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Transport Studies of Nanostructured Materials across the Buccal Mucosa

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Introduction: The oral cavity acts as a complex barrier and displays the first main hindrance against uncontrolled uptake of a variety of substances. The oral mucosa represents 60% of the total surface area within the oral cavity, offers a good opportunity for drugs to be absorbed and shows a 4 to 4.000 times greater permeability than the skin.The barrier function of this tissue is mainly guaranteed by i) the saliva, ii) the mucus layer, iii) the cell junctions in the epithelium and iv) the membrane coating granules. However, as the permeability of drugs through the oral mucosa is limited, new delivery carriers have to be developed. Nanostructured materials (NMs) are small enough to overcome this tissue. Within the development of such nano-carriers, the efficacy as well as the safety are important factors that cannot be neglected. Currently, no standardized physiological *in vitro* models, evaluating the permeability, transport route and toxic effects of NMs are available. *Methods:* NMs (polystyrene particles (PS), silver particles Ag)) were primarily characterized in terms of size and surface charge in physiological media. The penetration of the particles was investigated through excised buccal mucosa from pig. The *in vitro* permeability studies were carried out with Franz diffusion cells. It is a fact that the diffusion barriers in the buccal mucosa are only functional within living cell layers. Therefore, the viability (MTT) and the structural integrity of the membrane (methylene blue/PBS with and without EDTA) were investigated. The transport studies were carried out with Transwells® and the Trans-Epithelial Electric Resistance (TEER) was measured. The particle uptake into the cells was recorded with fluorescence/electron microscopy and the cell damage was evaluated. Results: The results demonstrate that the permeability of the particles depends on the size, surface charge, hydrophobicity and particle concentration. Particles in sizes of 20 nm (PS) and 35 nm (Ag) permeated the mucus layer and penetrated in the stratum superficiale of the top third region of the epithelium. They did not affect the tight junctions and were taken up by the cells. The cellular uptake correlated with the cell damage. Particles in sizes of 150 nm (Ag) and 200 nm (PS) aggregated in the saliva, were entrapped in the mucus layer and could not enter the top third region of the epithelium. Additionally, they also did not affect the tight junctions and no cellular uptake could be recorded. *Conclusion:* Independent from the material small (20–35 nm) NMs showed a much higher penetration than larger (150–200 nm) NMs.