



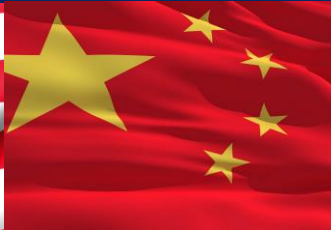
ANANDA Scientific



Israel



United States



China



Jamaica



Brazil

# Making Cannabinoids Effective Type 2 Diabetes Medicine



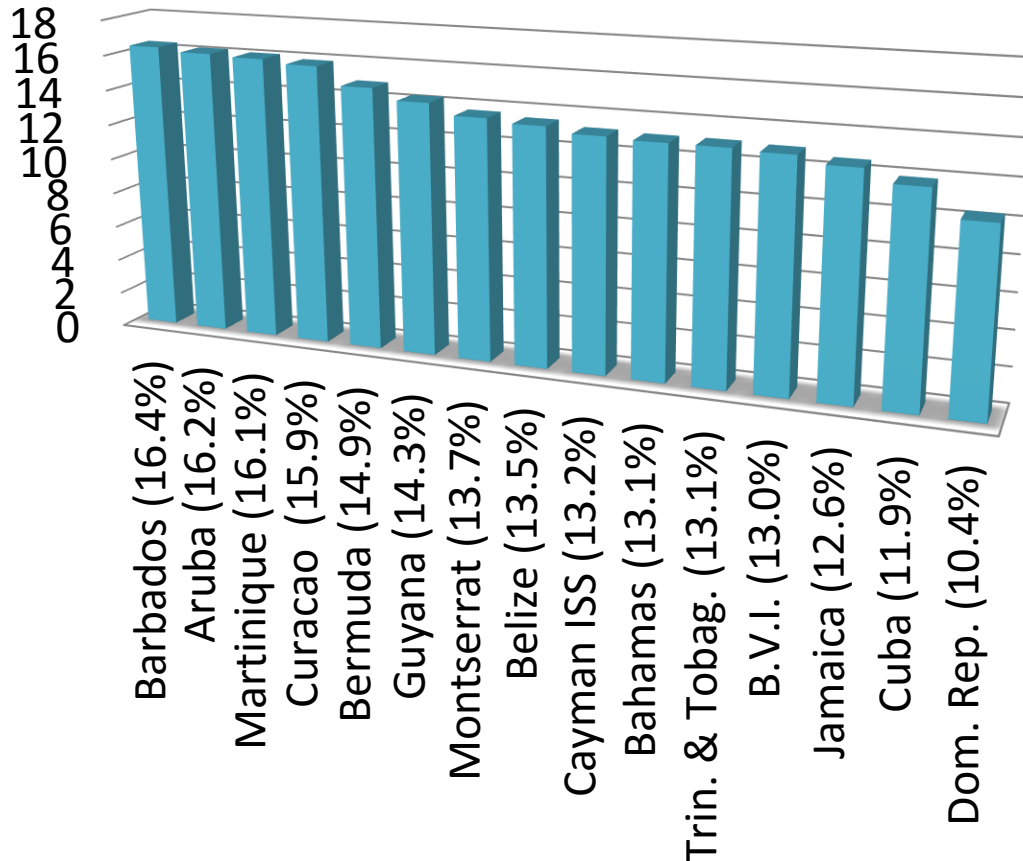
New Hope for Better  
Health with Innovative  
Cannabinoid Science

Mark J. Rosenfeld, M.S., Ph.D. – President & Chief Science Officer



# The Caribbean Nightmare

Prevalence Highest in the Americas



- 8.5% Worldwide (2014)
- Mortality Rate Among the World's Highest:  
60-80 per 100,000 people  
(24 in the United States)
- Complications Rampant  
End-stage kidney disease (28% of diabetics),  
retinopathy (37%),  
amputation (> 936 per 100,000 in Barbados)
- More Frequent in Poorer and Elderly



# Greatest Diabetes Prevalence -- Tokelau



37.5% — 4.4 Times the Global Average (8.5%)

