ultra nature®

amplifying the power of nature

Actiponin®

Encourages the body to burn fat

Uniquely able to restore balance and equilibrium to multiple bodily systems:

- Cardiovascular system
- Digestive system
- Immune system
- Nervous system
- Reproductive system

Product Overview

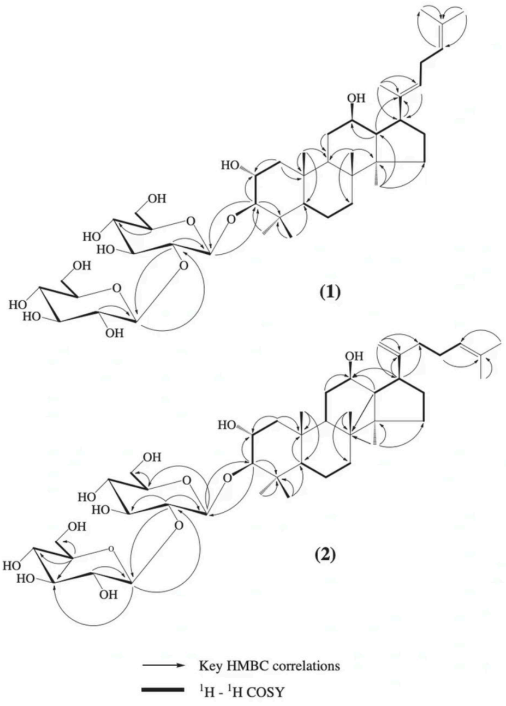
Actiponin® is a revitalizing botanical supplement that encourages the body to burn fat, particularly at the waistline. Patented in the US and supported by published clinical studies, Actiponin® promotes healthy metabolism at the cellular level. In clinical trials, Actiponin® reduced body fat mass, body weight, and abdominal fat in overweight people over a 12-week period.

Almost no anti-obesity drugs have been approved for long-term use by the US Food and Drug Administration. Drugs like orlistat (i.e. Xenical) reduce the absorption of fat in the intestines by inhibiting lipase, a pancreatic enzyme that catalyzes the breakdown of fats, while drugs like sibutramine (i.e. Meridia) suppress the appetite by blocking the re-uptake of certain neurotransmitters (dopamine, norepinephrine, and serotonin), though in 2010 Meridia was withdrawn from the markets in the United States and Canada because clinical studies revealed that it increased the risk of cardiovascular disease. Because they so often cause adverse side effects, anti-obesity drugs are generally prescribed only when the benefits of the treatment definitively outweigh the hazards. Proven to be both safe and effective, Actiponin® offers a novel—and natural—approach to weight loss.

Actiponin® is an ethanol extract of *Gynostemma pentaphyllum*, a five-leafed perennial that has been widely used as an herbal tea in Korea, China, and Japan for over five hundred years. Traditionally, *G. pentaphyllum* is used to regulate blood pressure, lower cholesterol, modulate inflammation, improve endurance, and increase longevity.

Derived from *G. pentaphyllum*, Actiponin® is uniquely able to restore balance and equilibrium to multiple bodily systems:

- Cardiovascular system
- Digestive system
- Immune system
- Nervous system
- Reproductive system



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Actiponin® activates the AMP-activated protein kinase (AMPK), an important intracellular sensor and regulator of glucose metabolism, lipid metabolism, and energy metabolism throughout the body. When activated, this powerful enzyme switches on catabolic ATP-generating pathways like fatty acid β-oxidation, glycolysis, and glucose uptake—processes that normally occur during intensive exercise or prolonged starvation—and switches off anabolic ATP-consuming pathways like fatty acid and cholesterol synthesis. The activation of the AMPK pathway has numerous physiological benefits:

- Reduction of body fat mass
- Reduction of blood glucose levels
- Reduction of blood cholesterol levels
- Increase of mitochondrial biogenesis
- Increase of exercise endurance
- Increase in longevity

Studies have shown that AMPK activation improves obesity and type-2 diabetes by stimulating fatty acid β-oxidation, glycolysis, and glucose uptake while simultaneously inhibiting the synthesis of fat and cholesterol in the liver. As such, AMPK activators like Actiponin® show immense promise as healthy solutions to obesity, diabetes, and dyslipidemia, a condition that increases the chance of heart attacks and strokes.

What's Novel about Actiponin®?

