Influence of poloxamer type on the structural changes upon autoclaving of trimyristin nanoemulsions: A DSC study

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The development of new drugs often involves poorly water-soluble compounds. In such cases, lipid-based nanoparticles can provide a suitable formulation option [1]. Drug delivery systems composed of lipid nanoparticles have particle sizes that typically range from 1 to 500 nm. Because of their nanoscale size, these drug delivery systems are suitable for intravenous administration [2]. One such system are lipid nanoemulsions, which are composed of a matrix lipid dispersed in an aqueous phase with an emulsifier. Trimyristin (TM) was used as the lipid matrix for our study. It is a saturated triglyceride of myristic acid with a melting point of around 56 °C. It forms a special type of colloidal lipid nanoemulsions, in which the disperse phase is a supercooled melt [3]. Different types of poloxamers (polyoxyethylene-polyoxypropylene block copolymers, Pol) were used as emulsifiers in our study. TM nanoemulsions were prepared by high-pressure homogenization. For parenteral formulations, sterility is required, and lipid nanoemulsions are usually sterilized by autoclaving. As has been observed previously, autoclaving of Pol 188-stabilized dispersions can lead to an increase in particle size and a change in particle size distribution [4].

This study aimed to examine the effect of autoclaving on the change in particle size and particle size distribution of the emulsions stabilized with different poloxamers. Additionally, the concentration of free poloxamer in the aqueous phase was of interest. The particle size (z-average diameter) and polydispersity index (PdI) of the emulsions was measured by photon correlation spectroscopy (PCS) before and after autoclaving. The z-average diameter had increased and the PdI decreased for all samples after autoclaving. Upon heating in DSC, the melting curves of non-autoclaved TM nanoemulsions exhibited broad and jagged peaks. This peak broadening, combined with multiple separated melting events and a shift towards lower melting temperatures, indicates the presence of small particles in the respective TM nanoemulsion [4]. After autoclaving, melting occurred in a single sharp event, indicating a narrow particle size distribution. Thus, the DSC results confirmed a growth in particle size and a decrease in polydispersity during autoclaving, supporting the results obtained by PCS. The concentration of free poloxamer in the aqueous phase was quantified by measuring the refraction index in the ultrafiltrate of the emulsions. After autoclaving, the free poloxamer concentration of all TM nanoemulsions had increased significantly. Larger particles have a lower specific surface area. It can be assumed that excess emulsifier was detached from the particle surface and resulted in an increased concentration of free emulsifier in the aqueous phase. Depending on the type of poloxamer used as emulsifier, changes in the crystallization behavior of the TM nanoemulsions were observed after autoclaving. The crystallization temperature of TM nanoemulsions stabilized with

poloxamers with a concentration-dependent adsorption behavior shifted to lower temperatures. In contrast, the use of poloxamers with a less concentration-dependent adsorption behavior displayed a slight increase in the crystallization temperature.

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