



*Metabolics*

*inventing the future of healthcare*

# Metabolic Disease Control

## Flavonoid-Based Amelioration of Carbohydrate Dysfunctional Metabolism

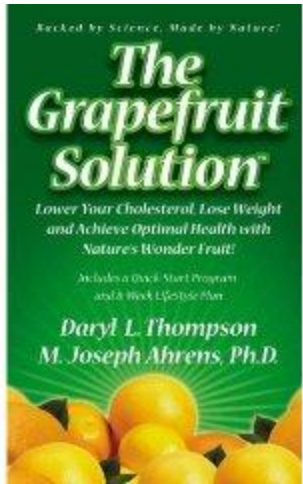
December 2013

Daryl L. Thompson and M. Joseph Ahrens

# The Path to Emulin

- ▶ 2002 Ahrens & Thompson designed Scripps grapefruit weight loss study
  - Fresh fruit, juice, dehydrated powder
  - Patients lost weight over 3 months
  - Glucose response decreased
  - Insulin levels affected





# The Path to Emulin

- ▶ Naringin early candidate



# The Path to Emulin

- ▶ Led to the discovery of a class of compounds more effective than naringin
- ▶ Understanding naringin structure and effect
- ▶ Understanding carbohydrate chemistry
- ▶ Awareness of Metabolic Syndrome, Diabetes

# The Path to Emulin

- ▶ To control carbohydrate chemistry
  - Complex sugars to simple sugars
  - Absorption from gut
  - Absorption to fat and muscle tissue
  - New glucose from storage or mfg
  - Fat storage
  - Insulin sensitivity and/or production

# The Path to Emulin

- ▶ No one getting diabetes eating mangoes, other sweet tropical fruits
- ▶ Survey of diabetes
- ▶ Survey of the plant kingdom
- ▶ Overlap



