



**INSULIN SECRETION EFFECT OF 2,17-  
DIOXOSPARTEINE, 17-  
THIONOSPARTEINE, MULTIFLORINE  
AND 17-HYDROXY-LUPANINE ON RAT  
LANGERHAN'S ISLETS**

**Carmen Magdalena Gurrola Díaz, Ph.D.**  
**Universidad de Guadalajara**



# Participants:

**Pedro Macedonio García López**

**Pedro Garzón de la Mora**

**Salvador García**

*Universidad de Guadalajara, Mexico*

**Anna K. Przybyl**

*Adam Mickiewicz University, Poland*

**Maria Inés Borelli**

*Universidad Nacional de la Plata, Argentina*

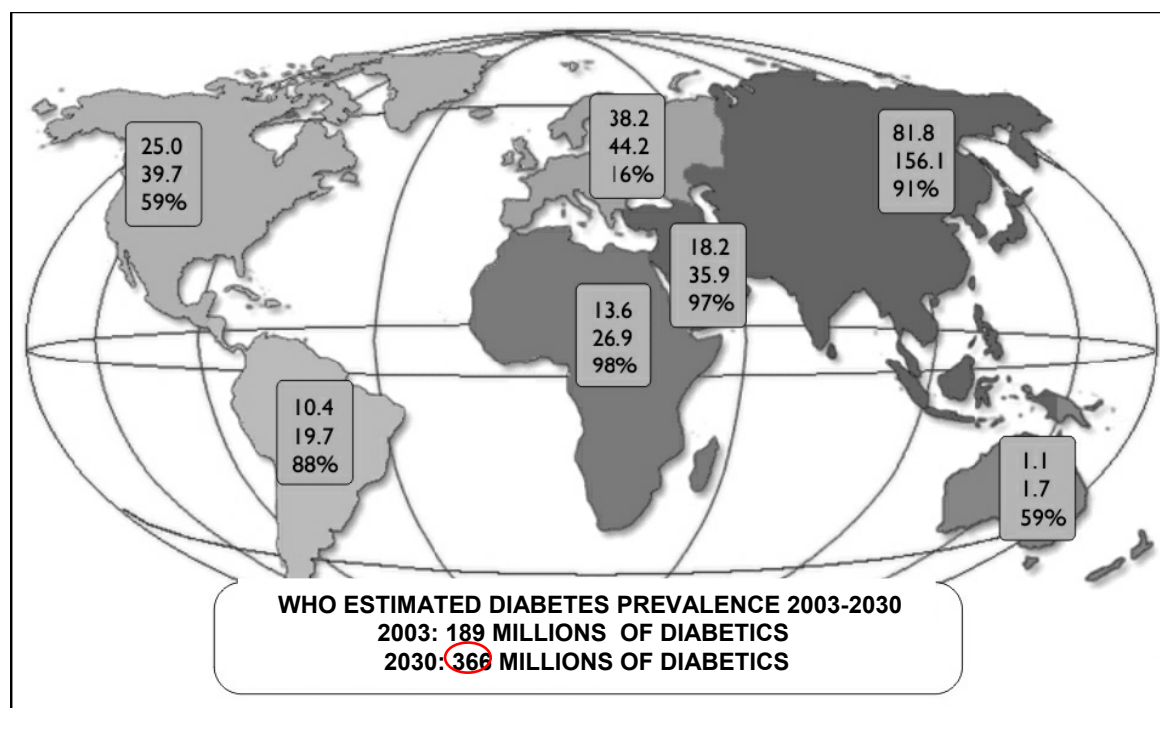


# Main Topics

- Diabetes
- Current and new alternative treatments for diabetes
- Secondary metabolites in lupin species → Quinolizidinic Alkaloids (QAs)
- Pharmacological properties of QAs
- Hypoglycemic activity of QAs

# Why is important to investigate compounds with hypoglycemic activity?

- Type 2 diabetes as **public health challenge**



# Diabetes: definition and classification



Diabetes is a metabolic disorder that arises when insulin secretion by pancreatic  $\beta$  cells fails to maintain **blood glucose levels** within normal range.

