

Preliminary Studies on the Effect of Manufacturing Process on Globule Size Distribution of Sunscreen Formulations.



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Abstract

Studies indicate that sunscreen UV filters are absorbed upon dermal application and systemic exposure was observed. Formulation properties such as globule size distribution may affect skin absorption of UV filters. Here we studied the effect of manufacturing process variables on globule size distribution and rheological properties of in-house manufactured sunscreen creams. Preliminary results indicated that process parameters appear to have confounding effect on globule size distributions.

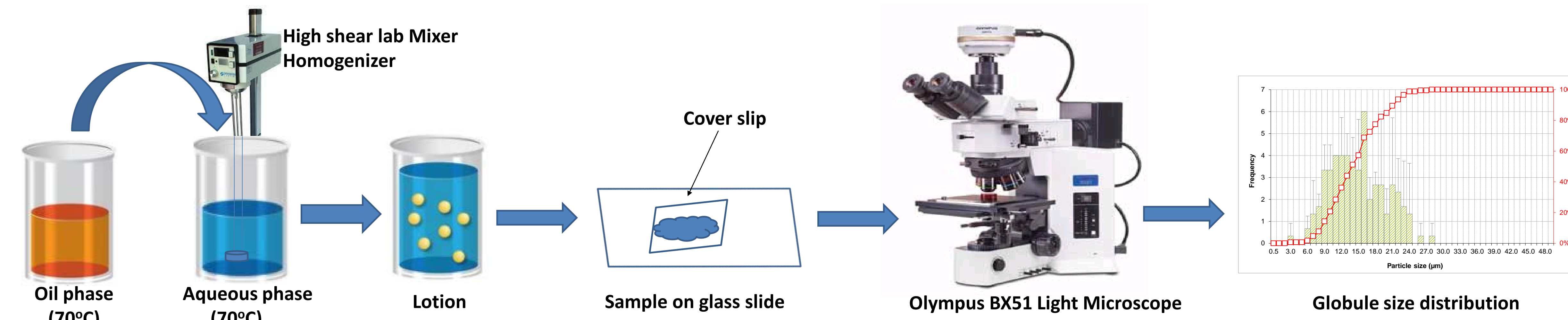
Introduction

UV filters used in sunscreen products are intended to act locally on the skin surface. However, studies have demonstrated that UV filters are in fact absorbed and results in significant systemic exposure. It may lead to safety concerns with the use of sunscreen products. Formulation properties such as globule size distribution, viscosity, and water activity are reported to affect product quality and skin absorption of active ingredients. The objective of the study was to better understand the effect of formulation properties and manufacturing process on the absorption potential of UV filters. For this purpose, a series of in-house sunscreen formulations were manufactured. **This poster reports the effect of manufacturing process variables on the globule size distributions which may affect dermal absorption of sunscreen UV filters. In addition, rheological properties of the sunscreen that may affect sunscreen stability and globule size distribution were also evaluated.**

Method

Formulations were prepared by varying process variables (temperature, homogenization speed and time) to study their effect on globule sizes. Aqueous and oil phases were prepared separately at 60 - 80 °C in a water bath. Oil phase (with or without UV filters) was added to the aqueous phase and homogenized at 1500 - 5000 rpm for 15, 30 or 45 minutes. Formulations were cooled at room temperature at a mixing rate of 1000 rpm, then dispensed into polypropylene centrifuge tubes and stored at 25 °C/60% RH. Samples for globule size measurements were applied onto glass slides and spread evenly using a cover slip. Images were acquired using an Olympus BX51 polarized light microscopy at 20X magnification. Around 200 globules from each formulation were measured using ImageJ to obtain size distribution information.

Method continued



Rheology assessment

- 25 mm sandblasted parallel plate geometry with peltier stage.
- Trimming gap was set to 525um, and measuring gap was 500 um.
- Measurements were done at 25 °C.
- studies were performed in triplicates and results were expressed as mean ± standard deviation (SD).

