

農業生物技術國家型計畫

## 抗代謝症候群 苦瓜保健食品研發-子計畫 1

苦瓜活化PPAR成份之萃取與化學鑑定及其供為  
調節胰島素敏感性與血脂保健食品之研發

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**Table 1. Abnormalities associated with the  
metabolic syndrome**  
(modified from [Reaven, 2002])

### The core Cluster

- |  |   |
|--|---|
| <ul style="list-style-type: none"> <li>➤ Central Obesity</li> <li>➤ Dyslipidemia             <ul style="list-style-type: none"> <li>hypertriglyceridemia</li> <li>-low HDL cholesterol</li> <li>-small, dense LDL particles</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>➤ Glucose intolerance             <ul style="list-style-type: none"> <li>-impaired fasting glucose</li> <li>-impaired glucose tolerance</li> <li>-type 2 diabetes</li> </ul> </li> <li>➤ Insulin resistance</li> <li>➤ Hypertention</li> </ul> |
|--|---|

Prevalence: ~1/4 in USA, 14% in Taiwan

## Definition of metabolic syndrome World Health Organization

- ◆ **The patient must have 1 of the following:**
  - Diabetes mellitus
  - Impaired glucose tolerance
  - Insulin resistance
  
- ◆ **Plus any 2 of the following:**
  - Central obesity
  - Dyslipidemia
  - Hypertension

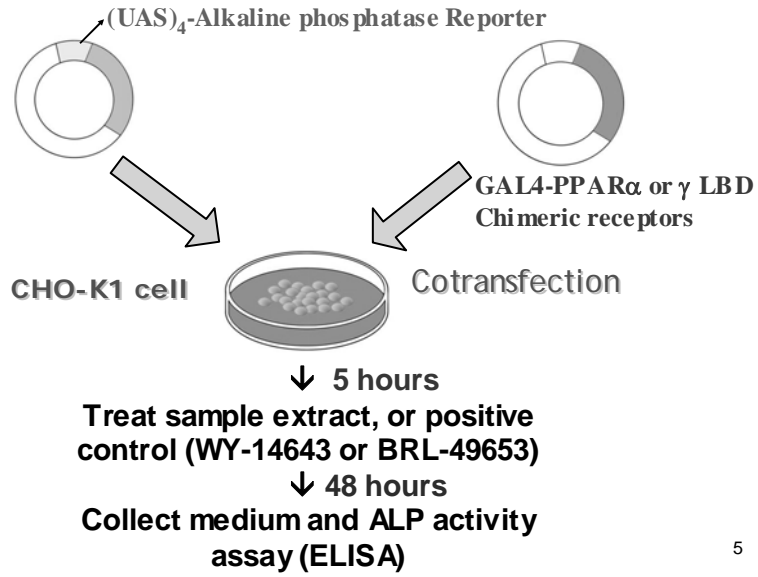
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*AmJ Clin Nutr* 2006;83:1237–47.

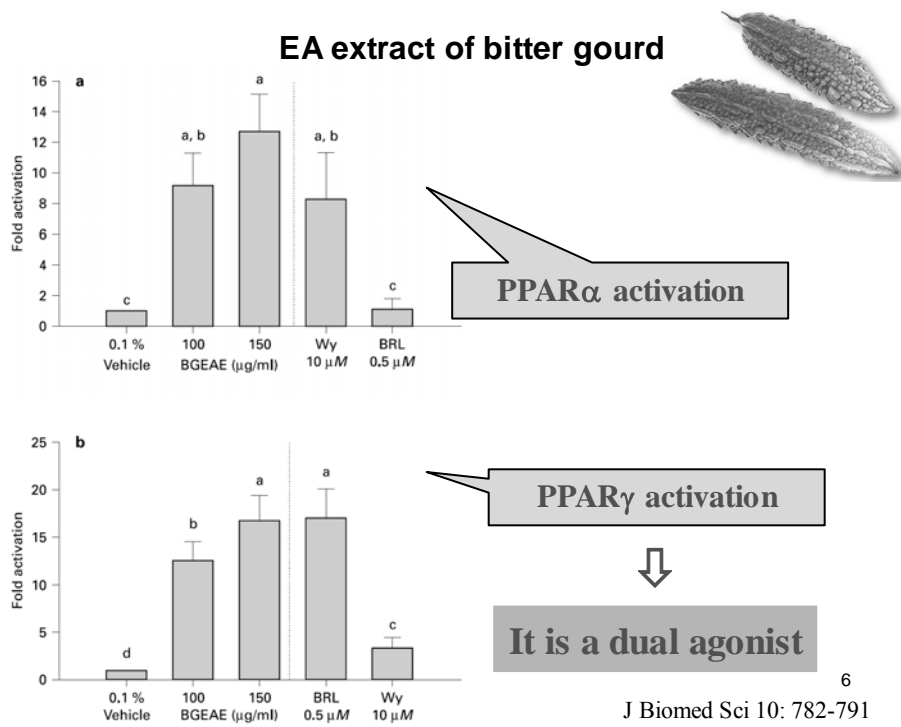
## PPARs : Peroxisome Proliferator Activated Receptor