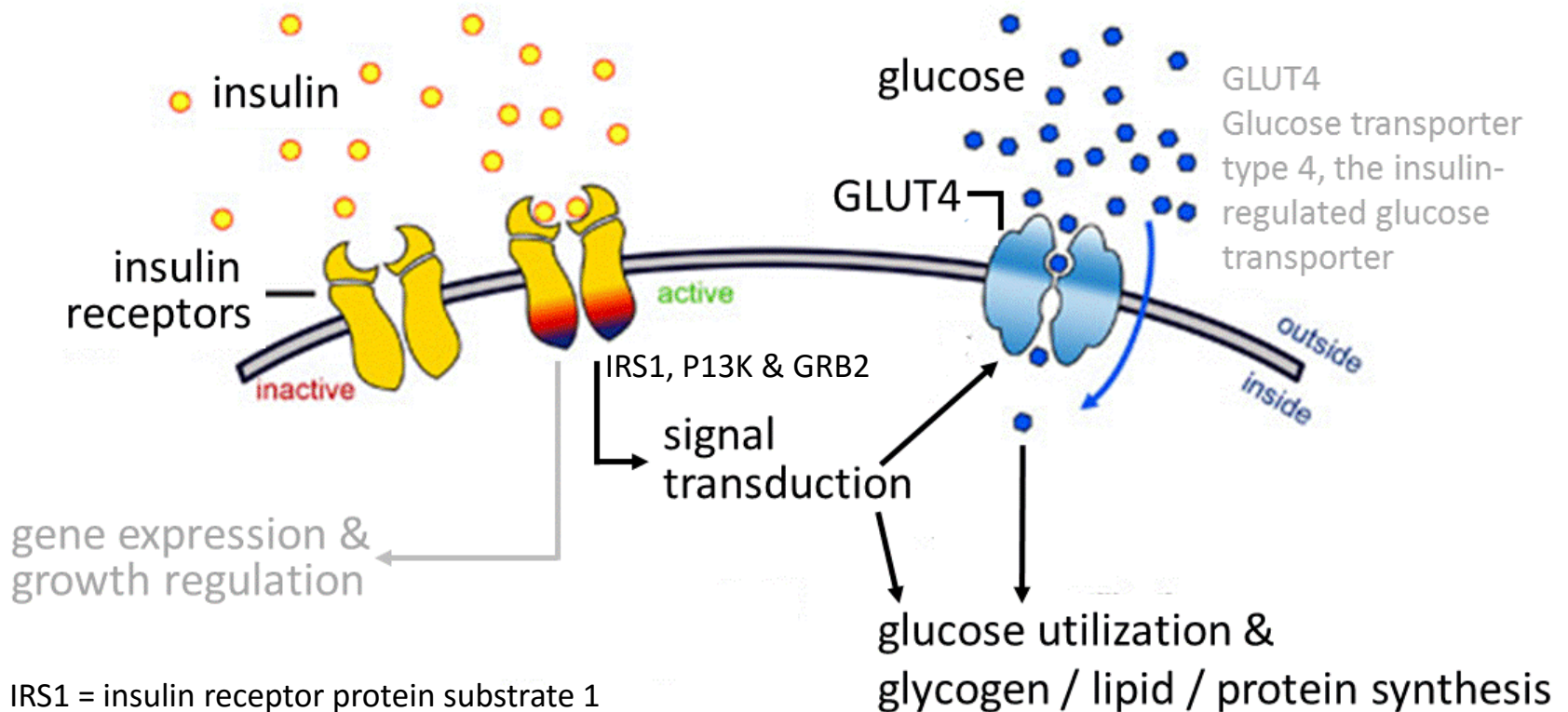


# The Most Diabetes -- China



150 Million Type 2 Diabetics ( $150/431 = 35\%$ )  
200-300 Million Pre-Diabetics  
11.6% of Chinese Adults

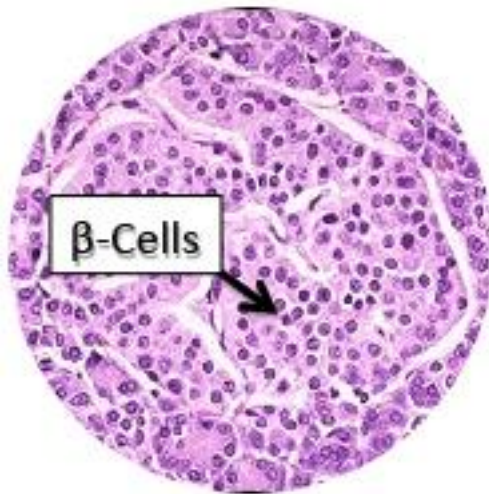
# How Insulin Works



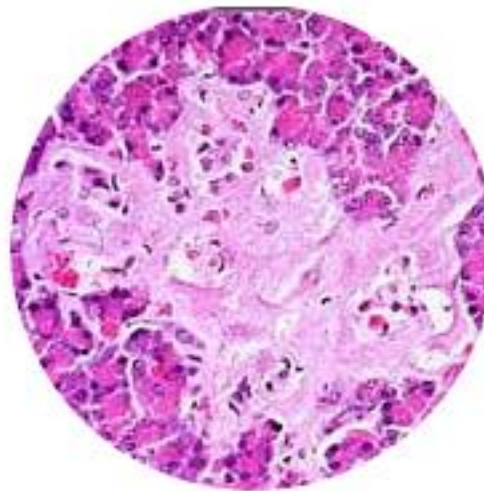
IRS1 = insulin receptor protein substrate 1  
P13K = phosphoinositide 3-kinase  
GRB2 = growth factor receptor binding protein 2

