Impact of Milk Components on Diffusion in Intestinal Mucus

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Introduction. Intestinal mucus acts as a barrier that selectively controls the diffusion of molecules, particulate matter, and microorganisms to the underlying epithelial layer. Different dietary components may alter mucus barrier properties and affect the absorption of nutrients, drugs, etc. For example, previous work in our lab has demonstrated that food-associated lipids such as soybean oil, can inhibit particle diffusion in mucus. Therefore, understanding the influence of a complex medium containing oils as well as protein, carbohydrate, and salts, such as milk, on particle diffusion in intestinal mucus is of great interest for enhanced understanding of physiological function as well as motivating strategies for enhancing oral absorption and/or preventing infection.

Materials and Methods. Native porcine small intestinal mucus was harvested within 2 hrs of slaughter. Multiple particle tracking experiments were completed using 200 nm carboxylate- and polyethylene glycol (PEG)- modified fluorescent nanoparticles (FluoSpheres, Invitrogen). Briefly, PEG-modified nanoparticles were synthesized using EDC crosslinking chemistry. Nanoparticle size and surface potential were characterized (Particle Size Analyzer 90 Plus, Brookhaven Instruments). Prior to addition to intestinal mucus, the nanoparticle solutions (2% solids in distilled water) were diluted (0.0025% wt/vol) in different test medias, which included deionized water (DI) and simulated milk solution. An Olympus IX51 microscope and attached Olympus DP70 camera were used to collect 20 sec videos. Particle trajectories were obtained using ImageJ software and analyzed to calculate mean-squared displacement (<MSD>) and effective diffusivity (D_{eff}). Where, MSD = $[x(t+\tau)-x(t)]^2 + [y(t+\tau)-y(t)]^2$ and $D_{eff} = MSD/(4\tau)$, x(t) and y(t) represent the particle coordinates at a given time and τ is the time scale.

Results and Discussion. The addition of simulated milk solution did not significantly affect the diffusion of neutral PEG-modified particles, while carboxylate-modified nanoparticles showed significantly reduced diffusivity (2.5-fold) in mucus when dosed in milk compared to DI water. The reduced diffusivity indicates that the charged particles may have increased particle interaction with mucin fibers in the presence of milk, while PEG-modified particles apparently do not. In summary, these results can be utilized to understand changes in intestinal mucus barrier properties and drug carrier absorption in the presence of external food stimuli such as milk.

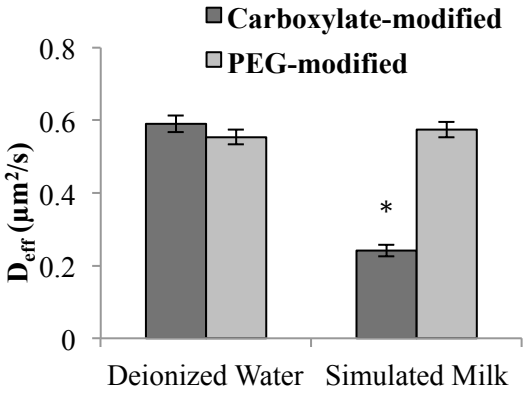


Fig. 1: Diffusivities of carboxylate- and PEG-modified nanoparticles dosed to mucus in deionized water or a simulated milk preparation. Data are ± standard error (N = 3 with at least 300 particles per sample). *$p < 0.05$ when comparing simulated milk with deionized water.