



**46<sup>th</sup>** APIMONDIA

International Apicultural Congress

MONTREAL, 8-12 SEPTEMBER, 2019

QUÉBEC - CANADA



# **Galangin and Pinocembrin from Propolis Relieve Insulin Resistance**

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*Research Article*

# Galangin and Pinocembrin from Propolis Ameliorate Insulin Resistance in HepG2 Cells via Regulating Akt/mTOR Signaling

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Journal of Apicultural Research, 2017  
<https://doi.org/10.1080/00218839.2017.1373512>



## ORIGINAL RESEARCH ARTICLE

### A plant origin of Chinese propolis: *Populus canadensis* Moench

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# Outline

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# 1 Insulin Resistance

- ❖ **In China, more than 92 million adults have diabetes, and 95 percent of them are type 2 diabetes.**
- ❖ **T2DM is characterized by impairing pancreatic  $\beta$ -cell and insulin resistance in target organs**
- ❖ **Insulin resistance represents a decreased sensitivity and reactivity to insulin in balancing and stabilizing glucose levels**
- ❖ **Insulin resistance can cause many severe complications, for example, hypertension, coronary heart disease, and so on.**
- ❖ **The treatments of insulin resistance seem to be worthy of more attention and investigation.**

# 1 Insulin Resistance

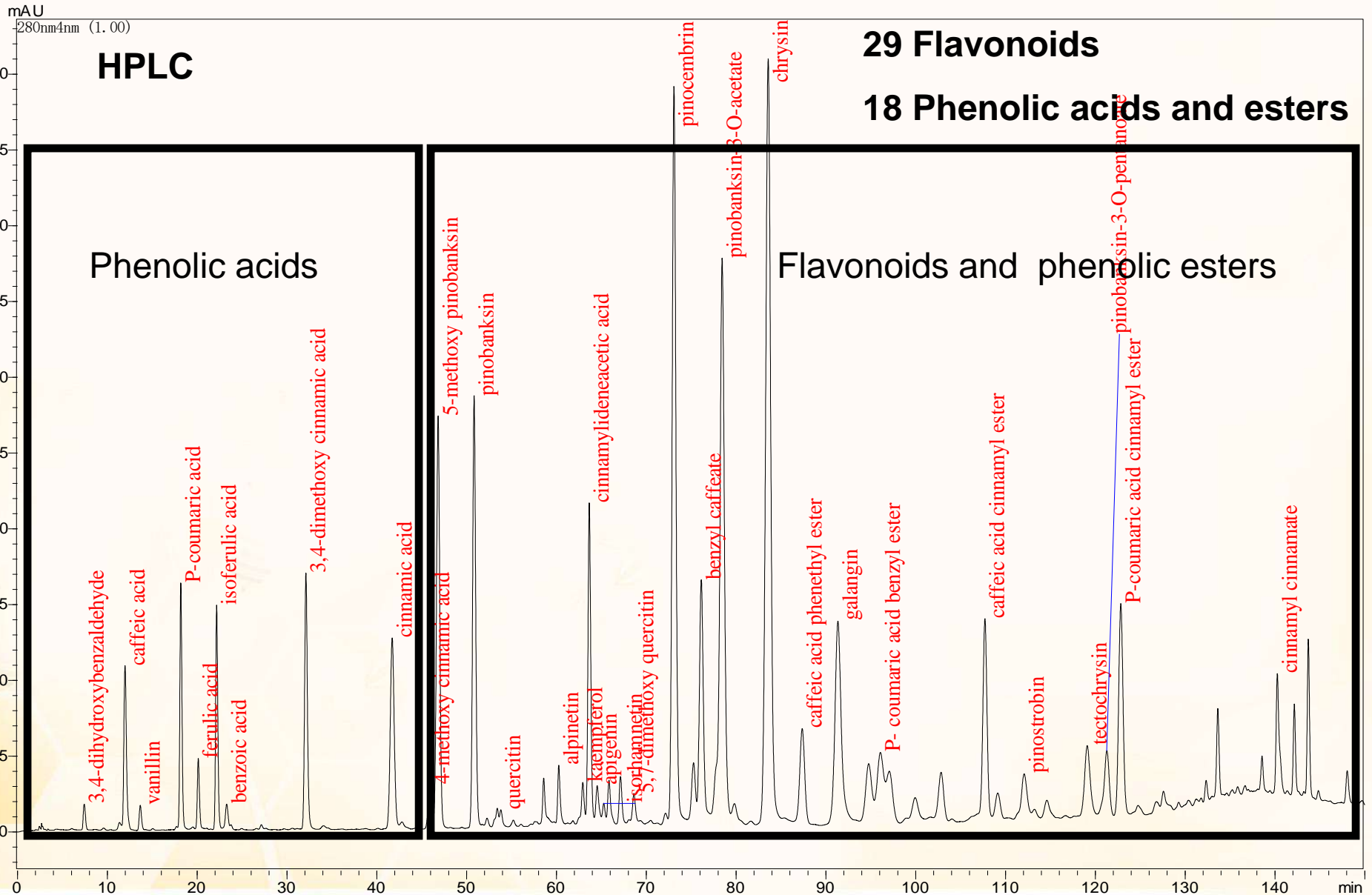
- ❖ Many studies show that **propolis** can **regulate glucose and lipid metabolism** in **diabetic rats**
- ❖ **Brazilian green propolis** also has therapy potential in **insulin resistance**
- ❖ In China, propolis has been approved to use in **functional foods with a health claim of controlling glycemia** in 1999 by the Ministry of Health
- ❖ Propolis has been accepted as **therapy drugs** for **diabetes** in 2005