Results

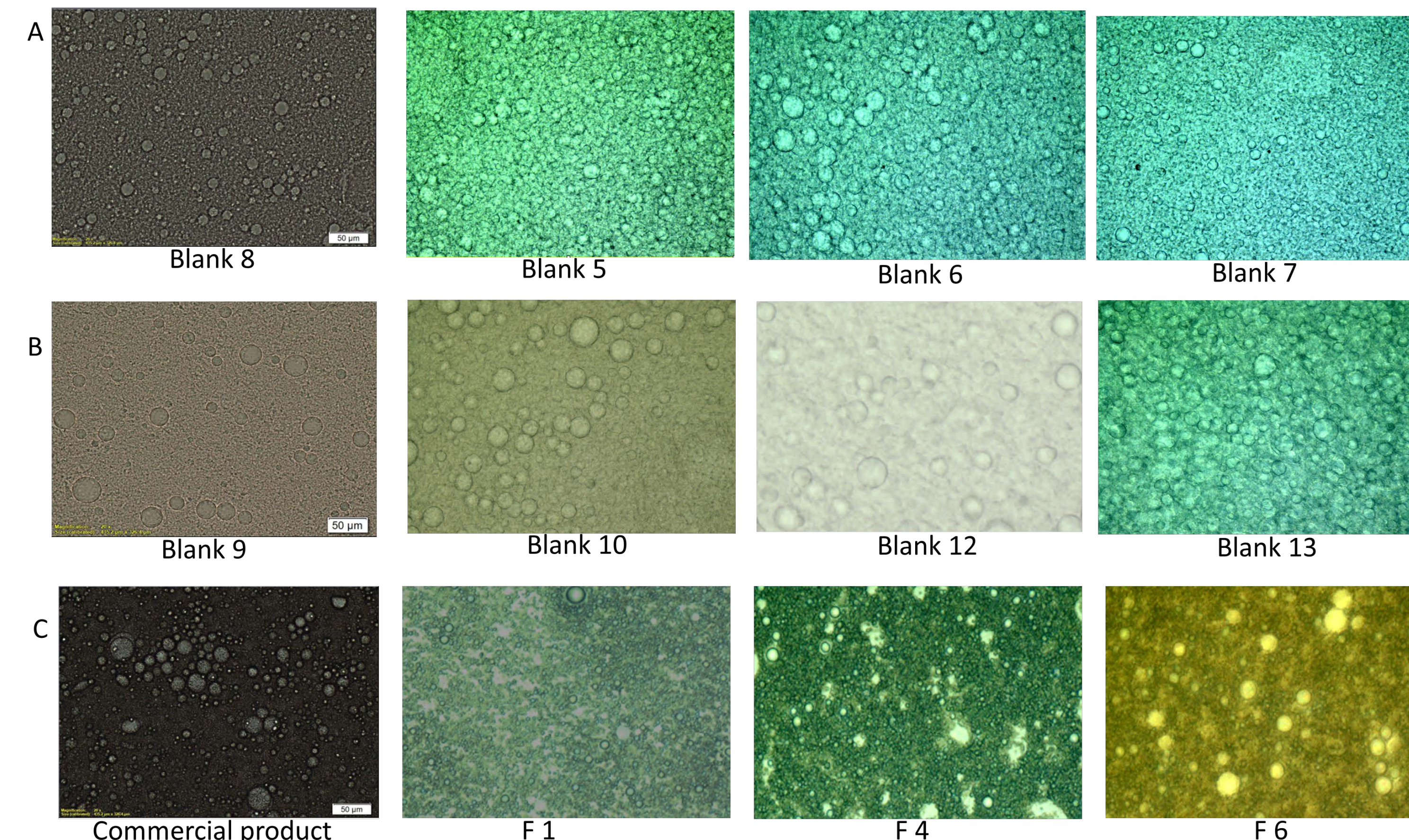


Figure 1. Representative images of oil phase globules in the formulations. A) Blank formulations B) Blank formulations C) Formulations with UV filters.

Time						
Formulation	Temp (°C)	RPM	Time (mins)	D10 (µm)	D50 (µm)	D90 (µm)
Blank #5	60	1500	15	7.72 ±0.41	11.12 ±0.62	15.1 ±0.78
Blank #6	70	1500	30	8.48 ±0.45	14.26 ±1.77	20.41 ±2.89
Blank #7	70	1500	45	5.83 ±0.92	9.2 ±0.34	13.23 ±0.74
Speed						
Formulation	Temp (°C)	RPM	Time (mins)	D10 (µm)	D50 (µm)	D90 (µm)
Blank #8	70	2500	15	7.03 ±0.85	10.47 ±1.07	15.65 ±1.55
Blank #9	70	4000	15	1.67 ±0.34	2.57 ±0.25	3.34 ±0.4
Blank #10	70	5000	15	10.11 ±0.66	16.83 ±0.88	25.4 ±2.41
Temperature						
Formulation	Temp (°C)	RPM	Time (mins)	D10 (µm)	D50 (µm)	D90 (µm)
Blank #10	70	5000	15	10.11 ±0.66	16.83 ±0.88	25.4 ±2.41
Blank #12	75	5000	15	7.12 ±0.74	11.23 ±0.88	18.07 ±0.84
Blank #13	80	5000	15	8.73 ±0.45	11.33 ±0.21	14.86 ±0.47

Table 1. Process parameters and globules size distribution for selected blank formulations.