Actiponin®'s patented extraction and treatment process increases the content of two novel dammarane-type glycosides—Damulin A and Damulin B—both of which are powerful AMPK activators. Actiponin® is enriched with *ten times* more Damulin A and Damulin B than standard extracts of *G. pentaphyllum*, dramatically boosting its ability to transform stored fat into energy.

Studies have shown that, in a dose-dependent manner, Damulin A and Damulin B activate AMPK, improve fatty acid β-oxidation, and increase glucose uptake, thereby lowering blood glucose levels. Conventional extracts of *G. pentaphyllum* take from the plant's root and rhizome, or rootstalks, through a water-extraction process that yields crude saponin powder. By contrast, Actiponin® is ethanol-extracted from the plant's leaf and extensively heat-treated, producing a proprietary powder extract. Through this patented process, Actiponin® becomes enriched with high levels of Damulin A and Damulin B, making it a powerful AMPK activator—and an emerging target for healthy solutions to obesity.

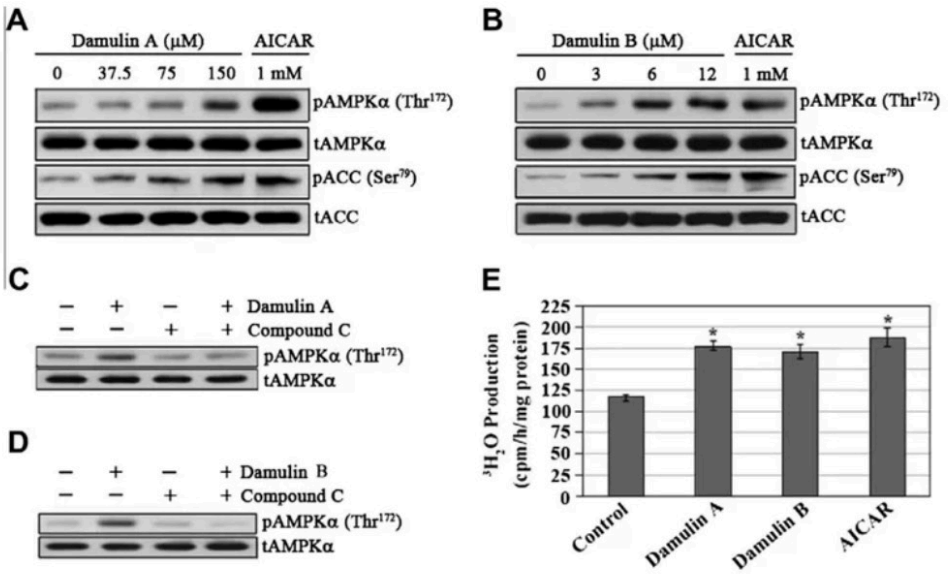

Figure 2. Effect of damulins A (**1**) and B (**2**) on AMPK activation and fatty acid oxidation in L6 myotube cells. L6 myotube cells were exposed to different doses of damulins A and B for 2 h or AICAR (1 mM) for 1 h, and phosphorylation of AMPK was analyzed with Western blotting. Damulins A (**A**) and B (**B**) increased phosphorylation of AMPK and ACC in a dose-dependent manner. Increased phosphorylation of AMPK induced by 150 μM damulin A (**C**) and 12 μM damulin B (**D**) was abrogated by pretreatment with compound C (10 μM) for 10 min. (**E**) Increased β-oxidation in cells by damulins A (150 μM) and B (12 μM). DMSO was used as a vehicle (control). AICAR (1 mM) was pretreated for 1 h. $^{*}P < 0.05$ compared with control.