## 2 Chinese Propolis Phenolics



- ❖ In China, Propolis is a resinous mixture that honey bees collect resin from populus tree buds.
- ❖ Chinese propolis is mainly from *Populus canadensis*
- ❖ Honeybees use propolis as a cement for small gaps in the hive
- ❖ Propolis biological properties can mainly be related with phenolic compounds

# 2 Chinese Propolis Phenolics





## 2 Chinese Propolis Phenolics

Main Composition	Average Contents (mg/g)
Benzyl Caffeate	25.47
Phenethyl Caffeate	12.03
Cinnamyl Caffeate	10.65
Cinnamyl <i>p</i> -Cinnamate	8.77
3-Acetate Pinobanksin	40.75
Chrysin	35.04
Pinocembrin	19.73
Galangin	12.99
Pinobanksin	12.15
5-Methoxy Pinobanksin	12.06

We collected and analyzed **98 samples** from China

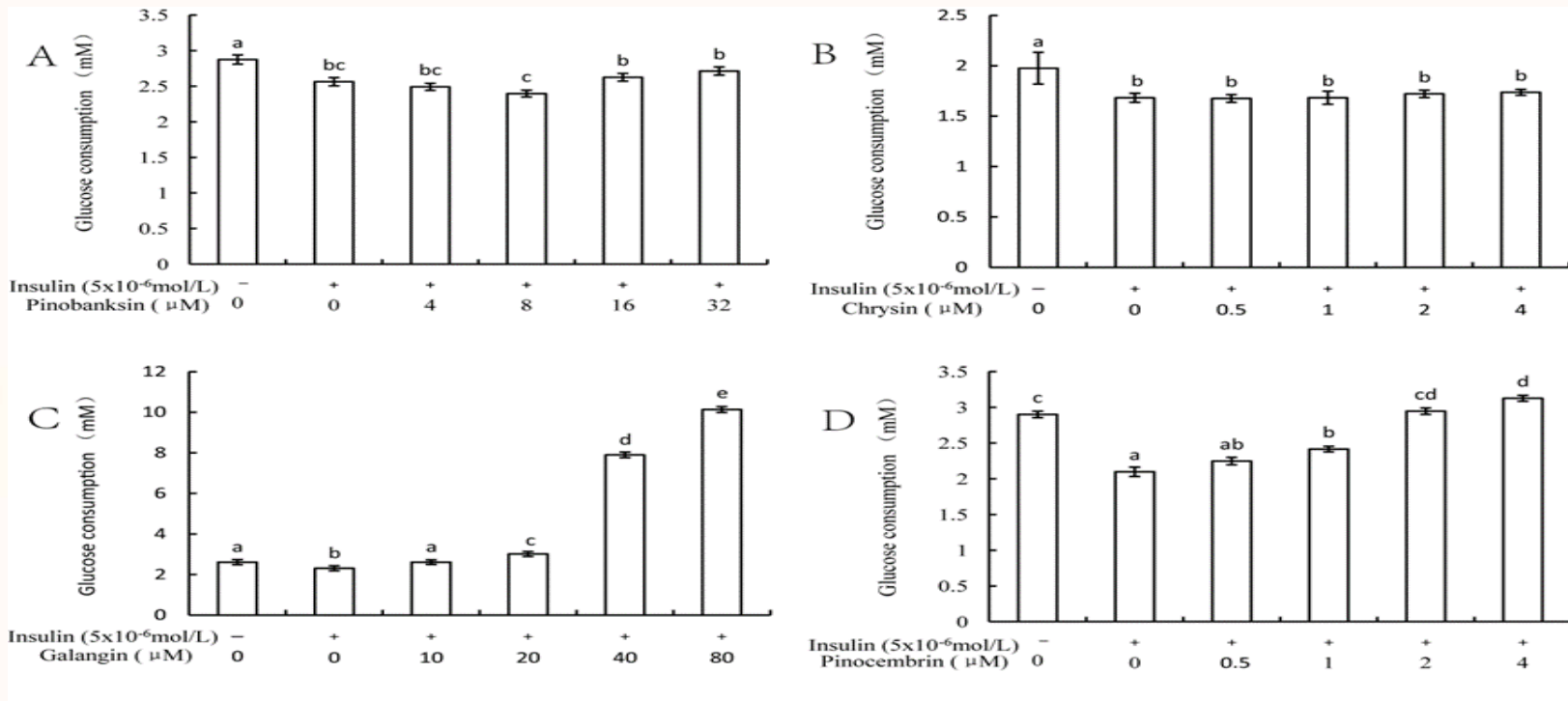
We find that **characteristic components included 4 phenolic esters and 6 flavonoids.**

