Long-term stability of in-house sunscreen formulations

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Abstract

The characteristics of sunscreen formulations can influence the transdermal absorption of chemical UV filters. The objective of this study was to evaluate the physical and chemical stability of in-house sunscreen formulations that were manufactured and stored at 25°C/60% relative humidity (RH) for one year. The formulations were found to be stable.

Introduction

Sunscreens are usually formulated as oil-in-water emulsions. It is a system where an oil phase is evenly dispersed as globules in a continuous aqueous phase. The active ingredients in sunscreen are UV filters, which protect the skin by absorbing, reflecting or scattering UV radiation at the skin surface. It has been shown that certain sunscreen active ingredients are dermally absorbed and result in systemic exposure. There are several factors that may affect the skin absorption including physical characteristics and composition of sunscreen formulation. The objective of this study was to investigate the physical and chemical stability of in-house prepared sunscreen formulations that were manufactured and stored at 25°C/60% RH for one-year. The stability of sunscreen formulation is necessary to ensure its safety and efficacy through its shelf life.

Methods

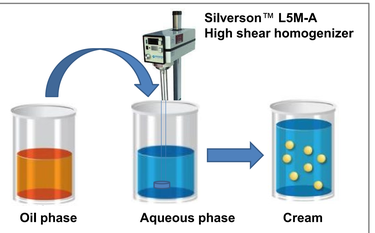
Manufacturing of sunscreen

The composition and manufacturing process variables are listed in Table 1 below. Aqueous and oil phases were prepared separately at 70 - 75°C in a water bath. Three formulations were manufactured. Figure 1 below show the manufacturing process.

Table 1. Composition & manufacturing process variables

Formulations	Process variables
S1	5000 rpm homogenization speed at 70°C
S2	5000 rpm homogenization speed at 75°C
S3	1500 rpm homogenization speed at 70°C
Compositions	
UV Filters	**Excipients**
3% (w/w) Avobenzone	Deionized water, glycerin, Tefose 63, cyclomethicone, propylene glycol, stearic acid, isopropyl palmitate, dimethicone, trolamine, stearyl alcohol, phenoxyethanol, Carbomer copolymer Type B, carbomer 940, hydroxypropylmethyl cellulose, edetate disodium
6% (w/w) Oxybenzone	
10% (w/w) Octocrylene	

Figure 1. Oil phase with UV filters was added to the aqueous phase and homogenized at 1500 - 5000 rpm for 15 minutes. Formulations were cooled at room temperature at a mixing rate of 1000 rpm, then dispensed into polypropylene tubes and stored at 25°C/60% RH.



Methods continued

Stability parameters

Physical stability:

— **Visual inspection:** Visually inspect for phase separation/ creaming/ or changes in color

— **pH:** Measuring the pH of emulsions

— **Globule size distribution:** Measuring the diameter of the dispersed oil globules (µm)

— **Rheology:** Measuring the yield stress and viscosity at different shear rates mimicking the in-use conditions, low shear rate represents initial stage, medium shear rate represent spreading, and high shear rate represent the end stage.

Figure 2. Instrumentation

pH
Mettler Toledo™ pH meter with Viscous Pro ISM pH probe

Globule size
Olympus Digital Microscope

Rheology
DHR-3 Hybrid Rheometer

Assay of UV filters
Waters Acquity I-Class UPLC system

Chemical stability:

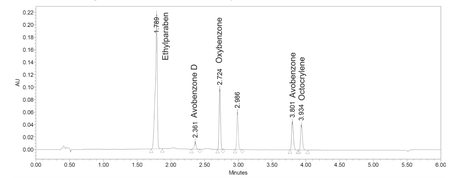
— **Assay and impurity by UPLC-UV:**

- Columns: Acquity BEH reverse-phase C18 (100 x 2.1 mm, 1.7 µm) with Acquity BEH C18 VanGuard pre-column (5 x 2.1 mm, 1.7 µm).
- MPA (4.5 mM H_3PO4 and 4.5 mM TBA in H_2O) and MPB (ACN)
- Flow rate: 0.6 mL/min, linear gradient program
- Internal standard: ethylparaben (255 nm, RT 1.82 min)

Table 2. Linearity of calibration curve.

Analyte	UV λ (nm)	RT (min)	Equation	R^2	Range
Avobenzone	354	3.80	$Y = 9.20e^{-5} X - 1.32e^{-4}$	0.9998	0.1-100 µg/ml
Oxybenzone	286	2.72	$Y = 6.34e^{-5} X + 7.03e^{-4}$	0.9986	0.1-100 µg/ml
Octocrylene	303	3.93	$Y = 3.44e^{-5} X + 1.20e^{-4}$	0.9995	0.1-100 µg/ml
Avobenzone D	283	2.36	$Y = 4.93e^{-5} X + 1.01e^{-2}$	0.9999	0.1-100 µg/ml

Figure 3. UPLC chromatogram of all the analytes. A mixed calibration standard, each 10 µg/ml, separated by UPLC method.