- **Ligand-activated transcription factors**
- **Member of**  
**Steroid hormone nuclear receptor superfamily**
- ❖ **PPAR $\alpha$** 為fibrates類降血脂藥物之作用分子標的
- ❖ **PPAR $\gamma$** 為Thiazolidinedione類抗糖尿病藥物之作用分子標的
- ❖ **PPAR 活化物促進****cholesterol reverse transport**
- ❖ **PPAR活化物抑制****巨噬細胞主導之發炎反應與動脈粥狀硬**

### Transactivation Assay for Nuclear Receptors



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## Animal Study : Bitter Gourd (*Momordica charantia*) and Metabolic syndrome

### Improvement study 改善

Experimental I: High fat diet - C57BL/6J mice

### Prevention study 預防

Experimental II: High fat diet- Wistar Rats  
Normal diet- C57BL/6J mice

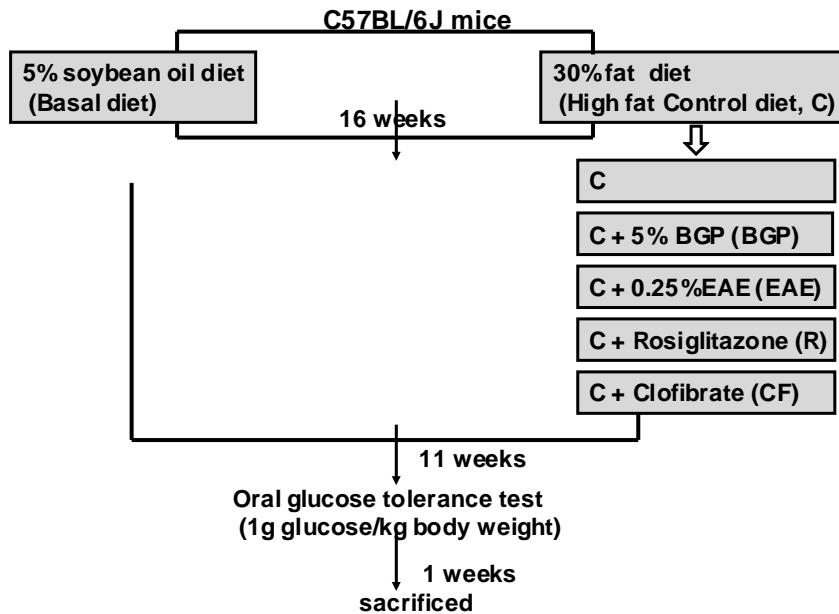
### Dose-Response study 劑量

Experimental III: High fat diet-Wistar Rats  
Normal diet- C57BL/6J mice

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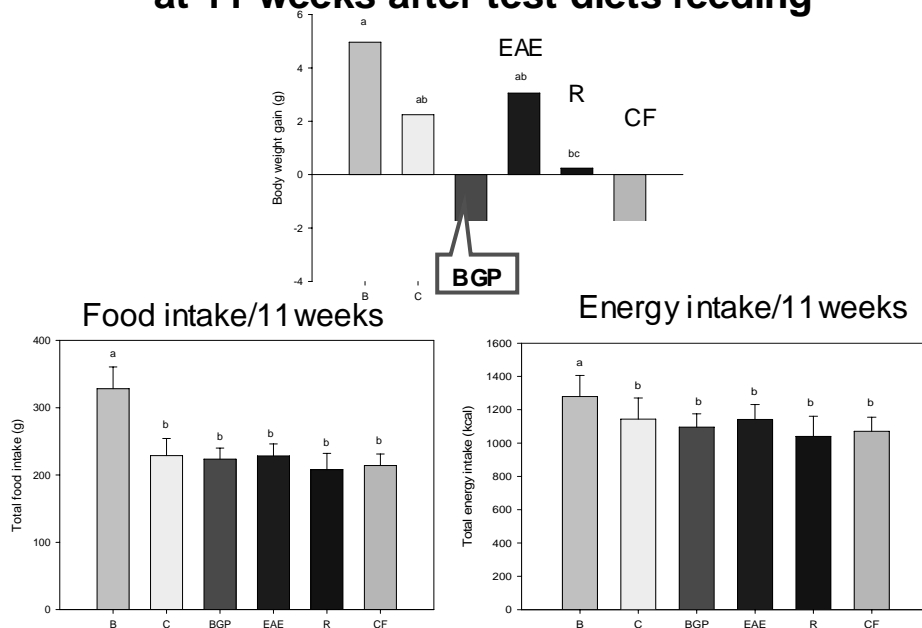
### Exp. I: Improvement study