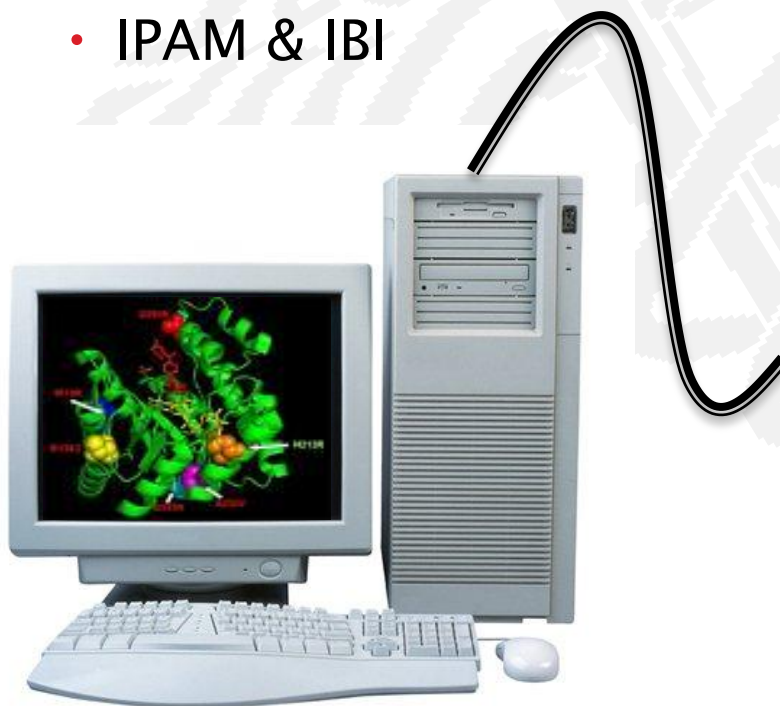


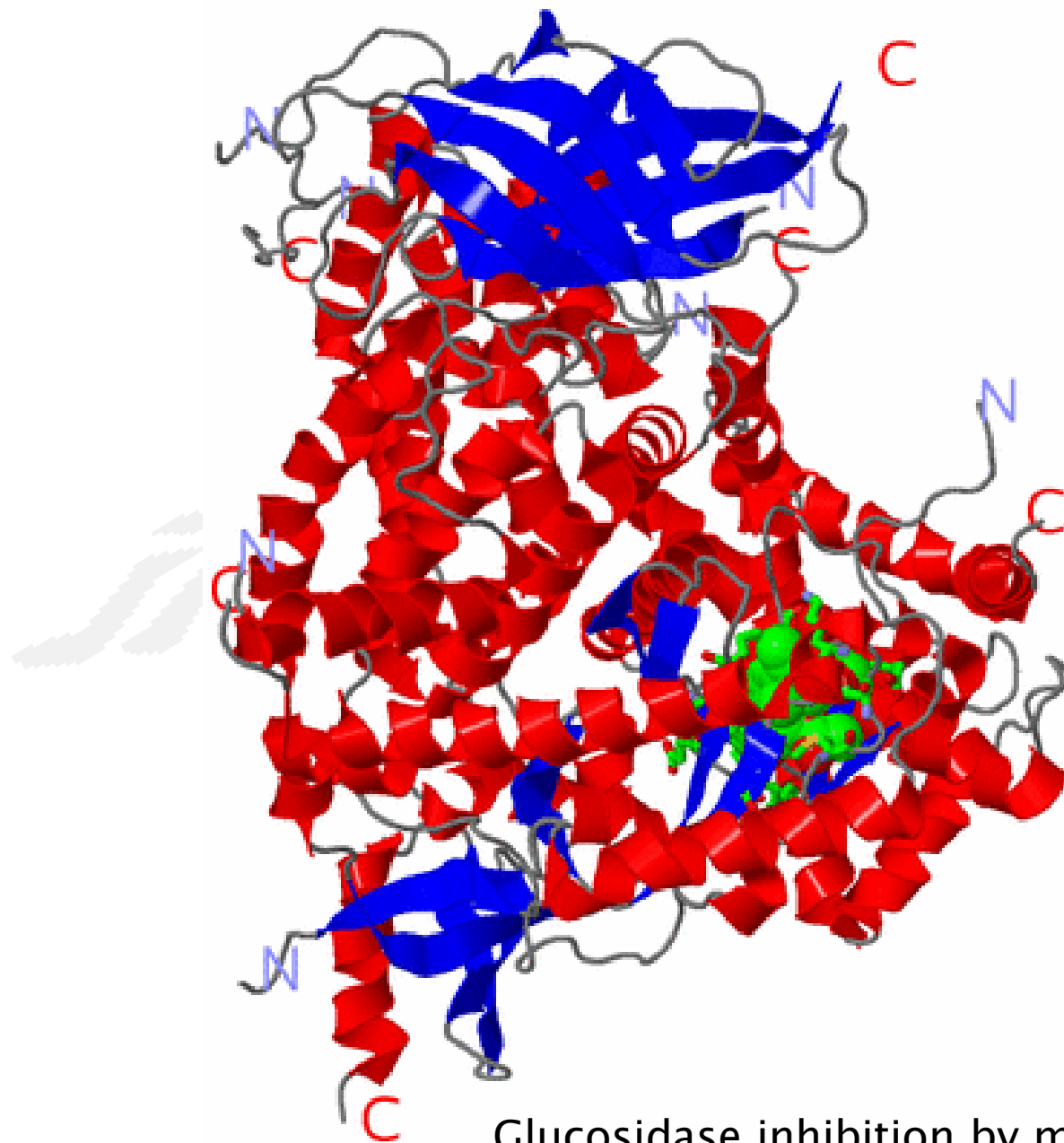
# The Path to Emulin

- ▶ Rational Drug Design
  - Candidate metabolic targets
  - Naringin-like phytochemicals
  - Drug-likeness
    - Optimal solubility
      - Balance in number of hydrogen bonds
    - Smaller molecular weight
    - Lipinski's "Rule of Five"
      - Not more than 5 hydrogen bonds
      - No more than 10 hydrogen bond acceptors
      - MW less than 500 g/mole
      - Partition log coefficient log P less than 5

