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# Rheological characterization of topical pharmaceutical foam products

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## PURPOSE & OBJECTIVE:

Pharmaceutical foams are essentially comprised of a dispersion of gas within a liquid phase (solution, suspension, or emulsion). The liquid phase exists as a single-phase system or a biphasic system, and the drug substance can be either completely dissolved or suspended in the final formulation. Therefore, the foams are thermodynamically and mechanically unstable once they are dispensed from the container closure system, and undergo rapid metamorphosis. They possess low yield stress and display shear-thinning behavior. An understanding of these rheological characteristics is crucial in understanding the microstructural differences between different types of foams, and can help to compare products which are similar in formulation composition. The present method development study was performed using an oil-in-water (O/W) emulsion-based foam (azelaic acid topical aerosol foam, 15%) and a hydroalcoholic solution based foam (clindamycin phosphate topical aerosol foam, 1%) as model drug products.

## METHODS:

Rheological measurements were performed using a stress-controlled rheometer, DHR-2, TA Instruments. The (O/W) emulsion-based foam was evaluated at 32° C, the temperature at the surface of the skin, however, the hydroalcoholic solution-based foams were evaluated at the closest feasible temperature to a physiological temperature (22° C) due to experimental limitations. The temperature was precisely controlled using a Peltier system. A 20 mm parallel-plate geometry with solvent trap was used. To minimize sample slippage adhesive backed sandpapers (grit number # 600), were attached to both upper and lower plates.

Two sets of experiments with the following steps were conducted on these samples. All data are presented as mean ±SD.

- **Set I**
  - ➢Time sweep (t = 300 s, σ =1 Pa, ω = 1 Hz, Gap = 500 µm)
  - ➢Frequency sweep (σ = 1 Pa, ω = 0.3-15 rad/s, Gap = 500 µm)
  - ➢Time sweep (t = 300 s, σ =1 Pa, ω = 1 Hz, Gap = 500 µm)
  - ➢Amplitude sweep (σ = 0.1-10 Pa, ω = 1 Hz, Gap = 500 µm)
  - ➢Time sweep (t = 300 s, σ =1 Pa, ω = 1 Hz, Gap = 500 µm)
- **Set II**
  - ➢Time sweep (t = 300 s, σ =1 Pa, ω = 1 Hz, Gap = 500 µm)
  - ➢Flow sweep ($\gamma_0$ = 0.002 $s^{-1}$ – 100 $s^{-1}$, Gap = 500 µm)
  - ➢Time sweep (t = 300 s, σ =1 Pa, ω = 1 Hz, Gap = 500 µm)

## RESULT(S)

**Figure 1: Amplitude sweep for O/W emulsion foam (n=3)**

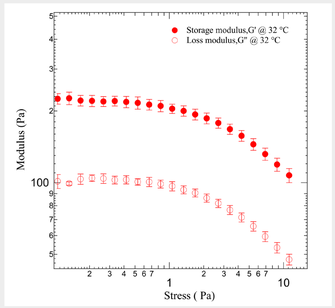



**Figure 2: Frequency sweep for O/W emulsion foam (n=3)**

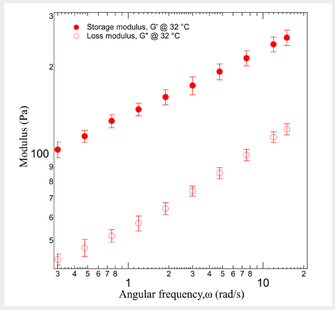
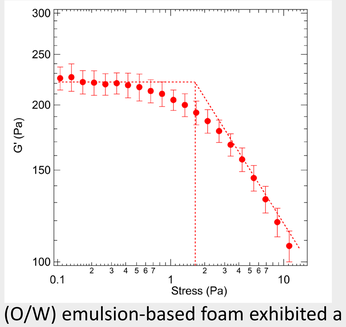



**Figure 3: Yield stress analysis of O/W emulsion foam (n=3)**




At 32 °C, the (O/W) emulsion-based foam exhibited a yield stress value of ≈1.6 Pa. The measured viscosity values using the flow-sweep test were 5807 ± 1011 Pa·s at the shear rate of 0.002 1/s and 5.26 ± 0.47 Pa·s at the shear rate of 10 1/s.

**Figure 4: Amplitude sweep for hydroalcoholic foam (n=3)**

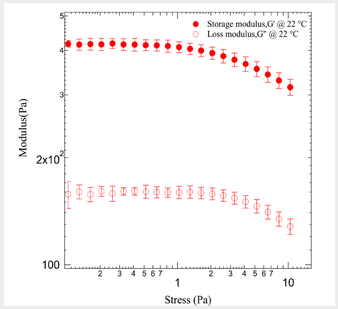



**Figure 5: Frequency sweep for hydroalcoholic foam (n=3)**

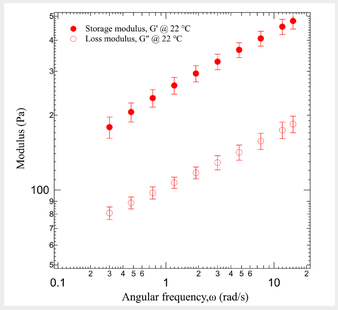
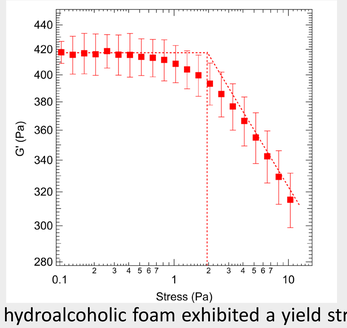



**Figure 6: Yield stress analysis of hydroalcoholic foam (n=3)**




At 22 °C the hydroalcoholic foam exhibited a yield stress value of ≈1.75 Pa. The measured viscosity values were 4005.64 ± 811.12 Pa·s at the shear rate of 0.002 1/s and 0.013 ± 0.01 Pa·s at the shear rate of 10 1/s. The hydroalcoholic solution-based foam collapsed rapidly as the sample was loaded in the rheometer at 32 °C. So, the rheological experiments were performed at 22 °C.

## CONCLUSION(S)

The foam samples display very low yield stress in general because a small amount of mechanical stress can cause the foam structure to collapse. In addition to the applied mechanical stress, temperature can cause drying and the corresponding collapse of the samples as illustrated by the challenges observed with the evaluation of the hydroalcoholic foam at 32 °C. An interesting finding of this work was that it may not always be practical to evaluate the rheology of foams at a physiologically relevant temperature (i.e., 32 °C); it may also be informative to assess (and/or compare) highly volatile foams at temperatures closer to room temperature. Based on our results, it is evident that yield-stress and viscosity values could be characterized for foam products, suggesting that these characteristics could be used to compare test and reference foam products and to evaluate correlations between the physical characteristics of the macro and micro-structure with the performance of the product.

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