RESEARCH OVERVIEW

InnoSlim®

Supporting Healthy Weight Management

GRAS Affirmed
GENERALLY RECOGNIZED AS SAFE

nulivscience.com

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We are committed to the dissemination of accurate and unbiased information. Our goal is to contribute to the understanding of its potential benefits and limitations. For any inquiries, clarifications, or further information, please do not hesitate to contact us.

Thank you for your interest in our research overview.

A NEW GENERATION METABOLIC NEUTRACEUTICAL

18 *in-vitro*, 2 *in-vivo*, 2 human clinicals

Published in Journal of Biochemistry and Biotechnology
Journal of Agricultural and Food Chemistry (2007 & 2010)
Molecular Pharmacology
Adaptive Medicine

NPN 80089461

Pennies per serving

KEY BENEFITS

↑ ACC IN FAT CELLS

↑ IN ADIPONECTIN

↑ AMPK IN FAT CELLS

INDICATORS OF METABOLIC WELLNESS

In the intricate web of human physiology, several key players influence our body's health and vitality.

- **Adiponectin** is a protein hormone that helps regulate glucose levels and the burning of fatty acids. When adiponectin levels are high, it reduces the formation of fat cells and increases the body's energy expenditure. This hormone plays a crucial role in maintaining a healthy weight & overall healthy body.

- **Adenosine monophosphate-activated protein kinase (AMPK)** is an enzyme that helps maintain the body's energy balance. When AMPK is activated, it encourages the burning of fatty acids in the liver and muscles, the uptake of glucose in muscles, and helps reduce cholesterol and triglyceride synthesis.

- **Glucose transporter type 4 (GLUT4)** is a glucose transporter that responds to insulin. When there are more GLUT4 transporters, it allows muscles to take in more glucose, helping the body manage blood sugar levels.

- **Acetyl-CoA carboxylase (ACC)** is an enzyme that influences the break-down of fatty acids from carbohydrates. Inhibiting or deactivating ACC reduces the formation of fatty acids.

- **Hypoxia-inducible factor 1 (HIF-1)** is a transcription factor that helps the body adapt to low oxygen levels and energy shortages. Activating HIF-1 has a positive impact on the process of glycolysis, oxygen levels, and overall energy balance.

- **Sodium-glucose cotransporter 1 (SGLT1)** is a transporter that moves glucose and galactose from the gut into the body, serving as the first
- step in absorbing sugars from the diet.

- **Plasminogen Activator Inhibitor-1 (PAI-1)** plays a role in regulating blood clotting and tissue repair processes within the body. While not a direct driver of weight gain, increased PAI-1 may contribute to health issues related to obesity, which could indirectly impact weight management.

INDICATORS OF METABOLIC WELLNESS

- **Retinol-Binding Protein 4 (RBP4)**: is linked to glucose regulation, changes in RBP4 levels may affect an individual's ability to manage their weight effectively.

- **Tumor Necrosis Factor-α (TNFα)** plays a role in various bodily functions. Within fat tissue, TNFα may be released in response to certain conditions, affecting the balance of inflammatory and anti-inflammatory factors and, consequently, overall health.

These physiological factors play vital roles in maintaining our body's equilibrium, influencing energy regulation, glucose control, and overall well-being. As we strive to promote a healthy lifestyle, it's important to recognize how these elements interact, with changes in fat tissue potentially affecting inflammation and holistic health.

DISCOVER INNOSLIM®

InnoSlim® is a stimulant-free, plant-based ingredient made from purified extracts of *Astragalus membranaceus* and *Panax notoginseng*.

InnoSlim® has been extensively studied, with 18 *in-vitro*, two *in-vivo*, and two human clinical trials published in the Journal of Biochemistry and Biotechnology, Journal of Agricultural Food Chemistry, Molecular Pharmacology, and Adoptive Medicine. These studies demonstrated an increase in adiponectin and activated AMPK pathway, promoting glucose uptake and fat oxidation to help stabilize glucose levels and improve energy utilization.

The release of adiponectin in fat cells triggers the AMPK pathway in muscles. This helps burn stored fat and helps improve the muscles' ability to use glucose. These effects were demonstrated in preclinical studies and further supported by two human trials, emphasizing the positive influence on glucose and fat levels.

Specifically, InnoSlim® has demonstrated:

- Increased adiponectin in normal cells by 103% and in insulin-resistant cells by 248%
- Increased AMPK expression levels in muscle by 52% and in fat cells by 300%
- Increased GLUT4 expression level in muscle by 46% and in fat cells by 488%
- Increased glucose absorption in muscle by 50%
- Increased glucose absorption in fat cells by 68% and enhanced fatty acid breakdown by 100%
- Decreased glucose absorption in Caco-2 cells by 41%
- Reduced glucose levels in rats by 11%
- Increased insulin sensitivity in rats by 38%
- Reduced inflammatory biomarkers PAI-1 by 11%, RBP4 by 31%, and TNFα by 61% in normal cells
- Reduced inflammatory biomarkers PAI-1 by 53%, RBP4 by 67%, and TNFα by 38% in insulin-resistant cells
- Increased ATP production in liver cells by 22%