Formulations with UV filters						
Formulation	Temp (°C)	RPM	Time (mins)	D10 (µm)	D50 (µm)	D90 (µm)
F #1	70	5000	15	2.3 ±0.15	3.53 ±0.34	5.22 ±0.62
F #4	75	5000	15	1.67 ±0.34	2.57 ±0.25	3.34 ±0.4
F #6	70	1500	15	6.22 ±0.17	8.96 ±1.05	13.32 ±2.03
Commercial Product	67	unknown	until uniform	1.67 ±0.11	2.85 ±0.63	6.84 ±0.17

Table 2. Process parameters and globules size distribution of selected formulations containing UV filters.

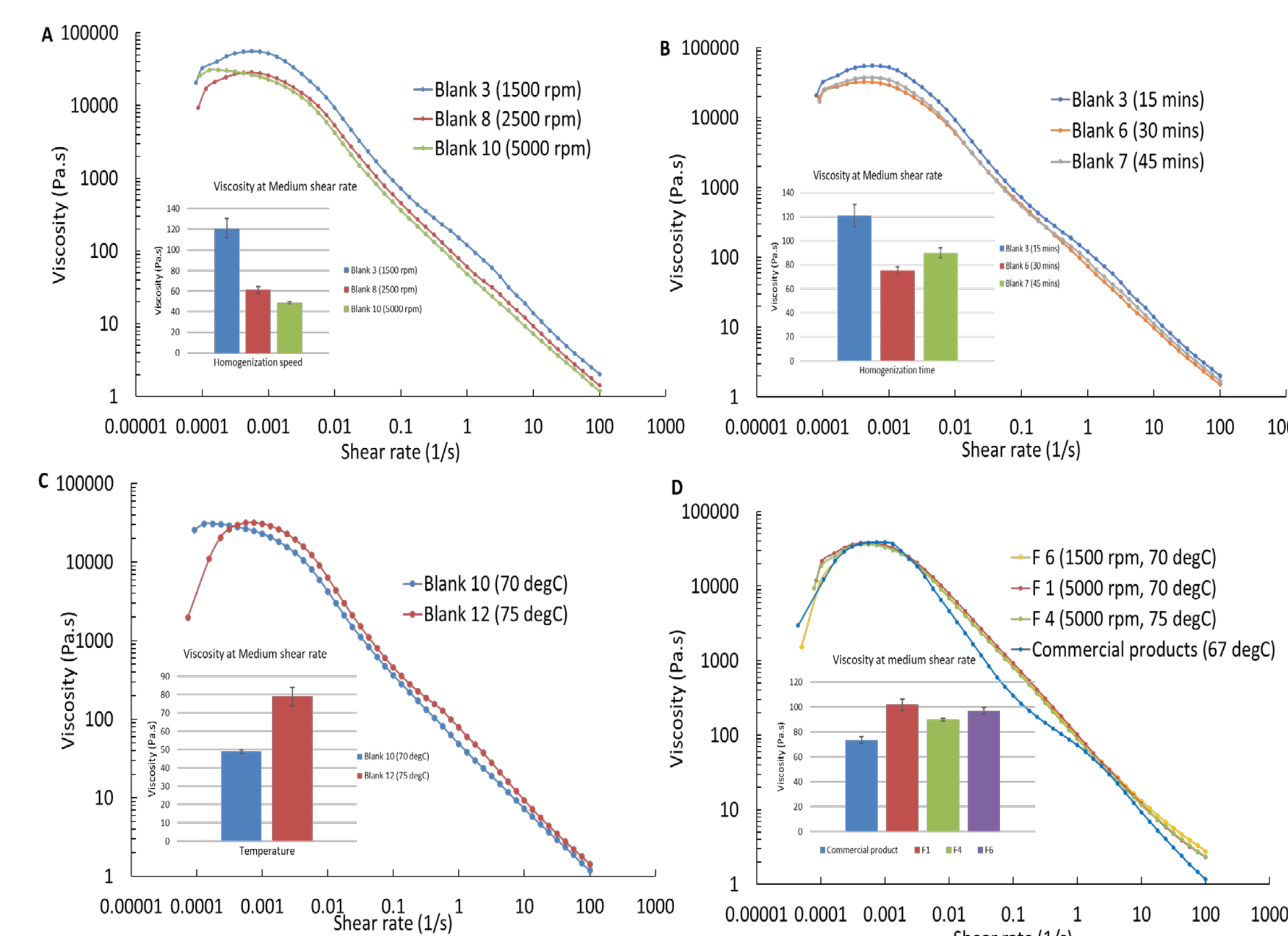


Figure 2. Viscosity profiles of selected formulations comparing A) Homogenization speed, B) Homogenization time, C) Temperature, and D) with UV filters.

