Layer-by-layer coated nanoliposomes for oral delivery of insulin

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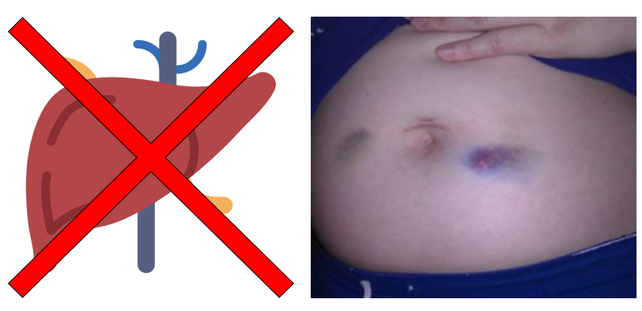
INTRODUCTION



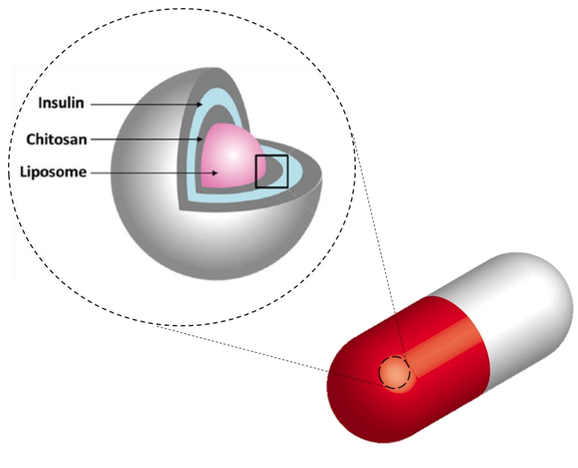
Subcutaneous Insulin

- Non-physiological
- Causes pain
- Poor compliance
- Complications

Solution

Oralized Insulin

The oral route has its own **challenge**: **lower bioavailability**	
Chemical Barriers	• Acidic Stomach • Hydrolytic Enzymes
Physical Barriers	• Enterocyte Barriers

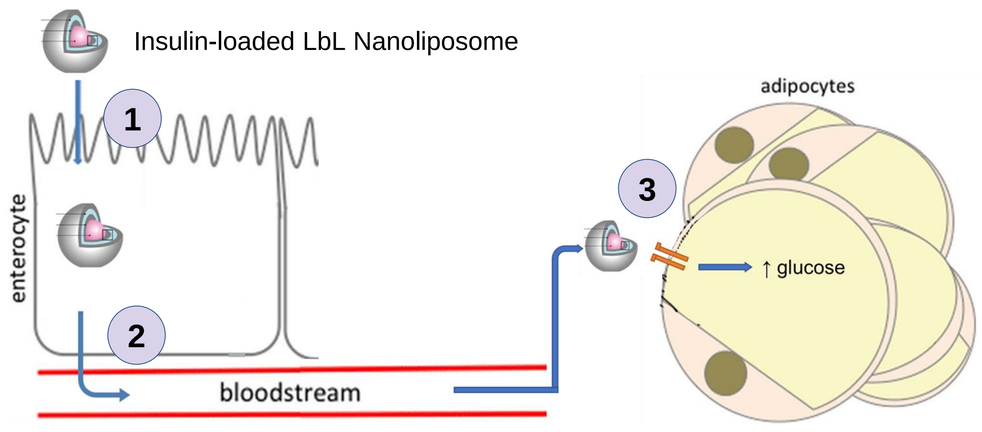


How we overcame these challenges:

- Using a **novel technique**
- **Layer-by-layer nanoliposome** insulin delivery

METHODS

In Vitro



1
Caco-2 **uptake** of LbL Insulin using confocal microscopy

2
Caco-2 **transcellular transport** of LBL Insulin (ELISA)

3
3T3 L1-MBX adipocyte glucose uptake assay for **LBL Insulin bioactivity**

In Vivo

Bloodstream assessment for **human insulin** post-Insulin loaded LbL nanoliposome gavage in **Wistar rats**