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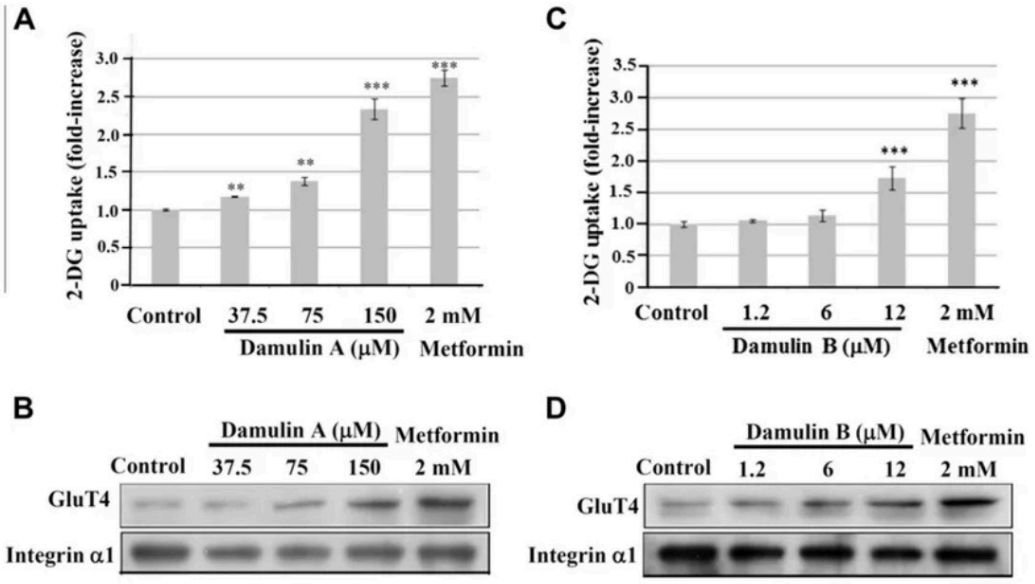

Figure 3. Dose-dependent increment of 2-DG uptake and GluT4 translocation to the cytoplasmic membrane in L6 myotube cells by damulins A and B. 2-DG uptake was increased by damulins A (**A**) and B (**C**). Stimulation of GluT4 translocation to the cytoplasmic membrane by damulins A (**B**) and B (**D**). Damulins A and B were treated to cells for 2 h and metformin was treated for 1 h. As a control DMSO was treated to cells. Cytoplasmic membrane faction of cell lysates (30 μg) was subjected to Western blot analyses. Data are the means ± S.D. of three experiments. $^{**}P < 0.01$; $^{***}P < 0.001$ versus control.

Differences between Actiponin® and conventional *Gynostemma pentaphyllum*

Name	Actiponin®	*Gynostemma pentaphyllum*
Source	*G. pentaphyllum* (leaf)	*G. pentaphyllum* (root and rhizome)
Production Method	Patented, ethanol-extracted, heat-treated powder extract	Water-extracted crude saponin powder
Effect	Reduces body fat mass	Adaptogen
Damulin A Content	NLT 1.2% (w/w)	No
AMPK Activation	Yes	N/A
QC Indicator (Active Biomarker)	Damulin A	N/A
Published Clinical Data	Yes	N/A
GLP Toxicology Data	Yes	N/A
Daily Dose	450 mg	1500-2000 mg

In-vitro and In-vivo Studies

In clinical studies, a heat-processed extract of *G. pentaphyllum* containing Damulin A and Damulin B stimulated fatty acid **β**-oxidation, glycolysis, and glucose uptake by activating AMPK. This extract (referred to as "actiponin" in the figures below) inhibited the formation of fat cells and increased the oxidation of fat cells. In other words, it burned fat—effectively *and* safely.

Rich in Damulin A and Damulin B, the proprietary extract of *G. pentaphyllum* activated AMPK, stimulated the uptake of glucose, and increased fatty acid **β**-oxidation, important steps towards treating diabetes and promoting health.

In clinical trials with pre-obese *ob/ob* mice, the extract of *G. pentaphyllum* reduced body weight gain and total cholesterol levels over the course of 8 weeks. Decreases in body weight gain were accompanied by reduced fat contents in the epididymis (the tube that connects a testicle to a vas deferens in the male reproductive system), the retroperitoneum (the space located behind the abdominal or peritoneal cavity), and the liver. As the study showed, Damulin A and Damulin B were successfully delivered to the skeletal muscle and liver, activating AMPK in these organs, stimulating fatty acid **β**-oxidation, and ultimately preventing or improving obesity.

