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Q-Sense | [Application Note] 24

Screening nanoparticle-protein interactions in nanotoxicology studies

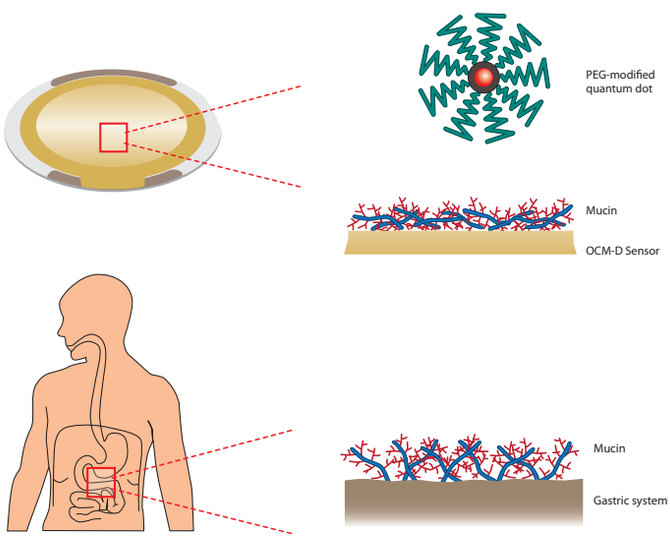
Pedersen et al.[1] have demonstrated how Quartz Crystal Microbalance with Dissipation (QCM-D) in combination with simplified model systems can be used as an early screening method of biodurability of potentially toxic nanoparticles. The presented results demonstrate how important information about the adhesive properties of nanoparticles to biomimetic surfaces can be assessed in straight-forward in vitro assays employing surface-based analytical techniques.

Introduction

Novel engineered nanomaterials are potentially hazardous and may have adverse effects on biological systems. Therefore it is important to develop methods to assess the degree of safety and toxicology hazards of nanoparticles. This includes methods for the characterization of physico-chemical properties of engineered nanomaterials and their interactions with model biological systems of varying complexity. The stability in solution of quantum dots (QDs) with different poly (ethylene glycol) (PEG)-coatings was studied under conditions which were designed to closely mimic those in the stomach and duodenum of the small intestine (figure 1). Mucin is a highly glycosylated protein which is present in the gastrointestinal tract. QCM-D experiments were used to investigate quantum dot adsorption to mucin-modified sensors. QCM-D is particularly useful in this context as structural rearrangements of polymers are readily observed by changes in frequency (f) and dissipation (D).

Experimental

Pedersen et al. propose a QCM-D assay to evaluate the gastrointestinal mucoadhesion of a wide variety of nanoparticles. Such an approach can be coupled to other in vitro systems to assess nanoparticle uptake by, and toxicity to, intestinal epithelia.

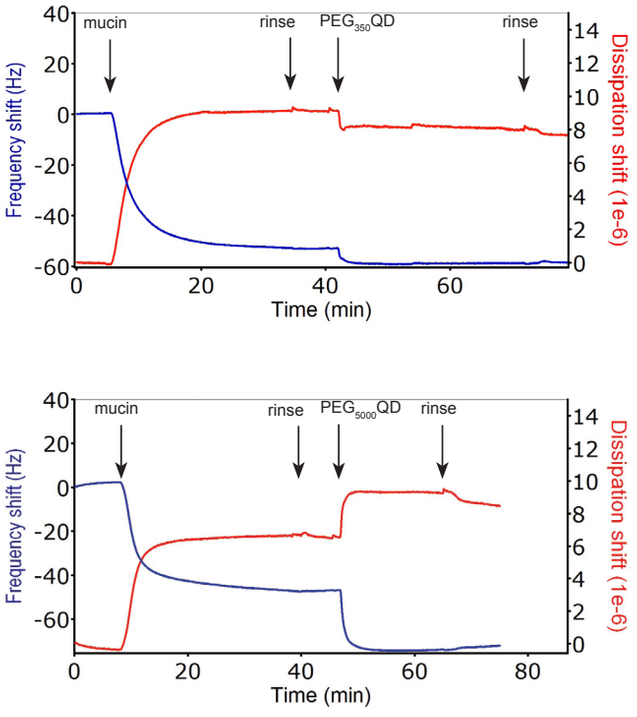


[Figure 1]: Illustration of a model system for nanoparticle interactions in the gastric system. Quantum dots (QDs) are one of the many interesting classes of nanoparticles for biomedical applications. QDs are semiconductors and their small size gives them remarkable physical properties.

Results and discussion

Mucin layers were deposited on gold-coated quartz crystals. The adsorption of mucin occurred rapidly, as indicated by the decrease in resonance frequency (corresponding to mass uptake) and the increase in dissipation (corresponding to a decrease of the layer rigidity) upon introduction of the glycoprotein (figure 2).

When exposing the mucin layer to the nanoparticles, an increase in mass (decrease in f) was observed for the two different PEG-coatings: PEG5000-QDs versus PEG350-QDs. Depending on the PEG coating molecular weight the dissipation either increased or decreased during the adsorption process. These results point towards an increased or decreased viscoelasticity, respectively, of the mucin layer associated with nanoparticles.



[Figure 2]: Frequency and dissipation shifts obtained upon adsorption of mucin to gold sensors, followed by the addition of PEG-coated QDs. Mucin layers were deposited at 25 µg/ml and the QD concentration was 2 µM, each in 0.03 M NaCl at pH 4. Presented data were obtained at the 3rd harmonic.

Conclusions

The association of the PEG-coated QDs with the mucin layer is suggested to explain the protective effect of mucin against acid-induced degradation of the nanoparticles.

Acknowledgements

The presented data were kindly provided by Prof. J. Pedersen at the University of Wisconsin, Madison.

References:

1. Wiecinski, P.N., Metz, K.M., Mangham, A.N., Jacobson, K.H., Hamers, R.J., and Pedersen, J.A. Gastrointestinal biodurability of engineered nanoparticles: Development of an In vitro assay, Nanotoxicology 3(3), 202-214 (2009).

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