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| **Solvent evaporation-based method for loading model proteins into mesoporous silica microparticles for oral delivery: Effects of protein size and solvent properties on diffusion and loading efficacy.** |
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| **Background:** Silica-based carriers are great candidates for protein-based molecules since they offer protection against degradation. They possess several characteristics that make them sought after; tuneable pore size and porous structure, surface area, and modified release. However, loading efficiency is affected by several factors, including protein size, solvent polarity, and diffusion. |
| **Methods:** Two proteins with different molecular weights (BSA and octreotide acetate) were loaded into a mesoporous silica microparticle carrier via solvent evaporation method using different solvents (ethanol, methanol, and water) and at different concentrations. Characterisation techniques included; confocal microscopy for protein fluorescence intensity, fourier-transform infrared spectroscopy (FTIR) for surface interactions, nitrogen porosimetry for surface area and pore volume, laser diffraction and dynamic light scattering for particle sizing, and scanning electron microscopy (SEM) for morphological properties. |
| **Results:** The molecular size of octreotide(0.67 nm) and BSA (2.69 nm) affected the loading process. Octreotide had a higher diffusion into the mesoporous carrier (5.92\*10-10 m2/s) than BSA (9.130\*10-11), presenting a higher recovery rate (71%) compared to 32% % of BSA. Octreotide samples were loaded more efficiently from methanol, where the protein diffused evenly through the silica carrier. At the same time, water and ethanol loading caused the drug to be concentrated on the surface due to the higher viscosity of both solvents and the higher polarity of water compared to methanol. BSA loading was affected by its solubility in the three solvents, where in water-based loading, the protein diffused to the outer parts of the carrier surface. In addition, BSA aggregation and the low solubility in methanol and ethanol affected the loading, where the dispersed particle size was 223 and 231 μm in ethanol and methanol, respectively, and the protein microcrystals adsorbed on the silica surface. |
| **Conclusions:** Protein loading into the silica carrier is based on diffusion, governed by the Stokes-Einstein equation, and is affected by the protein’s molecular size and solvent viscosity. The polarity of the loading solvent and protein solubility had a significant role in loading, as highly polar solvents (water) compete with the drug to interact with the carrier. In addition, aggregation-inducing solvents (ethanol and methanol for BSA) will decrease protein diffusion into the silica carrier as they will cause the dispersed particle size to increase. |