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Critical Quality Attributes of Topical Pharmaceutical Foams

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PURPOSE & OBJECTIVE:

- The objective of the study was to develop physical and structural characterization techniques to evaluate topical dermatological foam products in an effort to identify quality attributes that may be critical to the performance of these products.
- Two commercially available foams were selected as model drug products for the study, of which one was an oil in water (O/W) emulsion-based foam (azelaic acid topical aerosol foam, 15% w/w) and another was a hydro alcoholic foam (clindamycin phosphate topical aerosol foam, 1% w/w).
- Different quality attributes like drying profile, bubble size distribution, density, time to break, residual content and foam firmness were evaluated for each drug product.

METHODS:

- The metamorphosis (drying profile) of the foams was evaluated thermogravimetrically by dispensing the foam products into the cavity of a rubber ring placed on a pre-weighed glass slide. The excess foam was trimmed off with a scalpel blade, the rubber ring was removed, and the weight of the slide was noted. The slide was then placed in an incubator at 32°C and the weight was monitored at 3-minute intervals until a constant weight was reached. The percentage of product remaining at different timepoints was calculated, and the time it took for a loss of 50% of the weight of the foam was determined.
- The bubble size distribution of the foam products was measured using differential interference contrast (DIC) microscopy by dispensing the foam in a box slide. Bubble size distribution was determined and d_{10}, d_{50} and d_{90} values were calculated.
- The foam density was measured by determining the average weight of the foam at five different volumes.
- Time to break for a foam was determined by placing samples of the specific foam in an incubator at 30°C, 32°C, 33°C, 35°C, and 40°C, in each instance at 40% relative humidity. The energy of activation required for the collapse of the foams was determined using the rate constant values obtained at the 5 different temperatures, assuming zero-order processes.
- The residual content of the foams was evaluated by drying each foam at an elevated temperature for a prolonged time. The weight of the slide was recorded every 1h until a constant weight was attained. The presence of any crystals in each sample was also observed under a microscope.
- Foam firmness and work of adhesion (WOA) were determined using TA-3 Texture analyzer.
- All the studies were conducted in triplicate and data are reported as mean ± standard deviation (SD).

RESULTS

Figure 1. Drying profile of topical foams (mean ± SD; n=3)

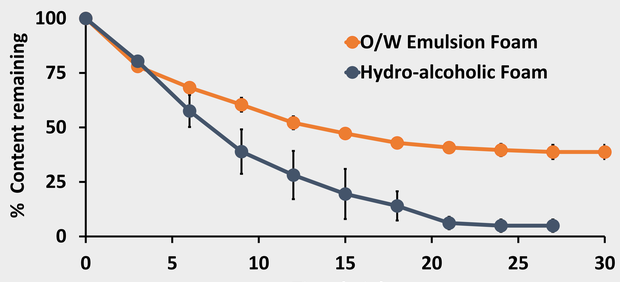


Figure 2: Representative DIC images (10X) of O/W emulsion foam (left) and hydro-alcoholic foam (right)

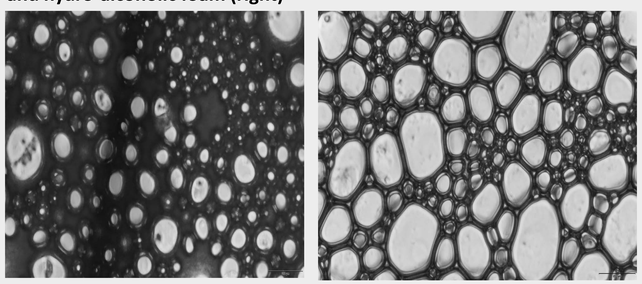


Table 1: Bubble size distribution of topical foams (n=3)

Diameter	O/W Emulsion Foam	Hydro-alcoholic Foam
d10	39.80	66.40
d50	66.00	119.00
d90	95.80	181.00

Figure 3: Residual content of topical foams (mean ± SD; n=3)

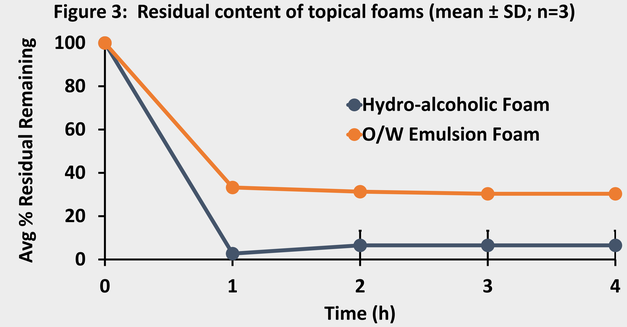


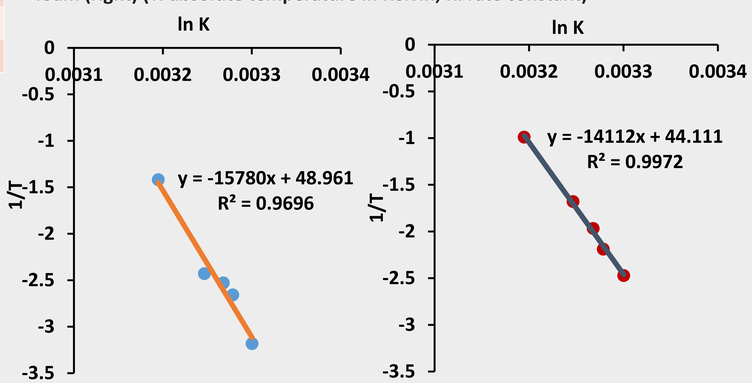
Table 2: Critical quality attributes of topical foams (mean ± SD; n=3)

Quality Attribute	O/W Emulsion Foam	Hydro-alcoholic Foam
Drying Rate (min)	13.00 ± 1.10	7.30 ± 1.50
Density (g/cm^3)	0.085 ± 0.001	0.104 ± 0.03
Residual content (% w/w)	30.35 ± 0.12	6.54 ± 6.74
Firmness (g)	169.19 ± 8.02	103.07 ± 6.45
WOA (g.sec)	161.67 ± 24.50	76.37 ± 13.76
Energy of Activation(KJ/mol)	133.75 ± 8.27	117.58 ± 12.09

Table 3: Mean (± SD) time to break analysis of topical foams (n=3)

Temperature (°C)/ Relative Humidity (%)	O/W Emulsion Foam (Min)	Hydro-alcoholic Foam (Min)
30°C-40%RH	40.22 ± 1.69	19.76 ± 1.61
32°C-40%RH	23.80 ± 1.15	14.90 ± 0.62
33°C-40%RH	20.92 ± 0.45	11.93 ± 0.31
35°C-40%RH	18.93 ± 0.54	8.95 ± 1.01
40°C-40%RH	6.69 ± 0.54	4.49 ± 0.54

Figure 4: Energy of Activation of O/W emulsion foam (left) and hydro-alcoholic foam (right) (T: absolute temperature in Kelvin; K: rate constant)



CONCLUSIONS

- Suitable methodologies for physical and structural characterization of topical dermatological foams were developed and evaluated during the study.
- The characterization of the two model drug products, an O/W emulsion-based foam and a hydroalcoholic solution-based foam, illustrated that the experimental techniques are sensitive to differences in the formulation and microstructure of the topical foams.
- The methods could be used as part of an evaluation of the physical and structural characteristics of generic and reference topical dermatological foams and to correlate the macro and micro-structure of the drug products with their performance.

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