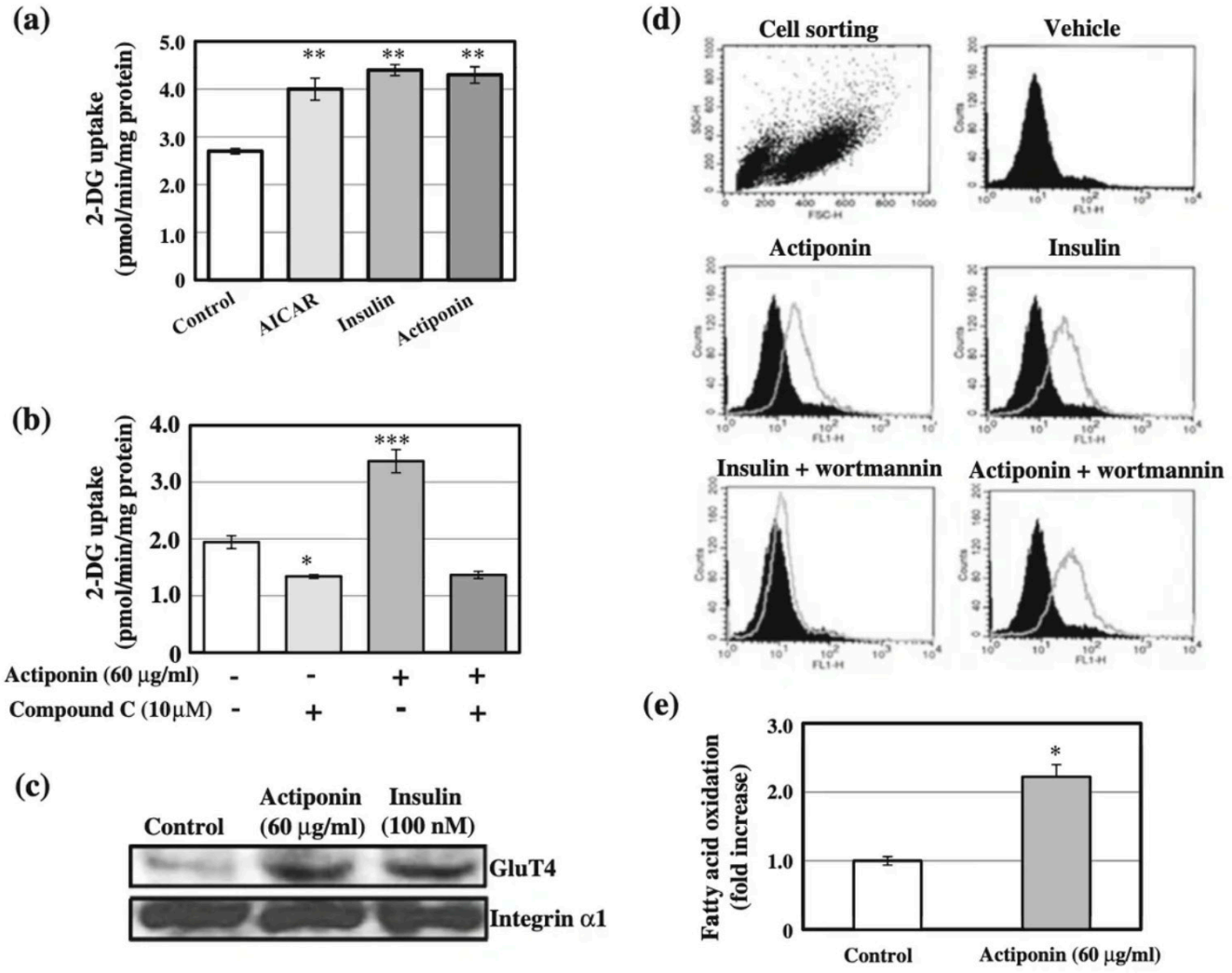

Fig. 3 Effect of actiponin on AMPK activation and GluT4 translocation in L6 myotubes. **a** Stimulation of 2-DG uptake in L6 myotubes by actiponin (60 μg/ml) treatment for 2 h. Cells were also treated with AICAR (1 mM) or insulin (100 nM) for 1 h and 10 min, respectively. **b** Increase in 2-DG uptake by L6 myotubes treated with actiponin (60 μg/ml) was blocked by pretreatment with compound C (10 μM) for 10 min. **c** Translocation of GluT4 to plasma membranes by actiponin and insulin. The plasma membrane fraction of cell lysates (30 μg) was subjected to Western blotting with respective antibodies. **d** FACS analysis of GluT4 translocation to the cell membrane. Cells were treated with actiponin (60 μg/ml, 2 h) and insulin (100 nM, 10 min) in the presence or absence of wortmanin (100 nM) pretreatment for 30 min. **e** Fatty acid oxidation increased by actiponin treatment for 2 h in L6 myotubes. Control cells were treated with DMSO. **a**, **b**, **e** Data were obtained for three independent experiments. $*P < 0.05$; $**P < 0.01$; $***P < 0.005$ compared to the control

