INTERACTION OF NANOPARTICLES WITH EPITHELIAL CELLS: PARTICLE PROPERTIES, INFLUENCING TOXICITY, CELL UPTAKE AND TRANSPORT

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The interaction of nanoparticles with cells has been under extensive interest during recent years because they can play a vital role in gene and drug delivery. The work we present involves the interaction of nanoparticles with epithelial cells (Caco-2 cells). *In vitro* experiments are focused on the physicochemical properties of nanoparticles, cytotoxicity and several factors such as duration of incubation, particle size, particle concentration, chemical surface properties and temperature and how these factors can influence cellular uptake and transport. Different sizes and concentrations of aminated polystyrene nanoparticles (50, 100, 200 nm) were used in this study. The size and zeta potential of nanoparticles in biological buffer were determined using dynamic light scattering and zetasizing. Toxicity studies of 50 and 100 nm nanoparticles were also investigated by using MTS assay (can measure metabolic function), LDH assay (measure the membrane integrity as a function of the amount of cytopasmic LDH released into the medium) and TEER. Higher concentrations of 50 and 100 nm aminated polystyrene nanoparticles can induce higher cellular toxicity when compared to lower concentrations.

Uptake and transport polystyrene nanoparticles (50, 100, 200 nm; aminated nanoparticles {positively charged} and 100 nm carboxylated nanoparticles {negatively charged}) across Caco-2 cells was also investigated. This work found that cellular uptake and transport was increased by increasing the concentration of nanoparticles (100 µg/ml > 50 µg/ml > 25 µg/ml), decreasing the diameter of aminated nanoparticles (50 nm > 100 nm > 200 nm) and increasing the temperature to 37°C. In this study we found the uptake of nanoparticles was decreased (60%) at 4°C which suggests that the uptake of these particles through Caco-2 cells can be energy dependent endocytic process. Furthermore, uptake and transport studies across Caco-2 cells were also conducted to investigate the effect of two different functional groups at the surface of polystyrene nanoparticles. Uptake and transport of 100 nm aminated and carboxylated polystyrene nanoparticles during 4 hours (100 µg/ml) was compared and we found that carboxylated nanoparticles experience a higher degree of repulsion from the negative cell membrane and can have a higher transport across the cells compared to aminated nanoparticles. This may be due to aminated nanoparticles (positively charged) becoming entrapped at the cell surface and undergo higher uptake, rather than transport across the cells than negatively charged particles. We propose this occurs through electrostatic interactions.

These findings create a field which explores surface modifications of nanoparticles and how these can be used to assess new formulations for oral administration of therapeutic proteins or peptides.

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