# Diabetes: Pancreatic $\beta$ -Cell Failure

Normal

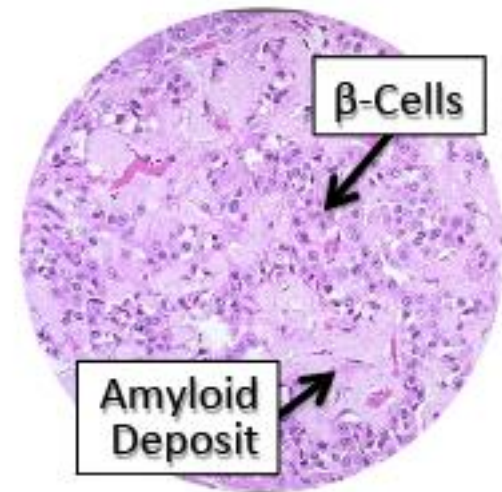


Type 1 Diabetes



$\beta$ -cells eliminated and replaced with hyaline connective tissue

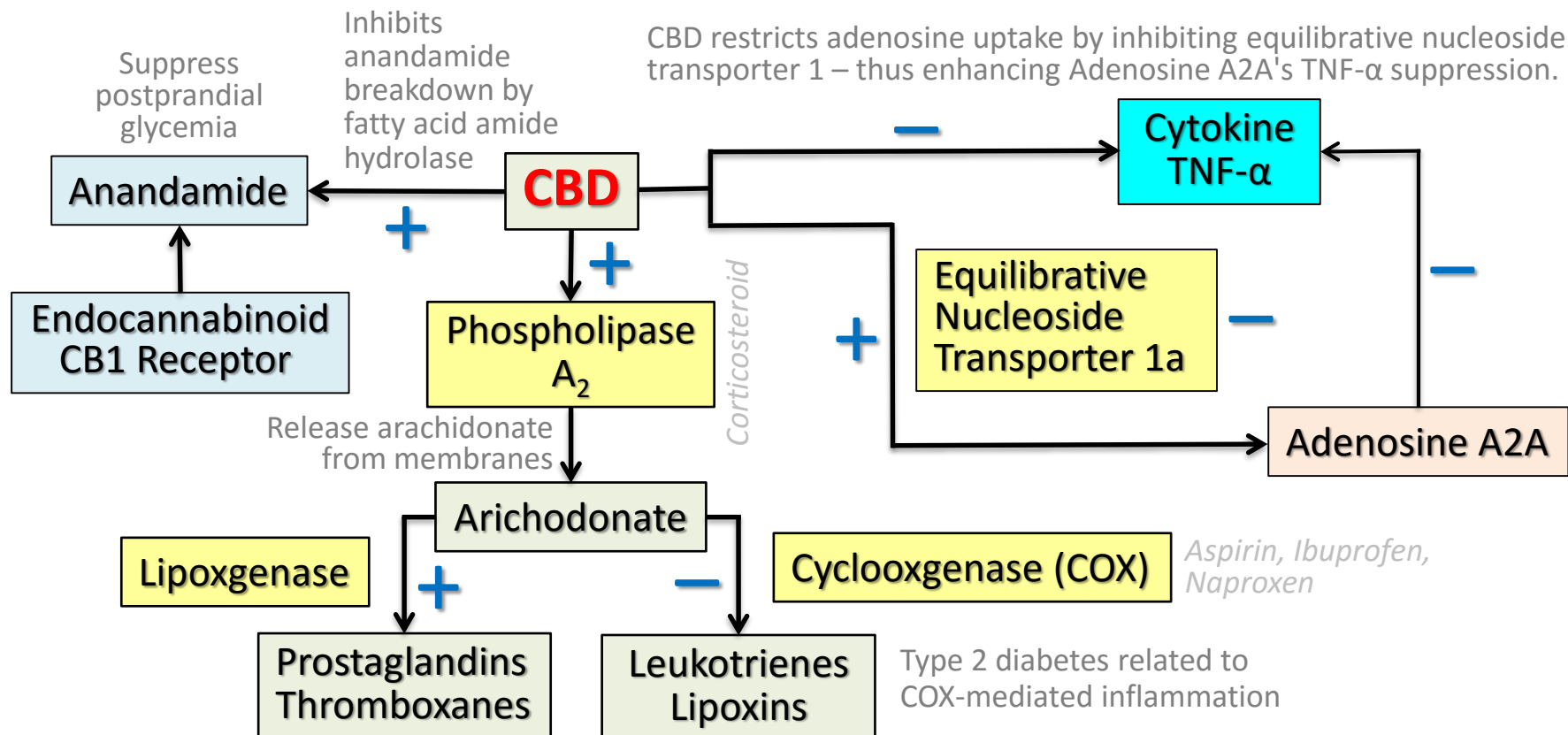
Type 2 Diabetes



$\beta$ -cells loss secondary to insulin resistance; islet amyloid made by  $\beta$ -cells with insulin B chains