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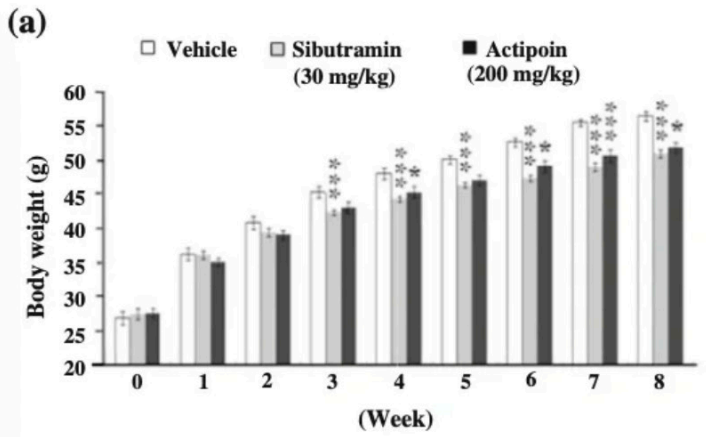

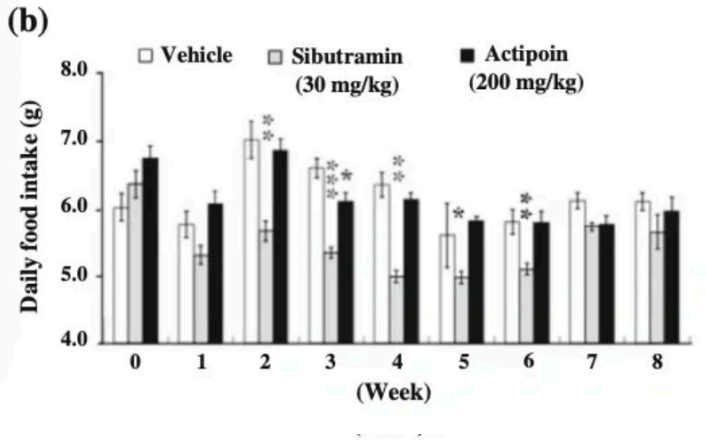

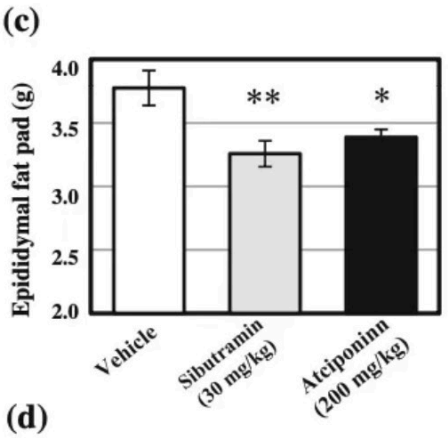

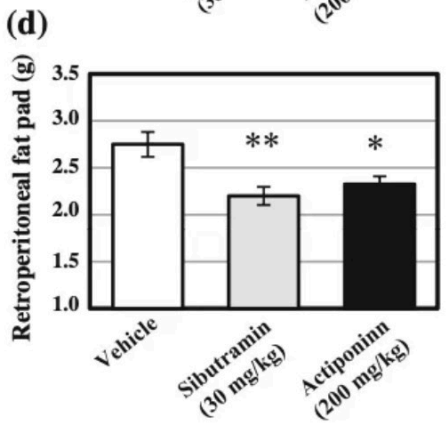

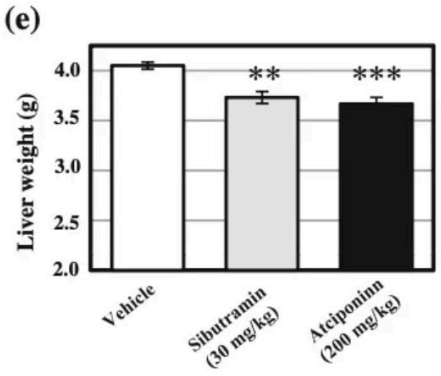

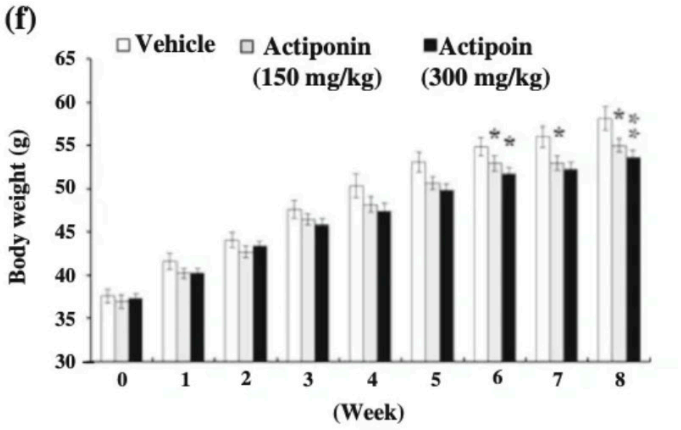

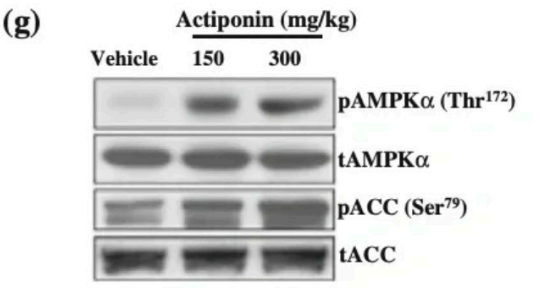

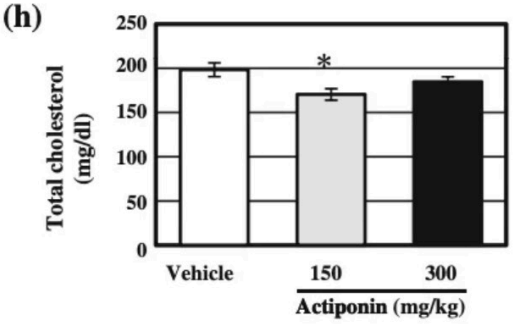

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Human Clinical Study Results

The human clinical study measured both the efficacy (abdominal fat distribution, anthropometric parameters, and blood lipid profiles) and the safety (adverse events, laboratory test results, electrocardiogram data, and vital signs) of the ethanol extract of *G. pentaphyllum*.

In a 12-week, randomized, double-blinded, placebo-controlled clinical trial, 74 obese participants were given either the *G. pentaphyllum* extract or a placebo. Each participant had a body mass index ≥ 25 kg. Males had a waist-hip ratio ≥ 0.90, and females had a waist-hip ratio ≥ 0.85.During the 12-week period, participants were asked to maintain their usual diets, refrain from consuming dietary supplements, and adhere to their normal levels of physical activity. Every four weeks, the participants were asked to report any changes in training, lifestyle, or eating patterns.

TABLE 2 Demographic characteristics of the study participants[a]

