Sensory panel tests for topical semi-solid creams: correlation between sensorial perceptions and product critical quality attributes

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PURPOSE

The sensory perception of topical products during and following product application on the skin can influence patient compliance and adherence to treatment. Nevertheless, conducting human sensorial panel tests for topical drug products, like any human subject study, can be expensive and challenging in both training human subjects and the subjective nature of outcomes. Moreover, topical dosage forms, in general, can vary widely in their composition, which in turn, has the potential to significantly impact the products' physical and structural attributes as well as patient's perception of therapeutic effect of the product. Our work aims to explore and understand how formulation composition impacts a subset of critical quality attributes (CQAs) and sensory feelings of topical creams, one of the most used dermatological dosage forms. This research is expected to provide helpful integration and prediction related to therapeutic equivalence of formulations from in vitro product characterization data.

METHODS

To perform this work, 8 creams with two blinded replicates, with different concentrations of ammonium lauryl sulphate (ALS), mineral oil, cetostearyl alcohol and poloxamer were selected from 25 lab-manufactured cream formulations, by using statistical analyses such as principal component analysis (PCA) and hierarchical clustering method to compare and group CQAs data (**Figure 1**). For in vitro characterization of CQAs, measurements of rheological parameters of creams (n=3) were carried out using an Anton-Paar rheometer system with the shear, temperature and strain sweep tests. Textural properties of cream samples (n=5) were examined by applying the texture profile analysis with a CTX Brookfield texture analyzer. Frictional property of creams (n=3) was determined by using the Anton-Paar rheometer system equipped with a tribology cell and a customized sample holder. For in vivo sensory panel test, skin biophysical properties of 32 subjects, 23 females and 9 males, aged between 18 and 70 years, (Ethics ID number: 2020/HE001995) were first tested using a non-invasive Courage + Khazaka (C+K) GmbH electronic equipment. Then, the subjects were trained on concepts and assessment criteria of the 11 different sensory attributes (i.e., spreadability, cooling sensation, immediate white residue, immediate shine, immediate oiliness, stickiness, smoothness, white residue, residue shine, residue oiliness, and dry touch). These visual and touch attributes can be classified as during and after-feel sensations. To start the panel test, at time 0, onto a marked area of the forearm (19.6 cm^2) of each subject, 25 µL of each cream sample was placed and spread by subject's forefinger at rotational speed of approximately 1 rotation/second for 15 seconds. After 15 seconds, subjects stopped spreading, and assessed cooling sensation, immediate white residue, immediate shine and immediate oiliness. The after-feel attributes of stickiness and smoothness were evaluated after waiting for 1 and 1.5 minutes, respectively. Finally, after 2 minutes, subjects assessed white residue, residual shine, residual oiliness, and dry touch. The intensity of each cream sensorial attribute was rated using a continuous 1-9 scale, representing from very low (1) to very high (9) intensity.

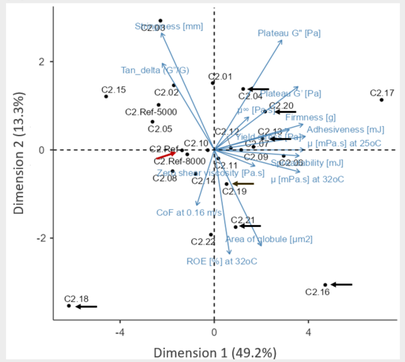
RESULTS

Skin biophysical parameters (by C+K instrument) of the 32 female and male subjects (with a wide age range) exhibited high interindividual variability, which represents a true sample from the general population. The recorded intensity scores of 11 sensory attributes for the 8 examined topical creams are depicted as spider graphs. Although subjects had differences in skin biophysical properties, they perceived sensorial attributes of the two sets of blinded replicates (named as SC2.Ref-1, SC2.Ref-2 and SC2.18-1, SC2.18-2), consistently.