High fat diet induced metabolic syndrome

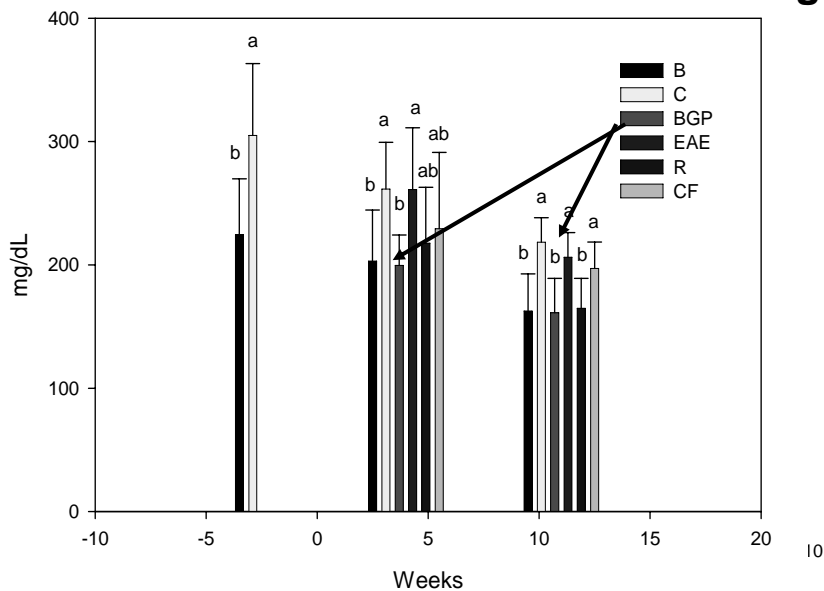


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### Body weight at 11 weeks after test diets feeding



### Plasma glucose at 4 and 11 weeks after test diets feeding



(二) OGTT

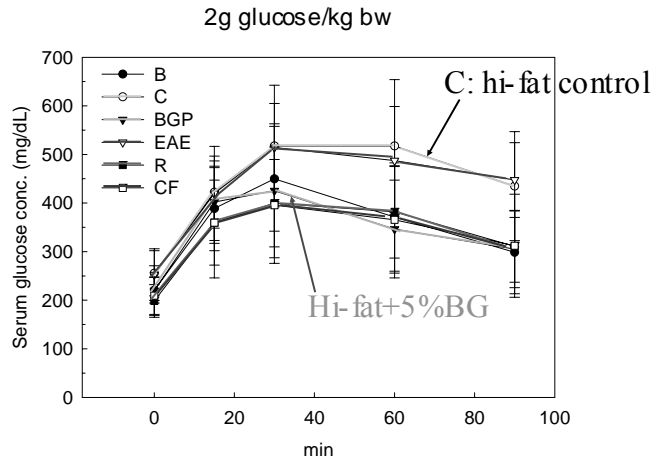
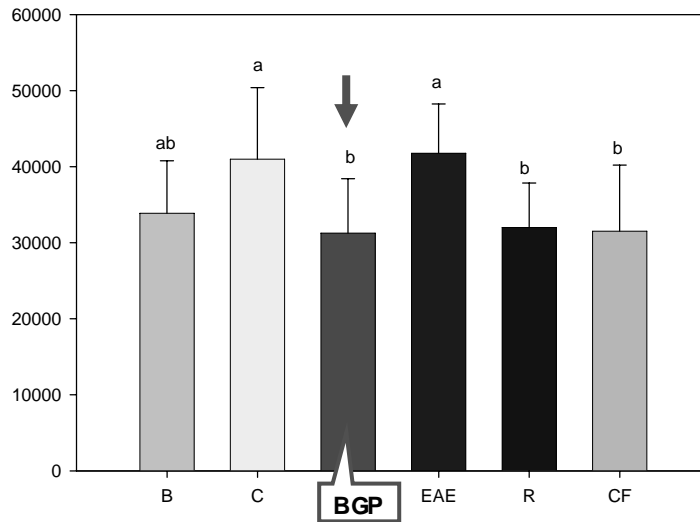


Fig. 7 B6 餵食實驗飼料九週後之 OGTT 結果

六組實驗動物皆於實驗進行三十分鐘後血糖達最高值

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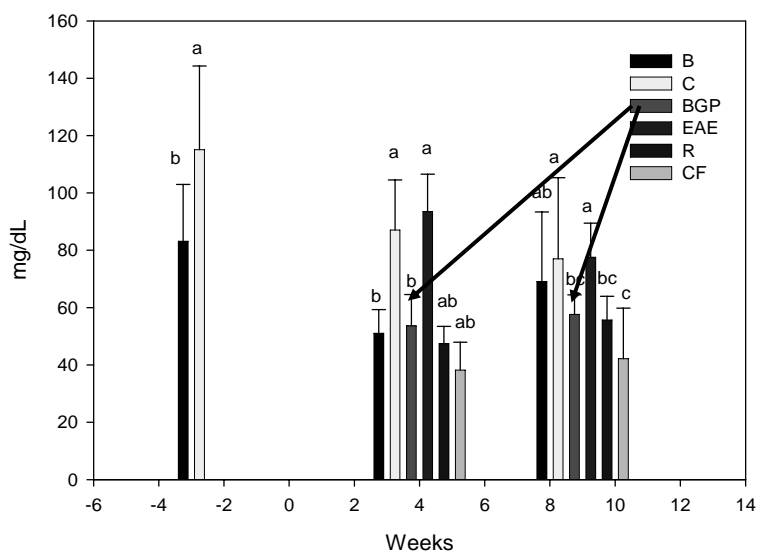
Area Under Curve of the OGTT after 11 weeks of test diets feeding