## **Type 1 Diabetes**

Autoimmune destruction of pancreatic  $\beta$  cells

10%

vs.

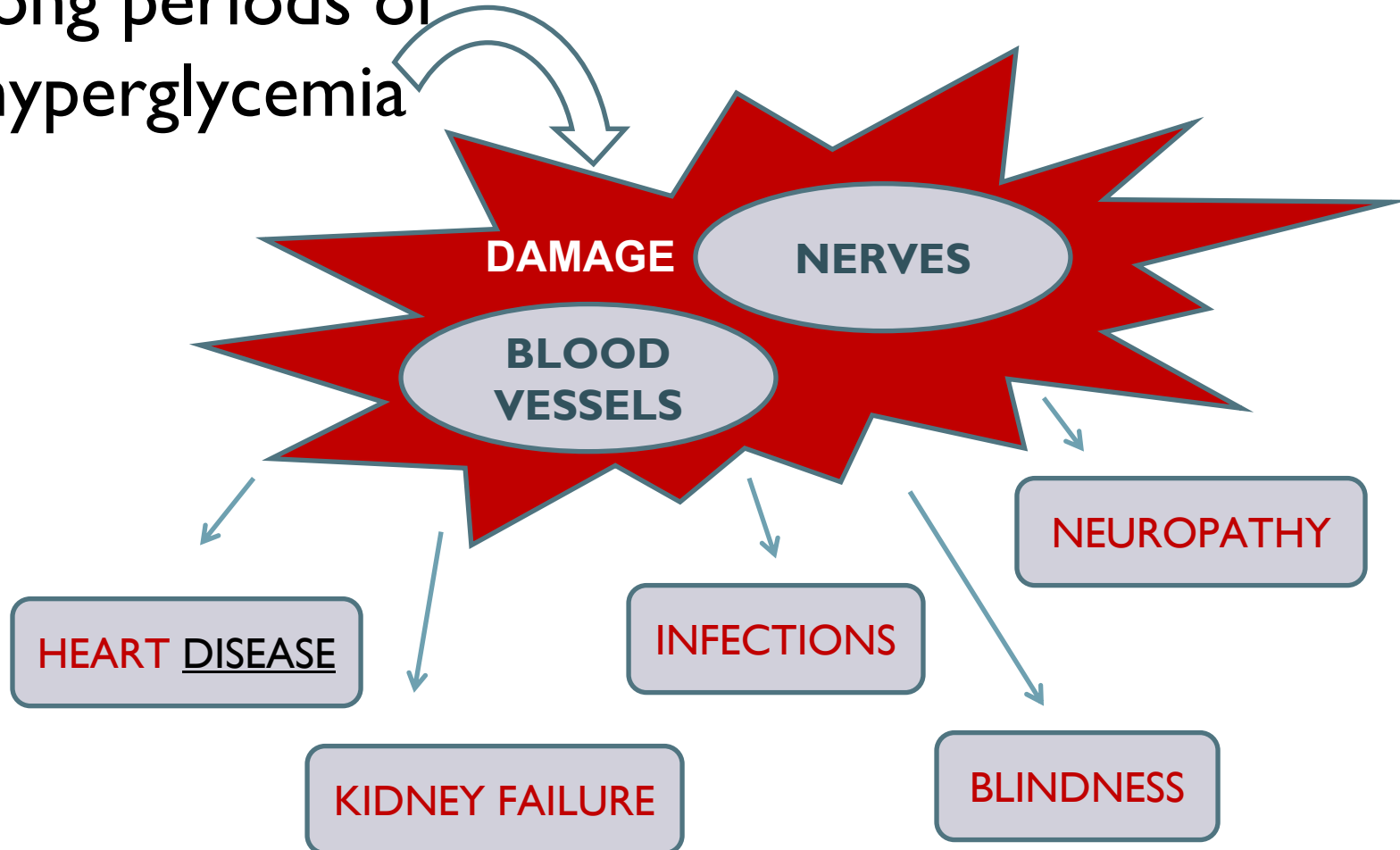
## **Type 2 Diabetes**

Failure of pancreatic insulin secretion contributing to peripheral insulin resistance