Amyloid – Regulates insulin and glucagon, satiation, and gastric emptying; but toxic in excess (an issue in both type 1 and type 2 diabetes)

# Diabetes and Cannabidiol (CBD)



Prostaglandins -- Regulators of glucose homeostasis, effects on glucose production and insulin secretion





# CBD Very Safe in Humans



- Non-Psychoactive
- No Impact on Psychomotor or Psychological Functions
- Chronic Use and High Doses (> 1,500 mg/day) Well Tolerated
- No Effect on Basic Physiological Parameters (Heart Rate, Blood Pressure, Body Temperature)
- No Effect on Food Intake or Gastrointestinal Transit
- No Catalepsy (Trance, Seizure, Unconsciousness)
- Co-administer CBD and Opioids without Consequence



# Resolving Unmet Needs: Efficient, Noninvasive (Oral) Drug Delivery



- **Entry into the Blood Low when Taken by Mouth**
  - 5-6% – Variable and unpredictable therapeutic results
- **Oral (Capsules, Pills) Overwhelmingly Preferred**
  - Convenience and ease-of-use
  - Greater adherence to treatment regimens

# Smoking: Unacceptable as Medicine



- **Harmful to Health**
  - Same toxins, irritants and carcinogens as tobacco smoke
  - 50-70% more cancer-causing substances
  - Precancerous lesions, bronchitis, heart disease
  - Most physicians view smoking unfavorably
- **Imprecise Dosing – Unpredictable Effects**
- **Oral Administration Safer – Preferred by Doctors and Patients, but with Its Own Challenges**



# Plant Extracts – Problematic and Unscientific



Alcohol-Processed,  
Whole-Plant Extract

- **Varying Treatment Outcomes**
  - Lack of standardization (challenging)
  - Diversity of plant strains and growing conditions
  - THC concentrates
- **Unsafe –Adverse Effects (40-47%)**
  - Upsurge in emergency room visits (Colorado)
  - Cardiovascular complications
  - THC-induced paranoia
- **Hyperalgesia (Increased Sensitivity to Pain)**







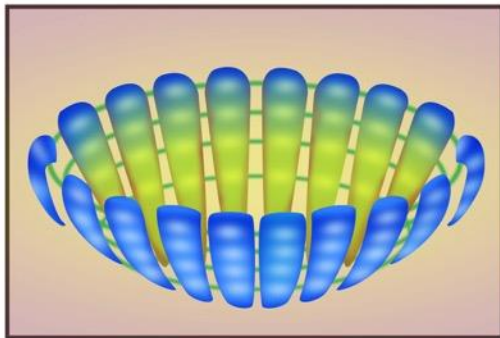
# Oral Bioavailability

- Degree to Which a Substance is Present in the Blood after Being Taken by Mouth
- **CBD – Low Bioavailability**
  - Most wasted – only 5-6% enters the bloodstream
- Predictive of Clinical Outcomes
  - Low
    - Variable dosing and unpredictable therapeutic results
    - Compensate with larger doses
      - Drug-induced idiosyncratic liver disease
      - Prohibitive or unaffordable drug costs
  - High
    - Key to therapeutic success
    - Consistent dosing and predictable treatment outcomes



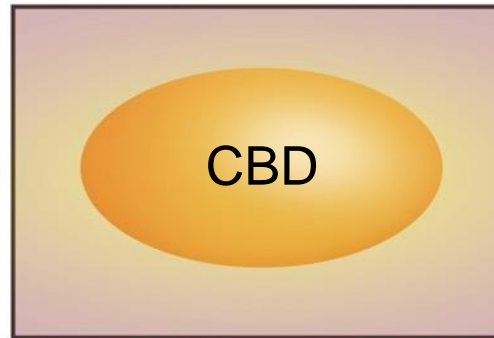
# ANANDA Particulate Technology: Increasing CBD Bioavailability & Performance

Nano-Micelle



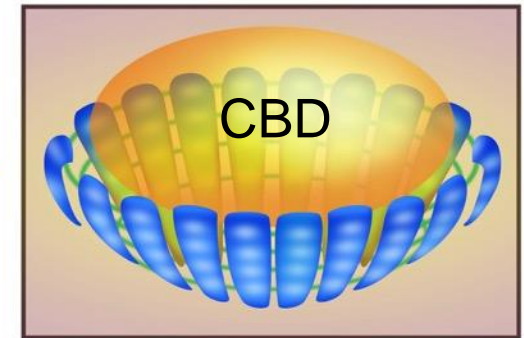
- Nanotechnology
- Below 50 nm in Size
- GRAS Compounds
- FDA Approved
- Cost Effective
- Unique, Patented

