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TOPICAL CREAMS SENSORIAL PERCEPTION: CORRELATION WITH PRODUCT CRITICAL QUALITY ATTRIBUTES

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PURPOSE

As some of the most commonly used topical pharmaceutical formulations, topical creams can vary greatly in their composition, which in turn, may have a significant impact on physical and structural attributes of the product and their interaction with skin surface, potentially impacting the sensorial feel of the product. However, conducting a sensory panel test can be costly and challenging as it involves training human subjects and yet, the outcomes measured can be subjective. Here we aim to explore the influence of inactive ingredient concentration (Q2) on assessed critical quality attributes (CQAs) of topical creams and how characterization of some CQAs can provide an understanding and prediction of their comparative sensory behavior.

METHOD(S)

To study the correlation between relevant CQAs and sensory attributes, 8 creams with two blinded replicates, having different concentrations of sodium lauryl sulphate (SLS), cetostearyl alcohol, petrolatum, and mineral oil, were selected from amongst 26 cream formulations (**Fig.1a**) by using statistical analyses such as principal component analysis (PCA) and Hierarchical clustering method to compare and group CQAs data. **Fig.1b** presents the first two-dimension scatter-plot accounting for total variation in CQAs for 26 cream formulations, and the positions of 8 creams selected according to their Q2 and a subset of CQAs for the sensory panel study.

For in vitro characterization of the creams, rheological evaluations were carried out using an Anton-Paar rheometer with the shear and strain sweep tests, at 32ºC. Textural properties of cream samples were examined by applying the texture profile analysis with a Brookfield texture analyzer. Frictional property of creams was determined by using the Anton-Paar rheometer equipped with a tribology cell and a customized sample holder.

For in vivo sensory panel test, skin biophysical properties of 30 subjects (n=30, ethics ID number: 2020/HE001995) were first measured using a non-invasive Courage + Khazaka (C+K) GmbH electronic equipment. Then, the subjects were trained on concepts and assessment criteria of 10 different sensory attributes (spreadability, immediate white residue, immediate shine, immediate oiliness, stickiness, smoothness, white residue, residue shine, residue oiliness, and dry touch). These sensory attributes can be classified as during and after-feel sensations (visual and touching attributes). To start the panel test, at time 0, 25 µL of each cream sample was placed onto a marked area of the forearm (19.6 cm^2) of each subject, and the subjects spread the sample using their forefinger at rotational speed of 1 circle/s for 15 s to assess spreadability. After 15 s, subjects stopped spreading, and assessed immediate white residue, immediate shine and immediate oiliness. The after-feel attributes of stickiness and smoothness were evaluated after waiting for 1 and 2 min, respectively. Subjects then assessed white residue, residual shine, residual oiliness, and dry touch. The intensity of each sensorial attribute was rated by subjects using a continuous 1-9 hedonic scale, representing from very low (1) to very high (9) intensity.

(a)