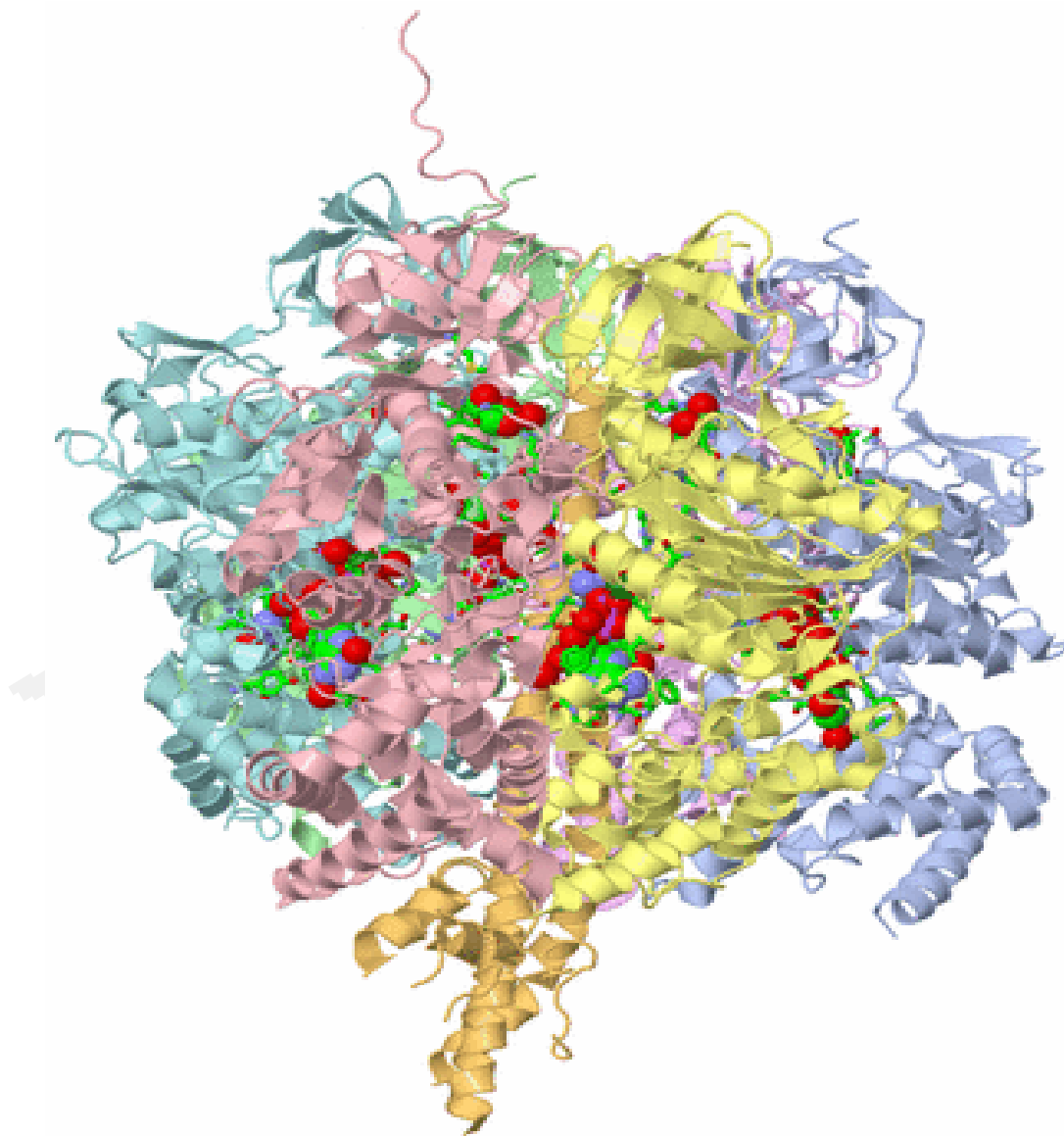
# The Path to Emulin

- ▶ Computer-Assisted Drug Design
  - BRENDA
  - Supercomputers
    - IPAM & IBI

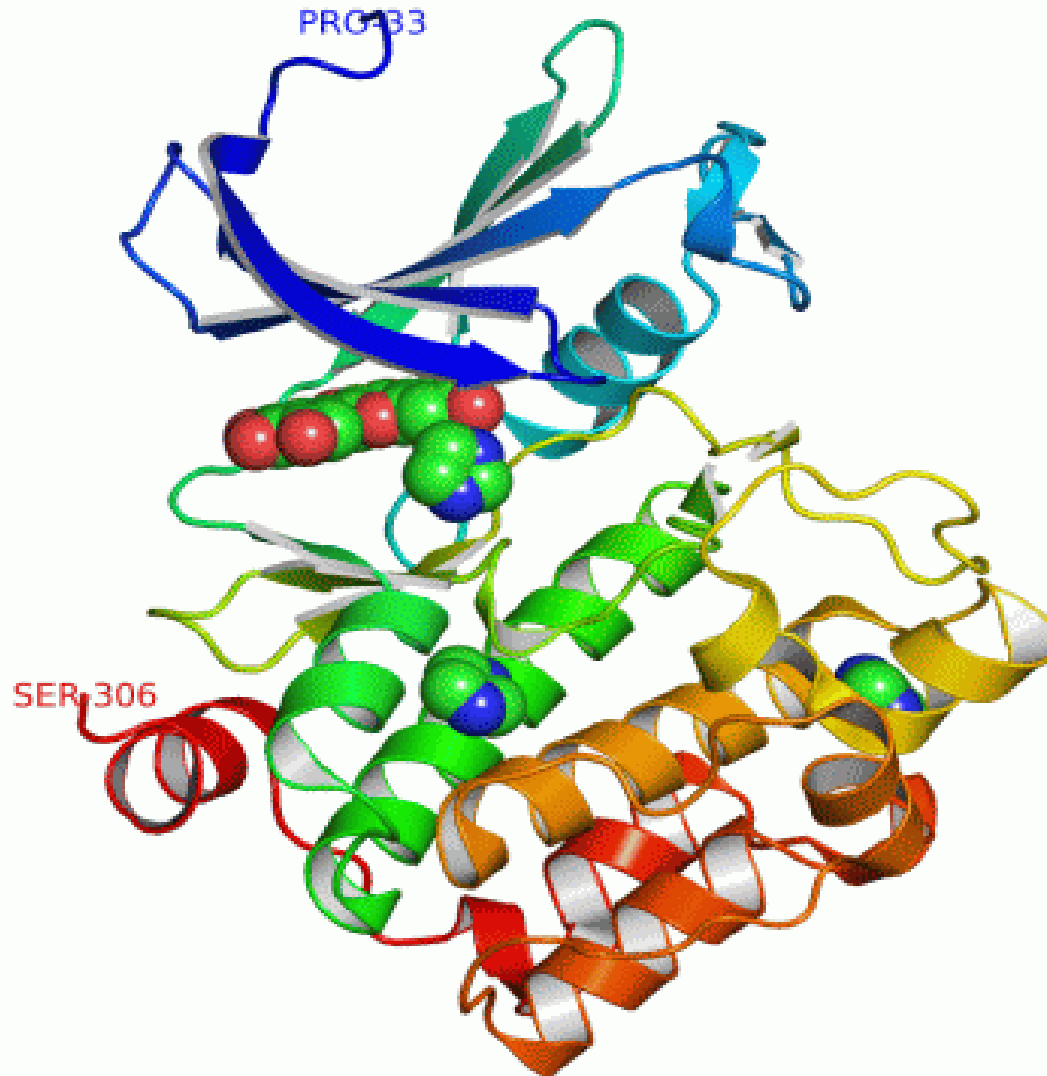




Glucosidase inhibition by myricetin



ATPase inhibition by quercetin



Alpha-amylase inhibition by chlorogenic acid

# The Path to Emulin

- ▶ Rodent Study by Eurofins Labs
  - STZ treated rats, stabilized at 300 ul/dL
  - Formulation & Dose
  - Fasting & mid-day glucose & OGT response decreased by
    - 18%, 27%, and 24%, respectively
  - Several rats became non-diabetic



# The Path to Emulin



Product Safety Laboratories

*“I have never seen anything perform like this in this severe of a model, other than insulin itself...you may be regenerating B-cells”*

Dr. Gary Grover, Principle Investigator  
Director, Eurofins Product Safety Laboratories

# Emulin – Human Clinical



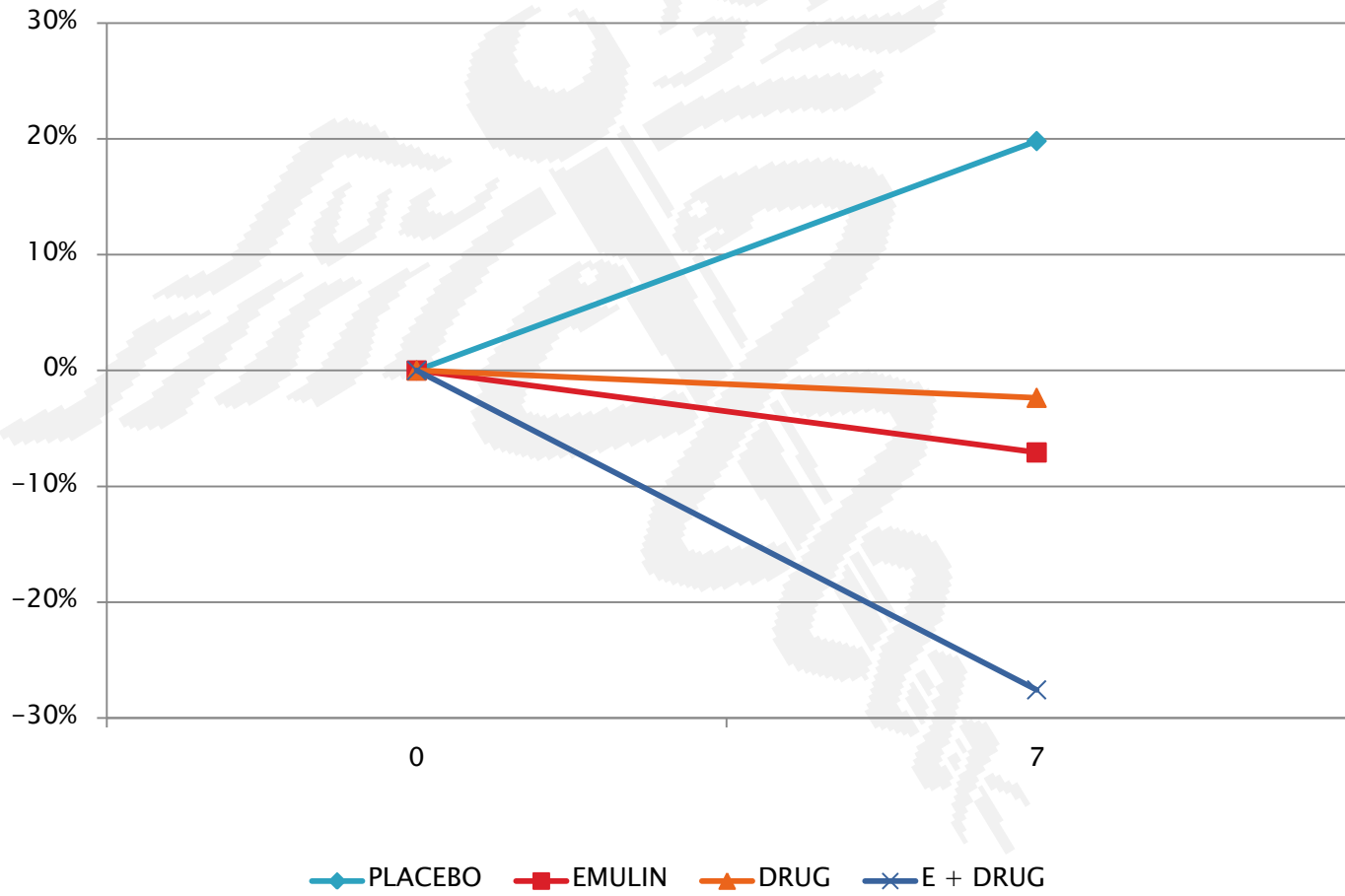
*Leading the search for better health*  
dgd Research is the largest, privately owned national endocrine and metabolic research organization in the United States.