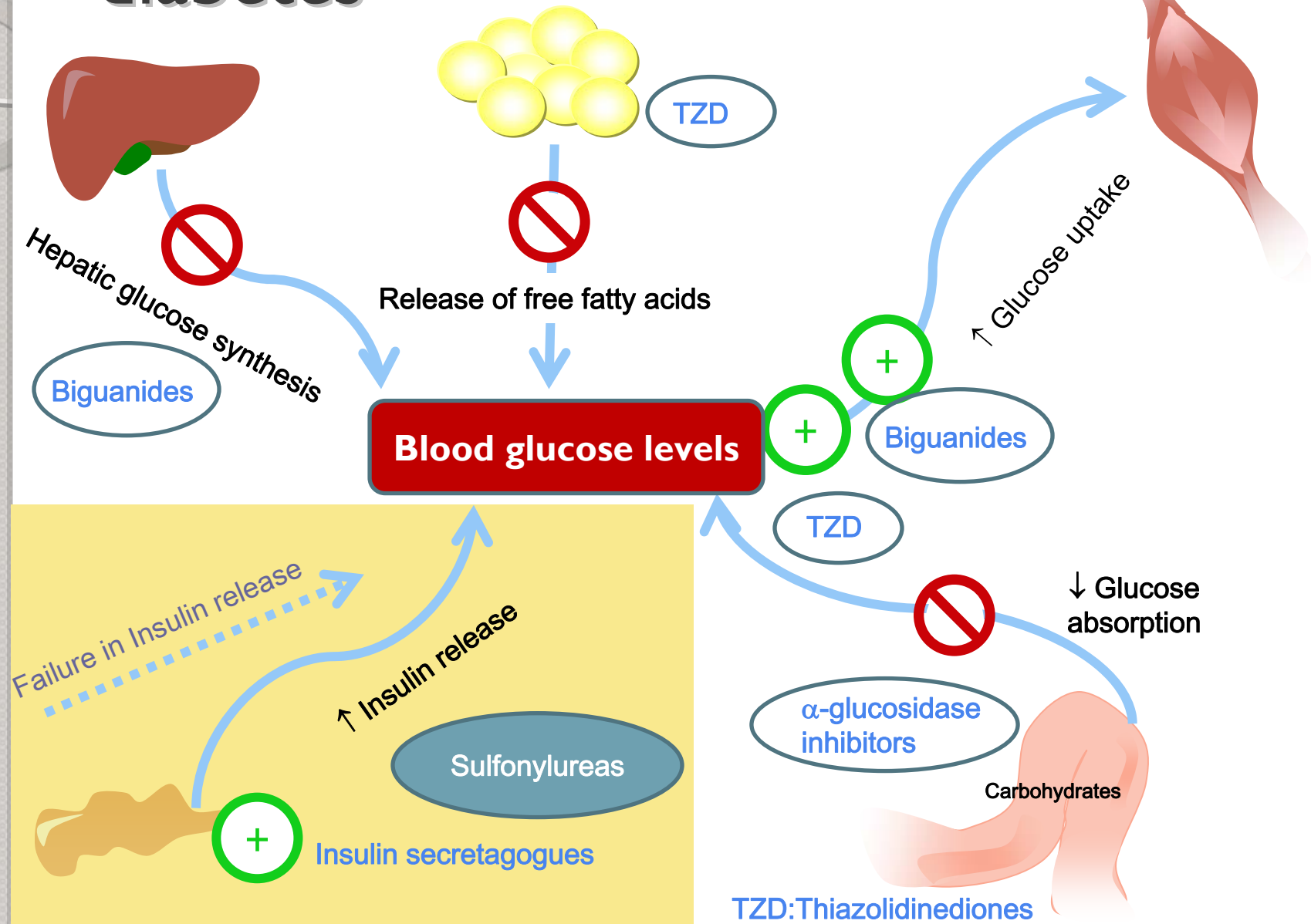
90%

# Diabetic complications

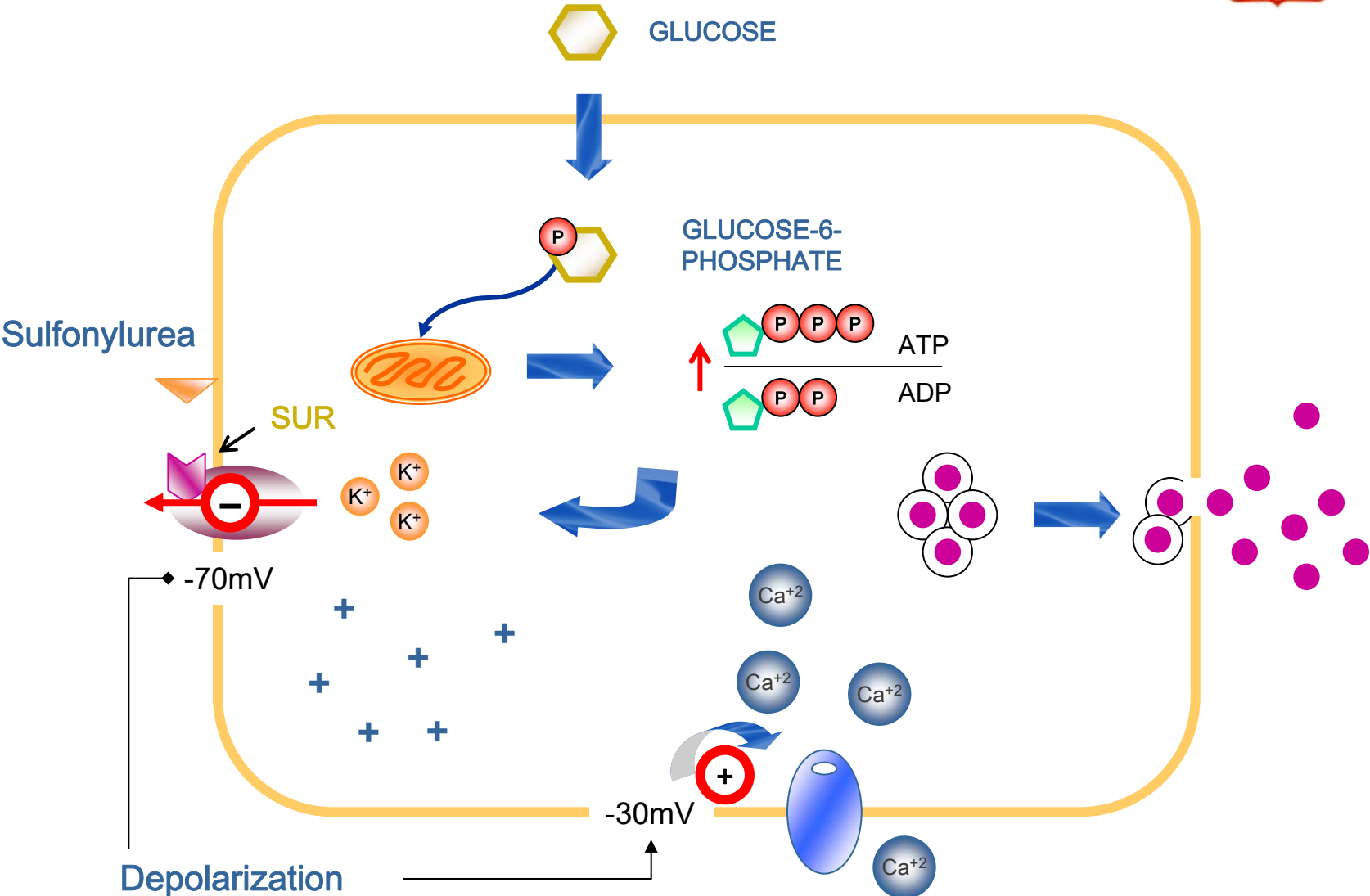
Long periods of hyperglycemia



# Current treatment of type 2 diabetes



# Enhancement of insulin secretion



# Insight of biological properties of lupin QAs



## Pharmacological activity:

Anti-arrhythmic, uterotonic, hypoglycemic,  
