TECHNICAL BRIEF (UST-001)

Oral prednisone nanoemulsions produced by Ultra Shear Technology

Summary: Nanodispersions of prednisone encapsulated in 30 nm oil droplets were stable for at least ten months of room temperature storage.

Background: Prednisone is a widely prescribed corticosteroid with systemic anti-inflammatory and immunosuppressant properties. Oral prednisolone has been shown to mimic the normal circadian rhythm better than other glucocorticoids [1]. However, it is sparingly soluble in water and ethanol and mean oral bioavailability of only 62% has been reported [2]. The absorption of such lipophilic bioactives by the intestinal mucosa has been shown to be significantly increased when administered as an oral nanoemulsion [3,4,5]. Water-miscible oil-in-water nanoemulsions are defined by extremely small droplet size and low polydispersity and are intrinsically transparent due to decreased Rayleigh light scattering. The localization of surfactant(s) at the droplet surfaces stabilizes nanoemulsions by increasing interparticle repulsion and curtails Oswalt effects such as coalescence and phase separation.

Methods: Prednisone was dissolved at 66 mg/mL in DMSO, then diluted to a final concentration of 1 mg/mL in the emulsified formulation. The carrier oil phase was either grapeseed oil (GSO) or argan oil (AO). Final composition of the formulation was 0.1% prednisone, 10% of the respective oil phase, 10% glycerol, 5% Phospholipon 85G (American Lecithin Company, Oxford, CT, USA) and 1.5% DMSO. The hydrophilic-lipophilic balance (HLB) of these formulations was adjusted to match the oil phase by addition of a polyoxyethylene sorbitan series co-surfactant. Current formulations were designed to provide a convenient dose of 5 mg prednisone per teaspoon. Course emulsions were prepared by rotor-stator homogenizer (control). Nanoemulsions were produced cycling the coarse emulsions through the Ultra Shear Technology™ (UST™) proprietary self-throttling, annular valve at 45,000 psi. Mean oil droplet size was measured after each cycle by dynamic light scattering (DLS). Sample clarification was quantified by UV/Vis spectroscopy at 595 nm.

Results: Course emulsions were highly polydisperse milky white suspensions in which mean oil droplet size exceeded 1000 nm. Course emulsions were prone to rapid phase separation. However, after only one pass through the UST valve, an approximately 80% reduction in mean oil droplet size was observed. GSO and AO formulations produced stable, visually clear nanoemulsions after 4-6 passes. The mean hydrodynamic diameter of oil droplets in the GSO nanoemulsion was approximately 50 nm after six UST passes and continued to decrease until reaching a minimum particle size of approaching 30 nm after 12 passes. **(Figure 1A).** No significant further particle size reduction was observed when additional UST cycles were performed. The AO nanoemulsions had similar clarity but slightly higher droplet size than GSO nanoemulsions following an equivalent number of cycles.

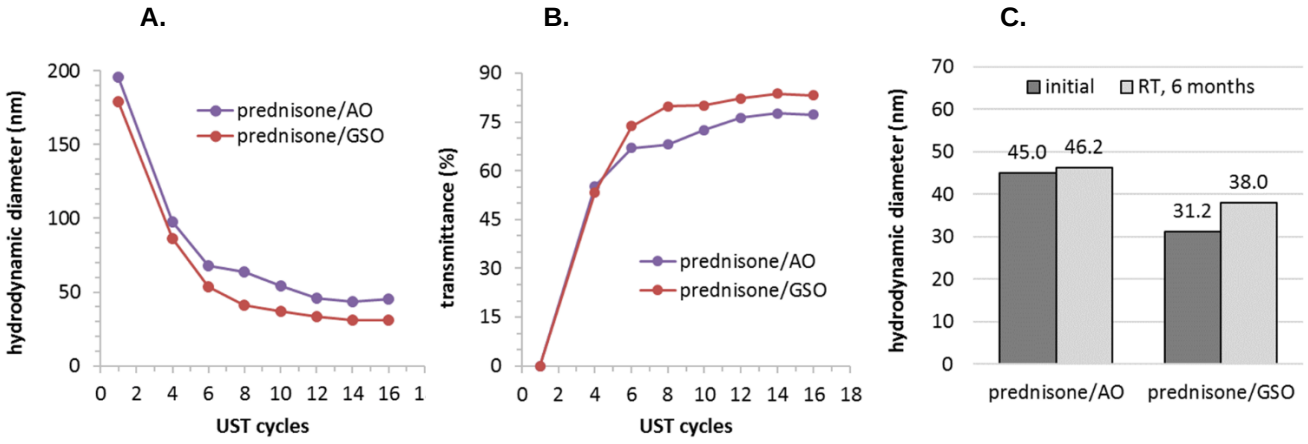

Figure 1. **(A)** Mean oil droplet size (nm) of prednisone AO and GSO nanoemulsions as a function of the number of UST cycles at 45,000 psi. **(B)** Optical clarity of prednisone AO and GSO formulations. **(C)** Stability of prednisone nanoemulsions stored at room temperature for six months.

References:

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