RESULTS

1

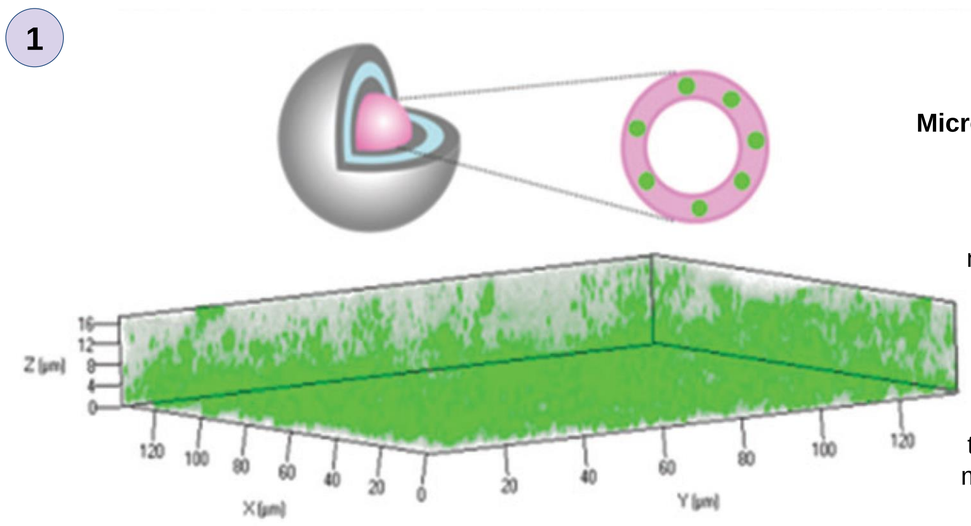


Fig 1: Confocal Microscopy of Caco-2 LbL Insulin Uptake

Confocal microscopy revealed that these nano-sized LbL coated **liposomes were heavily up-taken by Caco-2 cells** and the nanoparticles translocated to the basal side of the monolayer after 4 hours of treatment

2

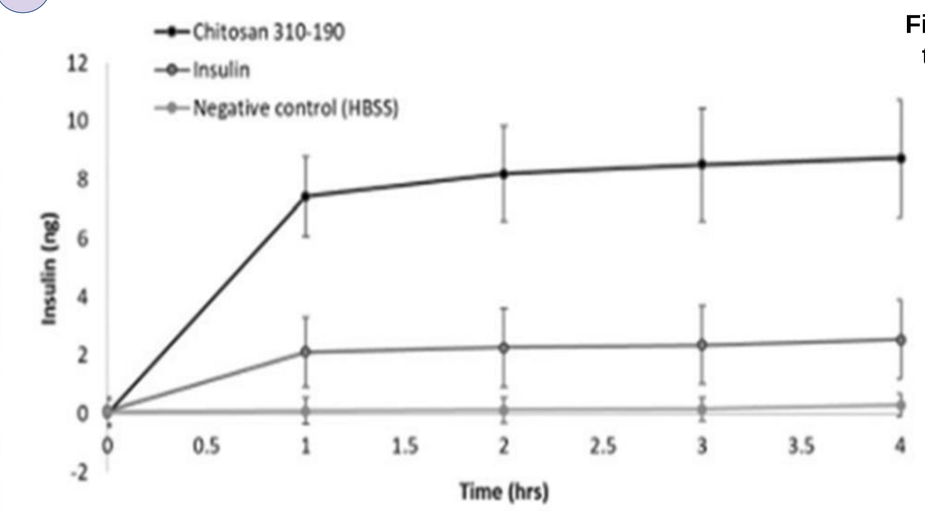


Fig 2: Caco-2 transcellular transport of LbL Insulin

The amount of **insulin** (measured by ELISA) transported across the Caco-2 monolayer was **3-fold higher when loaded in the LbL coated liposome compared to bare insulin solution**

