbA1c and (c) change in HOMA-β. Placebo (n=41), LD (n=50), MD (n=52) and HD (n=44). Data are presented as mean ± S.E.M. \**P*<0.05.



- Reducing HbA1C significantly and it is dose-dependent (HD, MD, LD and placebo reduce HbA1C is respectively **0.95%、0.79%、0.28% , 0.31%**).
- Real-time quantitative PCR confirmed that the Chinese herbal formula significantly enriched *Faecalibacterium prausnitzii*, and *Pseudobutyrvibrio* were significantly decreased.

## GQD on type 2 diabetes

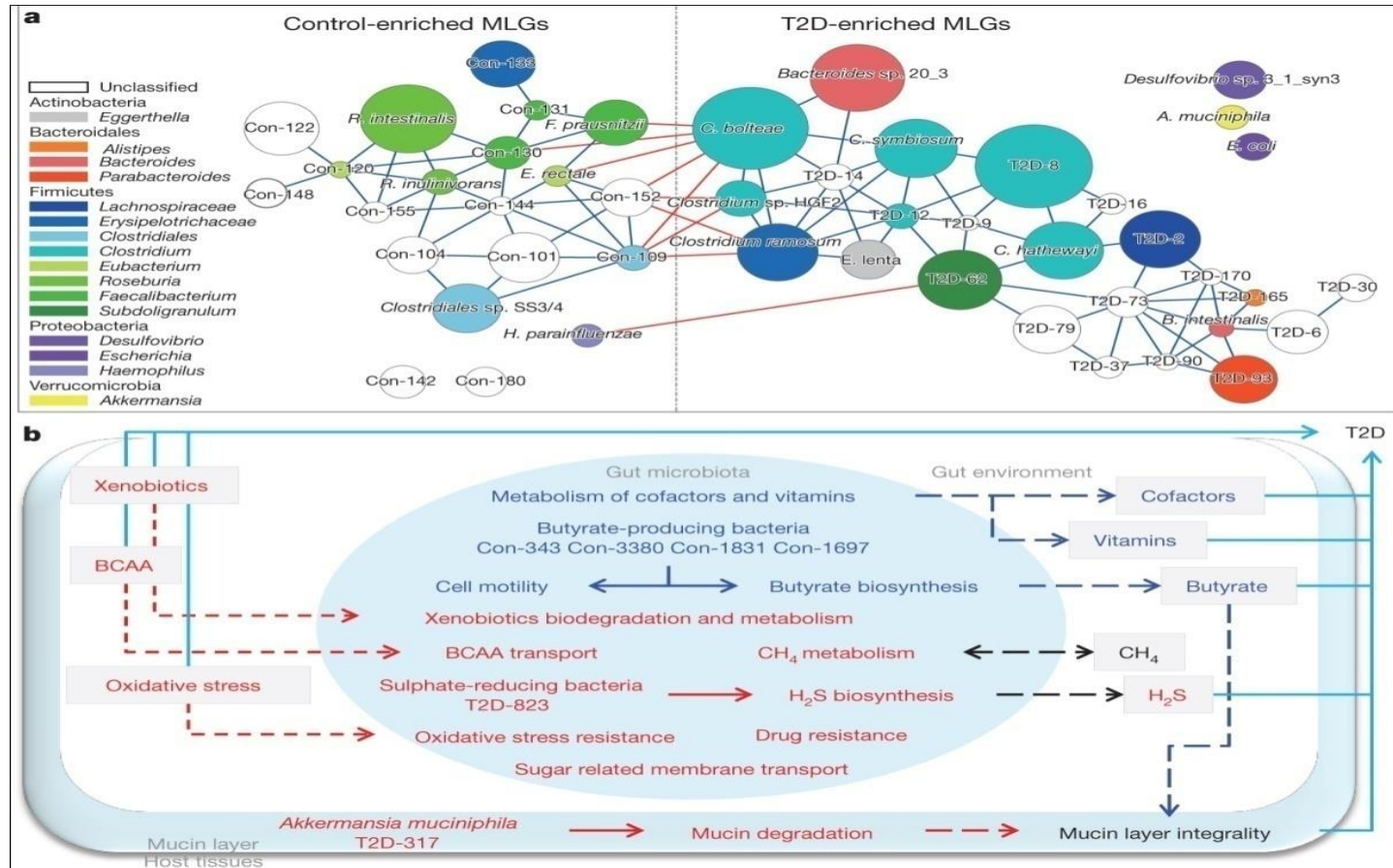


Supplementary Figure 5. Impact of GQD on plasma adiponectin, TNF- $\alpha$  and SAA. (a) Plasma adiponectin. (b) Plasma adiponectin. (c) Plasma TNF- $\alpha$ . (d) Plasma SAA. Placebo(n=40), LD(n=47), MD(n=50), HD(n=41). Data are means  $\pm$  S.E.M..  $\Delta P < 0.05$  vs. before treatment using Wilcoxon signed-rank test.