DISCOVER INNOSLIM®

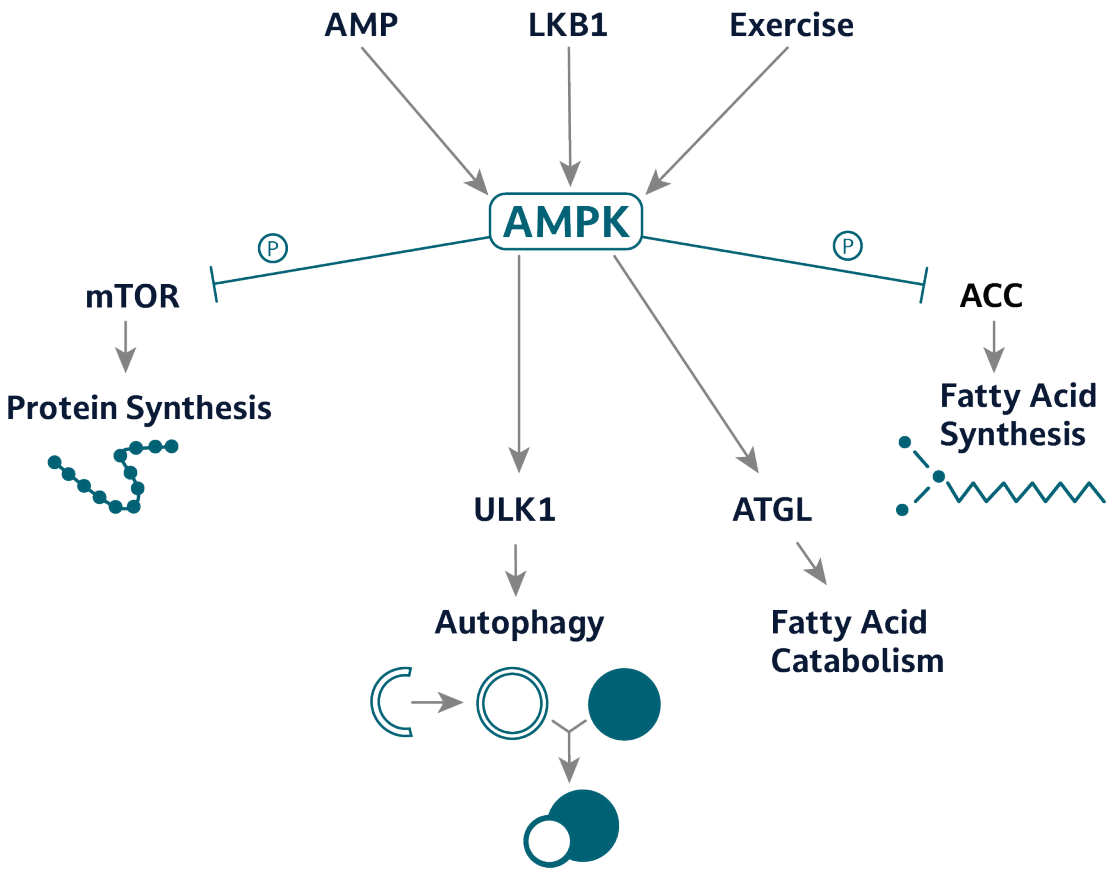
Excess glucose circulating in the bloodstream is typically stored as fat. Prolonged elevated blood glucose levels can lead to less efficient energy utilization in the body. InnoSlim® works by reducing glucose absorption in the intestines through the downregulation of the glucose transporter SGLT1. At the same time, it enhances glucose uptake in muscle and fat cells by increasing the activity of the glucose transport protein GLUT4. These combined effects could lead to a decrease in both circulating blood glucose levels and the accumulation of fat.

InnoSlim® has demonstrated to help mitigate fat accumulation by inhibiting ACC activation (ACC-P) through the Adiponectin-AMPK pathway. Furthermore, adipose tissue can contribute to inflammation and disruptions in glucose regulation. InnoSlim® effectively reduces inflammatory biomarkers such as PAI-1, RBP4, and TNFα within fat cells, potentially promoting better metabolic balance.

The cumulative impact of these effects suggests that InnoSlim® has the potential to initiate a shift in energy balance that favors the breakdown of fatty acids, which can have a positive impact on overall metabolic function. For more details, please refer to the specific scientific papers.