The **four flavonoids represent 50%** of the total flavonoid contents



# 3 Effects on Insulin Resistance

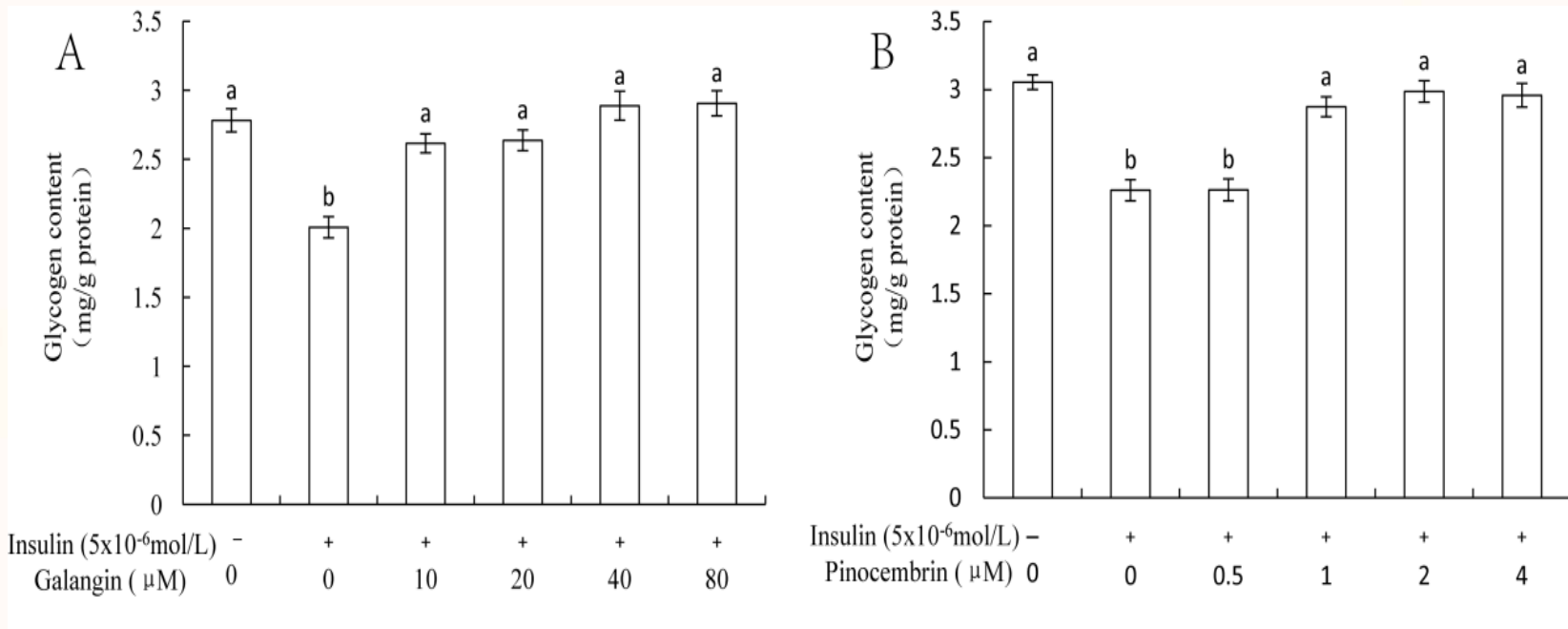
## Glucose uptake in Insulin-Resistant HepG2 Cells



- ❖ **Galangin** and **Pinocembrin** can promote the glucose uptake of insulin stimulation groups
- ❖ **Pinobanksin** and **Chrysin** show no significant differences in the amount of glucose uptake— not ameliorate insulin resistance

