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DISSERTATION TITLE: *Formulation and evaluation of polysaccharide- and liposome-based nanosystems for improved targeting to the oral cavity*

I denne avhandlingen har ulike nanopartikler blitt utviklet og testet for bruk i munnhulen. Liposomer og liposomer dekket med polysakkaridet alginat var de mest lovende partiklene da de festet seg til hydroksyapatitt en modellsubstans for tennene, de var ikke giftige mot en celletype som finnes i munnhulen og de var stabile i kunstig spytt. Partiklene kan ha et potensial som fysisk beskyttelse av tenner mot for eksempel erosjon.

The burden of oral diseases has increased worldwide in the last decades, which indicates the need for the developments of treatments with increased efficacy. A common reason of the poor efficacy of local treatments for oral cavity diseases is the short retention time of the active substance in the mouth, due to swallowing and oral function. This project is focused on the development of pharmaceutical preparations able to adhere onto the tooth surface, thus leading to an increase in the retention time in the mouth of the preparations and consequently to an improvement in their efficacy.
In specific, the pharmaceutical preparations investigated in the project were nanosystems, which can be described as systems constituted by particles with a size smaller than one micron. Two types of nanosystem were tested: nanoparticles (spheres made of polymer), and liposomes (vescicles made of lipids that can be coated with polymers). The polymers used for the preparation of the nanosystems were alginate, pectin, and chitosan.
The first part of the project was focused on the optimization of the preparation of the nanosystems in order to obtain particles with constant size that had no tendency to aggregate to each other. The size determines the properties of the particles, therefore it is particularly important to obtain particles not aggregated to each other and with homogeneous size, in order to assure homogeneous properties. The optimization was carried out by modifying important parameters during the preparation of the nanosystems (such as the concentration of polymer used).
The second part of the project tested the optimal nanosystems selected in the first part of the project in order to determine their suitability as formulations addressed to the oral cavity and to determine their potential ability of adhesion onto the tooth surface. Their suitability for oral cavity applications was assessed by measuring their toxicity on cells of

the oral epithelium, and by measuring their stability in artificial saliva. The surface of the nanosystems was charged (negatively or positively) and this characteristic determinant for the outcome of some test. Most of the formulations were bioadhesive onto the tooth model. However, the positively charged nanosystems were unstable in artificial saliva, since they tended to aggregate. The nanoparticles presented some cell toxicity due to the presence of positively charged components.
Based on the results of this project, the most promising nanosystems for oral cavity applications were the negatively charged uncoated liposomes, the pectin-coated liposomes and the alginate-coated liposomes. The findings in this thesis provide the basis for further studies for development of improved nanosystems for oral cavity applications.