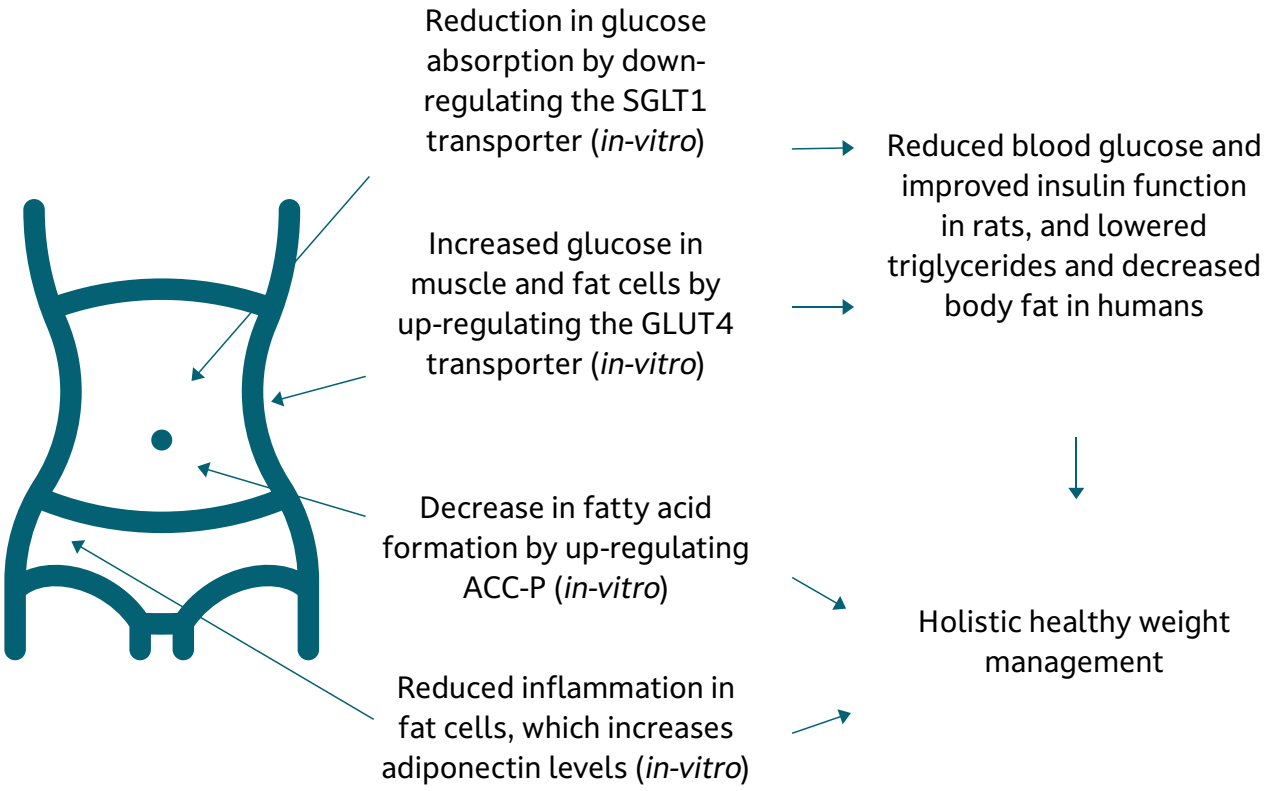
HOW INNOSLIM® WORKS

AMPK Signaling Pathway



Think of AMPK as a traffic controller influenced by AMP, LKB1, exercise, and InnoSlim®. When InnoSlim® activates AMPK, it sets off a chain reaction. AMPK boosts protein-making (mTOR), kickstarts cell cleaning (ULK1), encourages burning fat for energy (ATGL), and slows down fat production (ACC). InnoSlim's role is crucial in keeping this metabolic orchestra in tune.