OGTT: Oral Glucose Tolerance Test

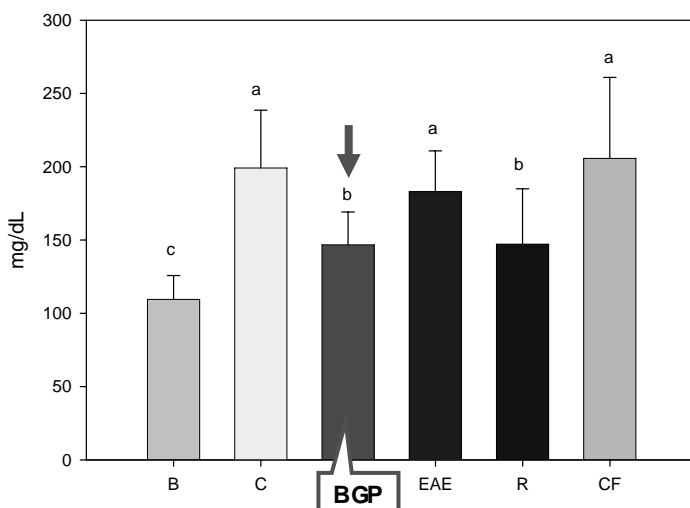
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### Plasma TG concentrations at 4 and 11 weeks of test diets feeding



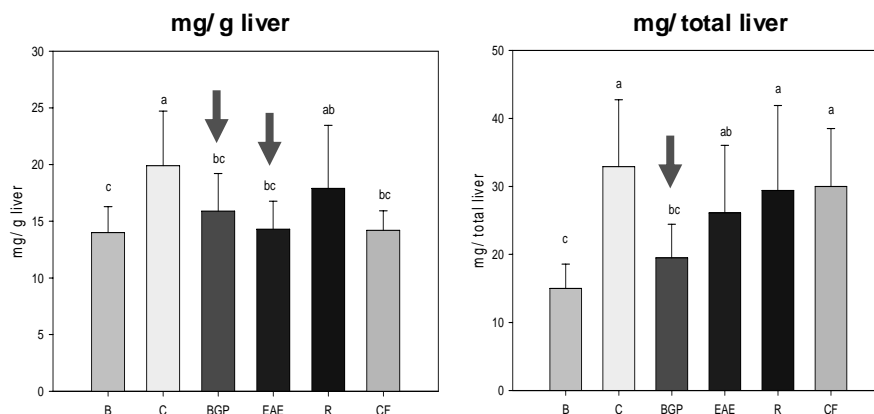
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### Plasma cholesterol concentrations after 11 weeks of test diets feeding



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## Liver TG after 11 weeks of test diets feeding



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## Summary

◆ **5% bitter gourd significantly improved**

1. Body weight gain
2. Hyperglycemia
3. Glucose intolerance
4. Hypertriglyceridemia
5. Hypercholesterolemia
6. Liver TG accumulation

◆ **0.25% EAE of bitter gourd**

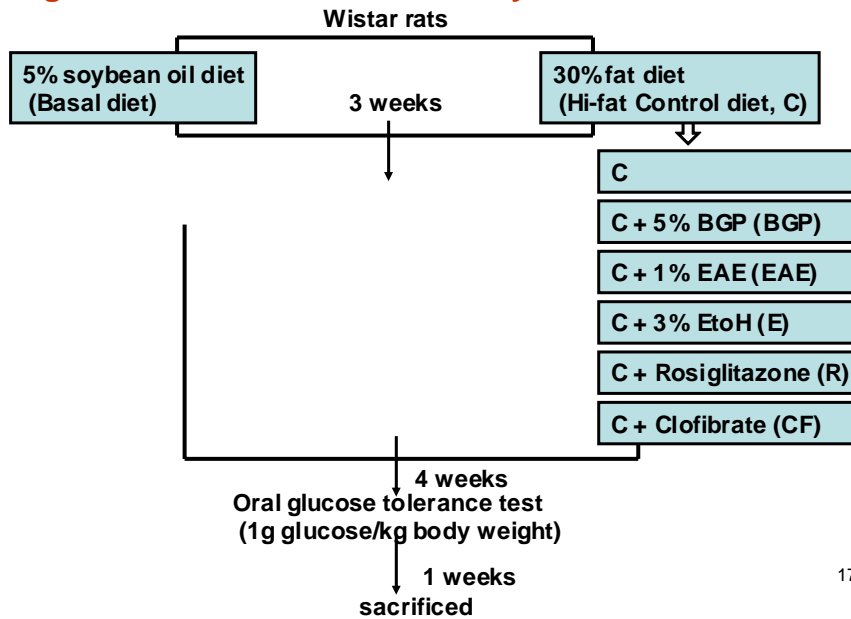
⇒ ameliorated the liver TG accumulation

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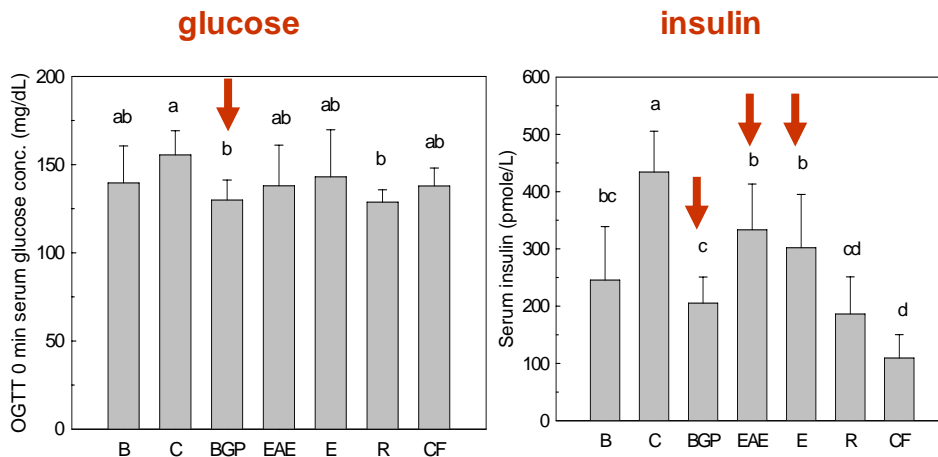