CNS depressants

*Alkaloids: Chemical and biological perspectives*  
*John Willey & Sons 1984; 105-148.*

## Main molecular target of QA

- Nicotinic and muscarinic acetylcholine receptors *J. Natural Products 1994; 57:1316-1319*
- Modulators of Na<sup>+</sup>, K<sup>+</sup> channels *Febs Lett 1998; 436:251-255 &*

# Recent insights....



## ☞ Hypoglycemic activity

QAs enhance insulin secretion *Eur. J. Pharmacol.*  
*2004; 504: 139-142.*

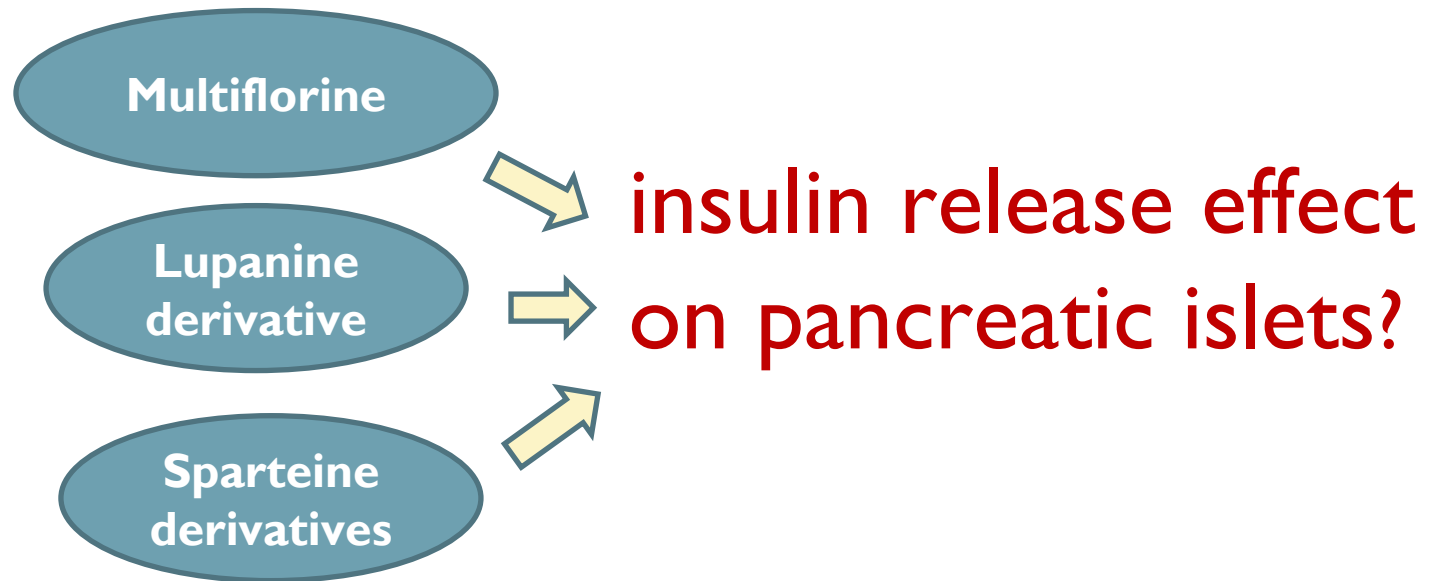
*In vitro*

Hypoglycemic effects of multiflorine *Biol.*  
*Pharm. Bull. 2006; 29: 2046-2050.*