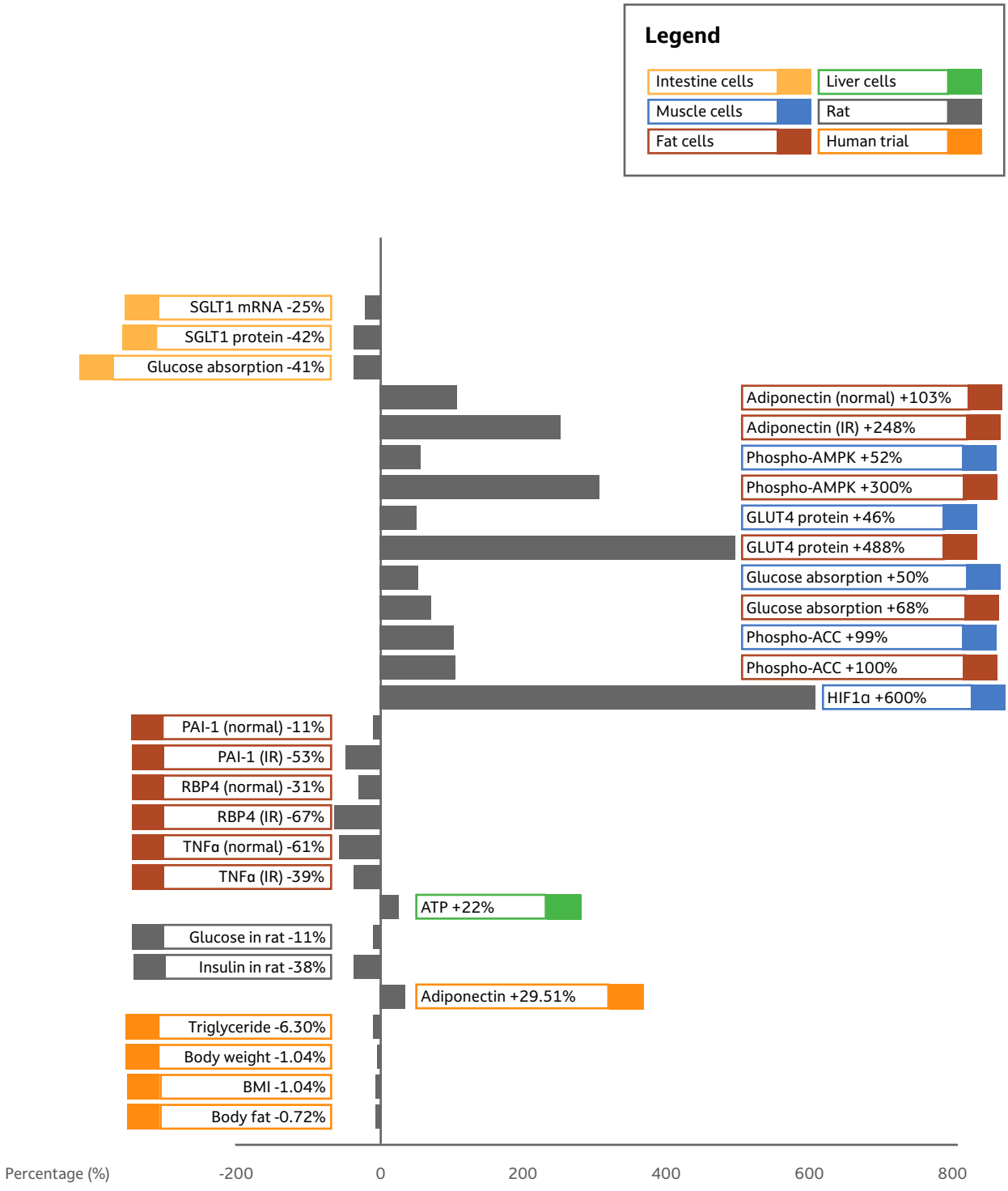
HOW INNOSLIM® WORKS



InnoSlim® demonstrates a multi-faceted approach to fostering holistic healthy weight management. It achieves this by helping to reduce glucose absorption, enhance glucose uptake by muscle and fat cells, inhibit fatty acid formation, and reduce inflammation in fat cells, which elevates adiponectin levels. These *in-vitro* mechanisms translate into meaningful potential benefits, including improved glucose levels and reduced fat accumulation in both rats and humans based on research findings to-date. These outcomes help to support the role InnoSlim® plays in supporting a holistic approach to maintaining a healthy weight.

Reference: 1, 2, 3, 5, 8, 10, 11, 12

KEY FINDINGS



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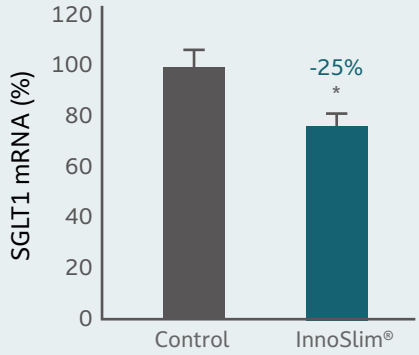
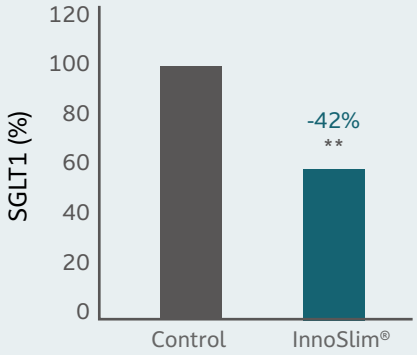
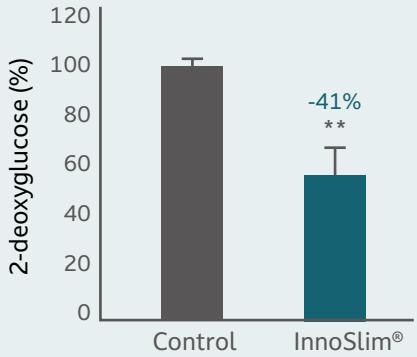
INNOSLIM® DECREASES GLUCOSE ABSORPTION IN THE INTESTINE (IN-VITRO)



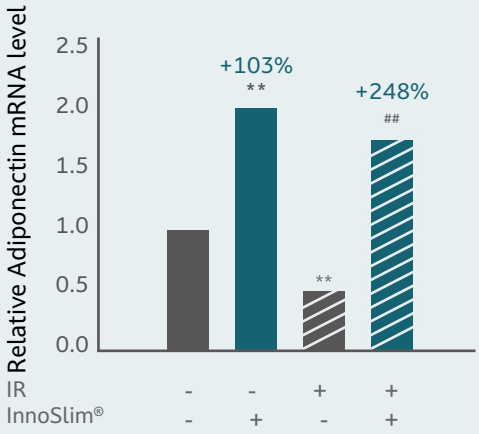




*p < 0.05, when compared to the control group
**p < 0.01, when compared to the control group