# 3 Effects on Insulin Resistance

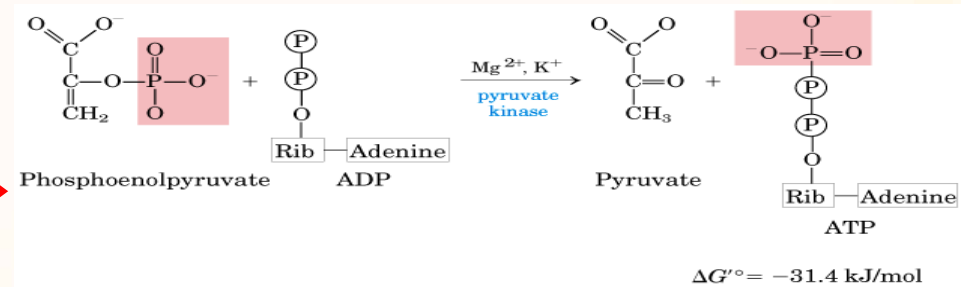
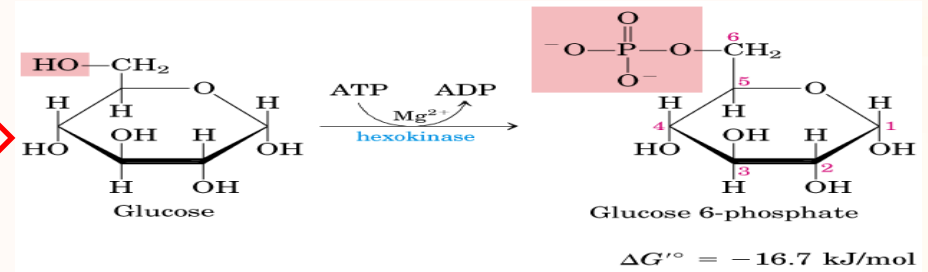
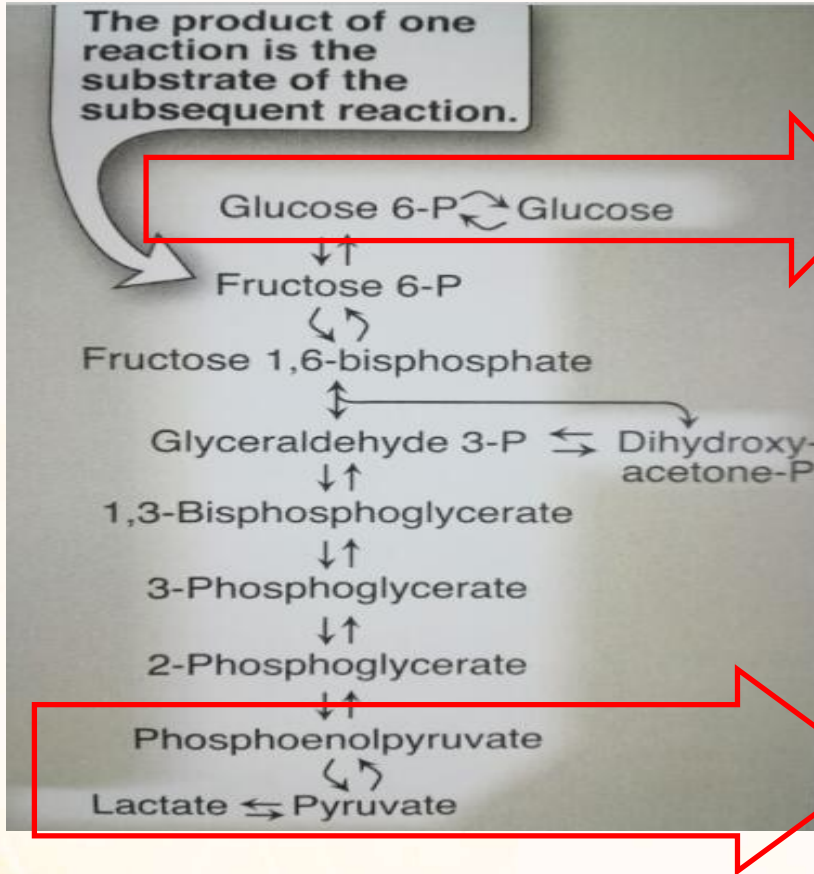
## Glycogen Synthesis in Insulin-Resistant HepG2 Cells



❖ **Galangin** and **Pinocembrin** can promote glycogen synthesis by 50% and 30%, respectively.

# 3 Effects on Insulin Resistance

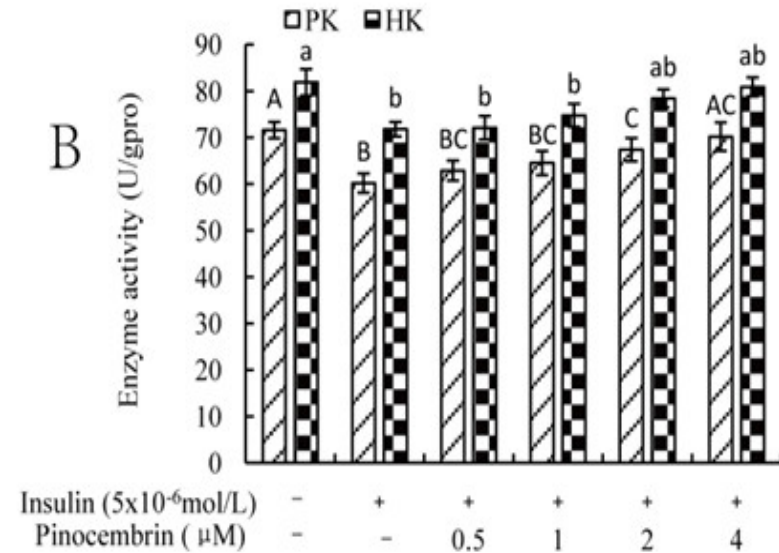
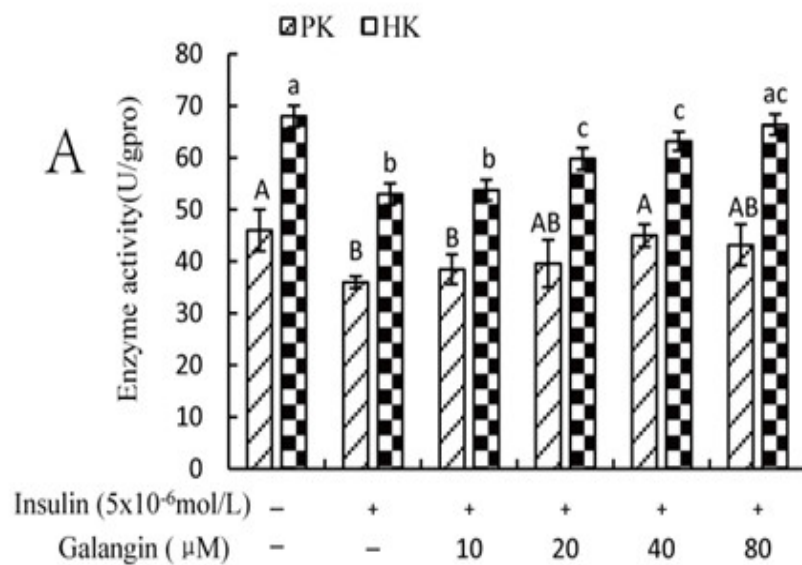
## Hexokinase and Pyruvate Kinase in Insulin-Resistant HepG2 cells