## Experimental II: Prevention study

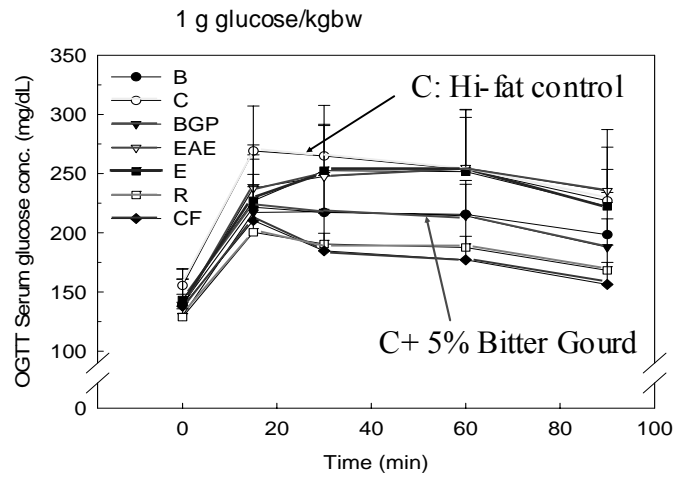
### A: High fat diet induced metabolic syndrome



## Plasma glucose and insulin at 4 weeks of test diets feeding



### (B) OGTT at Wk 4



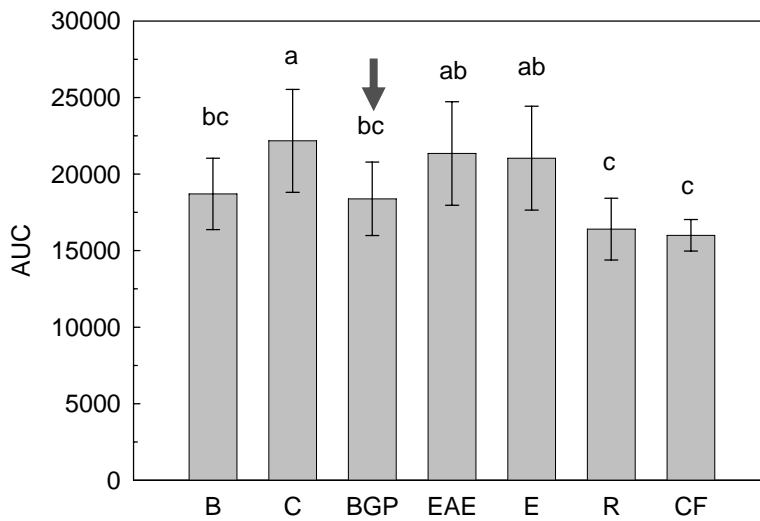
B, C, R, CF 組於實驗進行 15分鐘後血糖達最高值

BGP, E 組於實驗進行 30分鐘後血糖達最高值

EAE 組於實驗進行 60分鐘後血糖達最高值

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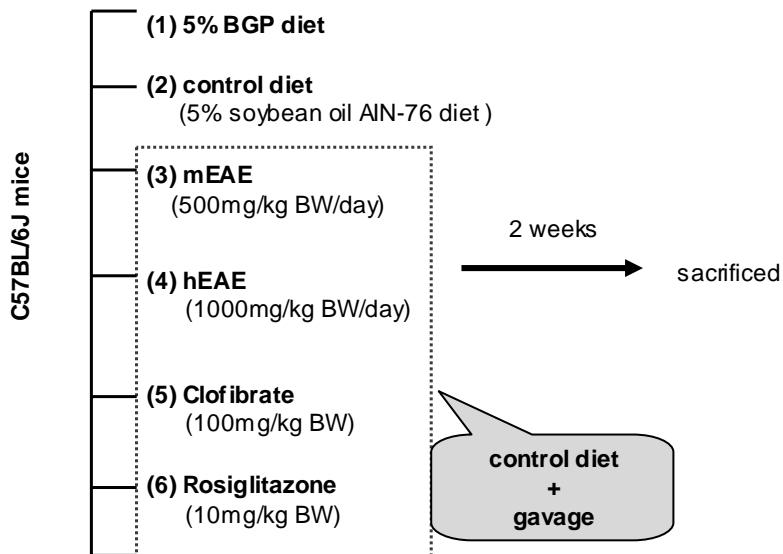
### Area Under Curve of the OGTT at 4 weeks of test diets feeding