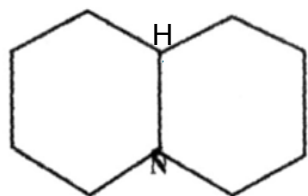
*In vivo*



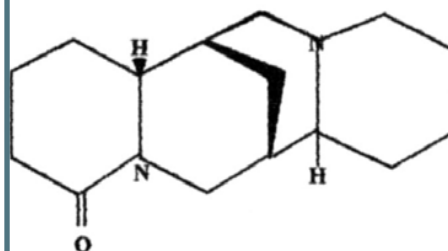
# Aim of the study



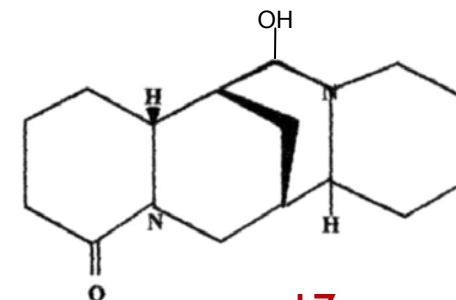
# Lupin QAs: Chemical structure



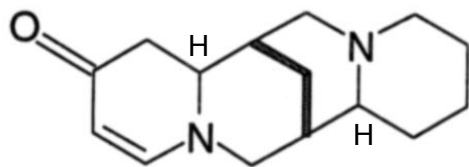
Quinolizidine



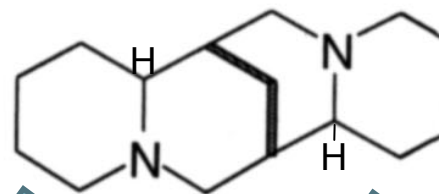
Lupanine



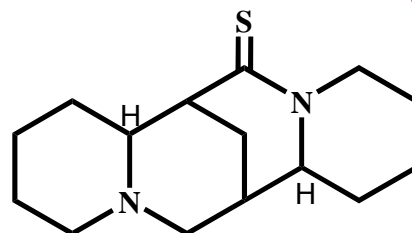
17-hydroxylupanine



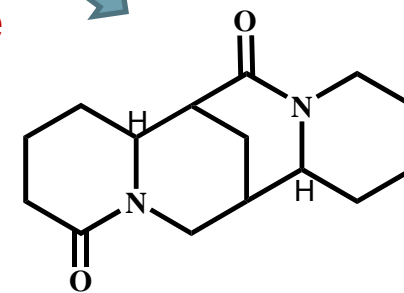
Multiflorine



Sparteine

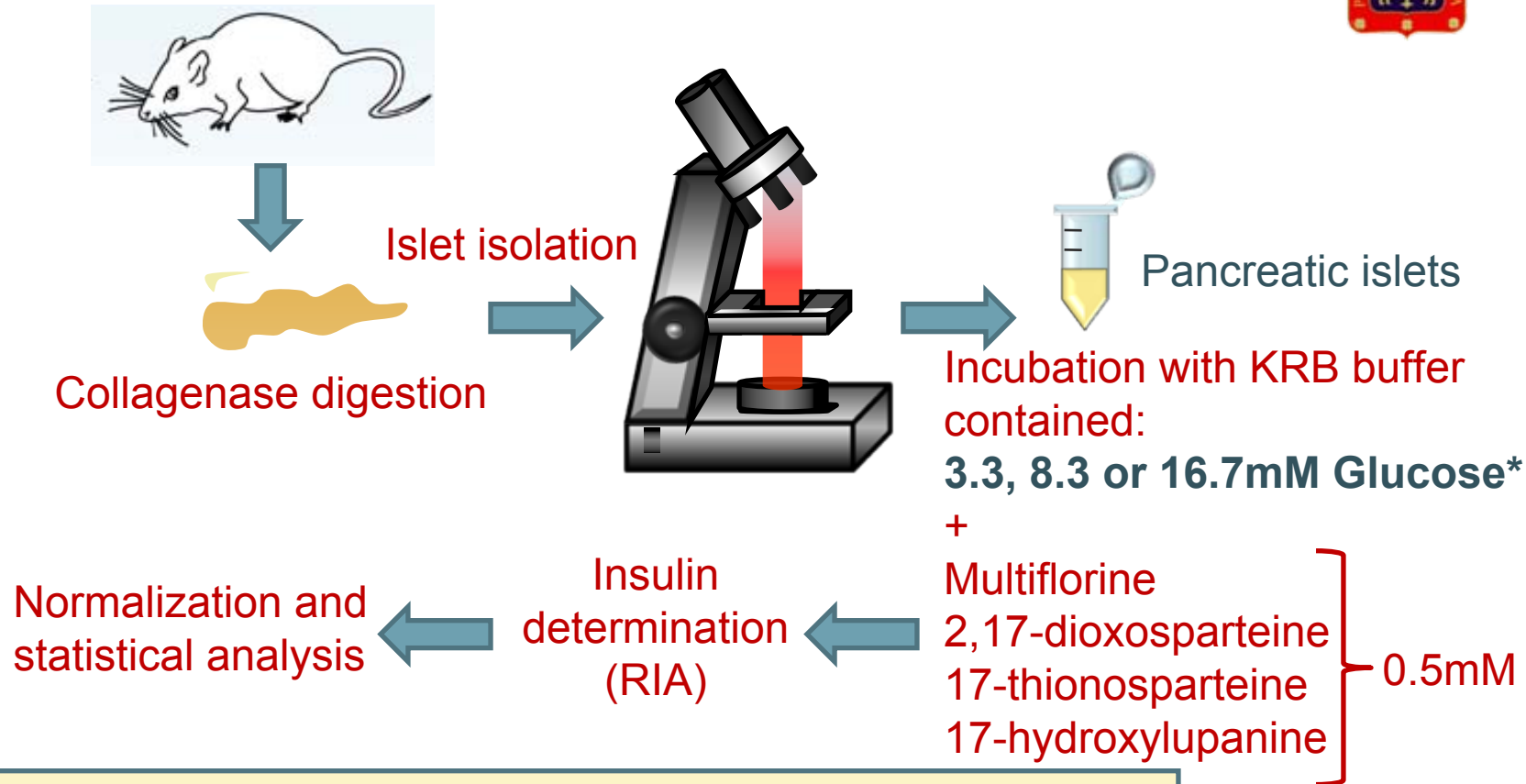


17-thionosparteine



2, 17-dioxosparteine