- ❖ **Hexokinase and pyruvate kinases** play an important role in glucose metabolism

# 3 Effects on Insulin Resistance

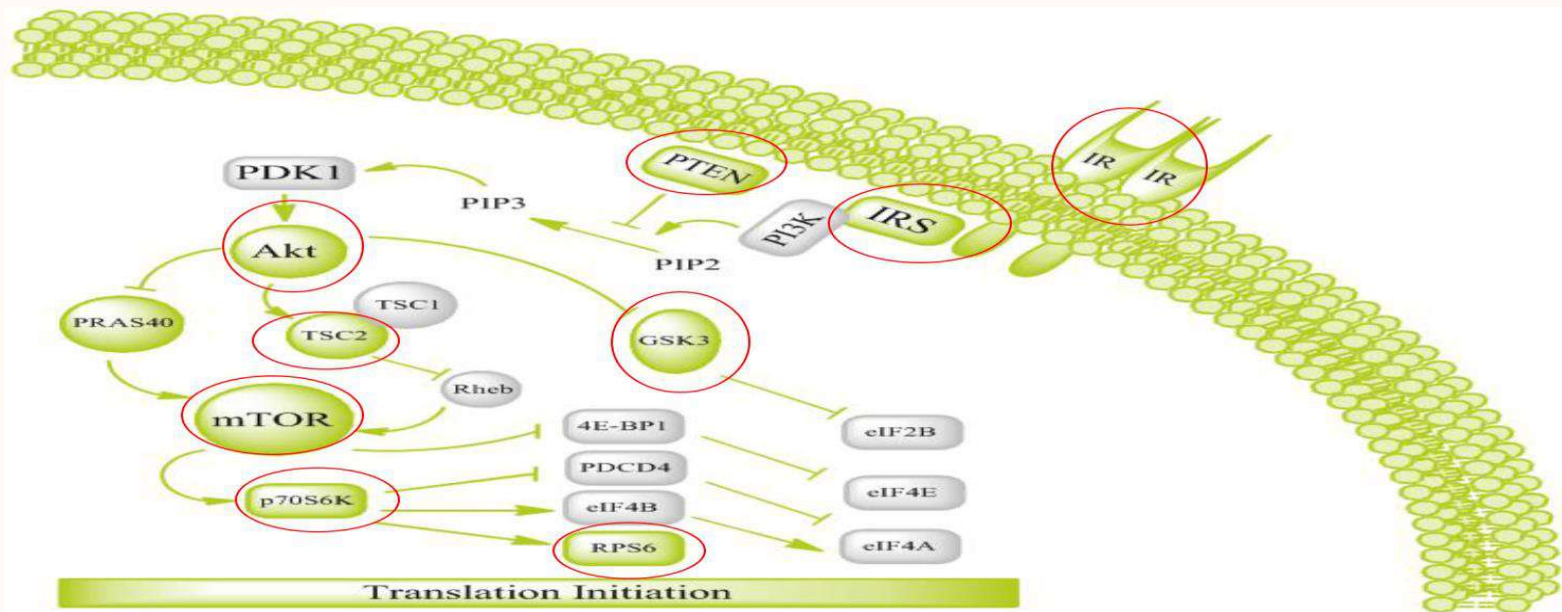
## Hexokinase and Pyruvate Kinase of Insulin-Resistant HepG2 cells



- ❖ **Galangin** and **Pinocembrin** increase the activities of hexokinase and pyruvate kinase by 22% and 30%, respectively.