	Actiponin group ($n = 40$)	Placebo group ($n = 40$)	P[b]
Age (years)	40.10 ± 1.53	40.05 ± 1.83	0.983
Height (cm)	165.78 ± 1.36	162.90 ± 1.41	0.146
Weight (kg)	76.56 ± 1.36	73.41 ± 1.55	0.126
BMI (kg m^{-2})	27.80 ± 0.19	27.55 ± 0.20	0.364
Sex			
Male	22 (55)[c]	10 (25)	0.006[d]
Female	18 (45)	30 (75)	

[a]All values are presented as the mean ± S.E.
[b]Derived from an independent student's *t* test. No significant differences between the two groups were observed.
[c]*N* (%)
[d]Derived from a chi-square test. Statistically significant compared to the placebo group ($P < 0.05$).

After 12 weeks, the study revealed statistically significant reductions in the following areas:

- Total abdominal fat area
- Body weight
- Body mass index (BMI)
- Body fat mass
- Percent body fat

Decreases were also found in:

- Areas of visceral fat in the abdomen
- Areas of subcutaneous fat
- Waist circumference
- Total cholesterol
- Triglycerides
- High-density lipoprotein (HDL cholesterol)
- Low-density lipoprotein (LDL cholesterol)

Blood test results and vital signs stayed within normal ranges, indicating an absence of adverse side effects.As the clinical trial shows, ethanol extracts of *G. pentaphyllum* like Actiponin®—enriched with AMPK activators Damulin A and Damulin B—are proven to reduce abdominal fat, body weight, body mass index, body fat, waist circumference, and cholesterol.