Decreased SGLT1 mRNA leads to decreased SGLT1 transport protein to decreased glucose absorption in intestinal cell (Caco-2 cell)

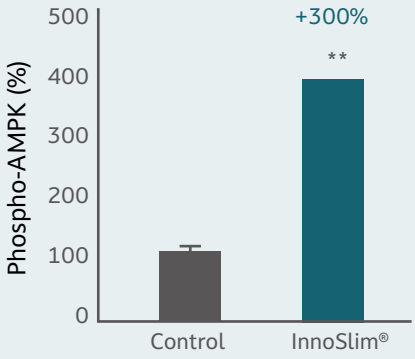
INNOSLIM® INCREASES ADIPONECTIN mRNA IN FAT (3T3-L1) CELL



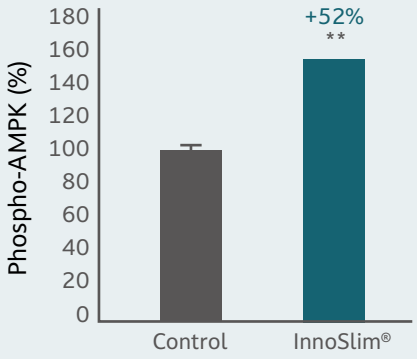
**p < 0.01, when compared to the control group
##p < 0.01, when compared to the IR group

Adiponectin is a protein hormone known for its role in regulating glucose levels and fatty acid oxidation. Increased adiponectin levels are associated with reduced fat cell formation and enhanced energy expenditure. InnoSlim® has demonstrated an ability to increase adiponectin levels in normal fat cells by 103% and in palmitate-induced insulin resistance (IR) fat cells by 248%.

INNOSLIM® INCREASES AMPK PHOSPHORYLATION IN FAT (3T3-L1) AND MUSCLE (HSMMT) CELLS



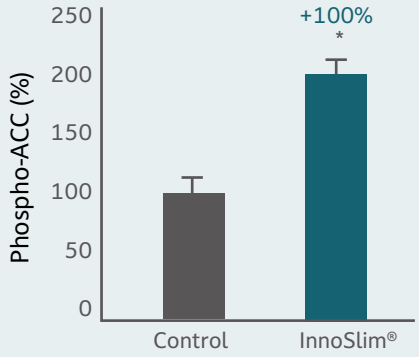
Fat cells
**p < 0.01, when compared to the control group



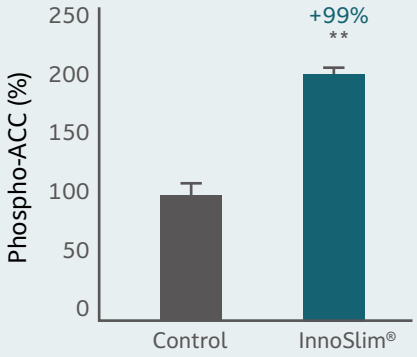
Muscle cells
**p < 0.01, when compared to the control group

Adenosine monophosphate-activated protein kinase (AMPK) is an enzyme involved in balancing cellular energy. When AMPK is activated, it boosts the burning of fatty acids, helps muscles take in more glucose, and helps to reduce the production of cholesterol and triglycerides. InnoSlim® has been shown to increase AMPK by 300% in fat cells and by 52% in muscle cells (*in-vitro*).

INNOSLIM® INCREASES ACC PHOSPHORYLATION IN FAT (3T3-L1) AND MUSCLE (HSMMT) CELLS



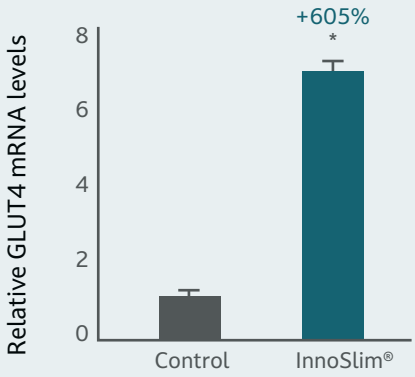
Fat cells
*p < 0.05, when compared to the control group



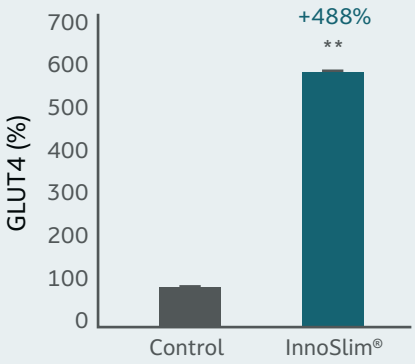
Muscle cells
**p < 0.01, when compared to the control group

Acetyl Coenzyme A carboxylase (ACC) is an enzyme that helps to regulates the metabolism of fatty acids. When ACC activity is inhibited, often through an increase in ACC phosphorylation (ACC-P), it can lead to a reduction in the formation of fatty acids. InnoSlim® has demonstrated the ability to boost ACC-P levels, with a 100% increase in fat cells and a 99% increase in muscle cells (*in-vitro*).