# 4 Akt/mTOR Signaling Pathway

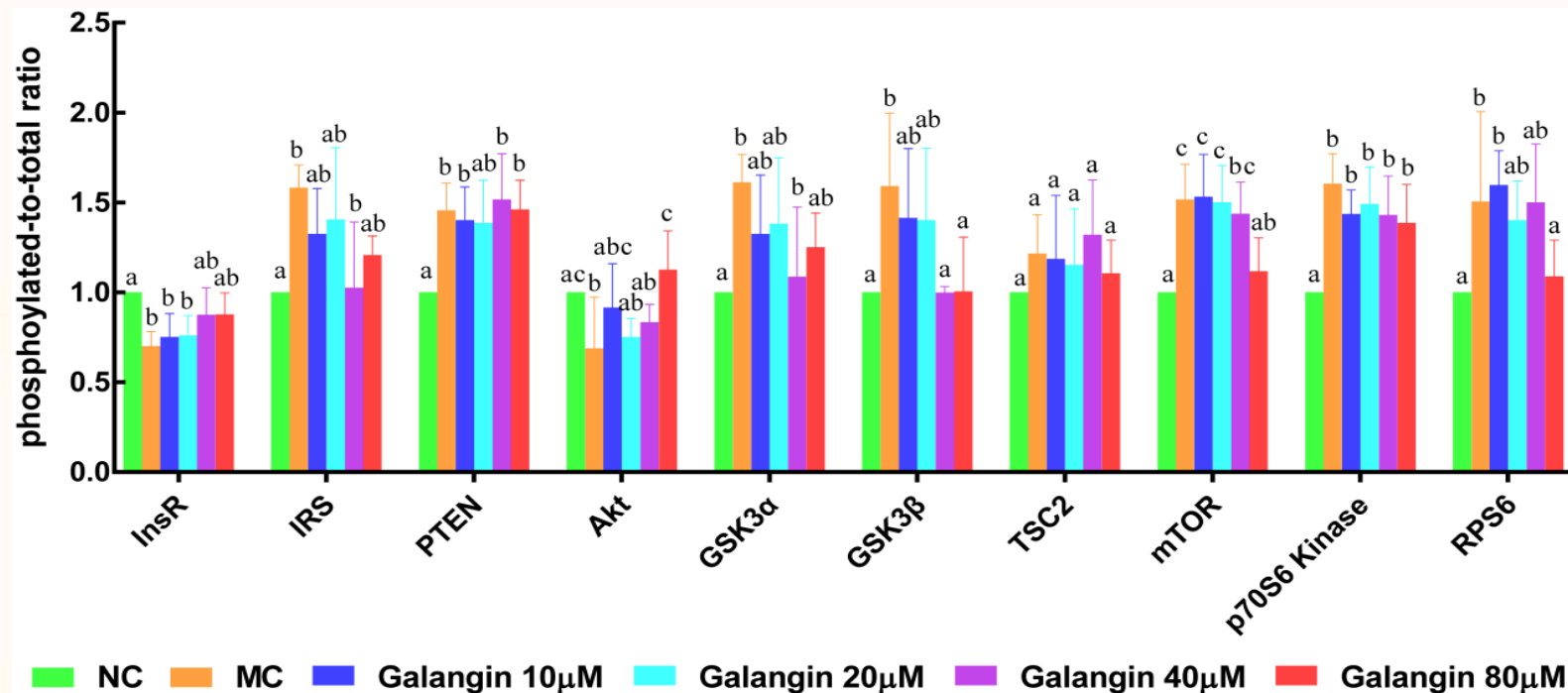
## AKT / mTOR signaling pathway in Insulin-Resistant HepG2 Cells



- ❖ Akt/mTOR is an important pathway of intracellular insulin transduction and energy metabolism in the liver
- ❖ Akt/mTOR also plays a very important role in glycolysis