3

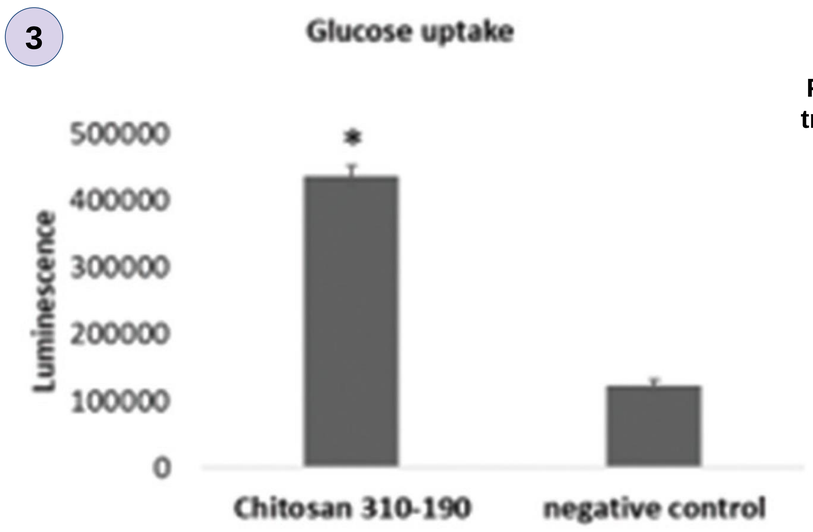


Fig 3: Glucose uptake on transported LbL insulin in matured 3T3 L1-MBX adipocytes

Luminescence detected for cells treated with the transport fluid was about **3.5× higher** than the cells treated with PBS negative control

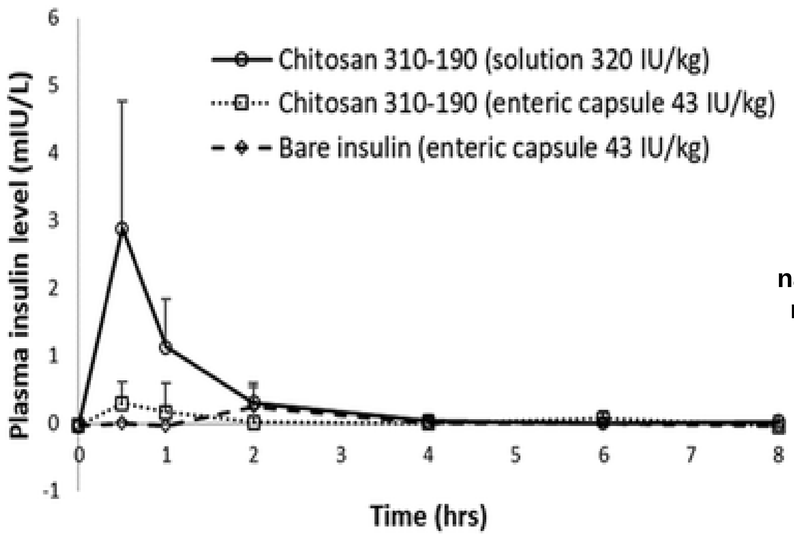


Fig4: *In vivo* pharmacokinetics of insulin loaded LbL nanoliposomes orally administered to Wistar rats

Oral administration of insulin loaded **LbL nanoparticles resulted in a rapid increase in plasma insulin concentration** which subsequently decrease to the baseline level
No significant insulin was detected using an enteric coated capsule

CONCLUSION

In vitro and *In vivo* results reveal the potential of the LbL technology using chitosan and insulin as an oral delivery system for treating diabetes mellitus. These LbL coated liposomes were **able to protect insulin during its GI transit and ensure its insulin payload reached the systemic blood circulation**.

LbL Technology

A layer-by-layer technique of surface modifying liposomes with alternating layers of chitosan and insulin was developed, leading to a **liposome-based nanocarrier with high insulin loading** (>10% by weight).

Uptake and Viability of LbL Insulin

The **outermost chitosan layer of the LbL coated liposome facilitated cellular uptake and transport** by Caco-2 cells and the transported **insulin demonstrated retention of bioactivity** through glucose uptake assay performed on 3T3 L1-MBX adipocytes.

Potential for Human Application

Considering the chemical and physical barriers of oralizing protein drugs, ***in vivo* detection of human insulin in rat sera** showcases the hurdles overcome using LbL nanoliposomes and is **potential in influencing blood glucose in humans**.