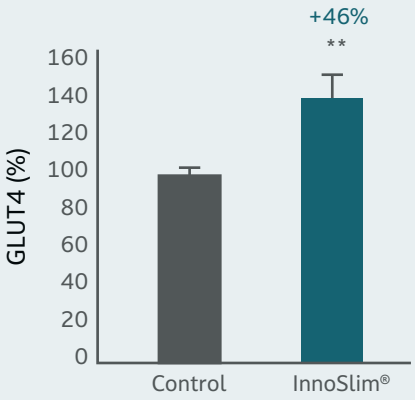
INNOSLIM® INCREASES GLUT4 TRANSPORT PROTEIN AND FAT (3T3-L1) AND MUSCLE (HSMMT) CELLS



Fat cells mRNA
**p < 0.01, when compared to the control group



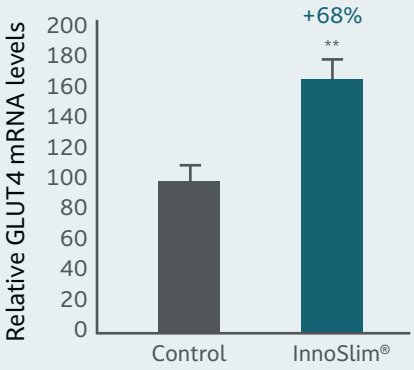
Fat cells transport protein
**p < 0.01, when compared to the control group



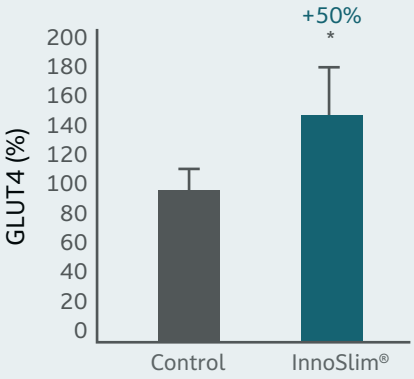
Muscle cells transport protein
**p < 0.01, when compared to the control group

Glucose transporter type 4 (GLUT4) is a insulin-regulated glucose transport protein found primarily in adipose tissues and skeletal and cardiac muscles. Increased GLUT4 level increases the absorption of glucose in muscles and decreases circulating glucose in blood stream. InnoSlim® has shown to increase GLUT4 mRNA and transport protein in fat cell by 605% and 488% respectively. InnoSlim® has also shown to increase GLUT4 transport protein in muscle cell by 46% (*in-vitro*).

INNOSLIM® INCREASES GLUCOSE ABSORPTION IN FAT (3T3-L1) AND MUSCLE (HSMMT) CELLS



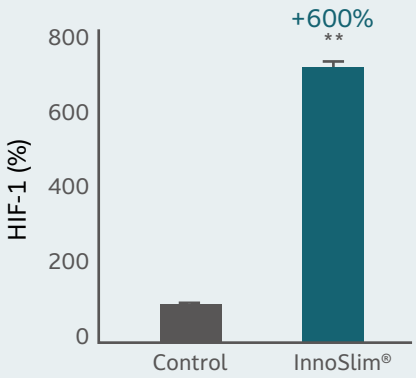
Fat cells
**p < 0.01, when compared to the control group



Muscle cells
*p < 0.05, when compared to the control group

InnoSlim® has shown to increase absorption of glucose in fat cell by 68% and in muscle cell by 50% as the result of increased GLUT4 mRNA and transport protein in fat and muscle cells (*in-vitro*).

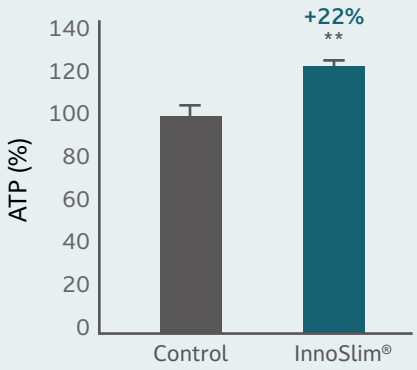
INNOSLIM® INCREASES HIF-1 IN MUSCLE (HSMMT) CELLS



HIF1
**p < 0.01, when compared to the control group

Hypoxia-inducible factor 1 (HIF-1), is a transcription factor that plays a role in maintaining homeostasis in response to changes in the body's environment, like low oxygen levels and reduced energy. When HIF-1 is activated, it has a beneficial impact on processes such as glycolysis, oxygen levels, and overall energy balance. InnoSlim® has demonstrated to increase HIF-1 levels, particularly in muscle cells by 600% (*in-vitro*).