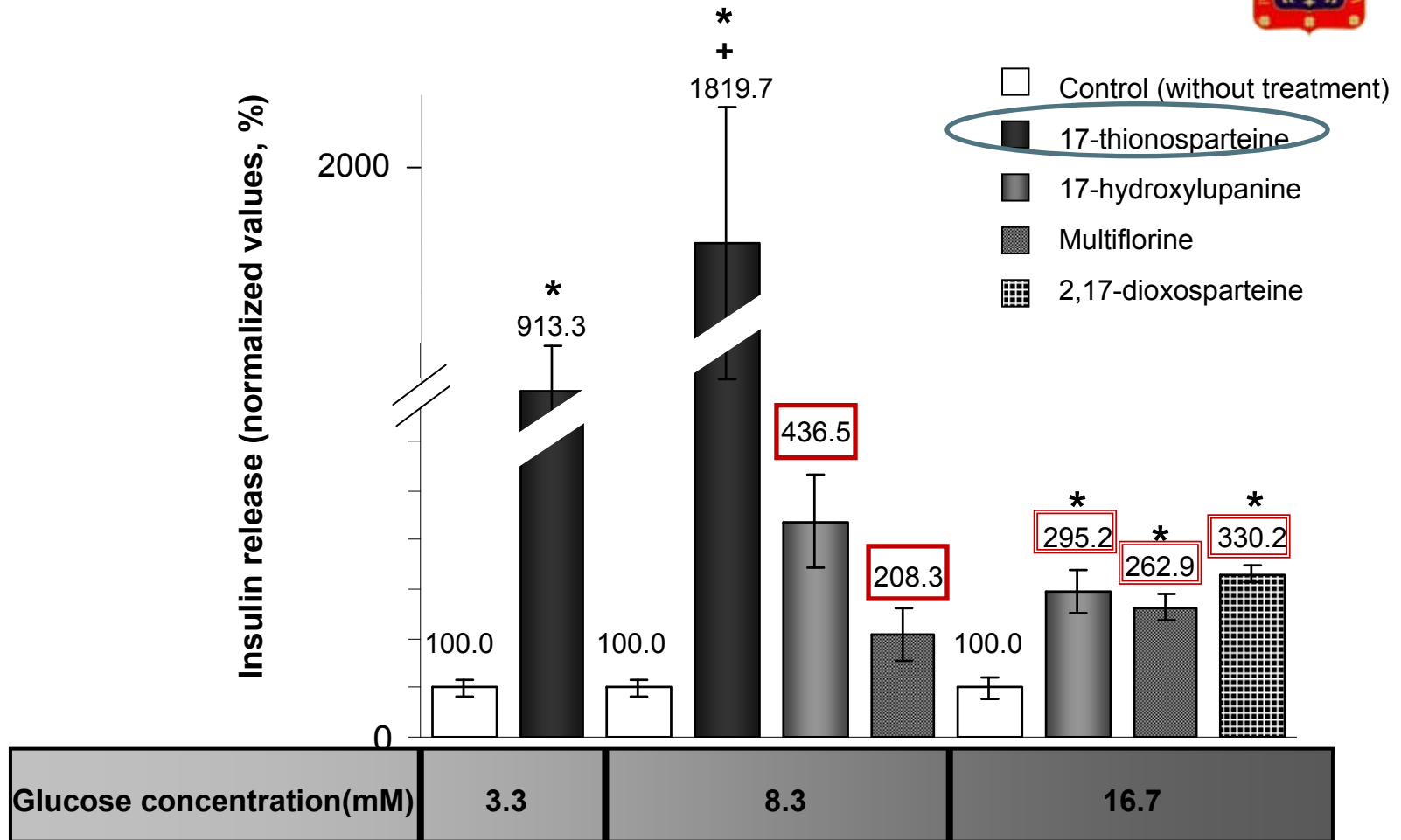
# Experimental design



## ☞ Principle of the insulin release test:

≠ **glucose concentrations\*** induced B cells to release insulin. Here, we used different glucose concentrations in combination with QA treatment to analyze the maximal enhancing effect upon glucose-induced insulin secretion.

# Results



\*  $P < 0.01$ , difference comparing each treatment vs its respective control

+  $P < 0.001$ , intertreatment difference at each specific glucose concentration



# Discussion

**Multiflorine in vivo effect** → ability to enhance insulin release

*Lupinus madrensis*: ↑ Multiflorine content

**Chemical modification of molecules** → enhance their biological activity

17-thionosparteine (Glucose [ ])

Mechanism of action of QAs → **Sulfonylureas**

.....but QAs only act at high glucose concentration, representing a potential therapeutic approach of these compounds.



# Perspectives

- ☞ Test of other [QAs]
- ☞ Test in Type 2 diabetes experimental induced model
- ☞ ED50 & LD50 in animal models

# Thank you !