- **Impact of GQD on plasma adiponectin, Tumor Necrosis Factor- $\alpha$ (TNF- $\alpha$ ) and serum amyloid A protein (SAA)**

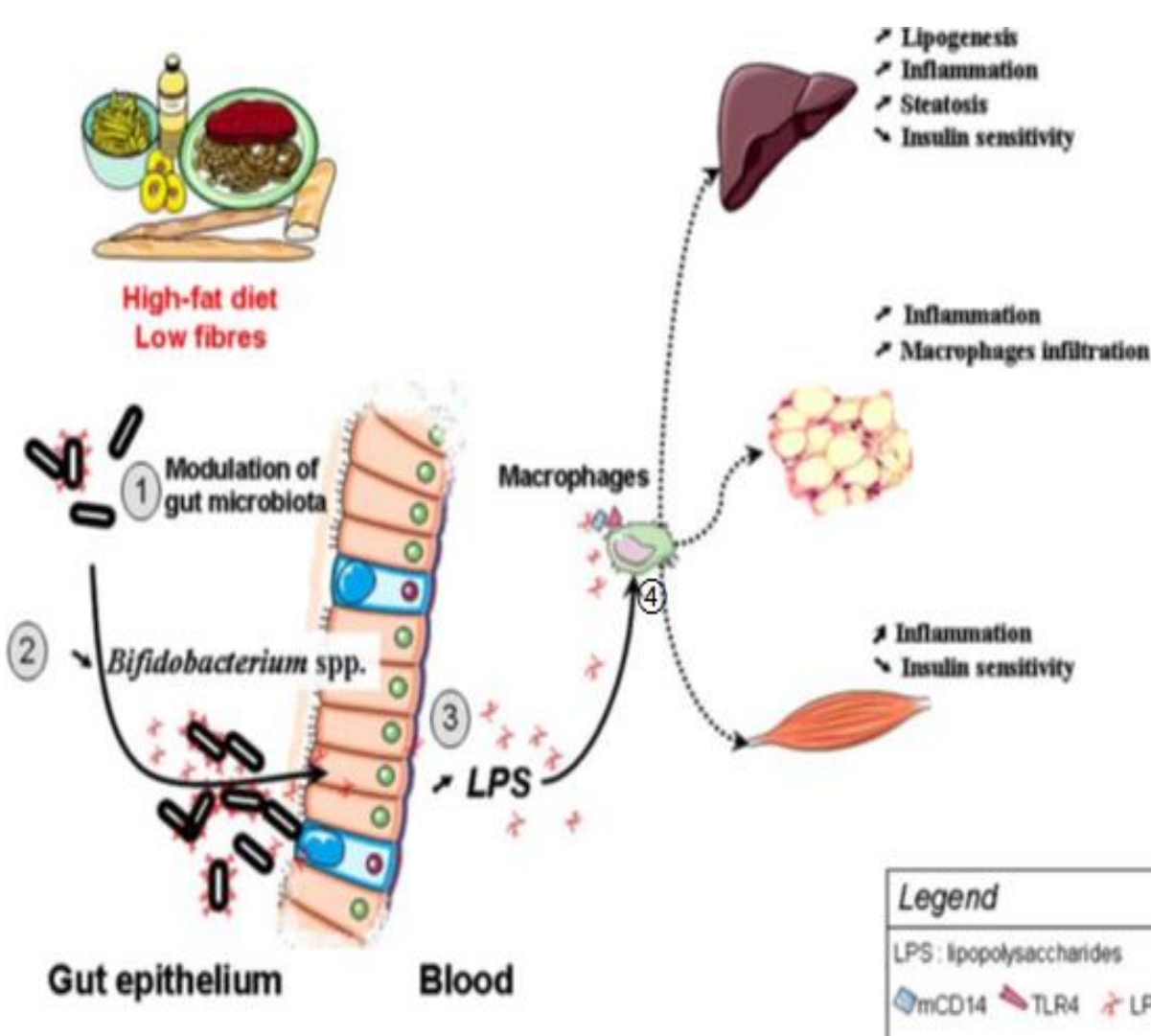
To our knowledge, this study is the first registered clinical trial to evaluate the dose-dependent efficacy and safety of a Chinese herbal decoction following a randomized, double-blinded and placebo-controlled design.