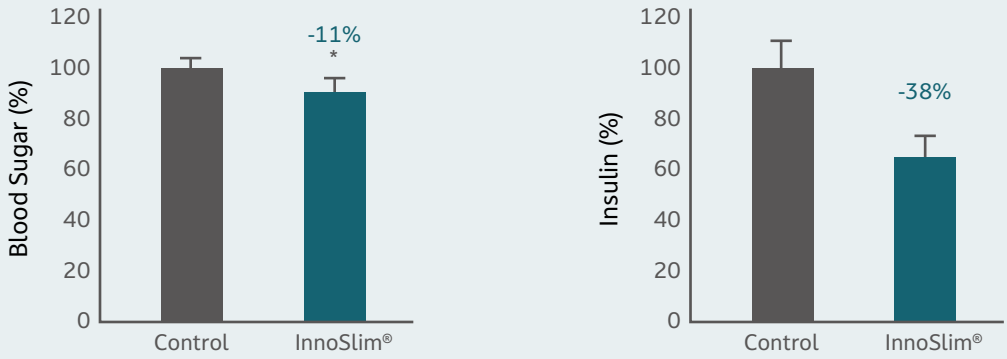
INNOSLIM® INCREASES ATP IN LIVER (HEPG2) CELL



ATP
**p < 0.01, when compared to the control group

Adenosine Triphosphate (ATP) is the primary energy source for all living organisms. Microorganisms store energy as ATP, which is then broken down to release energy for various cellular processes. InnoSlim® has been shown to increase ATP production in liver cells by 22%, supporting cellular functions (in-vitro).

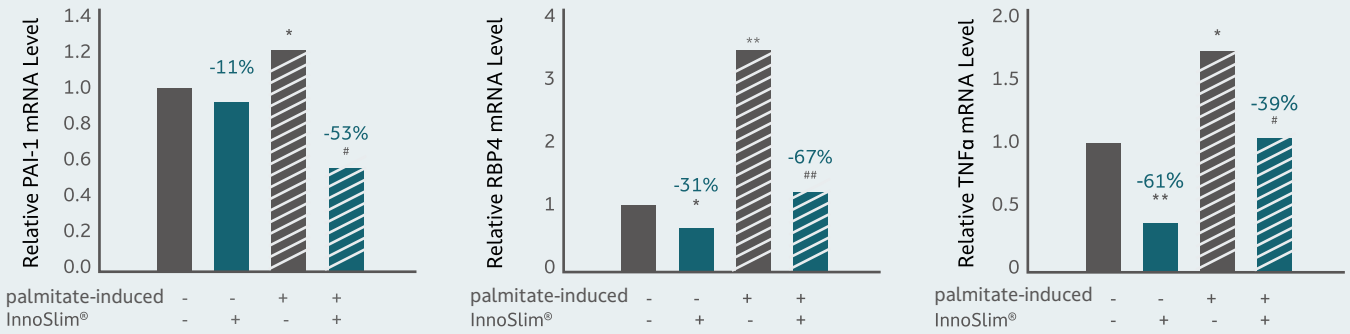
INNOSLIM® DECREASES GLUCOSE AND INSULIN IN RATS (IN-VIVO)



**p < 0.05, when compared to the control group

Blood glucose levels are carefully regulated within a specific range. Persistent elevation of glucose levels can lead to metabolic imbalances. InnoSlim® has shown to reduce blood glucose and insulin levels in rats by 11% and 38%, respectively.

INNOSLIM® DECREASES INFLAMMATORY CYTOKINES MRNA IN NORMAL AND PALMITATE-INDUCED FAT CELLS

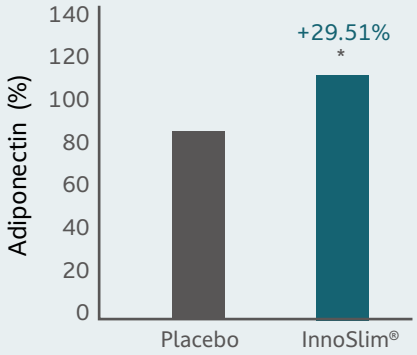


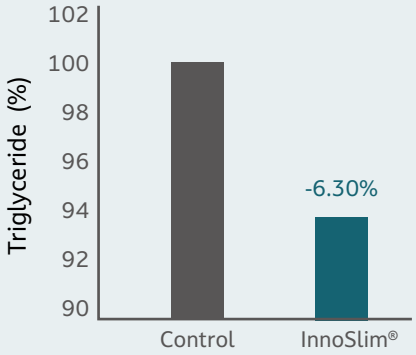
*p < 0.05, when compared to the control group
**p < 0.01, when compared to the control group
#p < 0.05, when compared to the IR group
##p < 0.01, when compared to the IR group

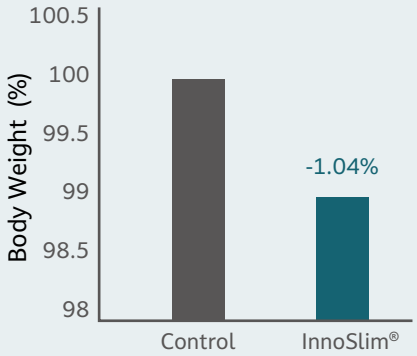
In a recent study, InnoSlim® has been observed to showcase positive effects on various markers related to metabolic cellular health. Specifically, InnoSlim® was shown to demonstrate favorable correlations, such as a reduction in PAI-1 in normal fat cells and a reduction in palmitate-induced stress in fat cells. Additionally, RBP4 levels were reduced in normal fat cells and in palmitate-induced fat cells. Finally, TNFα levels were lowered in normal fat cells and in palmitate-induced fat cells. These findings are based on an *in-vitro* cell study.