Ingredient	% w/w																									Manufacture variants	
	Ingredient concentration variants - 6600 rpm of homogenization																									5000 rpm	8000 rpm
	SC1.01	SC1.07	SC1.16	SC1.15	SC1.17	SC1.18	SC1.19	SC1.20	SC1.21	SC1.22	SC1.23	SC1.24	SC1.25	SC1.26	SC1.27	SC1.28	SC1.29	SC1.30	SC1.31	SC1.32	SC1.33	SC1.34	SC1.35	SC1.36		SC1.16-5000	SC1.16-8000
Sample ID	*C1.1*	*C1.7*	*C1.16R*	*C1.15*	*C1.17*	*C1.18*	*C1.19*	*C1.20*	*C1.21*	*C1.22*	*C1.23*	*C1.24*	*C1.25*	*C1.26*	*C1.27*	*C1.28*	*C1.29*	*C1.30*	*C1.31*	*C1.32*	*C1.33*	*C1.34*	*C1.35*	*C1.36*	*C1.16L*	*C1.16H*	
Mineral oil	10	10	10	10	15	15	10	10	10	10	10	10	10	10	10	10	10	10	10	10	20	20	15	15	10	10	
Sodium Lauryl Sulphate	0.75	1.50	0.75	0.50	0.75	1.50	0.79	0.71	0.83	0.68	0.90	0.60	0.75	0.75	0.75	0.75	1.13	0.38	0.75	0.75	0.75	1.50	0.75	1.50	0.75	0.75	
Poloxamer 407	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
Cetostearyl alcohol	6	8	8	6	8	8	8	8	8	8	8	8	8.40	7.60	8.80	7.20	8	8	9.60	6.40	8	8	8	8	8	8	
Petrolatum	10	10	10	10	0	0	10	10	10	10	10	10	10	10	10	10	10	10	10	10	0	0	5	5	10	10	
Propylene Glycol	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	30	
Methyl Paraben	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	
Propyl Paraben	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	
Water	42.12	39.37	40.12	42.37	45.12	44.37	40.08	40.16	40.04	40.19	39.97	40.27	39.72	40.52	39.32	40.92	39.74	40.49	38.52	41.72	40.12	39.37	40.12	39.37	40.12	40.12	

(b)

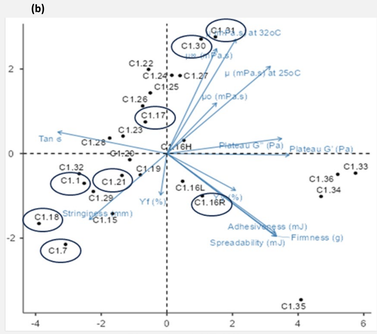

Figure 1. (a) *Formulation table of 26 topical creams that varied in %w/w of sodium lauryl sulphate (highlighted in yellow), cetostearyl alcohol (highlighted in blue), petrolatum (highlighted in green), and mineral oil (highlighted in pink) composition;* ***(b)*** *Eight cream formulations including SC1.16 (the reference formulation, highlighted in orange), SC1.30, SC1.21, SC1.07, SC1.01, SC1.31, SC1.17 and SC1.18 (in red font in 1.(a)), identified as C1.16R, C1.30, C1.21, C1.7, C1.1, C1.31, C1.17, and C1.18, respectively, were selected out of the 26 formulations for the sensory panel study by using statistical analysis, according to their formulation composition and a subset of CQAs.*