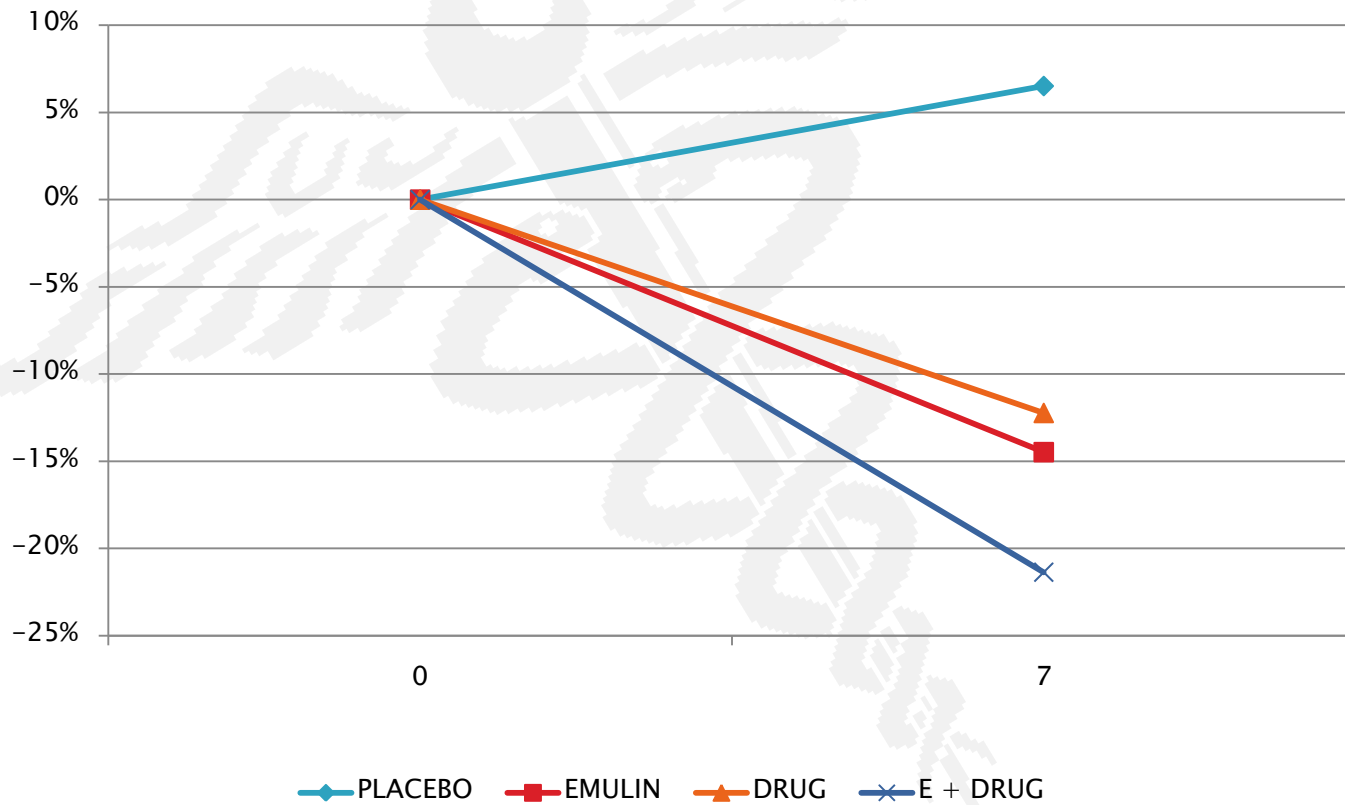
- ▶ 40 patients type 2 diabetics
- ▶ Half on metformin
- ▶ Half on no control
- ▶ Half of each group received placebo
- ▶ Half of each group received Emulin
  - 250mg with each meal



