In vitro-In vivo Comparison of Cooling Sensation in Topical Gel Products

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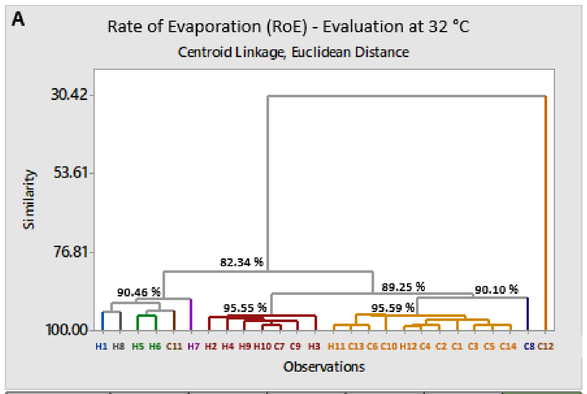
Introduction

Cooling sensation can play a crucial role in the perception/sensorial feel of topical products. This sensation can be the result of both, the solvent evaporation, as well as inherent sample temperature. In this work, in vitro and in vivo assessment of the cooling sensation generated by carbomer (Carbopol® 980P, CBP) and hydroxyethyl cellulose (HEC) gels, was studied. Two gel products, coded HEC08 and CBP02, were selected among 26 different formulations of HEC and CBP gels (as showed in Figure 1) by clustering and centroid linkage-based grouping information of in vitro cooling effect, evaporation data, and other critical quality attributes (CQAs) based on statistical analysis.

A



B

Gel	Zero-shear viscosity η_0	Yield stress τ_y	Consistency index K	Plateau elastic modulus G'_p	Plateau loss tangent $Tan\delta_p$	Cooling sensation (ΔT)
HEC	-0.044 *	-0.176 *	-0.198 *	-0.234 *	0.495 *	0.23 *
CBP	-0.25 *	-0.24 *	-0.242 *	-0.421 *	0.681 ***	0.721 ****

**** p<0.01; *** p<0.05; ** p<0.1; * p>0.1

C

No.	Formulation	Polymer, %	Propylene glycol, %	Ethanol/iso-propanol, %	Mean temp. difference (°C)
1	CBP12 (C12)	0.5	15	50	25.23
2	HEC01 (H1)	1	15	20	14.34
3	HEC08 (H8)	2.2	15	50	**13.28**
4	HEC07 (H7)	2.2	15	45	12.99
5	HEC05 (H5)	2.2	15	25	12.18
6	HEC06 (H6)	2.2	15	30	11.43
7	CBP11 (C11)	0.5	15	35	10.69
8	HEC03 (H3)	3	15	20	9.96
9	HEC02 (H2)	2.2	15	20	9.31
10	CBP09 (C9)	0.1	15	--	9.08
11	HEC09 (H9)	2.2	20	20	8.77
12	CBP07 (C7)	0.5	15	20	8.51
13	HEC04 (H4)	5	15	20	8.42
14	HEC10 (H10)	2.2	30	20	8.12
15	HEC11 (H11)	2.2	40	20	6.87
16	CBP10 (C10)	1	15	--	6.78
17	CBP13 (C13)	0.5	15	10	6.75
18	CBP06 (C6)	0.5	35	--	6.34
19	CBP01 (C1)	0.5	15	--	5.88
20	CBP02 (C2)	0.25	15	--	**5.65**
21	HEC12 (H12)	2.2	50	20	5.47
22	CBP04 (C4)	0.25	25	--	5.30
23	CBP03 (C3)	0.65	15	--	4.86
24	CBP14 (C14)	0.5	25	--	4.65
25	CBP05 (C5)	0.25	35	--	4.48
26	CBP08 (C8)	0.5	50	--	3.03

Figure 1: Statistical analysis of Critical Quality Attributes (CQAs) of hydroxyethyl cellulose (HEC) and carbomer (Carbopol® 980P, CBP) gels. Correlation coefficient was employed to analyze the relationships between the rate of evaporation (RoE), temperature difference, and CQAs. Centroid linkage and Euclidean distance were used as the average linkage method to assess the distance or similarity between the clusters (groups) of observations (gel formulations) (1A). HEC gels showed insignificant correlation with cooling sensation when compared to CBP gels (1B). From statistically grouping information, HEC08 and CBP02 gels (highlighted in the table of gel formulations) (1C) were selected for the in vitro and in vivo comparison of cooling sensation.

Methodology

Evaporation rate of gels was measured using gravimetric method. A 100 µL gel product was placed inside a rubber ring (1.64 cm^2 area) on a temperature-controlled plate, maintained at 32°C for 60 min. Simultaneously, infrared thermal (IRT) camera system was set up from the above to record the temperature. In the in vivo study, first an IRT camera recorded the temperature dynamics of a subject's forearm. At time 0, a gel sample was placed onto a marked skin area (12.5 cm^2) of the forearm, one at a time for 3 gels (one blinded replicate). The gel was spread using a circular motion by the forefinger at 1 rotation/sec. Then, thermal images were captured every 15 s to record the temperature of the un-treated and treated area for 2 min (Figure 2). Simultaneously, at time 0, the subject started a sensorial assessment to evaluate immediate cooling sensation and evaporative cooling sensation (during solvent evaporation) and ranked the intensity.