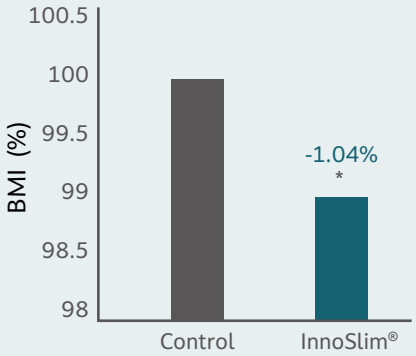
*A complete dossier detailing the study is available upon request for qualified professional review.

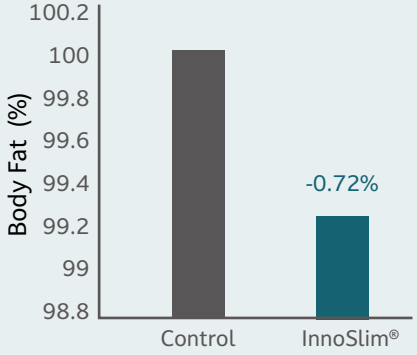
THE EFFECT OF INNOSLIM® IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSSOVER HUMAN STUDY WITH AN UNRESTRICTED CALORIE DIET











*p < 0.05, when compared to the placebo group

THE EFFECT OF INNOSLIM® IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSSOVER HUMAN STUDY WITH AN UNRESTRICTED CALORIE DIET

In this human study, InnoSlim® demonstrated a statistically significant change in adiponectin and BMI. As well as a decrease in triglyceride, body weight, and body fat among the study subjects. These findings align with the outcomes of 18 in-vitro and 2 in-vivo studies conducted previously.

The mechanisms behind these effects involve several key pathways:

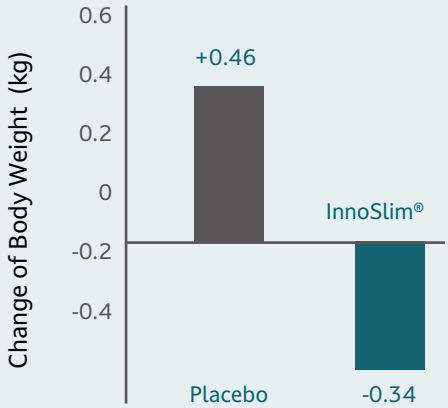
- InnoSlim® supports lowered blood plasma glucose levels, subsequently decreasing triglycerides that are associated with fat buildup and impaired glucose regulation. This is accomplished by diminishing glucose uptake in the intestines while enhancing glucose uptake in muscle and fat cells[1, 2, 3, 5].

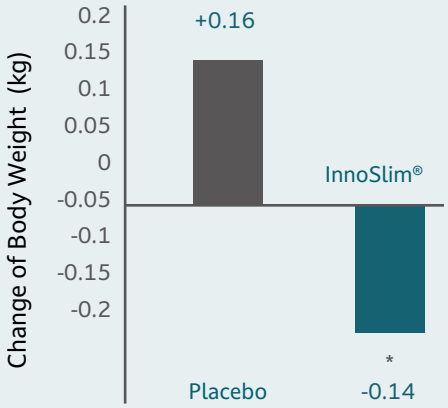
- InnoSlim® helps to lower inflammation in fat cells, supporting glucose regulation and elevated Adiponectin levels in blood plasma[10, 11, 12].

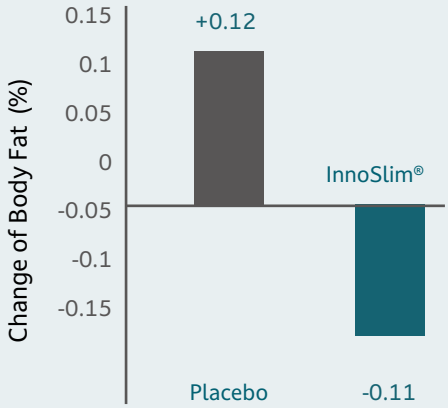
- InnoSlim® promotes the increase of adiponectin, which activates AMPK, GLUT4, ACC-P, and HIF-1. This activation could contribute to a decrease in fat cell formation and an increase in energy expenditure[4, 5, 8, 1].

Collectively the effect of InnoSlim® on glucose and fat metabolic pathways brings about a shift in energy balance, favoring reduced fat accumulation and enhanced breakdown of fatty acids. This correction supports the underlying issues in glucose and fatty acid metabolism that contribute to overall metabolic wellness.

THE EFFECT OF INNOSLIM® IN A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSSOVER HUMAN STUDY WITH AN UNRESTRICTED CALORIE DIET







*p < 0.05, when compared to the placebo group

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