***In vitro* skin permeation test (IVPT)**

— Skin samples: purchased from Science Care, TEWL< 10 g/cm².hr

— Apparatus: PermeGear in-line flow-through diffusion cells

— Exposure area: 1.76 cm²

— Flow rate: 25 µL/min

— Surface temperature: 32°C

— Receptor solution: phosphate buffered saline (PBS) with 4% bovine serum albumin (BSA)

— Finite dose application: 10 mg/cm²

— Sampling time points: 0, 2, 4, 6, 8, 10, 12, 14, 16, 20, and 24 h

— Quantification: UPLC-UV

Results and Discussion

Table 3. Long term stability of in-house sunscreen creams

Parameters		Formulation S1		Formulation S2		Formulation S3	
		Time 0	One year	Time 0	One year	Time 0	One year
Appearance		Rich white cream, no phase separation					
pH		7.5	7.8	7.5	7.7	7.5	7.6
Globule size distribution (µm)	D10	1.4 ± 0.2	2.1 ± 0.1	1.8 ± 0.1	1.6 ± 0.2	2.1 ± 0.2	1.8 ± 0.1
	D50	2.2 ± 0.2	3.9 ± 1.4	2.7 ± 0.2	2.6 ± 0.4	3.2 ± 0.5	3.2 ± 0.3
	D90	4.6 ± 0.2	6.8 ± 1.0	5.8 ± 0.5	4.3 ± 0.5	7.8 ± 1.2	5.9 ± 0.3
Yield Stress (Pa)		84.1 ± 2.4	115.3 ± 4.0	70.4 ± 1.6	107.8 ± 0.1	69.6 ± 2.5	123.9 ± 2.3
Viscosity at different shear rate (Pa.s)	Low (0.001 s^{-1})	35623.7 ± 3623.0	40471.6 ± 4211.2	33578.2 ± 3763.3	36283.4 ± 1183.7	35228.2 ± 2638.5	51492.5 ± 7525.6
	Medium (1 s^{-1})	101.8 ± 4.6	127.3 ± 7.6	89.8 ± 1.2	117.9 ± 6.0	98.3 ± 1.5	170.8 ± 5.8
	High (> 50 s^{-1})	3.2 ± 0.1	3.0 ± 0.3	3.3 ± 0.4	3.0 ± 0.2	4.0 ± 0.04	4.1 ± 0.4
%Assay	Avobenzone	95.2 ± 4.8	99.2 ± 2.1	98.4 ± 5.9	98.7 ± 1.4	109.6 ± 4.1	107.2 ± 1.5
	Oxybenzone	100.3 ± 4.7	100.6 ± 2.3	102.9 ± 5.7	99.6 ± 1.3	107.6 ± 4.3	107.0 ± 1.2
	Octocrylene	98.7 ± 4.8	99.4 ± 2.1	106.4 ± 6.2	103.7 ± 1.6	103.5 ± 4.2	108.3 ± 1.5
Impurity (NMT 3%)	Avobenzone D	-	1.0 ± 0.2	-	0.9 ± 0.2	-	0.9 ± 0.2

— No significant changes were found in the visual appearance (cream color, phase separation), pH, viscosity, and globule size distribution in the in-house sunscreen formulations after one year storage. All three UV filters remained chemically stable with assay and impurity% levels at satisfaction.

— The yield stress significantly increased after one year storage and might be due to water evaporation from the permeable part of the container.

Figure 4. Microscopic pictures of dispersed oil globules in sunscreen formulations. The diameter of dispersed oil globules are generally < 10 µm.

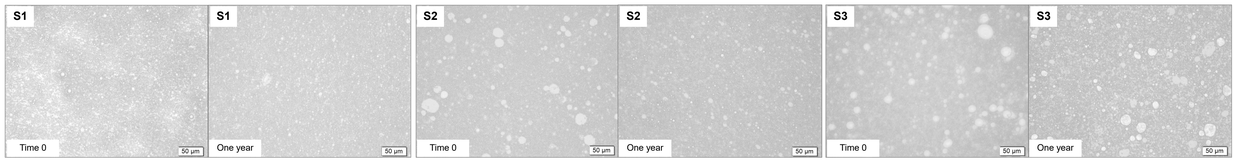
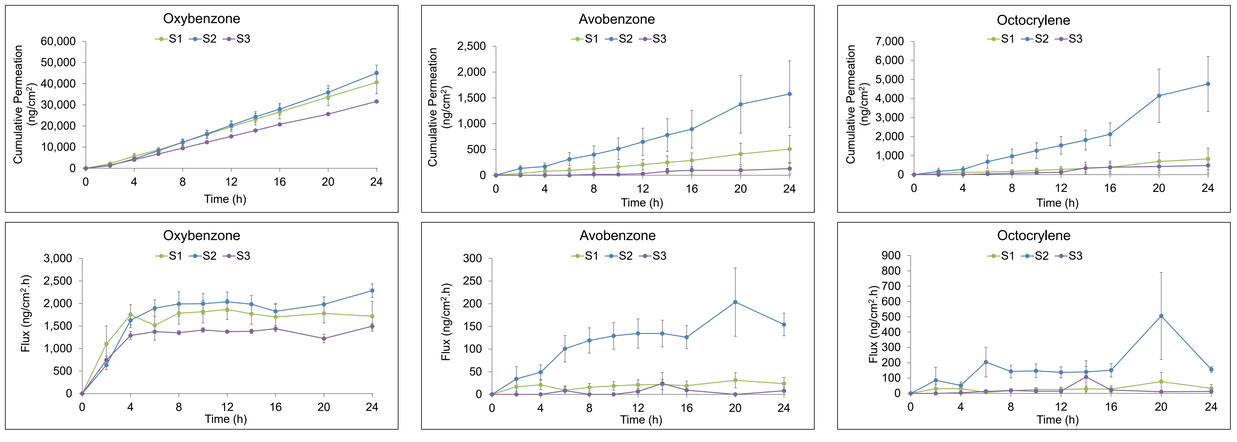


Figure 5. Skin permeation (cumulative) and flux of UV filters from in-house sunscreen formulations. Mean ± SEM, n = 3-6.



Conclusion

All in-house sunscreen formulations remained physically and chemically stable during the long-term storage (25°C/60% RH) for one year.

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