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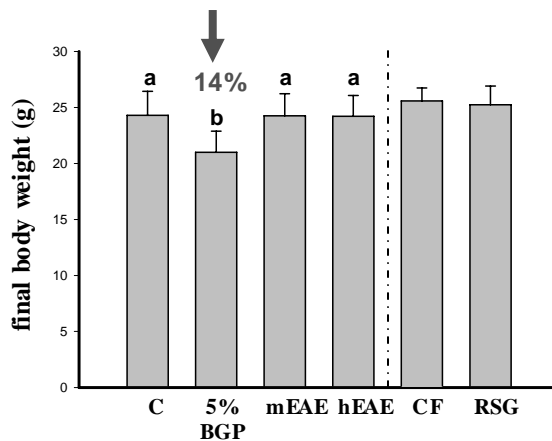
## Experimental II: prevention study

### B: Freeze-Dried Wild Bitter Gourd diet effects on C57BL/6J mice



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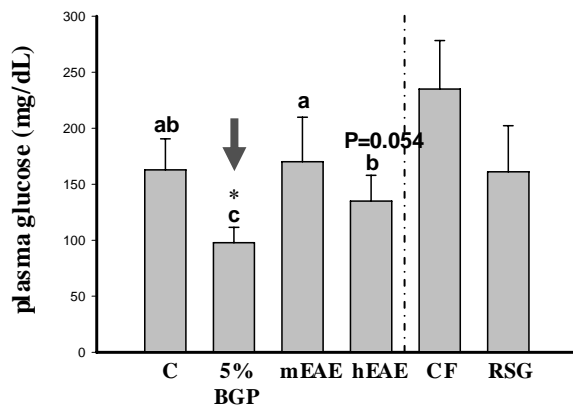
### Body weight



(Food and energy intake have no significant difference)

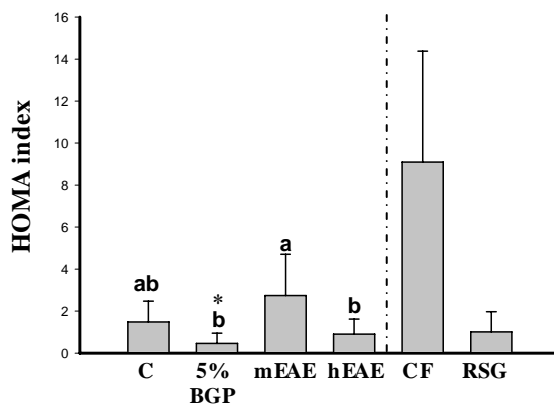
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### Plasma glucose concentrations



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### HOMA index



**HOMA (homeostasis model assessment) index**  
 = [fasting plasma glucose (mmol/L) x fasting plasma insulin ( $\mu$  M/mL) / 22.5] <sup>24</sup>

## Summary

### ◎ High fat diet induced obesity (Wistar rats)

- ◆ 5% bitter gourd significantly prevented
  1. Hyperglycemia
  2. Hyperinsulinemia
  3. Glucose intolerance
- ◆ 1% EAE of bitter gourd significantly prevented Hyperinsulinemia

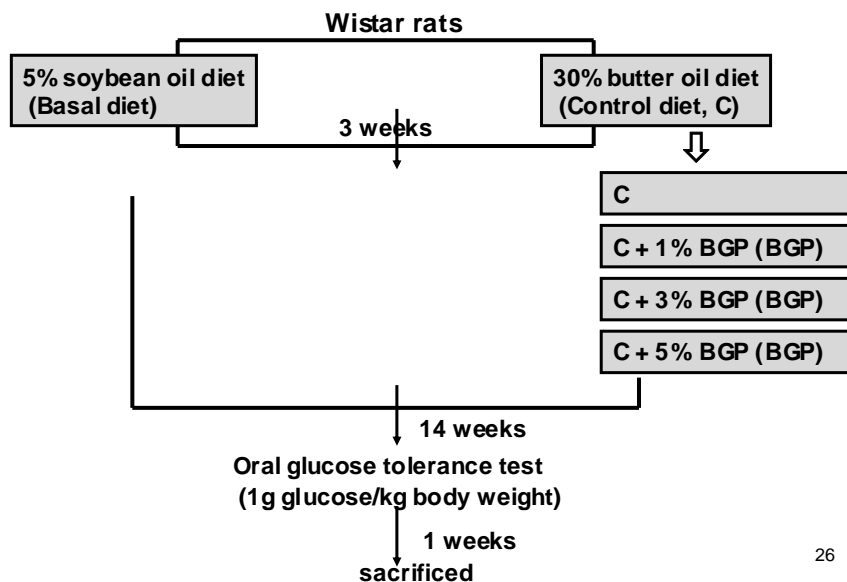
### ◎ C57BL/6J mice

- ◆ 5% bitter gourd significantly prevented
  1. Body weight gain
  2. Hyperglycemia

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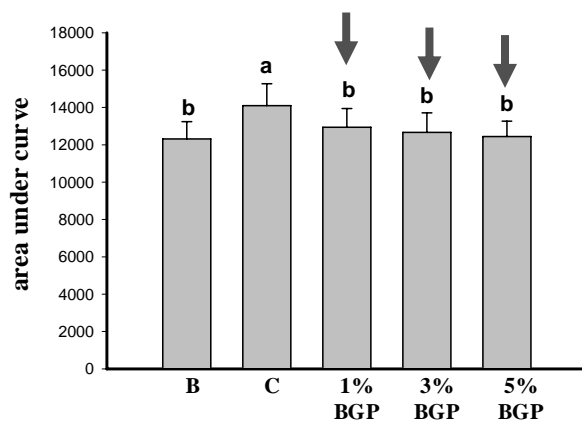
## Experimental III: dose-response study

