TECHNICAL BRIEF (UST-007)

Retinol nanoemulsions produced by Ultra Shear Technology

Summary: Ultra Shear Technology™ (UST™) produced nanodispersions of encapsulated retinol with long term storage stability.

Background: The percutaneous absorption of retinol induces cell proliferation, regulates keratin expression, and stimulates collagen production causing the plumping of skin and lessening the appearance of wrinkles. Transdermal diffusion is extremely low, and retinol is almost entirely sequestered in the lipid-rich stratum of the epidermis [1]. In the epidermis, retinol is metabolized to retinoic acid, its biologically active form.

Retinol and retinoic acid are susceptible to UV photooxidation where nascent reactive oxygen species induce lipid peroxidation and the potential for DNA damage. Moreover, the cytotoxicity of the products of retinoid photodegradation is not fully known [2]. However, the half-life of retinoids is significantly increased when encapsulated [3]. The encapsulation of retinol in nanoemulsions has recently been shown to be photoprotective and increases the storage stability of retinol [4, 5, 6].

Methods: Retinol (Millipore-Sigma, Burlington, MA, USA) was dissolved in dimethyl sulfoxide, then diluted 20 times in organic argan oil (Cliganic, Walnut, CA, USA). The oil phase comprised 10% of the final formulation. Surfactant phase consisted of Phospholipon 85G (American Lecithin Company, Oxford, CT, USA) in which the hydrophilic-lipophilic balance (HLB) was adjusted to match the oil phase with a polyoxyethylene sorbitan series cosurfactant. The final formulation contained 0.5% retinol. Course emulsions were prepared by rotor-stator homogenization at 35,000 rpm for two minutes. Course emulsions were cycled through the UST valve for 1-10 cycles at 45,000 psi. The progression of particle size reduction was monitored by dynamic light scattering (DLS) measurements after each cycle. Increased optical clarity was quantified by UV/Vis spectroscopy. For stability studies, retinol nanoemulsions were stored at 4°C protected from light for a minimum of ten months.

Results: Coarse retinol emulsions prepared by conventional homogenization were milky suspensions of large polydisperse oil droplets prone to rapid phase separation. After only one pass through the UST NanoGap™ valve, the mean hydrodynamic diameter of oil droplets was decreased by an order of magnitude. Oil droplet size continued to decrease with each addition UST cycle, reaching a minimum of 50-60 nm after ten cycles **(Figure 1A)**. Decreased light scattering commensurate with decreasing particle size marked the transition from translucent to transparent nanoemulsions, typically after four cycles. Nanoemulsions continued to clarify with each additional cycle **(Figure 1B)**. Retinol nanoemulsions were stable for at least ten months, with no significant change in oil droplet size or optical clarity **(Figure 1C)**.

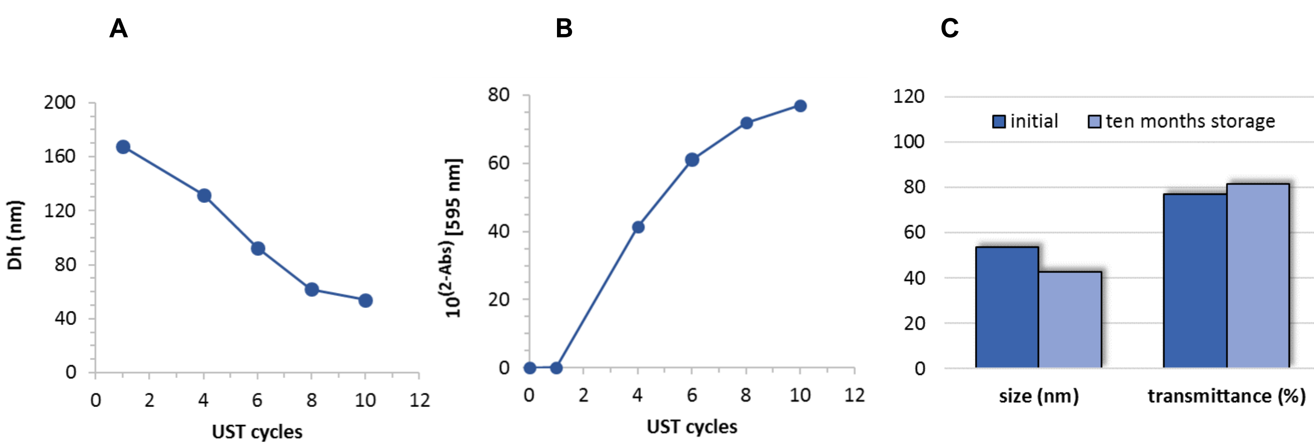

Figure 1. (A) Progressive reduction in the mean hydrodynamic diameter (Dh) of oil droplets as a function of the number of UST cycles reaching a minimum particle size of 54 nm. **(B)** Increasing clarification was commensurate with decreasing particle size. Optical clarity was quantified from turbidity measurements at 595 nm and expressed as transmittance. **(C)** Stability of retinol nanoemulsion following ten months storage at 4°C protected from light.

References:

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