



# LOESYN™

## Maintenance of Healthy Glucose Levels\*

### What is Loesyn™?

Loesyn™ is a proprietary composition containing a unique combination of *Aloe* chromone in *Aloe vera* leaf gel powder clinically proven to maintain healthy glucose levels and normal insulin sensitivity already in normal ranges<sup>1,\*</sup>

### What makes Loesyn™ unique?

- LOESYN (UP780) is a patented Aloe composition with pre-clinical and clinical evidence for maintain novel insulin sensitivity within already normal ranges.\*
- LOESYN (UP780) was shown to be maintaining already healthy fasting plasma glucose and normal fasting insulin with improvement in HOMA (insulin sensitivity index) in human clinical study.\*
- LOESYN (UP780) was found to be effective in maintaining healthy and novel long term and short-term glycemic control (HbA1C and fructosamine) in human clinical study.\*
- LOESYN (UP780) was shown to result in statistically significant reduction in oxidative stress (F2-isoprostanes) in human clinical study.\*

### Key Benefits\*

- Supports already normal insulin sensitivity
- Maintains normal healthy blood glucose levels

- Reduces oxidative stress
- Maintains already healthy blood triglycerides (based on pre-clinical studies)
- Safe, well-tolerated and natural with high compliance to oral supplement
- Easily formulated with other ingredients

### Plant Origin

Derived from leaf of *Aloe barbadensis* and *Aloe ferox*.

### Applications

An alternative natural aid for maintaining already healthy glycemic control and insulin sensitivity in normal healthy individuals.

### Formulation

Can be used as an active agent in tablets, capsules and liquids.

### Physical Properties

Off-white to tan colored powder that is water soluble.

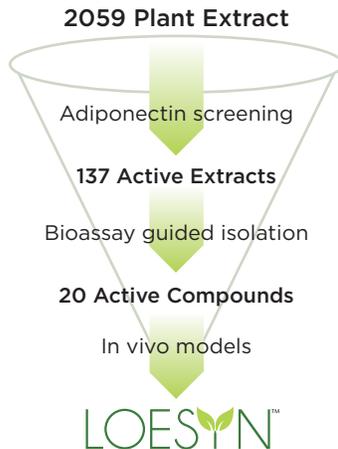
### Regulatory Status

Self-Affirmed Medical Food GRAS Ingredient

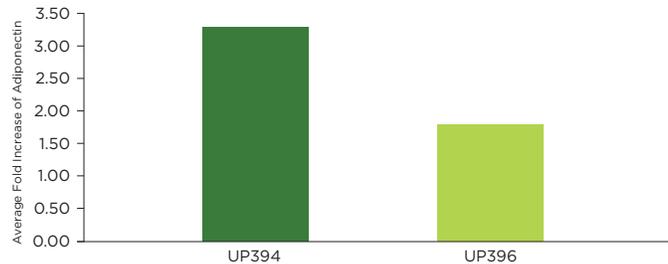
## SUMMARY

- Loesyn™ was discovered by screening 2059 plant extracts to identify natural substances that increase adiponectin production by adipocytes.
- Adiponectin is a protein in blood to help maintain normal healthy insulin sensitivity
- The active components from the screen were identified by HPLC-Mass Spectrometry and NMR and shown to be highly specific components in extracts from *Aloe*.

**Figure 1: Screening Process for Loesyn™**



**Figure 2: Two Aloe chromones identified that increase adiponectin secretion from adipocytes**



## Mechanisms of Action

**Genomic Study of Loesyn™ (UP780) with Microarray and Quantitative RT-PCR: An analysis of genome-wide gene transcription was used to better understand Loesyn's mechanism of action.**