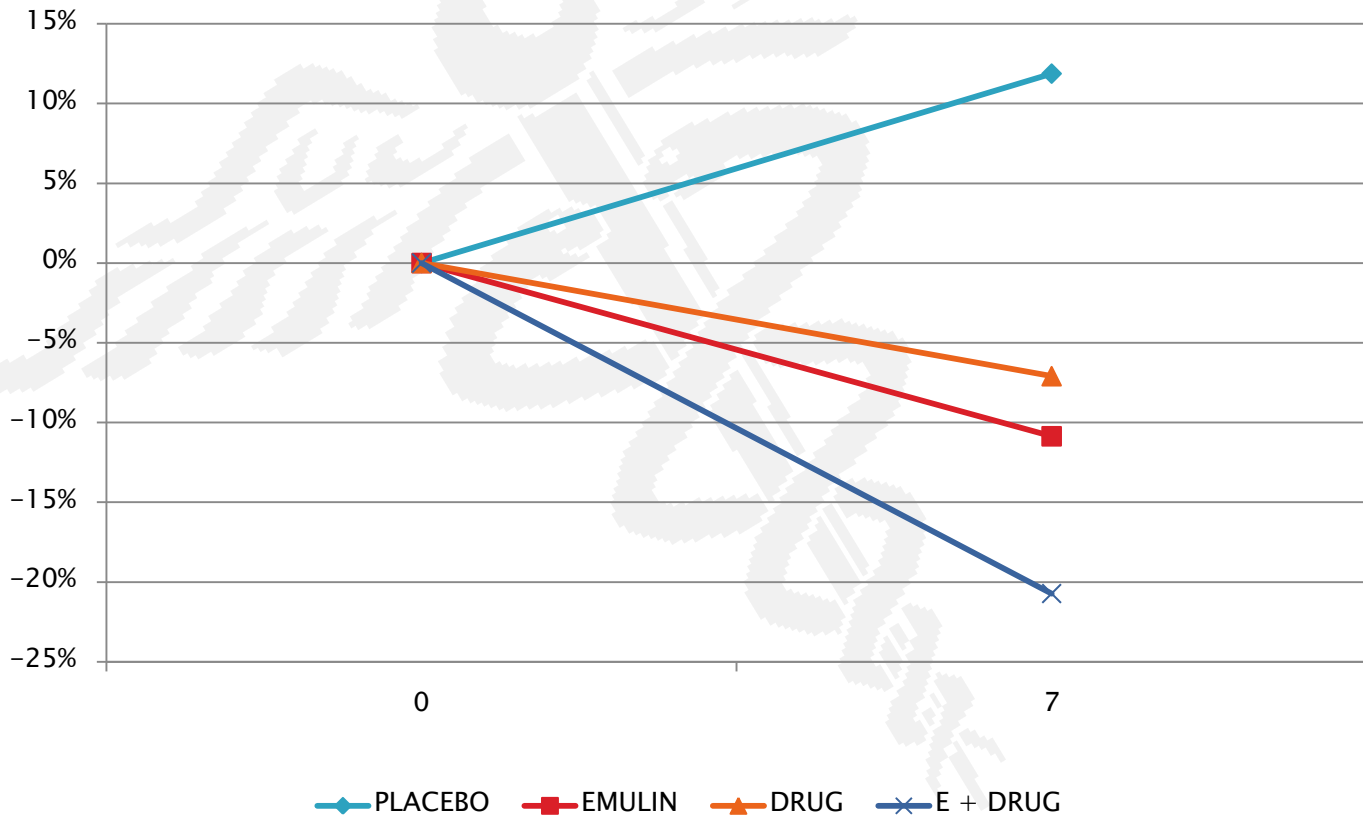
# Change in Fasting Glucose



## Change in 2 Hr Postprandial Glucose



# Change in AUC



# The Path to Emulin



*Leading the search for better health*  
dgd Research is the largest, privately owned  
national endocrine and metabolic research  
organization in the United States.



*“Emulin does a better job at reducing blood sugar levels in type II diabetes than metformin, the most commonly prescribed drug. Emulin...[is] a genuine breakthrough.”*

Dr. Mark Kipnes, Principle Investigator  
Director, dgdresearch/Cetero Labs

# The Science Behind Emulin

Three naturally-occurring phytochemicals that do not occur together in nature

Each with specific major activity toward a key control point in carbohydrate metabolism, but with some overlap

3 “skeleton keys” that together unlock or lock a group of related metabolic pathways

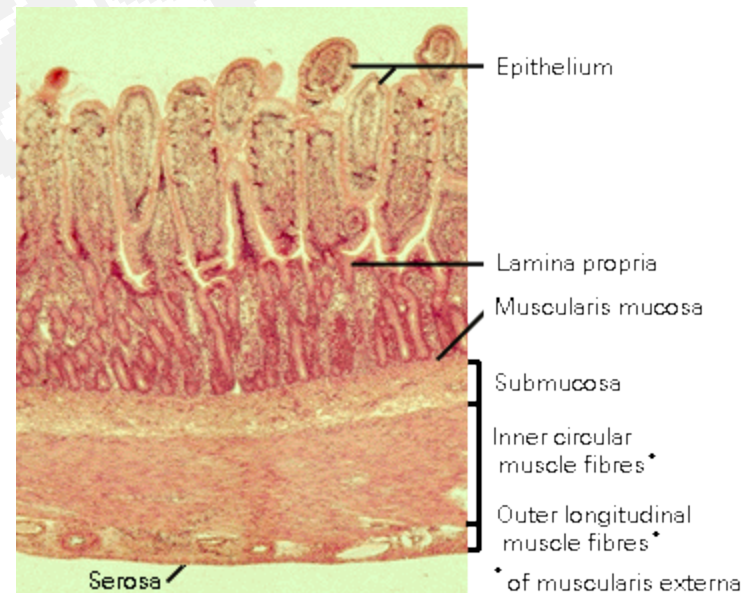
# Glucosidase Inhibition

- ▶ Inhibits several  $\alpha$ -glucosidases
- ▶ Inhibits  $\alpha$ -amylase
- ▶ Inhibits release of pancreatic  $\alpha$ -amylase



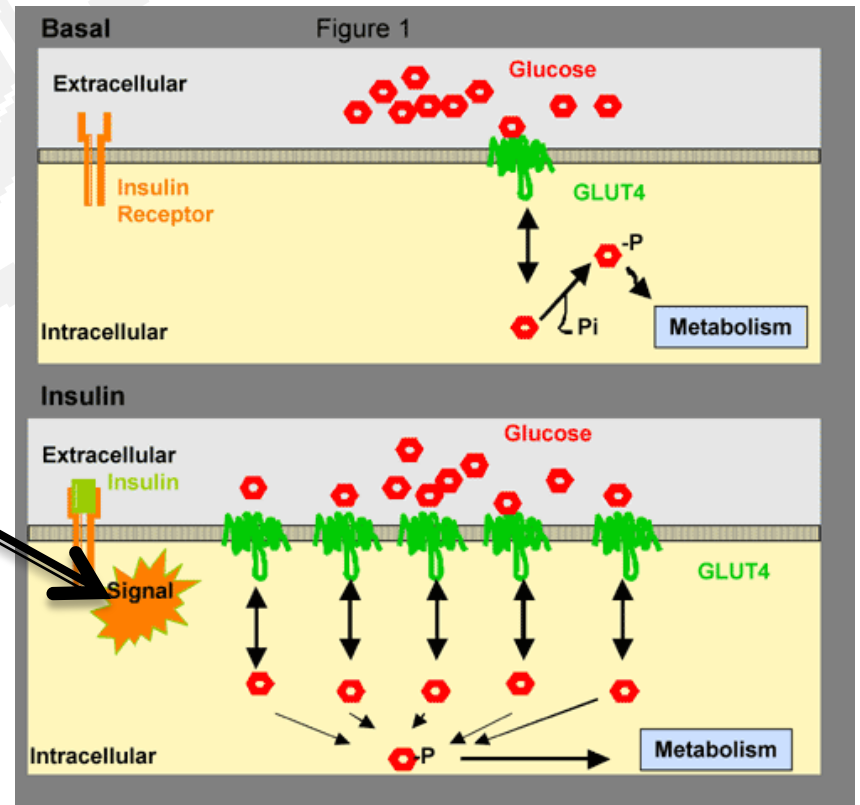
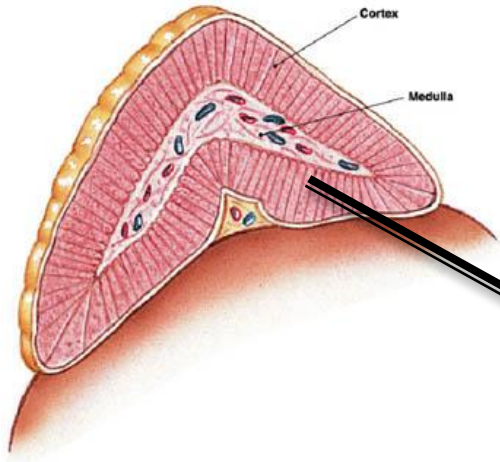
# Inhibition of GLUT2