CBD



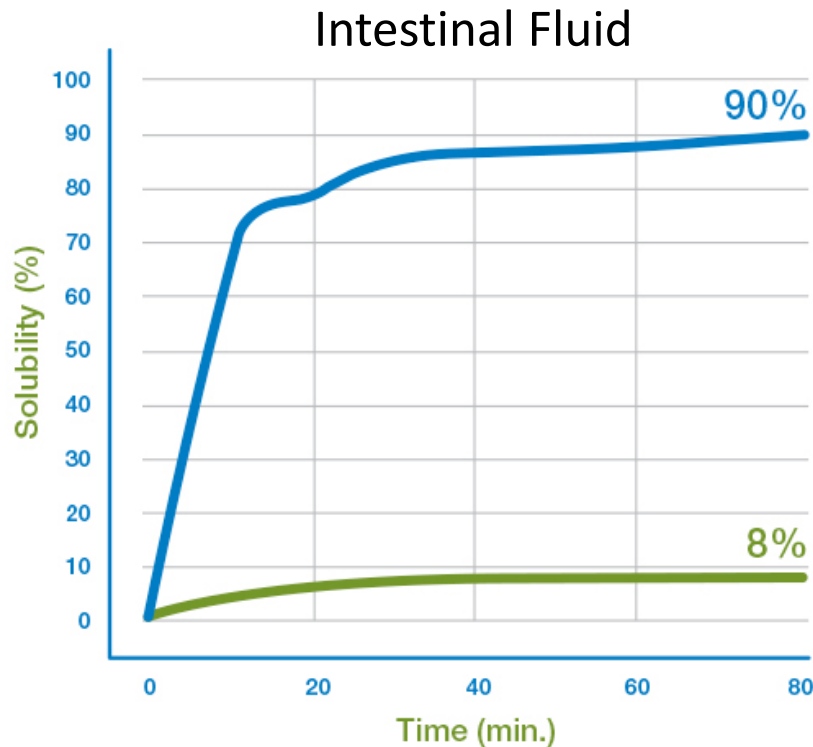
- Insoluble in Water
- Low Bioavailability
- Barely Absorbed after Oral Administration
- Sizable Degradation in Weeks or Months

Enhanced CBD



- 100% Water Soluble
- High Bioavailability
- Enhanced Biological Performance
- Stable for Years, Even at 40 °C

# Solubility Is Key



CBD with ANANDA  
Particulate Technology  
Phase 1

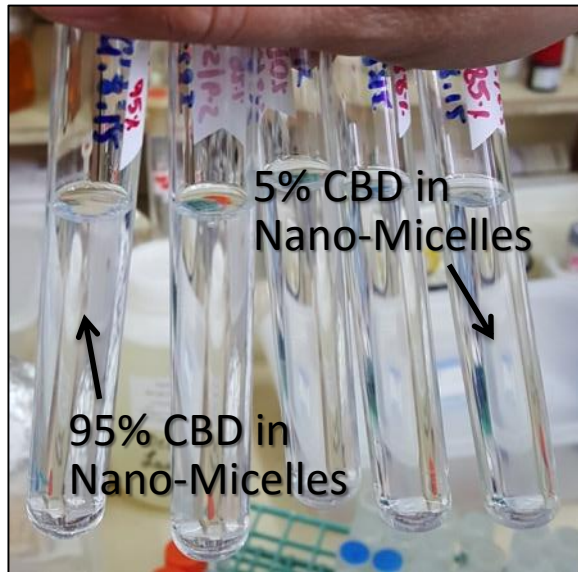
**Unmet Need  
Successfully Resolved**

CBD Only

CBD's Poor Solubility Limits Bioavailability Partly  
Due to Low Dissolution in Gastrointestinal Fluid

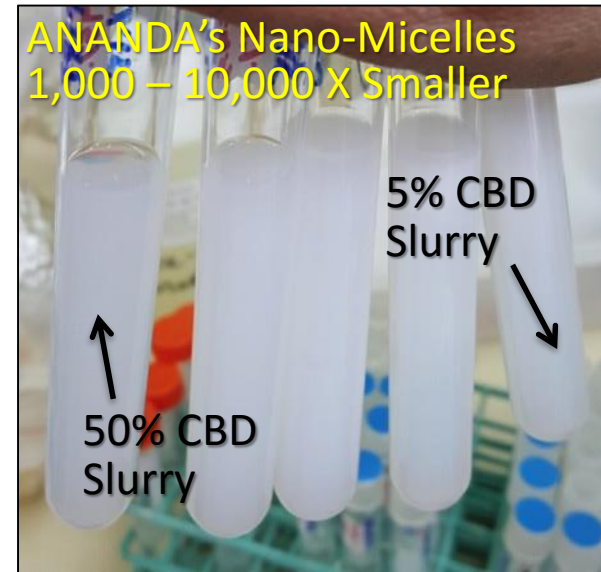


## ANANDA's Unique Nano-Micelles



- 100% Water Soluble
- Crystal Clear
- Odorless
- Tasteless
- Bacteriostatic
- Stable for 3 years (at 40 °C)

