SELECTING THE BEST NANOPARTICLE-BASED DELIVERY SYSTEMS FOR TRANSPORT ACROSS INTESTINAL BARRIER

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The intestinal barrier represents a serious challenge for drug delivery. Its intricate architecture, mucus layers, and tight junctions act as gatekeepers, leading to degradation and poor absorption of conventional drug formulations [1]. In the quest for more effective drug delivery systems, nanoparticles (NPs) show a great promise. NPs-based delivery systems offer enhanced stability, targeted delivery, improved bioavailability, and controlled release, promising solutions to these issues [2].

In this context, we aimed to study the transport mechanism of NPs with different characteristics (chemical structures, sizes, surfaces) across intestinal barrier over time in order to provide a deeper understanding of NPs behavior in these biological systems and further innovative, mechanistic strategies for preventing toxicity and designing more effective drug delivery systems.

Gold, magnetic iron oxide and polymeric poly(lactic-co-glycolic acid)-PLGA NPs were selected for this study in order to cover the most common NPs that are used in biomedical applications.

Obtaining the intestinal barrier model first targeted the differentiation of HT-29-MTX cells towards goblet-like, mucus-producing cells by using a MTX solution (10^{-4} M). Afterwards, both cell types were seeded at the same time in a ratio of 7:3 (Caco-2 : HT-29-MTX) at a final density of 5×10^4 cells per 24-well insert on Transwell® plates with polyester membrane and 3 µm pore diameter, in DMEM medium with 10% fetal bovine serum. The medium was changed 2-3 days before the start of the transport study (day 21 after seeding).

The Caco2/HT-29-MTX co-culture was exposed apically to 25 µg/mL NPs and subsequently the level of NPs internalized and released into the basal medium was monitored over time (after 24, 48 and 96 h). The quantity of transported NPs, penetration times and permeability coefficients were calculated using a calibration curve for each type of nanoparticle.

To evaluate the proliferation of the obtained cell cultures, but also the permeability effect induced by NPs, the transepithelial electrical resistance (TEER) was monitored using the Millipore® Millicell Electrical Resistance system (ERS).

Our results showed that all three types of NPs tested showed increased internalization in the intestinal model and none of them were transported to the basal part in the first 24 hours. Instead, a transport rate of 14.6% was recorded in the case of gold NPs after 48 hours, and the permeability of the intestinal barrier to magnetic nanoparticles (6%) appeared only after 96 hours.

In conclusion, our findings revealed that gold NPs have the best transport rate across the gut barrier and they can be used in developing more effective medications in order to significantly impact the treatment of various gastrointestinal conditions.

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References

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Figures

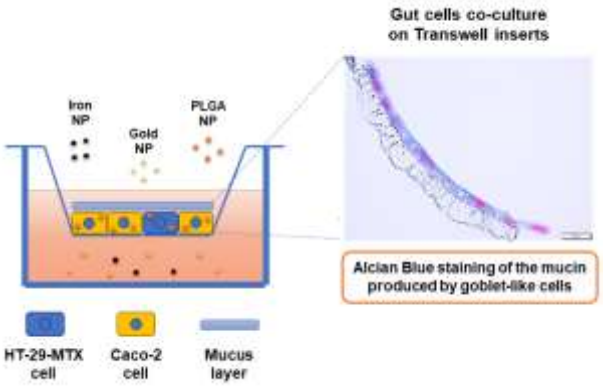

Figure 1. Dynamic transport of magnetic (iron), gold and polymeric (PLGA) NPs across intestinal barrier model.