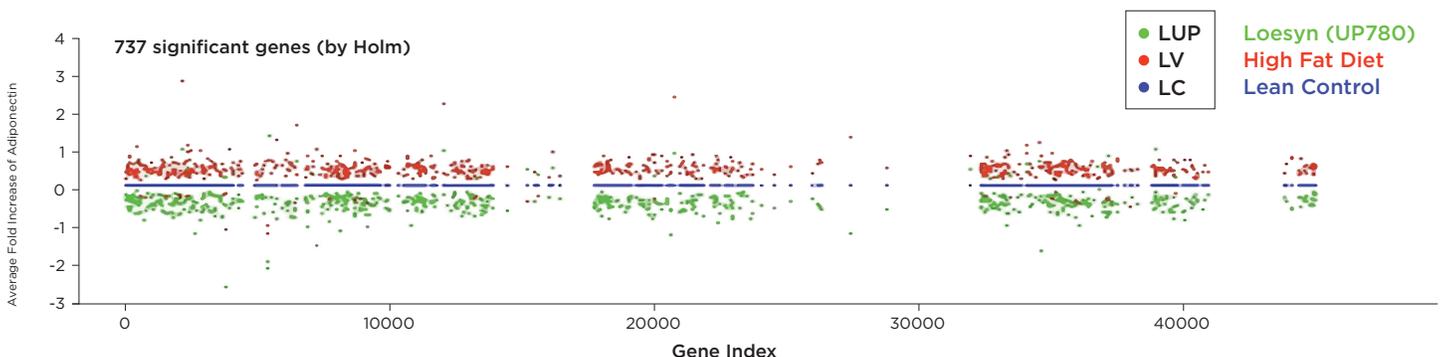
Data analysis using the Ingenuity pathway analysis software identified significant Canonical Pathways affected by Loesyn™. In particular, gene expression in white adipose tissues was increased for multiple key genes in the insulin receptor signaling cascade:

- Insulin receptor (INSR)
- Insulin receptor substrate 1 (IRS1)
- Glucose transporter 4 (GLUT4)

Loesyn™ supplementation also modified multiple metabolic pathways in liver for lipid metabolism:

- Decreased fatty acid biosynthesis
- Increased fatty acid binding proteins
- Decreased lipid uptake
- Increased bile biosynthesis

**Figure 3: Results of Genomic Study of Loesyn™**



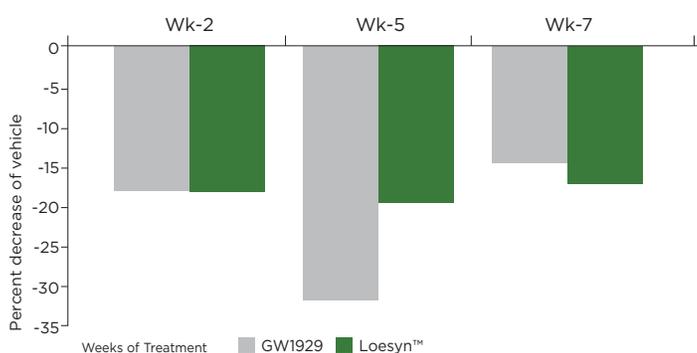
# Pre-Clinical Efficacy

## SUMMARY HIGHLIGHTS

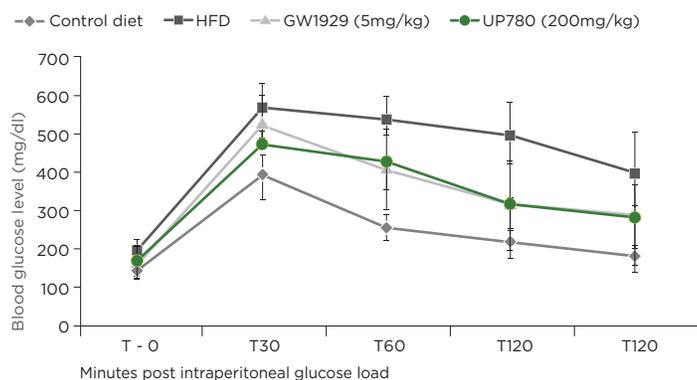
As illustrated in Figures 4 - 10, Loesyn™ supplement relative to vehicle given mice demonstrated the following results:

- Reduced fasting plasma glucose levels comparable to that achieved with GW1929 treatment (Figure 4)
- Significantly improved glucose tolerance, as measured by intraperitoneal glucose tolerance tests, comparable to that achieved with GW1929 (Figure 5)
- Significantly improved insulin sensitization as measured by intraperitoneal insulin tolerance tests (Figure 6)
- Reduced fasting blood triglyceride concentrations comparably to GW1929 (Figure 7)
- Significantly reduced hepatic triglyceride and cholesterol content to levels comparable to that of lean mice fed with normal chow (Figure 8)

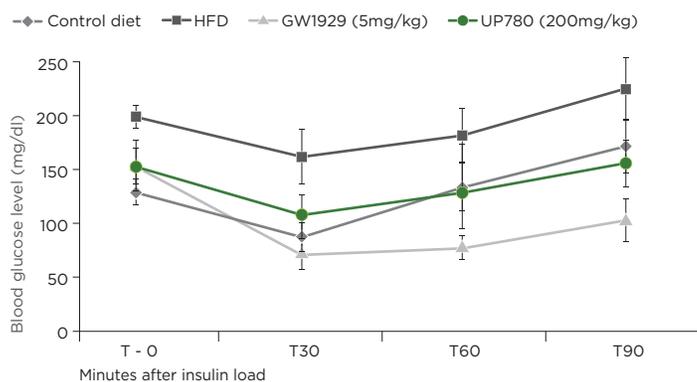
**Figure 4: Loesyn™ significantly supports healthy fasting blood glucose levels after 2, 5 or 7 weeks of oral administration**



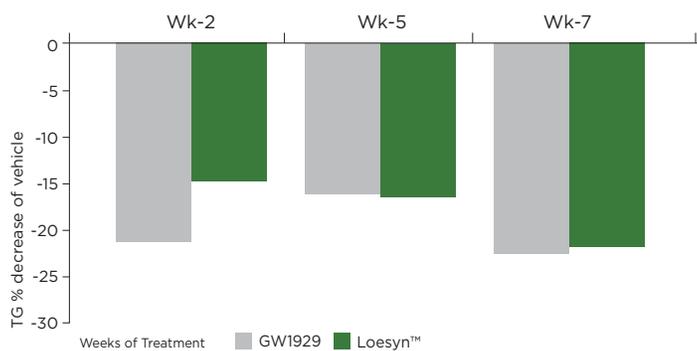
**Figure 5: Loesyn™ improved glucose tolerance of overweight mice**



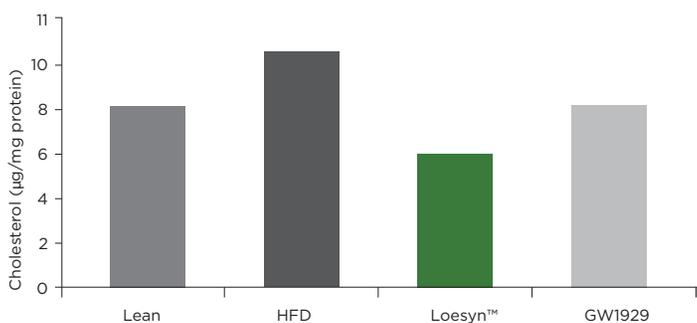
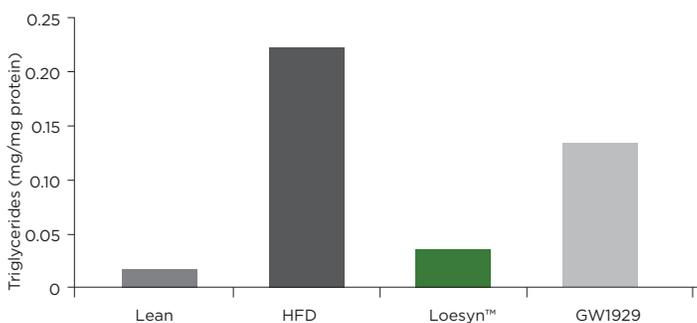
**Figure 6: Loesyn™ improved insulin sensitivity of overweight mice**