# 4 Akt/mTOR Signaling Pathway

## Galangin on AKT / mTOR signaling pathway in Insulin-Resistant HepG2 Cells

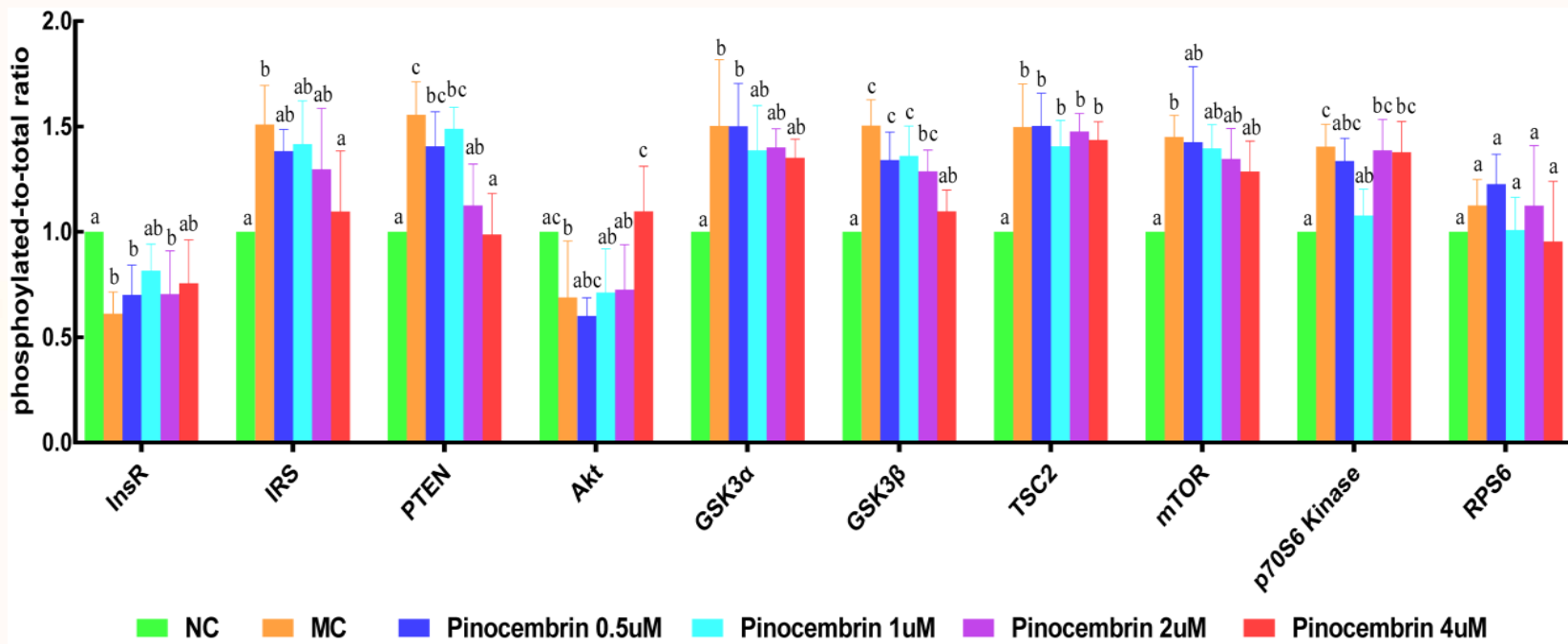


- ❖ **Galangin** can significantly promote phosphorylation levels of IR, Akt, GSK3 $\alpha$ , and GSK3 $\beta$
- ❖ significantly reduce IRS, mTOR, and RPS6 levels



# 4 Akt/mTOR Signaling Pathway

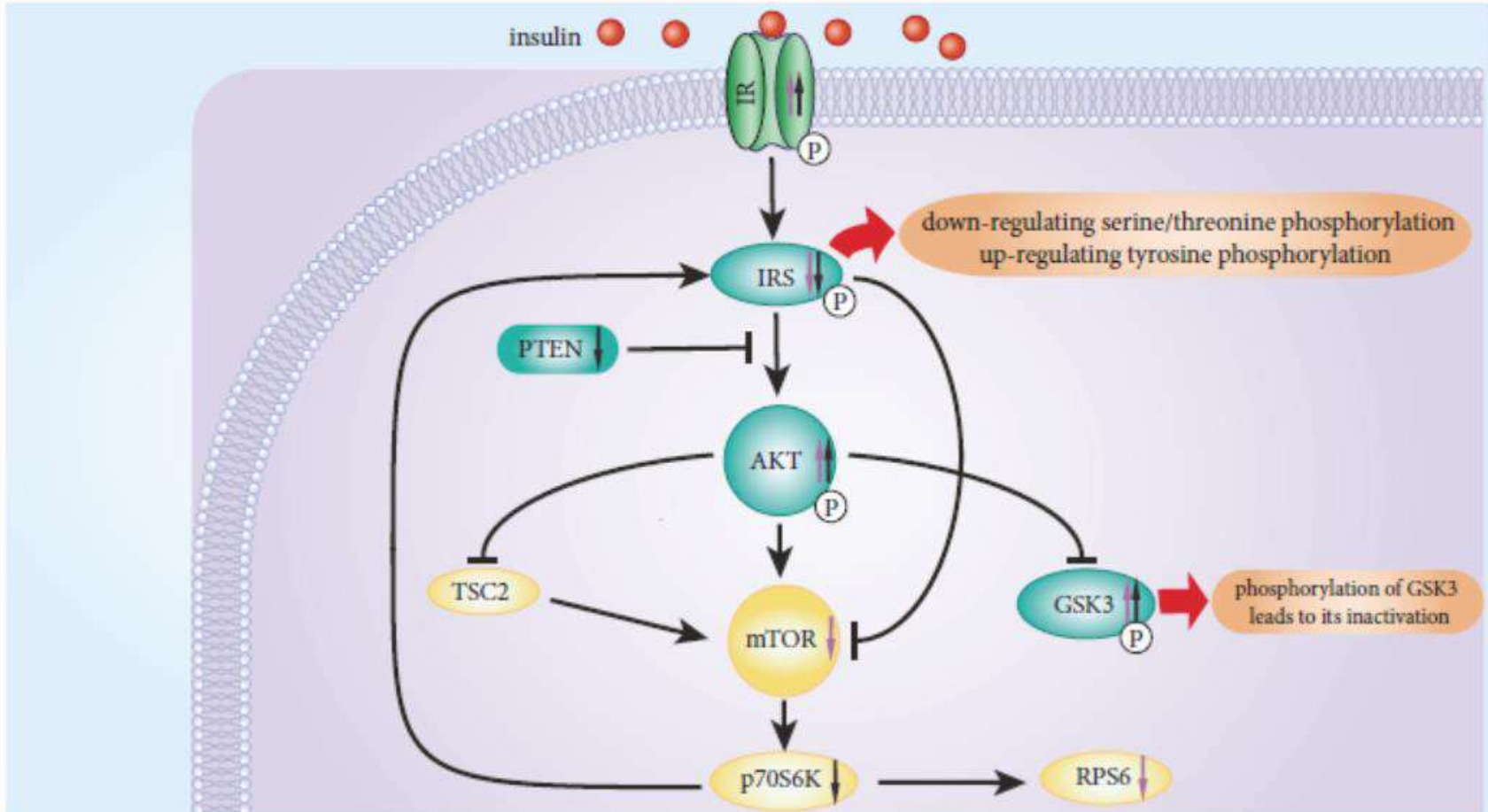
## Pinocembrin on AKT / mTOR signaling pathway in Insulin-Resistant HepG2 Cells