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TABLE 3 Abdominal fat area of the actiponin and the placebo groups measured at 0- and 12-week of the study[a]

	Actiponin group ($n = 40$)				Placebo group ($n = 40$)				
Parameters	0-wk	12-wk	Difference	P^b	0-wk	12-wk	Difference	P^b	P^c
Total abdominal fat (cm^2)	332.24 ± 10.65	311.35 ± 9.04	−20.90 ± 8.29	0.016	335.36 ± 7.24	333.05 ± 8.36	−2.87 ± 3.73	0.447	0.044
Visceral fat (cm^2)	106.84 ± 6.61	95.97 ± 5.23	−11.70 ± 5.65	0.046	98.78 ± 4.85	96.68 ± 4.79	−2.92 ± 2.21	0.195	0.146
Subcutaneous fat (cm^2)	225.40 ± 8.55	215.38 ± 8.06	−8.70 ± 3.54	0.019	236.57 ± 9.08	236.37 ± 10.17	0.05 ± 3.85	0.990	0.092
VSR[d]	0.51 ± 0.04	0.47 ± 0.04	−0.04 ± 0.02	0.075	0.47 ± 0.04	0.47 ± 0.04	−0.00 ± 0.02	0.801	0.203

[a]All values are presented as the mean ± S.E.
[b]Derived from a paired *t* test. Statistically significant compared to the baseline ($P < 0.05$).
[c]Derived from the linear mixed-effects model adjusted for gender. Statistically significant compared to the placebo group ($P < 0.05$).
[d]VSR, visceral subcutaneous ratio.

TABLE 4 Anthropometric parameters of the actiponin and the placebo groups measured at 0-, 4-, 8-, and 12-week of the study[a]

	Actiponin group ($n = 40$)					Placebo group ($n = 40$)					
Parameters	0-wk	4-wk	8-wk	12-wk	P^b	0-wk	4-wk	8-wk	12-wk	P^b	P^b
Body weight (kg)	76.56 ± 8.31	76.26 ± 8.35	75.57 ± 8.18[c]	75.21 ± 8.20[c]	<0.0001	73.41 ± 9.79	73.53 ± 9.79	73.33 ± 9.98	73.33 ± 10.17	0.187	0.021
Body mass index ($kg\ m^{-2}$)	27.80 ± 1.21	27.69 ± 1.17	27.44 ± 1.28[c]	27.31 ± 1.24[c]	<0.0001	27.55 ± 1.27	27.61 ± 1.36	27.54 ± 1.45	27.55 ± 1.54	0.159	0.029
Body fat mass (kg)	22.65 ± 3.12	22.28 ± 3.45	21.89 ± 3.35[c]	21.40 ± 3.62[c]	<0.0001	23.04 ± 3.55	23.17 ± 3.61	23.15 ± 3.8	23.32 ± 3.82	0.147	<0.0001
Percent body fat (%)	29.95 ± 5.4	29.56 ± 5.73	29.31 ± 5.56[c]	28.79 ± 5.87[c]	<0.0001	31.76 ± 5.39	31.91 ± 5.62	31.96 ± 5.68	32.13 ± 5.4	0.018	<0.0001
Waist circumference (cm)	93.69 ± 4.85	92.26 ± 5.03[c]	91.65 ± 4.62[c]	91.07 ± 5.11[c]	<0.0001	92.23 ± 4.03	91.57 ± 4.55	91.46 ± 4.25[c]	91.04 ± 4.50[c]	0.0001	0.060
Hip circumference (cm)	99.85 ± 3.30	99.41 ± 3.28	99.21 ± 3.39[c]	98.85 ± 3.40[c]	<0.0001	99.86 ± 4.28	99.81 ± 4.62	99.76 ± 4.59	99.68 ± 4.83	0.257	0.127

[a]All values are presented as the mean ± S.E.
[b]Derived from the linear mixed-effects model adjusted for gender. Statistically significant compared to the placebo group ($P < 0.05$).
[c]Multiple comparison by Bonferroni correction. Statistically significant difference compared to baseline (0-wk).