## Solubilization Technologies by Others



- Poorly Water Soluble
- Turbid or Cloudy
- Pungent Odor
- Bitter, Unpalatable Taste
- Supports Bacterial Growth
- Refrigeration Needed





# Enhanced CBD in Capsules and Soft Gels



- Enhanced CBD Capsules
- Both Gelatin and Vegetable
- Behaves Like an Oil-Based Substance, but Still 100% Water Soluble
- Stable Shelf-Life – Over 12 Months

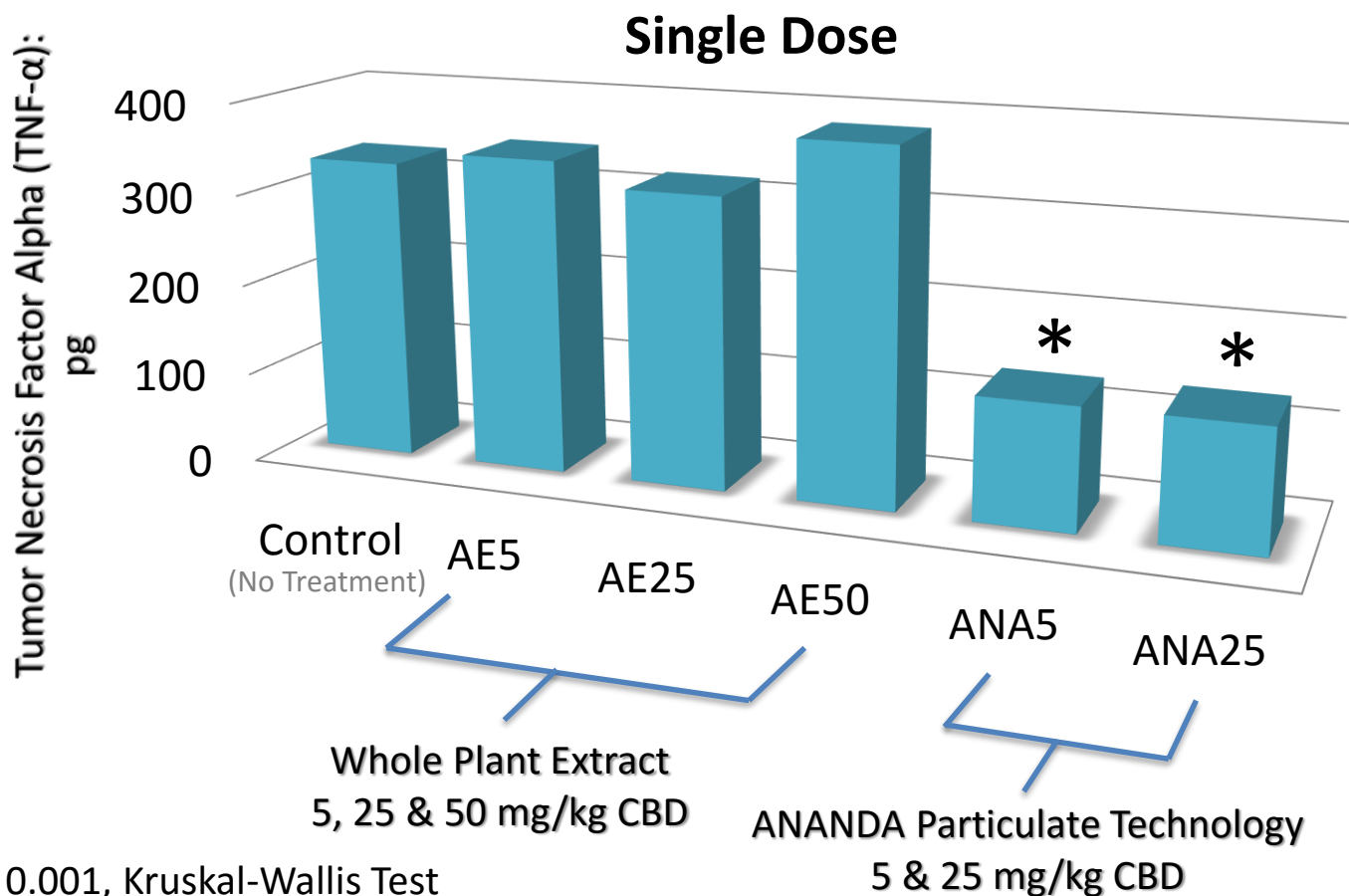
- Enhanced CBD Soft Gels

# Tumor Necrosis Factor Alpha (TNF- $\alpha$ ): A Potent Immune System Cytokine

- Key to the Inflammatory Response
  - Made by activated macrophages, T lymphocytes and other immune cells
- Central to the Pathogenesis of Insulin Resistance and Type 2 Diabetes
  - Obesity typified by elevated TNF- $\alpha$  levels
  - Negative impact on insulin signaling and glucose uptake
  - **Glucose uptake normal with TNF- $\alpha$  antibodies**
- Critical Factor in the Autoimmunity That Leads to Type 1 Diabetes
  - **Type 1 disease progression arrested with TNF- $\alpha$  antibodies**