# In patients with type 2 diabetes, there is a moderate imbalance of intestinal flora



*Faecali* and many kinds of butyrate bacteria reduced; sulfate reducing bacteria of opportunity pathogenic bacteria increased.

# The development of intestinal flora in the development of type 2 diabetes mellitus

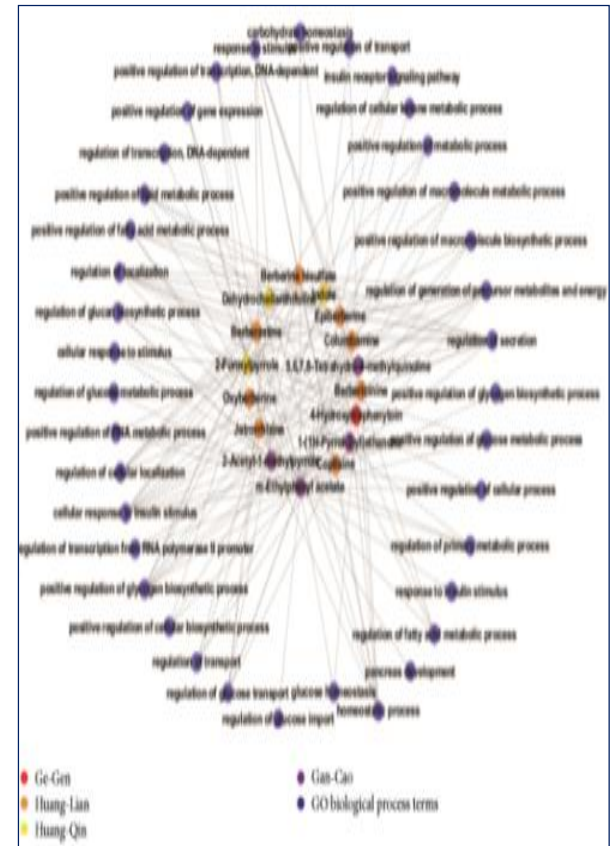
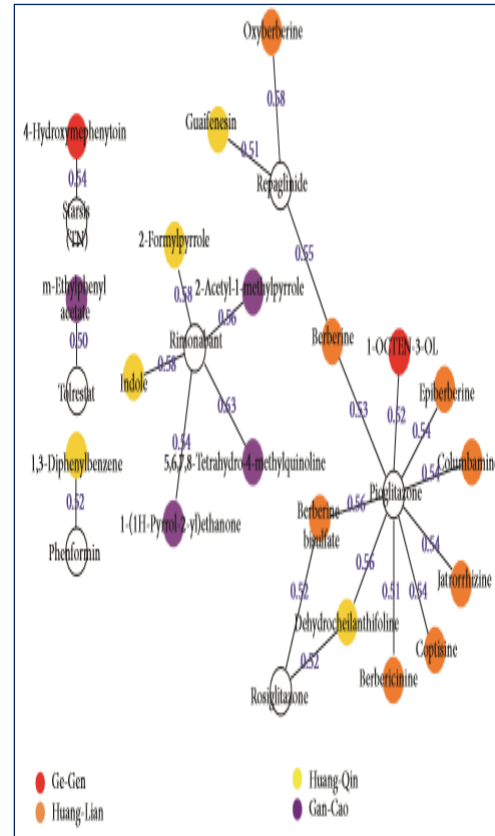


- ① The intestinal flora changes in high fat diet :probiotics reduce and harmful bacteria increase.
- ② Harmful bacteria damage the intestinal mucosa, intestinal mucosal barrier function is reduced, the level of blood endotoxin increased.
- ③ low levels of chronic inflammation is induced;
- ④ The insulin resistance is triggered and which leading to disorder of glucose metabolism.





Through the study of network pharmacology of Gegenqinlian Decoction effective components were explored.



- Consistent with the dose-dependent manner of T2D amelioration, GQD also exerted a dose-dependent modulation on the gut microbiota, suggesting a strong association between the modulation of gut microbiota and T2D alleviation.
- Our study suggests that gut microbiota might be involved in the effect of a widely used TCM formula, GQD.



- The study is still continuing, furthermore, we will do some animal study to confirm whether changes of gut microbiota by GQD directly contribute to the improvement of glucose homeostasis.

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**Thanks for your attention!**