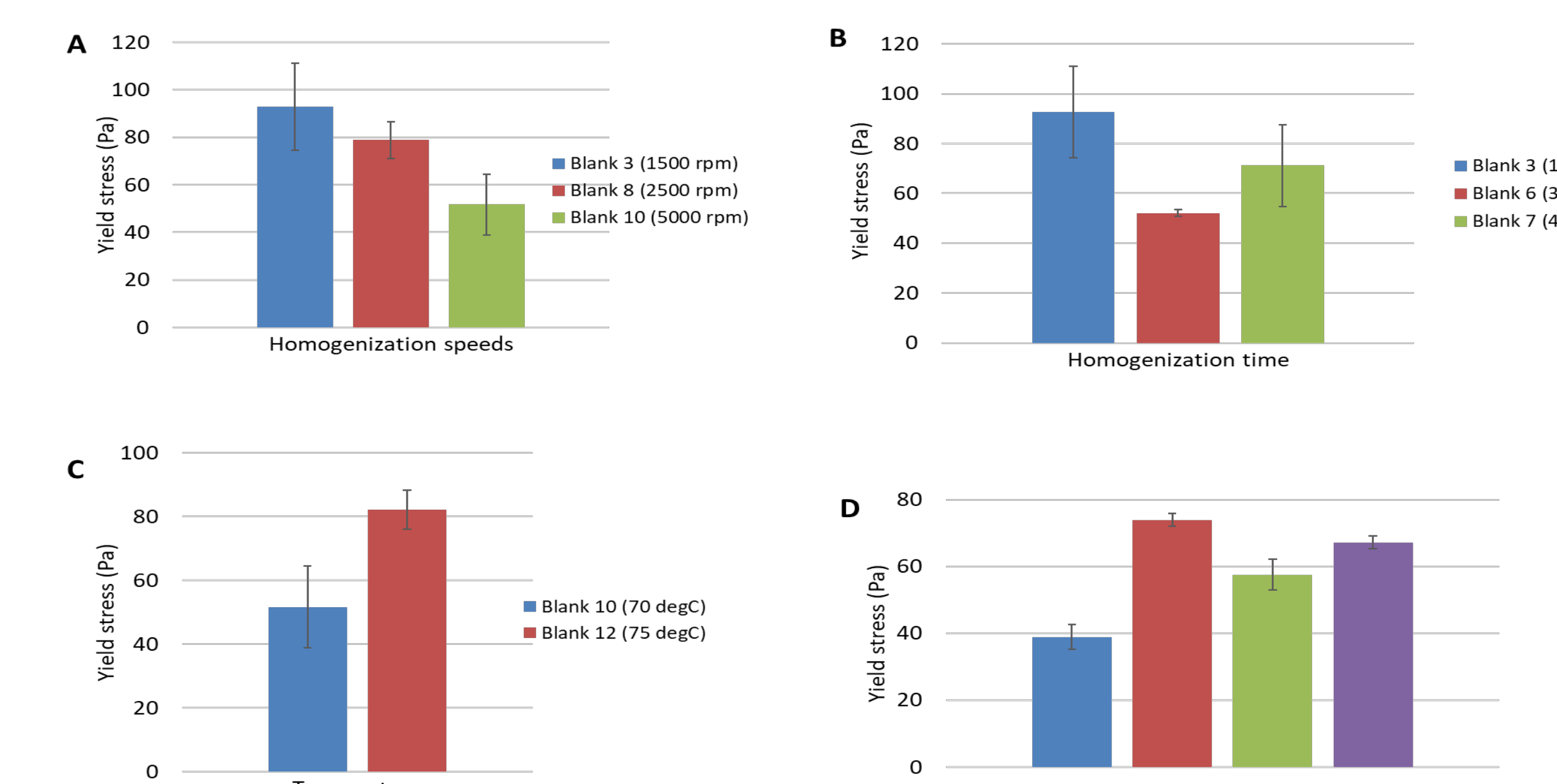


Figure 3. Yield stress of selected formulations comparing A) Homogenization speed, B) Homogenization time, C) temperature, and D) with UV filters.

Conclusion

Preliminary results indicate that manufacturing process parameters appear to have confounding effect on the globule size distributions and product viscos. These results also call for a more systematic design-of-experiment to elucidate the relationships between process variables and formulation characteristics that may lead to skin absorption of UV filters.

On-going studies

- Stability studies are on-going to evaluate changes in globule size distribution over time, particularly for formulations prepared at high homogenization speed.
- For formulations containing UV filters, a series of in vitro permeation tests (IVPT) will be performed on human cadaver skin to further evaluate the impact of the globule size distribution differences observed among the formulations on skin absorption of the UV filters.
- Using process parameter ranges established from the preliminary studies, DOE formulations will be prepared and evaluated for UV filters absorption.

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Disclaimer

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