- ▶ Non-competitively inhibit GLUT2
- ▶ No effect on GLUT5 & SGLT1



# Stimulates Muscle Uptake

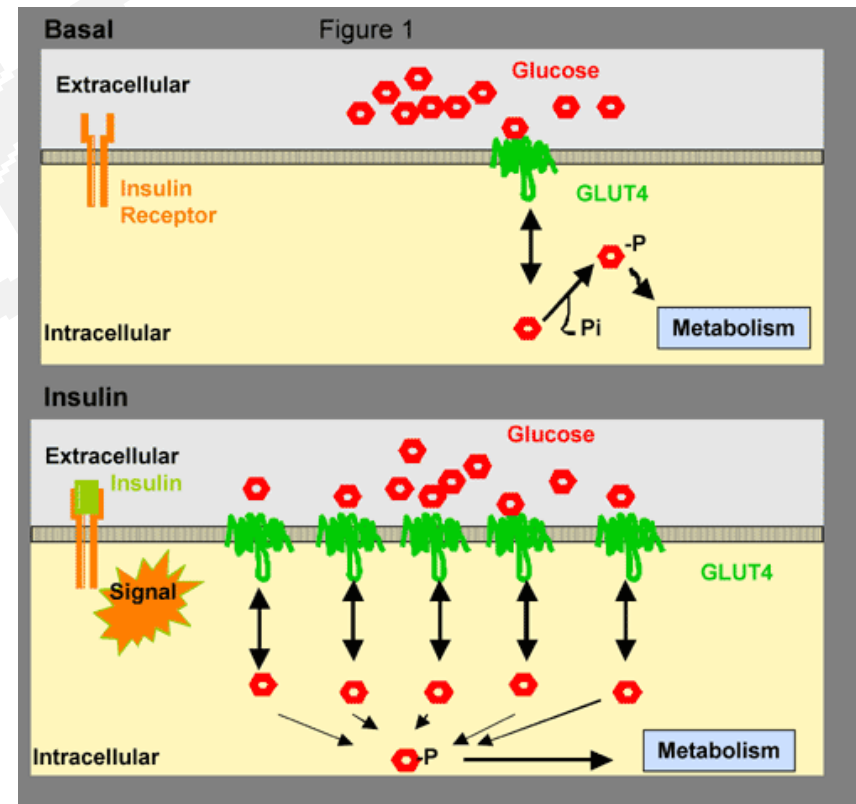
- ▶ Stimulates GLUT4 expression in muscle tissue via beta endorphin-like immunoactivity





# Increased Insulin Sensitivity

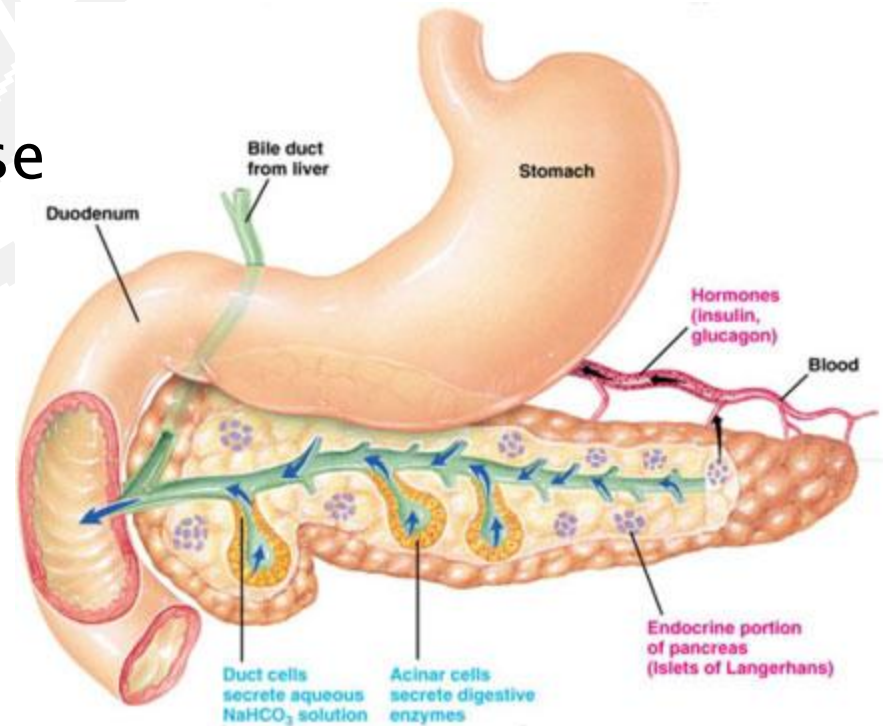
- ▶ A broad category
- ▶ Increases insulin receptor expression in muscle tissue
- ▶ Competes with rosiglitazone
- ▶ Stimulates glucose uptake by muscle in the presence of insulin