- ❖ **Pinocembrin** can significantly promote phosphorylation levels of IR, Akt, GSK3
- ❖ significantly reduce IRS, PTEN, and p70S6K

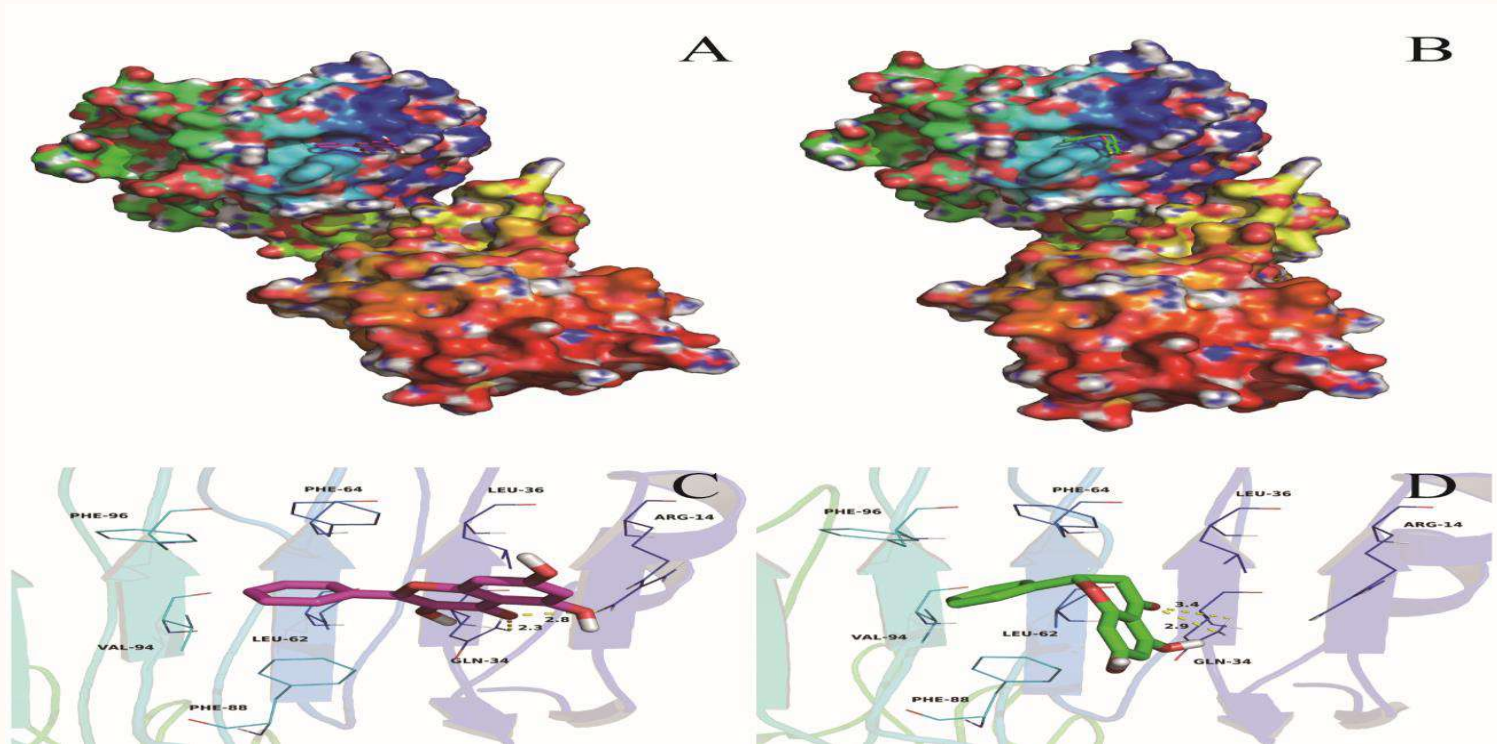


# 4 Akt/mTOR Signaling Pathway



- ❖ We hypothesize that **galangin** and **pinocembrin** can synergistically relieve insulin resistance through regulating the protein phosphorylation of key Akt/mTOR signal proteins.

# 4 Akt/mTOR Signaling Pathway



- ❖ We performed **Molecular Docking** between **Galangin/Pinocembrin** and **Human Insulin Receptor (IR)**
- ❖ Galangin and pinocembrin can **change insulin receptor conformation** by binding to the **hydrophobic pocket** of insulin receptor, therefore **increasing insulin receptor sensitivity**

## 5 Conclusions



- **Pinobanksin and chrysin** are **ineffective** for promoting glucose metabolism
- **Galangin and pinocembrin** can **relieve insulin resistance** by increasing the activities of hexokinase and pyruvate kinase, promoting glucose consumption and glycogen synthesis
- Galangin and pinocembrin may have a **synergistic effect** through **Akt/mTOR** signaling pathway
- Galangin and pinocembrin can change **insulin receptor conformation** to **increase insulin receptor sensitivity**