Synthesis of Solid Lipid Nanoparticles and their Interaction with Skin

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Statement of Purpose: The skin is a prominent target organ for numerous inflammatory and stress-related biomarkers, making it an excellent site for early detection of physiological imbalance. Solid lipid nanoparticles (SLNs) are a promising platform for sensing such biomarkers due to their biocompatibility, stability, and the ability to accept a wide range of active ingredients. Their small size has been shown to increase their skin penetration, and the higher surface area promotes efficient detection. In this study, a systematic Design of Experiments (DOE) approach was used to study the synthesis of SLNs for sensory applications using phase inversion temperature (PIT) method and the correlation of the properties of SLN and their interaction with skin.

Methods: SLNs were prepared by the phase inversion PIT method[1-2]. The fluorescent dye, 1-1'-oxalyldiimidazole, methanol, and decanol were combined into a vial. The following step was the addition of Brij O10 and the lipid. The resulting mixture was co-melted and stirred. DI water was added to the mixture, heated and stirred. Under continued stirring, cooling the sample causes inversion of the water-in-oil emulsion to an oil-in-water emulsion, creating a nanoemulsion in the process. A further decrease in temperature below the melting point of the lipid converts the liquid nanoemulsion into SLNs. In this study, the DOE processing variables are lipid composition, dye composition, lipid concentration, surfactant concentration, dye concentration, processing temperature, and thermal mass. The dye solubility, phase inversion temperature, particle size, polydispersity, melting point, latent heat of melting, penetration depth, and absorbance loss per wash were measured.

Results: SLNs for sensory applications have been developed previously by our group[3]. In this study, the demonstration of the synthesis of SLNs with ultra-small size, and the penetration and permanence of the loading compounds is dominated strongly by the compound chemistry. SLNs with 7.59 nm particle diameter and polydispersity of 1.644% were synthesized using tetracosane (C24) as a lipid, 2.0% oil concentration, 2.02% surfactant concentration, a processing temperature of 50 ˚C, and thermal mass of 10mL. In addition, varying the lipids facilitates control of the thermal properties of the SLNs (Figure 1) with the potential of expanding their applications.

The interaction of the loading compounds with skin depends strongly on the compound chemistry (Figure 2). Statistical analysis indicated that the most influential factor on the penetration depth is the dye solubility with a confidence level of 97.7%.

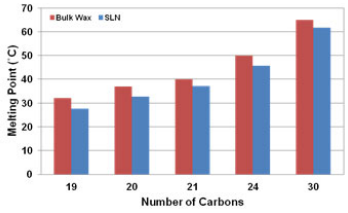

Figure 1: Melting points as function of bulk lipid and plain SLNs.

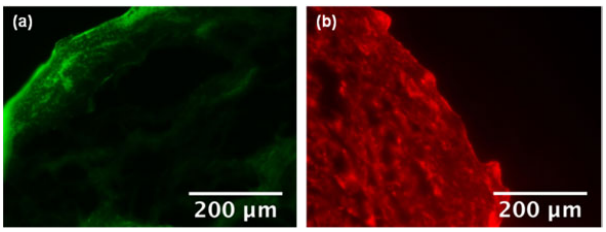

Figure 2: Fluorescence microscopy micrographs of (a) sample with the blue/green dye (Bis(N-methylacridinum)nitrate) and (b) sample with the red dye (Rhodamine B). Observe that SLNs loaded with the red dye penetrated throughout the entire viable epidermis. Penetration of the SLNs loaded with the blue/green dye was limited to approximately 77 µm.

Conclusions: The main conclusions of this study are: (1) the PIT method is a versatile method with which to synthesize SLNs with ultra-small sizes and low polydispersity and (2) the interaction of the loading compounds with skin depends strongly on the compound chemistry. The DOE analysis showed that dye solubility, dye polarity, and latent heat of melting were the most significant parameters effecting particle interactions with skin. Overall, we conclude that when using this method, it is possible to consistently produce SLNs with particle diameters less than 20 nm and low polydispersity, almost regardless of synthesis conditions or payload.

References:

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