(a)

Ingredient	% w/w																						Manufacture variants	
	Ingredient concentration variants - 6600 rpm of homogenization																						5000 rpm	8000 rpm
	SC2.Ref	SC2.01	SC2.02	SC2.03	SC2.04	SC2.05	SC2.06	SC2.07	SC2.08	SC2.09	SC2.10	SC2.11	SC2.12	SC2.13	SC2.14	SC2.15	SC2.16	SC2.17	SC2.18	SC2.19	SC2.20	SC2.21	SC2.22	SC2 Ref 5000	SC2 Ref 8000
	C2.Ref	C2.01	C2.02	C2.03	C2.04	C2.05	C2.06	C2.07	C2.08	C2.09	C2.10	C2.11	C2.12	C2.13	C2.14	C2.15	C2.16	C2.17	C2.18	C2.19	C2.20	C2.21	C2.22	C2.Ref -5000	C2.Ref -8000
Mineral oil	5	5	5	5	5	5	5	5	5	5.25	4.75	5	5	5	5	5	5	5	5	6.00	4.00	5	5	5	5
Ammonium Lauryl Sulphate	1.25	1.31	1.19	1.38	1.12	1.50	1.00	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.88	0.63	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Poloxamer 407	1	1	1	1	1	1	1	1	1	1	1	1.05	0.95	1.10	0.90	1	1	1	1	1	1	1.20	0.80	1	1
Cetostearyl alcohol	6	6	6	6	6	6	6	6.30	5.70	6	6	6	6	6	6	6	6	7.20	4.80	6	6	6	6	6	6
Isopropyl myristate	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Glycerol	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30
Phenoxy ethanol	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8
Water	53.95	53.89	54.01	53.82	54.08	53.70	54.20	53.65	54.25	53.70	54.20	53.9	54.00	53.85	54.05	53.32	54.57	52.75	55.15	52.95	54.95	53.75	54.15	53.95	53.95

(b)



(c)

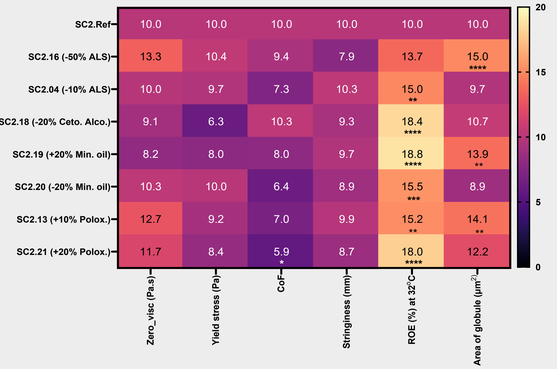


Figure 1. (a) *Formulation table of 25 topical creams varied in %w/w of ammonium lauryl sulphate (ALS, highlighted in yellow), cetostearyl alcohol (Ceto. Alco., highlighted in blue), poloxamer (Polox., highlighted in green), and mineral oil (Min. oil, highlighted in orange) composition;* ***(b)*** *Eight cream formulations including SC2.Ref (the reference formulation, highlighted in pink), SC2.04, SC2.13, SC2.16, SC2.18, SC2.19, SC2.20 and SC2.21 (in red font in 1.(a)), identified as C2.Ref, C2.04, C2.13, C2.16, C2.18, C2.19, C2.20 and C2.21, respectively, were selected out of 25 formulations for the sensory panel study by using statistical analyses, according to their formulation composition and a subset of CQAs; (c) A subset of CQAs-Q3 normalized for different units including, zero shear viscosity (zero_visc), yield stress (rheological property), coefficient of friction (CoF) (tribology), stringiness (texture property), rate of evaporation (ROE) at 32°C, and area of globule (globule size) of the eight selected SC2 creams (in red font in 1.(a)). The number of "*" summarizes the p values/significant levels: without "*" meaning p>0.05 or no significant difference, with "*" significant difference at p<0.05, "**" significant difference at p<0.01, "***" significant difference at p<0.0005, and "****" significant difference at p<0.0001 between the formulations.*