# Tumor Necrosis Factor Alpha (TNF- $\alpha$ ): ANANDA-Enhanced CBD & Conventional Extracts

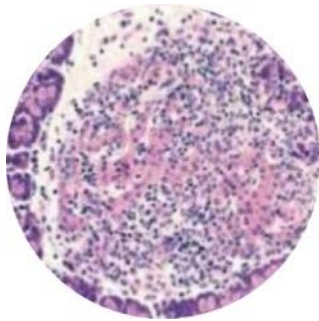


\* =  $P < 0.001$ , Kruskal-Wallis Test  
 pg = one billionth of a gram



## ANANDA-Enhanced CBD & Conventional Extracts

- Significant and Sizeable Reduction in TNF- $\alpha$  with Lesser Amounts of ANANDA-Enhanced CBD
- Extracts – Statistically Irrelevant Impact on TNF- $\alpha$



Early Type 1 Diabetes (Honeymoon)  
Lymphocytic Infiltration into Islets

**ANANDA-Enhanced CBD a Prospective Therapy for Stabilizing, Reversing and Maybe Even Preventing Type 2 and Type 1 Diabetes**





## Type 2 Diabetes – Animal Model



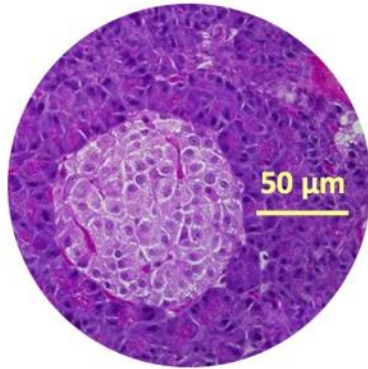
- Desert Sand Rat (*Psammomys obesus*)
- Dead Sea Valley, Israel
- Naturally Eat Low-Caloric Vegetation
- Obesity and Type 2 Diabetes with a Laboratory Diet
  - Reach an irreversible hypoinsulinemic state within 4-6 weeks



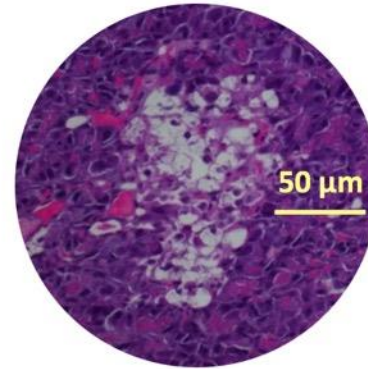
## Type 2 Diabetes – Animal Model

- Pancreas in Hyperinsulemic Rodents Protected by Enhanced CBD, Decreased Islet and  $\beta$ -Cell Destruction