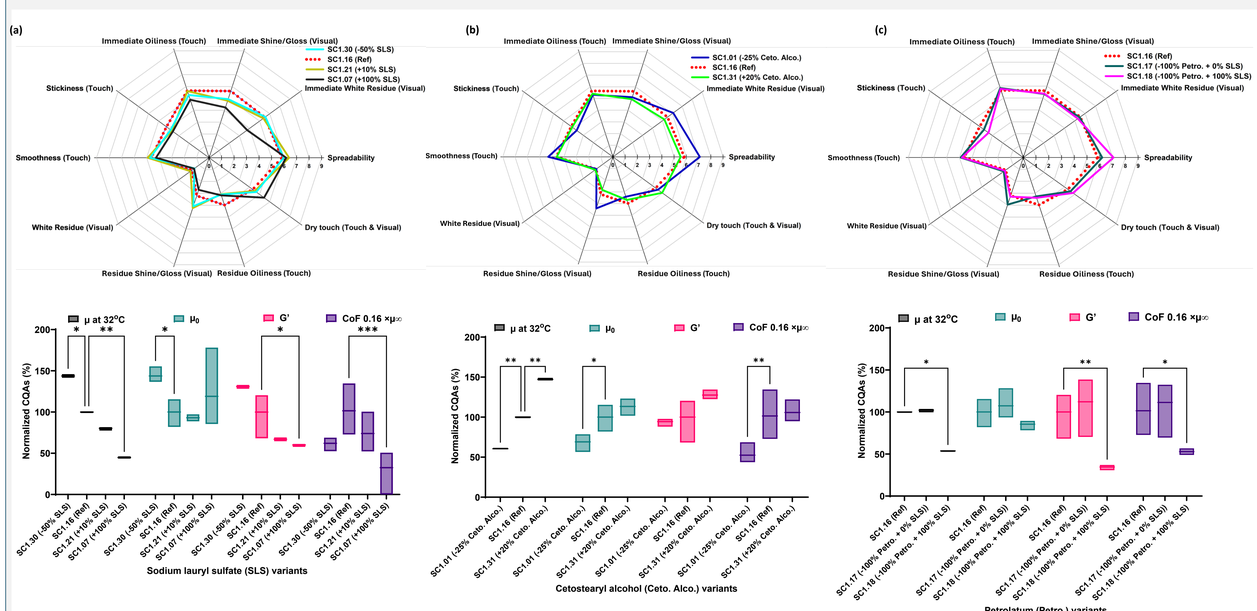

Figure 2. *Three groups of formulation variants:* ***(a)*** *sodium lauryl sulfate (SLS),* ***(b)*** *cetostearyl alcohol (Ceto. Alco.) and* ***(c)*** *petrolatum (Petro.) (formulations presented in Figure 1a) showing correlations among sensory perceptions: spreadability, immediate white residue, immediate shine, immediate oiliness, stickiness, smoothness, white residue, residue shine, residue oiliness, and dry touch assessed using 9-point hedonic scale; cream formulation composition differences in -/+ % w/w compared with that of the reference (Ref) formulation (SC1.16); and a subset of critical quality attributes (CQAs) assessed including viscosity at 32ºC (µ at 32ºC), zero shear viscosity (μ_0), storage modulus (G'), coefficient of friction at 0.16 m/s (CoF 0.16) and infinite shear viscosity (μ_∞). 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.*

RESULT(S)

Subject (n=30) skin biophysical parameters (by C+K instrument) exhibited high interindividual variability, which are representative of the general population. The recorded intensity scores of the 10 sensory attributes for the 8 examined topical creams are depicted as spider graphs (**Fig.2**). Although subjects had high interindividual variability in skin biophysical properties, they perceived sensorial attributes of the two sets of blinded replicates (SC1.01 and SC1.31), consistently. To clearly observe the impact of Q2 changes on CQAs and sensorial properties of the tested creams, the outcomes were divided into 3 groups according to SLS (**Fig.2a**), cetostearyl alcohol (**Fig.2b**) and petrolatum (**Fig.2c**) variants. The subjects perceived significant dissimilarities in spreadability and visual sensory attributes including immediate white residue, immediate shine and residue shine between the reference formulation (SC1.16) and some of Q2 variant formulations, which meaningfully correlate with the formulation composition and in vitro characterization data. As shown in **Fig.2**, the SC1.01 (-25% cetostearyl alcohol) and SC1.18 (-100% petrolatum and +100% SLS) creams, with significantly ($p<0.05$) lower rheological values (viscosity at 32ºC, zero shear viscosity and storage modulus), were ranked higher in intensity of spreadability as compared to the reference formulation (SC1.16). Additionally, a significant difference ($p<0.01$) in friction and viscosity values of the SC1.07 (+100% SLS) cream could impact the disappearance of cream when applied onto the skin area, leading to the changes in immediate white residue and immediate shine of the variant compared to the reference formulation (**Fig.2a**). Further, a higher perception score for residual shine was recorded in SC1.01 (-25% cetostearyl alcohol), which could be related to the amount of stabilizer.

CONCLUSION(S)

The findings demonstrate that, it may be possible to understand and even predict some sensory aspects from the physicochemical and structural characteristics assessed instrumently. Our data suggest that large differences in some of CQAs, such as rheological and tribological behaviors are likely to be perceptible to human subjects. Our outcomes demonstrate that data from selected CQAs may be predictive of the impact of Q2 changes on sensory perception of topical products.

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