# Stimulates Insulin Secretion

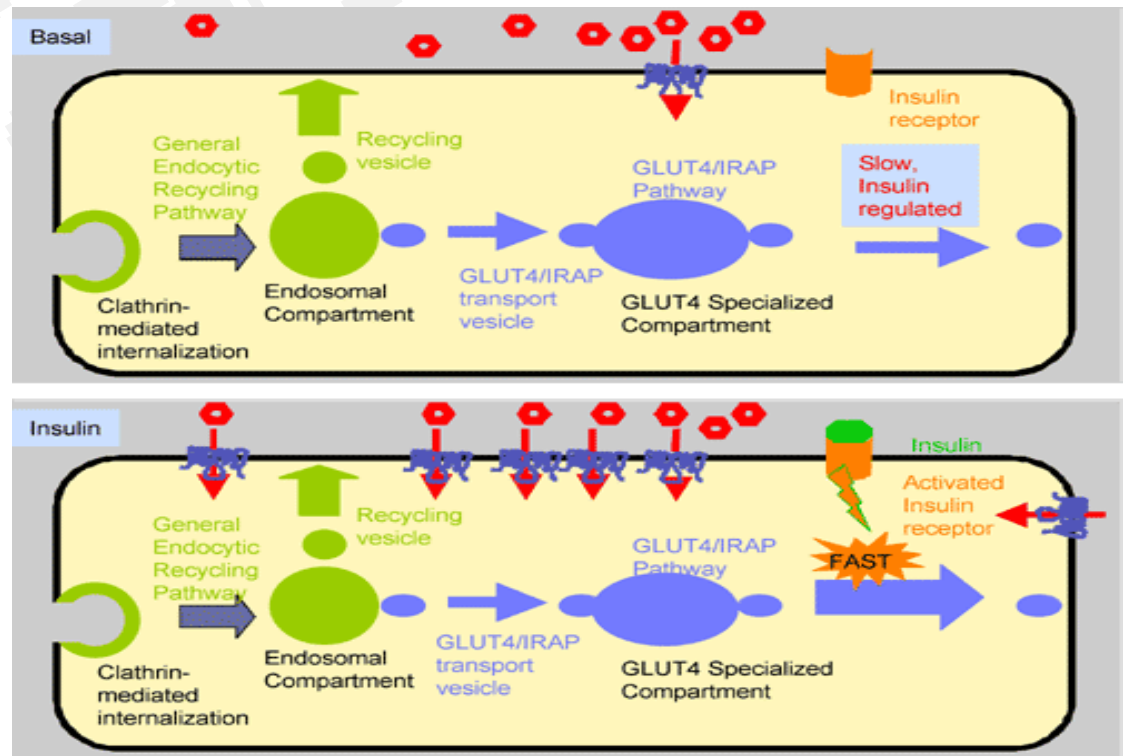
- ▶ Stimulates GLP-1, via cAMP, promoting IDX-1, maintaining  $\beta$  cells responsiveness to glucose.

Stimulates islets to release insulin via non  $\text{Ca}^{++}$ , K channels

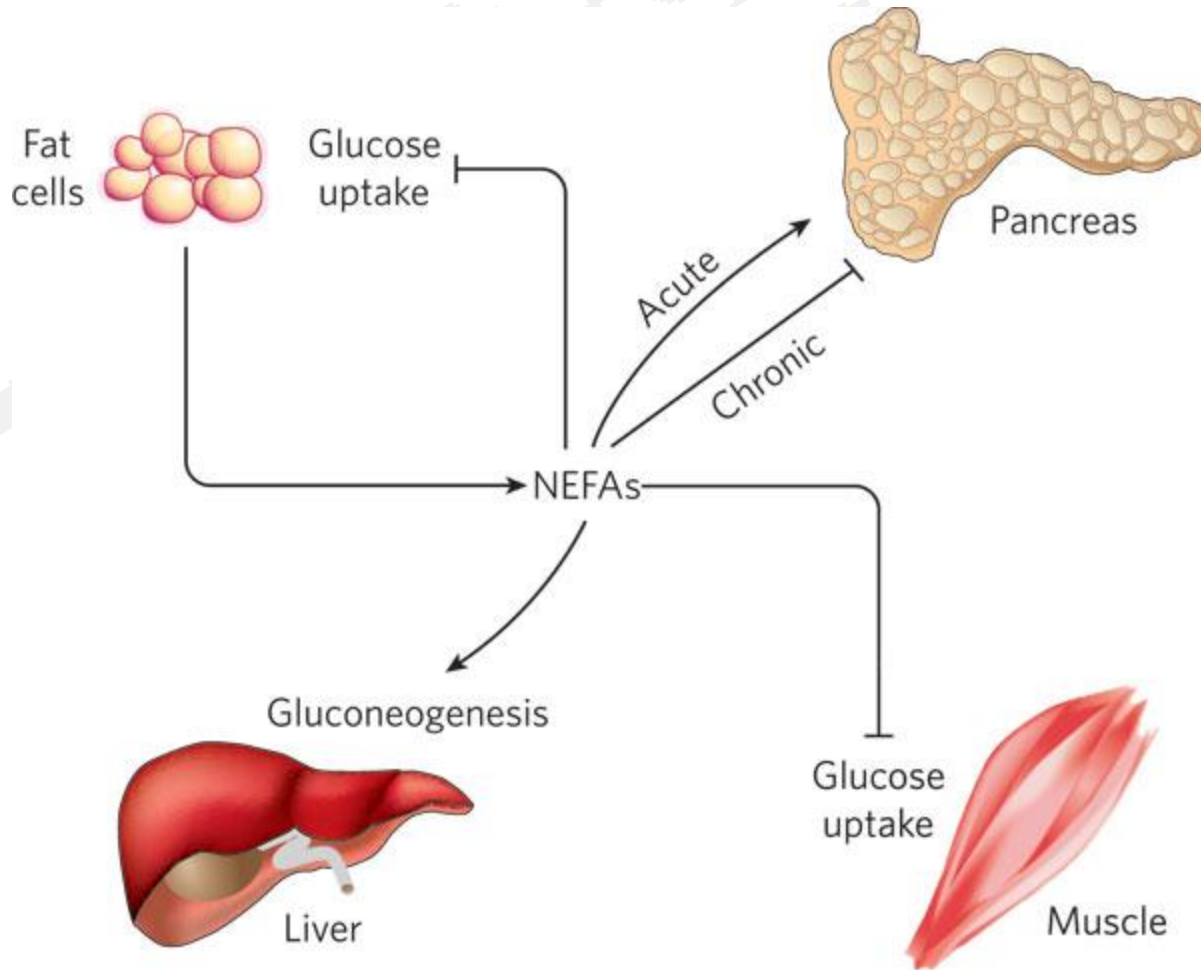


# Inhibits Uptake by Adipocytes

- ▶ Inhibits GLUT4 in adipocytes by:
  - inhibiting protein kinase C
  - phosphorylation of receptor sites
  - Suppressing translocation of GLUT4

