Chapter 2

Aim of the thesis and study objectives
Aim and scope of this thesis

The aim of the work described in this thesis was to improve the immunogenicity of antigens in transcutaneous immunization (TCI) by using microneedle arrays, immune-modulators, and antigen-containing vesicle formulations. The study objectives include:

i). To investigate the use of microneedle arrays to potentiate immune responses of topically applied antigen;

ii). To combine microneedle arrays with adjuvants to modulate immune responses induced in TCI;

iii). To prepare, characterize and evaluate surfactant- and lipid-based vesicle formulations for vaccine delivery across the stratum corneum into the viable layers of the skin;

iv). To investigate the immunogenicity of topically applied antigen using antigen-loaded vesicular carrier systems in vivo;

v). To improve TCI by combining antigen-loaded vesicle formulations with microneedle array pretreatment of the skin.

Organization of the thesis and experimental approaches

Chapter 1 provides a comprehensive review of the current research status of TCI, including a brief introduction to vaccines and adjuvants, the structure and barrier functions of the skin, and the innate and adaptive immunity involved in cutaneous immune defense. The main part of this chapter summarizes the strategies and experimental approaches of enhancing transcutaneous antigen delivery and improving/optimizing the immunogenicity of vaccine formulations.

Chapter 3 describes the microneedle arrays and the impact insertion applicator developed for TCI. This system was first evaluated for effective piercing of mouse skin in vivo. Then, the effect of microneedle array pretreatment on TCI of DT and influenza vaccine is presented. The 300 μm-long assembled microneedle array is used in the research described in Chapter 4 --- a comparative study on the immune potentiation and modulation functions of various adjuvants in TCI of DT onto microneedle-pretreated skin.
In Chapter 5 and 6 studies are presented on the potential of DT-containing vesicle formulations in TCI. Two types of DT-containing vesicle formulations, i.e. negatively charged surfactant vesicles and positively charged (elastic) liposomes, are prepared and characterized in vitro. Selected formulations are tested in TCI onto intact and microneedle array-pretreated mouse skin. These vaccinations were compared with vaccination through intradermal and subcutaneous injection. Human peripheral blood mononuclear cell-derived immature dendritic cells are used to assess the immune-stimulatory potential of these formulations.

A summary of the outcome of this work, a general discussion and perspectives are provided in Chapter 7.