Healthy Islet in  
a CBD-Treated  
Sand Rat

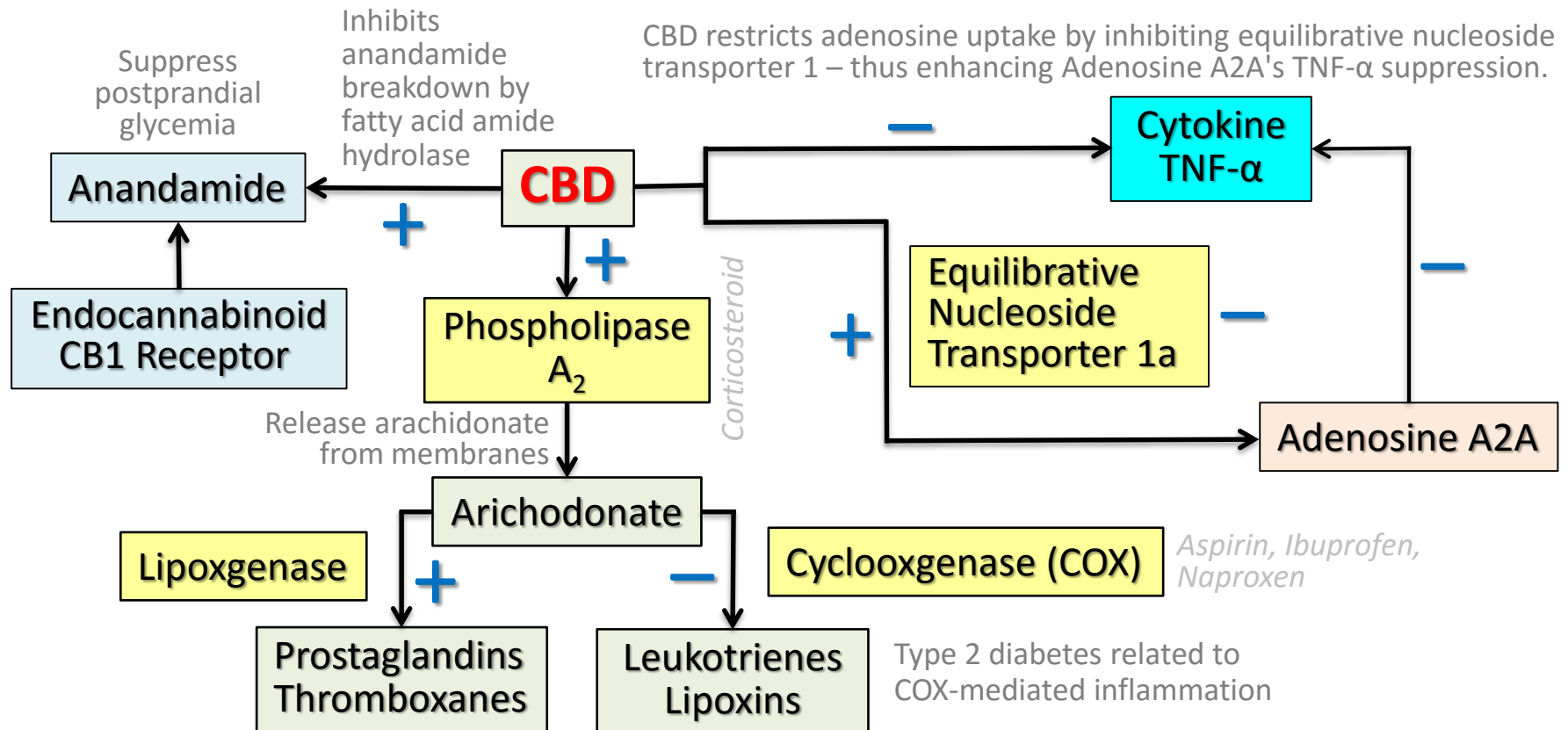


Damaged Islet in an  
Untreated Sand Rat



- Minimization of Amyloid Deposits, Virtually Disappear
- Increased Insulin Levels
- Blood Glucose Levels Reduced
- Lower Weight with Enhanced CBD – No Obesity

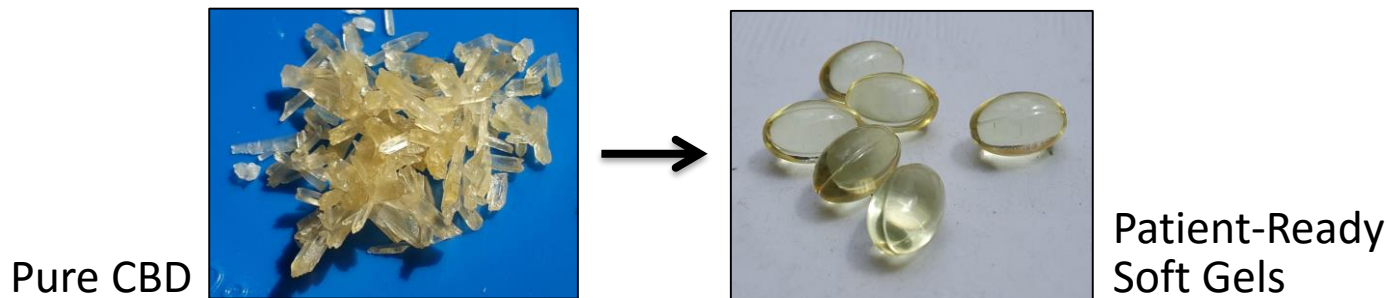
# CBD: A Diabetes Therapy



Prostaglandins -- Regulators of glucose homeostasis, effects on glucose production and insulin secretion



# Unmet Need: CBD Purification Very Costly



- Affordable Drugs = Pervasive Health Care
- Unique, Patented Methods
- Set the Stage for Affordability
  - Also, use less with enhancement technology





Thank You  
Gracias  
Merci  
תודה  
谢谢

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