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Interaction of mucins with bioinspired polymers and drug delivery particles

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Mucins are glycoproteins with high molecular weight and an abundance of negatively charged oligosaccharide side chains, representing the main components in the mucous gels apart from water. Mucin structure consists of a flexible backbone (mainly serine and threonine residues) which serves as anchoring points for oligosaccharide side chains, and hydrophobic "naked domains" enriched in cysteine residues [1,2]. The latter can form inter-molecular bonds via disulphide links, promoting mucin association in solution. Therefore, mucins can establish adhesive interactions with particulates/biomacromolecules via electrostatic interactions, van der Waals forces, hydrophobic forces, hydrogen bonding, or chain entanglement. Mucosal drug delivery vehicles can either penetrate rapidly or establish prolonged contact. However, their development is of great challenge because little is still known about the interactions between mucin and other macromolecules. We are currently working on a comprehensive study of the interaction between mucin and macromolecules of interest for pharmaceutical developments by complementary techniques. To this scope, we employ biocompatible natural and synthetic polymers with different physical-chemical characteristics. Among them, linear polyamidoamines with amphoteric character are particularly interesting for their cyto-biocompatibility [3-5]. It is indeed crucial to characterise such interactions not only in the bulk but also at the interface, since complexation between mucins and biomacromolecules takes place close to the cell membrane surface. Moreover, the strategy to overcome mucus barrier and achieve long retention time in the cell surface is to develop nano-agents which can effectively penetrate the mucus layer and accumulate at the epithelial surface. In this framework we present preliminary investigations in the bulk by small angle x-ray scattering (SAXS) and at the solid-liquid interface by employing quartz crystal microbalance (QCM-D).

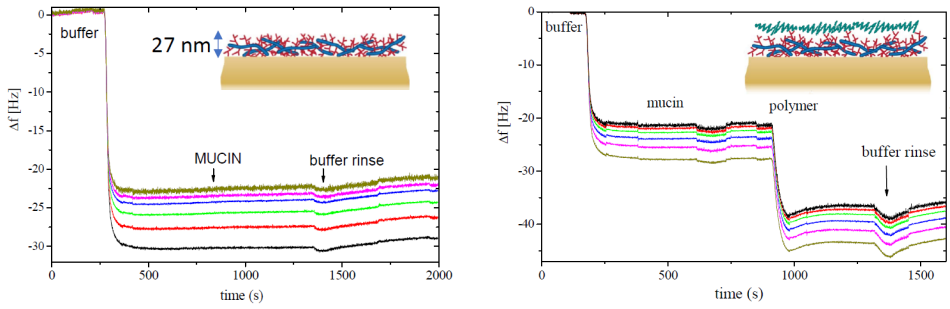

Figure 1. Monitoring individual mucin-polymer interactions and their effects on the layer properties using QCM-D.

References

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