### A: High fat diet induced metabolic syndrome



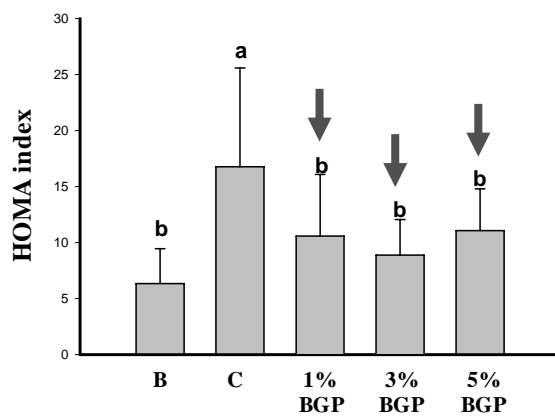
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### Area Under Curve of the OGTT



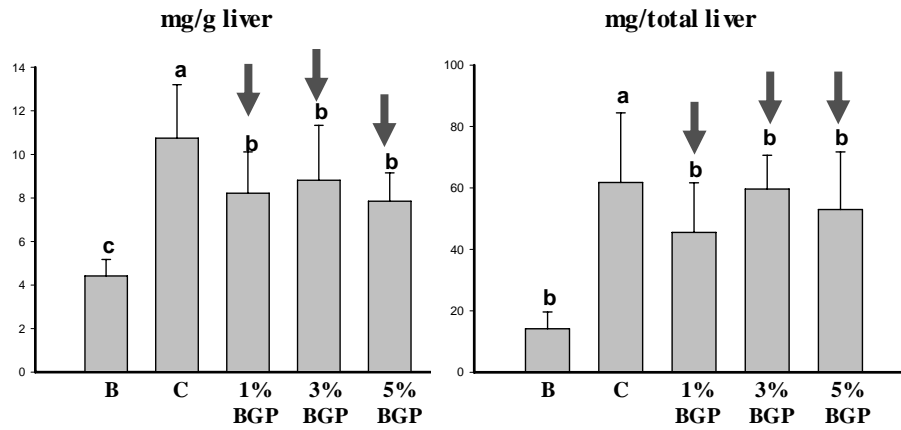
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### HOMA index



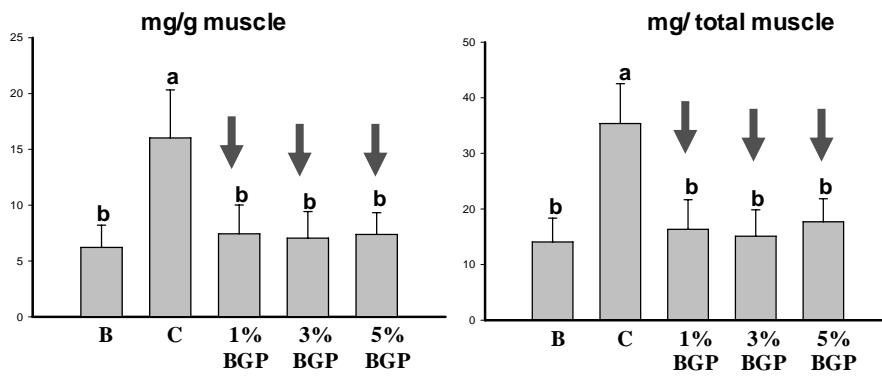
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### Liver cholesterol contents after 15 weeks of test diets feeding



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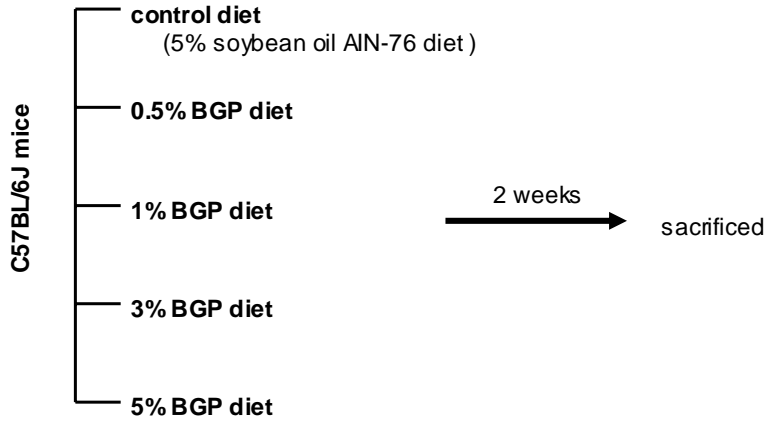
### Muscle TG contents after 15 weeks of test diets feeding



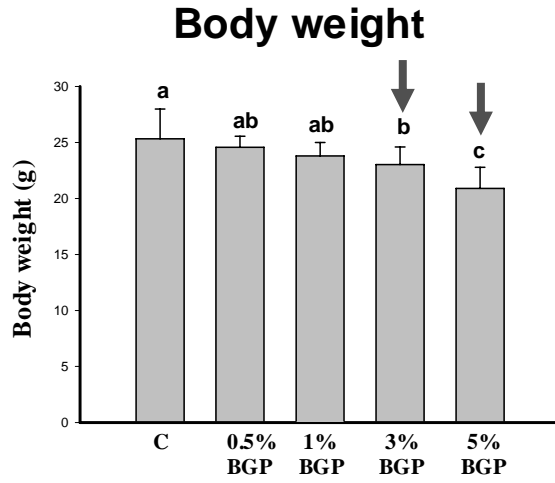
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## Experimental III: Dose-Response study

