The Alexander Kofkin Faculty of Engineering
Bar-Ilan University

BINA Bar-Ilan Institute of Nanotechnology & Advanced Materials
Bar-Ilan University

Tiny Particles, Big Plans: Nanoparticles for Controlling Drug Transfer through the Placental Barrier

Shiri Katzir, *Menachem Motiei, Tamar Sadan and Rachela Popovtzer*
Faculty of Engineering and the Institute of Nanotechnology & Advanced Materials, Bar-Ilan University

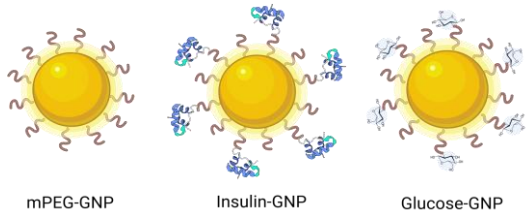
Introduction

Conventional, non-selective drug treatments during pregnancy pose significant risks to the developing fetus, as many medications can freely cross the placenta and disrupt growth or cause toxicity. Controlling drug transfer through the placental barrier is essential to ensure safe and effective treatments for pregnant women and the well-being of their babies.

Nanoparticles provide a promising solution to this challenge. When drugs are incorporated onto nanoparticles, their pharmacokinetics and biodistribution change dramatically. These engineered particles can be designed with "big plans" in mind - minimizing placental crossing to reduce fetal exposure or enhancing placental targeting to treat pregnancy complications, which mostly originate in the placenta. Understanding the design principles that govern nanoparticle behavior at the placental interface is essential for developing safe and effective pregnancy therapeutics.

In this research, we investigate how different surface functionalizations (mPEG, insulin, and glucose) influence the biodistribution of 20nm gold nanoparticles (GNP) in pregnant mice, focusing on their ability to control placental barrier penetration, for optimizing maternal-fetal drug delivery profiles.

Methods



Injection to pregnant mouse at gestational day 14.5

Harvesting placentas, fetuses and maternal organs

Determining gold content by ICP-OES

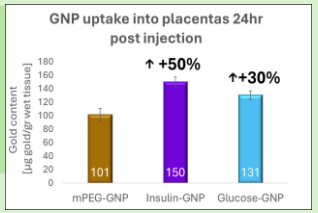
Results

Biodistribution of GNP in the fetoplacental unit

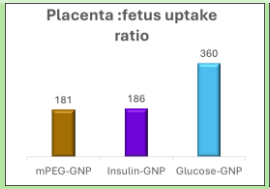
Figure 1. Uptake of GNPs in placentas, fetuses and yolk sac 24 hours post-injection.
Gold content (µg gold/g wet tissue) was quantified 24 hours after administration of mPEG- (n = 19), insulin- (n = 20), or glucose-GNPs (n = 16).

Insulin and glucose coatings significantly increase placental accumulation by 50% and 30% *Compared to mPEG-GNPs*

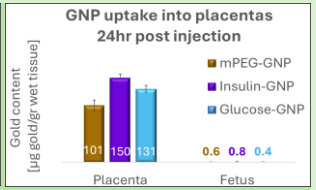
($p \leq 0.0001$ and $p \leq 0.05$ respectively)



Negligible fetal exposure (<1% of placental levels)



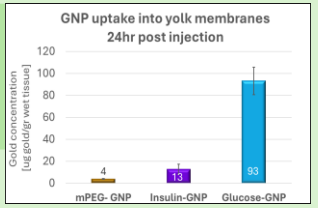
GNP accumulate 180-360 times more in placentas than in fetuses



fetal accumulation remained extremely low across all groups

Glucose-GNPs show high selectivity to extraembryonic tissue

Glucose-GNPs showed remarkably higher accumulation in the yolk sac ($p \leq 0.01$): x23 compared to mPEG-GNP and x7 compared to insulin-GNPs



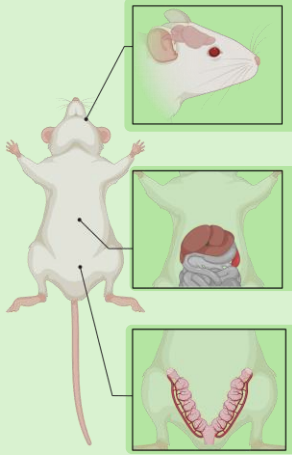
Gold nanoparticles share similar physicochemical properties

functionalization	Zeta potential (mV)	hydrodynamic diameter (nm)	UV absorbance (nm)
mPEG	-8.9 (±1.2)	41.1 (±1.1)	524
Glucose	-10.4 (±0.9)	47.4 (±0.3)	523
Insulin GNP	-9.9 (±0.8)	51.4 (±0.8)	524

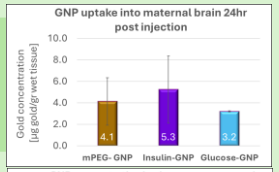
Table 1: Characterization of gold nanoparticles. Zeta potential, Dynamic Light Scattering- size measurements (hydrodynamic diameter) and UV-vis spectroscopy (SPR) of mPEG-, insulin-, and glucose-coated gold nanoparticles. Absorption around 520nm indicating formation of 20nm core size particles.

Biodistribution of GNP in the mother

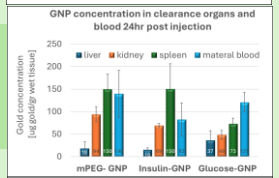
Figure 2. Biodistribution of functionalized gold nanoparticles in maternal tissues 24 hours post-injection. Gold nanoparticle concentrations following intravenous administration of mPEG-modified (n=3), insulin-modified (n=4), and glucose-modified (n=3) GNPs.



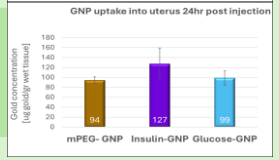
Accumulation in brain was LOW.
It was enhanced by insulin and reduced by glucose compared to mPEG-GNPs.



All three GNPs showed preferential accumulation in the spleen



Insulin dramatically enhanced uterine accumulation



Conclusions

Our study demonstrates that surface functionalization of gold nanoparticles (GNPs) significantly influences their biodistribution in pregnant mice. Functionalizing GNPs with glucose or insulin enhances their accumulation in the placenta while maintaining minimal fetal exposure (<1%). Additionally, Insulin-GNPs showed high uterine accumulation, whereas glucose-GNPs preferentially targeted the yolk sac membranes. Compared to free drugs, which often cross the placental barrier and reach the fetus, these nanoparticles offer a safer and more targeted strategy for treatment during pregnancy. Future studies will focus on conjugating these particles with therapeutic agents and evaluating their potential to treat pregnancy-related complications