**Figure 7: Loesyn™ supported fasting blood triglyceride level**



**Figure 8: Loesyn™ significantly supported healthy triglyceride & cholesterol levels in livers**

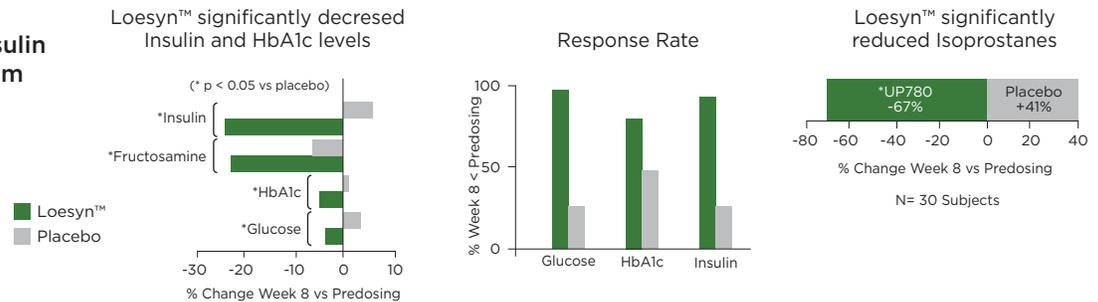


## SUMMARY

In a randomized, double-blind, placebo controlled, IRB approved clinical trial:

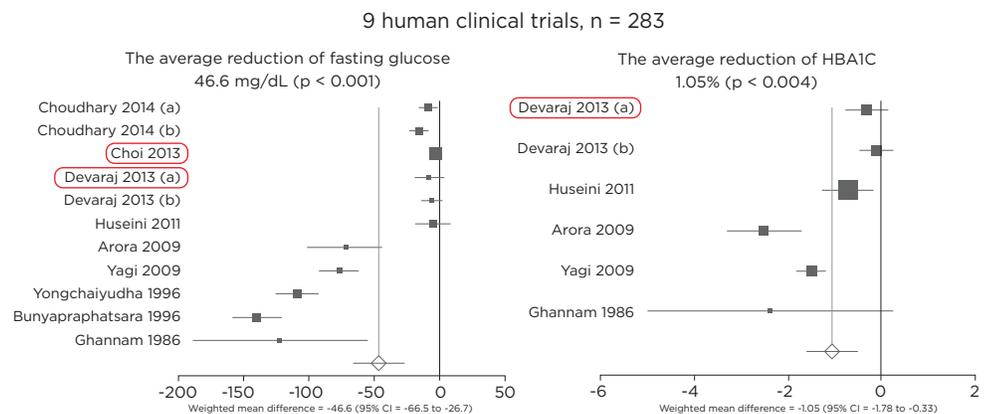
- Loesyn™ has been shown to be safe and well-tolerated.
- Loesyn™ has been shown significant maintenance of normal healthy levels of fasting plasma glucose and insulin with improvement in HOMA (insulin sensitivity index).\*
- Loesyn™ has been shown significant support in healthy long term and short-term glycemic maintenance (reduced HbA1C and fructosamine).\*
- Loesyn™ has shown reduction in oxidative stress (F2-isoprostanes) in certain populations.\*

**Figure 9: Data from human clinical study showing key insulin sensitivity, glucose metabolism and oxidative stress related impact of Loesyn™**



Loesyn™ human clinical data has been used in both clinical trial meta-analyses with significance.

**Figure 10: Meta-analysis for Aloe Effects on Fasting Blood Glucose & Glycated Hemoglobin**



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## REFERENCES

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6. Mesfin Yimam, Jifu Zhao, Brandon Corneliusen, Mandee Pantier, Lidia Alfaro Brownell, Qi Jia. UP780, a Chromone-enriched aloe composition improves insulin sensitivity. *Metabolic Syndrome and Related Disorders.* Vol. 11, No. 4. 267-275, 2013.