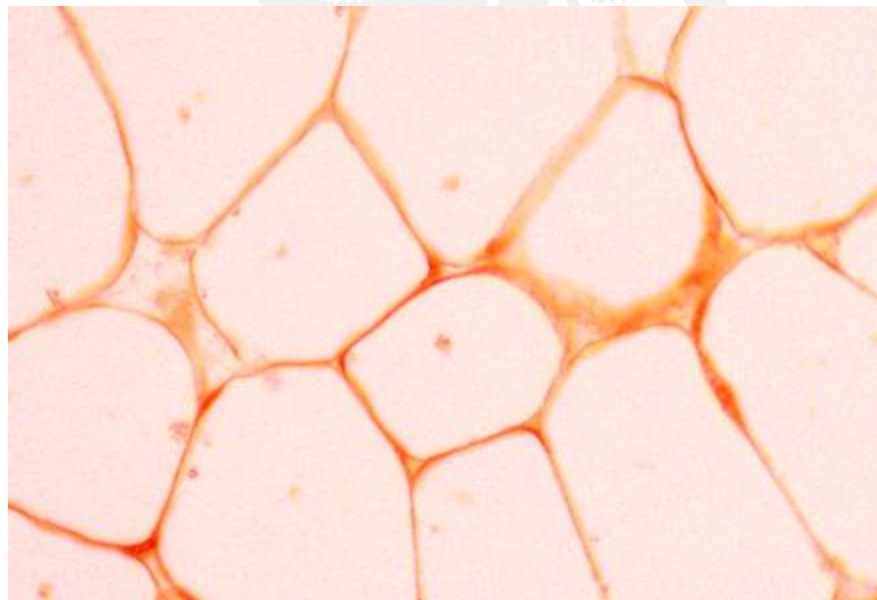


# Stimulates Lypolysis, Inhibits Gluconeogenesis



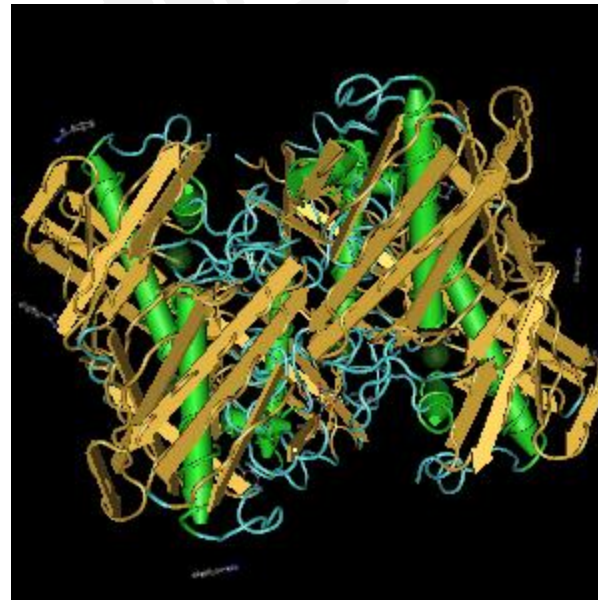
# Inhibits Adipocyte Initiation and Maturation

- ▶ Inhibits at G1 cell expansion phase
- ▶ Inhibits maturation via activation of AMPK pathway



# Digestive Track Therapuetic

- ▶ Inhibits the growth of helicobacter in GI
- ▶ Promotes healthy upper and lower GI lining
- ▶ Ameliorates colitis and diarrhea



# Hypothesis

- ▶ Plants high in simple carbohydrates evolved to:
  - Provide a “buffer” or carbohydrate manager for higher life forms to be consumed with their high sugar load
- ▶ Higher life forms co-evolved to use these carb managers in carbohydrate metabolism
- ▶ Consuming refined sugars without these components results in an inflammatory response
- ▶ The components of Emulin have been left out of the modern diet, resulting in the obesity and diabetes epidemics

# Scientific Paper Published

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FULL COMMUNICATION

## Effect of Emulin on Blood Glucose in Type 2 Diabetics

Milton Joseph Ahrens and Daryl L. Thompson

*ATM Metabolics LLC, Winter Haven, Florida, USA.*

**ABSTRACT** Emulin™ is a patented blend of chlorogenic acid, myricetin, and quercetin that has shown efficacy in reducing midday and post-oral glucose tolerance test (OGTT) area under the curve (AUC) glucose in streptozotocin-treated rats. The purpose of this study was to determine if similar effects would be evident in type 2 diabetic humans. Forty human subjects with confirmed type 2 diabetes (10 each in 4 groups: placebo/no medication, Emulin/no medication, placebo/metformin and Emulin/metformin) were evaluated. At the end of 1 week, fasting blood glucose, 2 h postprandial, actual peak glucose, and AUC (post-50 g OGTT) were determined. The placebo-only group had a large (5%–13%) increase in all parameters. The Emulin group and those on metformin performed similarly with reductions between 1% and 5%, with Emulin slightly outperforming the medication-alone group. The most significant reduction occurred in the Emulin/metformin group, with decreases in the parameters by up to 20%. These results suggest that Emulin, if consumed regularly, could not only have the acute effect of lowering the glycemic impact of foods, but chronically lower background blood glucose levels of type 2 diabetics.

**KEY WORDS:** • *chlorogenic acid* • *flavonoids* • *flavonols* • *myricetin* • *polyphenols* • *quercetin*

### INTRODUCTION

**T**YPE 2 DIABETES IS CONSIDERED an epidemic worldwide in industrialized nations.<sup>1,2</sup> Historically, the incidence of type 2 diabetes has tracked the increased consumption of

Traditional treatment for diabetes has included alterations in diet to avoid refined carbohydrates and prescribing of drugs to inhibit hyperglycemia and increase insulin release. Common drugs for the treatment of diabetes or its symptoms are



# Patents

- ▶ COMPOSITION AND METHOD FOR TREATING DIABETES AND METABOLIC DISORDERS
- ▶ USP 7,943,164 and 8,198,319
- ▶ CIP 13/961524 and worldwide
- ▶ Others Pending
  - Food Additive
  - Food Supplement
  - Functional Food
  - Pharmaceutical Composition
    - Unique Combination not found in Nature
    - No digestive issues
    - Equal to or greater efficacy than current drugs

# Released to Public April 2011



- ▶ Currently available at GNC and online
- ▶ Seeking to license/sell IP in other channels
  - Glucose control foods
  - Sports Drinks/Bars
  - Replacement meals
  - Diet aid
  - Diet Foods & Beverages
  - Diabetic Treatment
    - No drug claims at present
  - Medical Foods

# “Sugir” Sugar recrystallized with Emulin





Thank You