### B: Freeze-Dried Wild Bitter Gourd diet effects on C57BL/6J mice



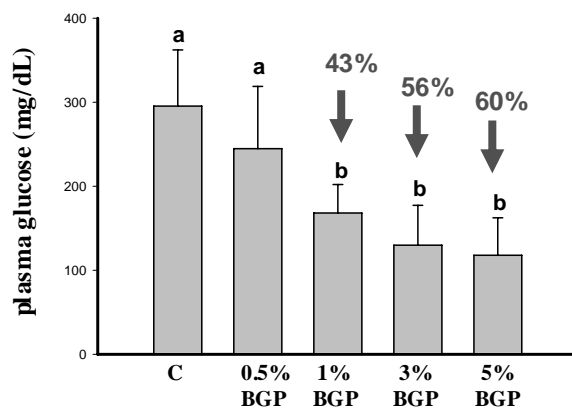
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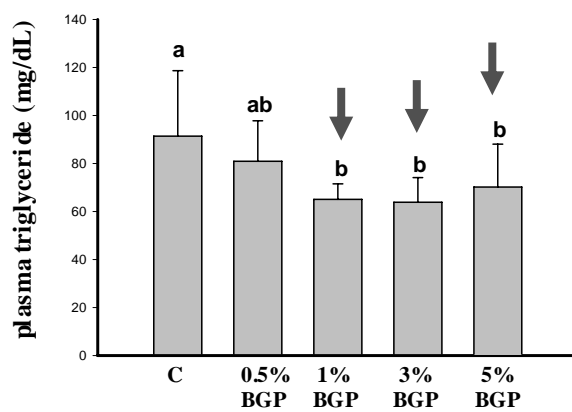


### Plasma glucose concentrations



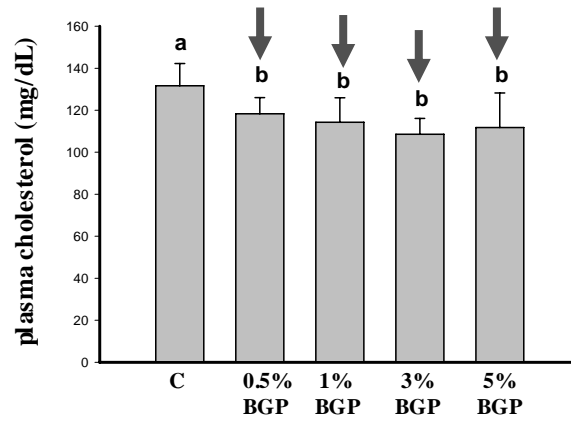
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### Plasma TG contents



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## Plasma CHOL concentrations



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## Conclusion

### ◎ 1% bitter gourd diet significantly prevented

#### ◆ High fat diet induced obesity (Wistar rats)

1. Hyperinsulinemia
2. Glucose intolerance
3. Liver CHOL accumulation
4. Muscle TG accumulation

#### ◆ C57BL/6J

1. Hyperglycemia
2. Hypertriglyceridemia
3. Hypercholesterolemia

### ◎ 1% bitter gourd diet

- ≈ 4.5 g dry bitter gourd powder/day
- ≈ 75 g fresh bitter gourd / day

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### summary

	Improved exp.		Prevented exp.			Dose-dependent exp.	
	C57BL/6J		Wistar		C57BL/6J	Wistar	C57BL/6J
	5% BGP	0.25% EAE	5% BGP	1% EAE	5% BGP	1% BGP	
Body weight	↓	-	-	-	↓	-	-
Hyperglycemia	↓	-	↓	-	↓	↓	↓
Glu. intolerance	↓	-	↓	-		↓	
Hyperinsulinemia	-	-	↓	-	↓	-	
Hypertryglyceridemia	↓		-	↓	-	-	↓
Hypercholesterolemia	↓	-	-	-	-	-	↓
Liver TG accumulation	↓	↓	-	-		-	
Liver CHOL accumulation	-	-	-	-		↓	
Muscle TG accumulation						↓	37

### Liver damage index: GOT and GPT

Group	GOT (U/I)	GPT (U/I)
Control	32.2 ± 15.4 <sup>b</sup>	11.3 ± 3.5 <sup>ab</sup>
5% BGP	39.7 ± 11.0 <sup>b</sup>	16.6 ± 6.6 <sup>a</sup>
mEAE	33.9 ± 10.7 <sup>b</sup>	10.6 ± 2.6 <sup>b</sup>
hEAE	65.3 ± 31.1 <sup>a</sup>	9.4 ± 4.9 <sup>b</sup>
Clofibrate	28.1 ± 5.6 <sup>b</sup>	10.2 ± 1.5 <sup>b</sup>
Rosiglitazone	40.7 ± 11.9 <sup>b</sup>	10.6 ± 1.0 <sup>b</sup>

Normal range:

GOT = 50~100 U/I

GPT = 20~50 U/I

吃得苦中苦，方為人上人