TABLE 5 Lipid profiles of the actiponin and placebo groups at 0-, 8- and 12-wk[a] of the study

	Actiponin group ($n = 40$)				Placebo group ($n = 40$)				
Parameters	0-wk	8-wk	12-wk	P^b	0-wk	8-wk	12-wk	P^b	P^b
Total cholesterol ($mg\ dL^{-1}$)	195.50 ± 5.03	185.97 ± 4.98	185.97 ± 29.9	0.055	190.40 ± 4.93	190.42 ± 5.89	190.42 ± 36.3	0.865	0.461
Triglycerides ($mg\ dL^{-1}$)	134.35 ± 9.60	117.28 ± 8.71	117.28 ± 52.26	0.336	136.40 ± 13.88	143.03 ± 12.44	143.03 ± 76.67	0.717	0.316
HDL-C ($mg\ dL^{-1}$)	44.43 ± 1.32	41.64 ± 1.01	41.64 ± 6.05	0.018	47.35 ± 1.71	44.37 ± 1.59	44.37 ± 9.78	0.052	0.946
LDL-C ($mg\ dL^{-1}$)	119.75 ± 4.22	111.61 ± 4.11	111.61 ± 24.67	0.060	113.03 ± 4.71	107.97 ± 4.88	107.97 ± 30.11	0.155	0.901
FFA ($uEq\ L^{-1}$)	582.48 ± 29.50	602.03 ± 31.42	602.03 ± 188.53	0.592	591.83 ± 33.47	608.45 ± 27.97	608.45 ± 172.39	0.223	0.197
Apo A1 ($g\ L^{-1}$)	1.41 ± 0.04	1.35 ± 0.03	1.35 ± 0.18	0.165	1.43 ± 0.04	1.43 ± 0.04	1.43 ± 0.25	0.158	0.202
Apo B ($g\ L^{-1}$)	0.89 ± 0.03	0.85 ± 0.03	0.85 ± 0.19	0.119	0.85 ± 0.03	0.86 ± 0.03	0.86 ± 0.19	0.846	0.692

[a]All values are presented as the mean ± S.E.
[b]Derived from the linear mixed-effects model adjusted for gender. No statistically significant differences between the two groups were observed.
Multiple comparison by Bonferroni correction. Statistically significant difference compared to baseline (0-wk).

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Safety Study Results

1. A Single-Dose Oral Toxicity Study in Sprague-Dawley rats revealed:
   - No animal deaths were observed
   - In clinical signs, diarrhea and soiled perineal region were observed in males and females at 2,000 and 5,000 mg/kg on the day of administration
   - No abnormal body weight changes were observed during the study
   - No abnormal necropsy findings were observed in any animals
   - The minimal lethal dose (MLD) of TG1022F in rats is higher than 5,000 mg/kg
2. 4-week Oral Dose Range Finding (DRF) Toxicity Study in Sprague-Dawley rats revealed:
   - The 4-week repeated oral administration of Actiponin® induced no adverse effects in clinical signs, mortality, body weight changes, food and water consumption, ophthalmology, urinalysis, hematology, serum biochemistry, necropsy findings, and organ weights at all dose levels tested
   - Based on these results, 2,000 mg/kg/day is considered to be an appropriate high dose
3. A Bacterial Reverse Mutation Test revealed:
   - Actiponin® does not induce reverse mutation in the tester strains used in the present study
4. Micronucleus Tests in the Bone Marrow Cells of Male Institute of Cancer Research (ICR) Mice revealed:
   - There was no statistically significant increase in the frequency of micronucleated polychromatic erythrocytes (MNPCEs) at all dose levels tested
5. A 13-Week Repeated Dose Oral Toxicity Study in Sprague-Dawley Rats revealed:
   - No animal deaths were observed
   - Continuous diarrhea and soiled perineal regions were observed in male and female 2,000 mg/kg/day groups during the study period
   - There were no treatment-related changes in body weight, food and water consumption, ophthalmology, urinalysis, blood related examinations, organ weights, necropsy and histopathological findings
   - Under the present experimental conditions, the no observed effect level (NOEL) for male and female rats is considered to be 1,000 mg/kg/day, and the NOAEL (no observed adverse effect level) is 2,000 mg/kg/day

Published Studies

1. "New dammarane-type glucosides as potential activators of AMP-activated protein kinase (AMPK) from *Gynostemma pentaphyllum*," P. H. Nguyen, et al., *Bioorganic & Medicinal Chemistry*, 19, 6254-6260 (2011).
2. "Heat-processed *Gynostemma pentaphyllum* extract improves obesity in ob/ob mice by activating AMP-activated protein kinase," R. Gauhar, et al., *Biotechnology Letters*, 34, 1607-1616 (2012).
3. "Antiobesity Effect of Gynostemma pentaphyllum Extract (Actiponin): A Randomized, Double-Blind, Placebo-Controlled Trial," S. Park, et al., *Obesity*, 22(1), 63-71 (2014).

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