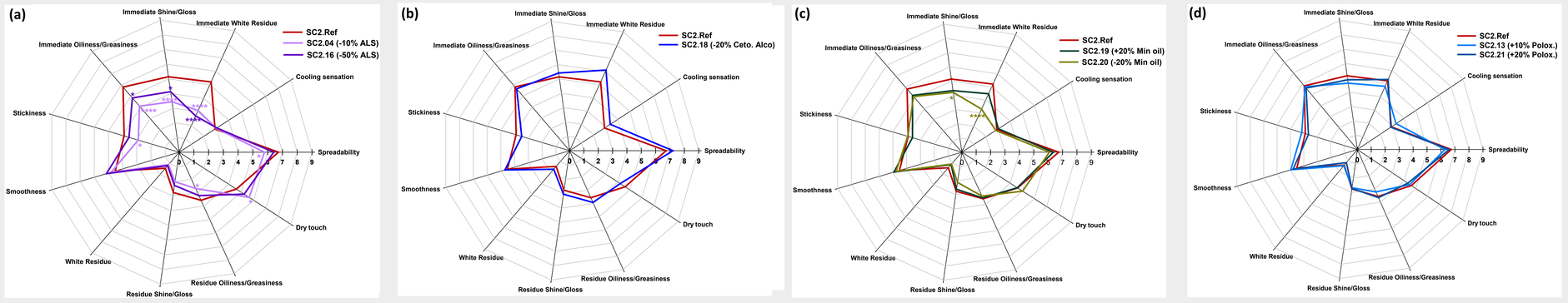


Figure 2*. Spider diagram of sensory perceptions of spreadability, cooling sensation, immediate white residue, immediate shine, immediate oiliness, stickiness, smoothness, white residue, residue shine, residue oiliness, and dry touch assessed using 9-point hedonic scale of the 4 groups of formulation variants:* ***(a)*** *ammonium lauryl sulphate (ALS),* ***(b)*** *cetostearyl alcohol (Ceto. Alco.),* ***(c)*** *mineral oil (Min oil),* ***(d)*** *poloxamer (Polox.) (formulations presented in Figure 1a), showing correlations among sensory perceptions of the cream formulation composition differences in -/+ % w/w compared with that of the reference (Ref) formulation. The number of "*" summarizes the p values/significant levels: without "*" meaning p>0.05 or no significant difference, with "*" significant difference at p<0.05, "**" significant difference at p<0.01, "***" significant difference at p<0.0005, and "****" significant difference at p<0.0001 between the cream formulations.*

RESULTS

To clearly observe the impact of inactive ingredient concentration (Q2) changes on CQAs and sensorial properties of the samples, the outcomes were divided into 4 groups for ALS (**Figure 2a**), cetostearyl alcohol (**Figure 2b**), mineral oil (**Figure 2c**) and poloxamer variants (**Figure 2d**). The participants perceived notable differences in several sensory attributes including spreadability, immediate white residue, immediate shine, immediate oiliness and stickiness when comparing the reference formulation to ALS and mineral oil variants. These perceived differences may be linked to variations in formulation composition and corresponding in vitro characterization results (**Figure 1b and 1c**). As shown in **Figure 1b**, these variants, are positioned at considerable distances from the reference formulation and occupy different quadrants of the PCA plot. The greater separation suggests more differences in CQAs, such as rheological, tribological behaviour, and textural properties between the reference and composition variant formulations, which are more likely to be perceived differently by human subjects.

CONCLUSION(S)

The obtained data demonstrate that substantial differences in some of CQAs are likely to be perceptible by human subjects. The findings also suggest that it may be possible to understand and predict some potential differences in sensorial attributes between two topical formulations from their physicochemical and structural characteristics assessed instrumentally.

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