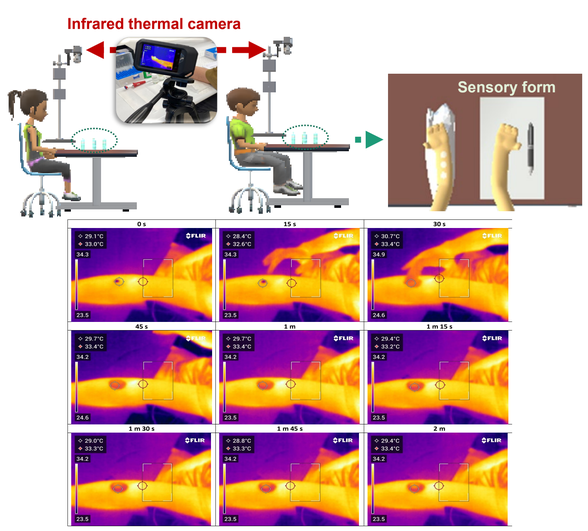


Figure 2: Setting up infrared thermal (IRT) camera-based method for in vivo cooling sensation assessment, and simultaneously sensory evaluation with human subjects (5 subjects/replications, n=5). Pictures were captured every 15 s by the IRT camera to record the temperature of the untreated and treated skin area with the gel sample.

Results

The skin temperatures recorded by the IRT camera showed a higher mean temperature difference (ΔT) between untreated and treated skin areas during the 2 min period with the HEC08 gel compared to the CBP02 gel (Figure 3), expectedly showing a greater cooling effect based on in vitro results. The findings also revealed a higher cooling intensity for the HEC08 gel compared to the CBP02 gel as evaluated by subjects on a 9-point hedonic scale (Figure 4). A correlative observation indicated that the gel (HEC08) with higher evaporation rate and ethanol content had more cooling effect compared to the CBP02 gel.

Gel samples	Time (s)	Skin temperature (°C) Treated skin spot	Control skin spot	Mean difference
HEC08-1st	0	28.1 ± 2.2	33.5 ± 1.3	5.4
	15	27.8 ± 2.1	33.5 ± 1.2	5.7
	30	30.9 ± 0.9	33.4 ± 1.2	2.5
	45	30.4 ± 0.9	33.4 ± 1.3	3.0
	60	30.4 ± 0.9	33.6 ± 1.3	3.2
	75	30.2 ± 1.1	33.4 ± 1.2	3.3
	90	30.3 ± 1.2	33.5 ± 1.2	3.2
	105	30.4 ± 1.2	33.7 ± 1.0	3.3
	120	30.7 ± 1.2	33.7 ± 1.1	3.0
HEC08-2nd	0	27.8 ± 1.2	33.4 ± 1.5	5.6
	15	28.8 ± 1.0	33.4 ± 1.3	4.6
	30	31.1 ± 0.6	33.6 ± 1.1	2.5
	45	30.6 ± 0.5	33.7 ± 1.1	3.1
	60	30.5 ± 0.8	33.5 ± 1.2	3.0
	75	30.3 ± 1.0	33.7 ± 1.2	3.3
	90	30.0 ± 1.1	33.4 ± 1.3	3.4
	105	30.2 ± 1.1	33.5 ± 1.3	3.3
	120	30.4 ± 0.9	33.5 ± 1.4	3.1
CBP02	0	30.1 ± 1.4	33.9 ± 1.3	3.8
	15	31.0 ± 1.6	33.9 ± 1.4	2.9
	30	31.8 ± 1.3	33.6 ± 1.4	1.8
	45	31.1 ± 1.4	33.3 ± 1.4	2.2
	60	31.1 ± 1.1	33.5 ± 1.2	2.4
	75	30.9 ± 1.2	33.4 ± 1.2	2.6
	90	30.9 ± 1.3	33.3 ± 1.3	2.4
	105	30.7 ± 1.1	33.7 ± 1.3	3.0
	120	31.1 ± 0.7	33.4 ± 1.4	2.3

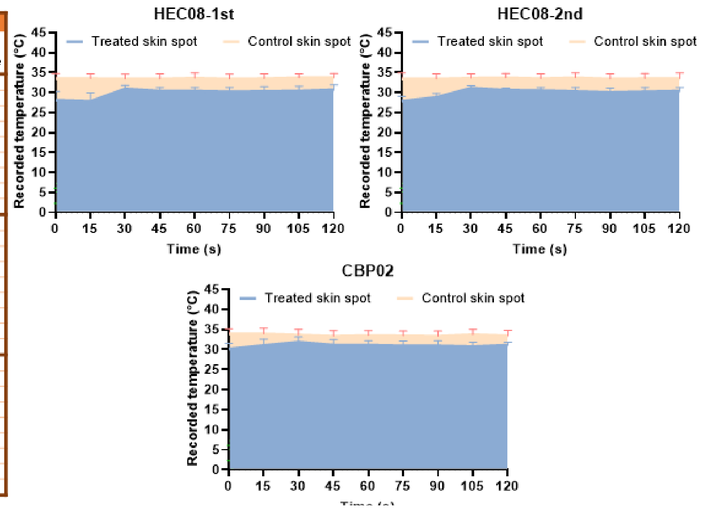


Figure 3: Temperature difference of the treated and untreated skin areas with the gel samples recorded by the infrared thermal (IRT) camera during 2 min period. Data are presented as mean ± standard deviation (SD). The HEC08 gel was blindly replicated and named as HEC08-1st and HEC08-2nd.

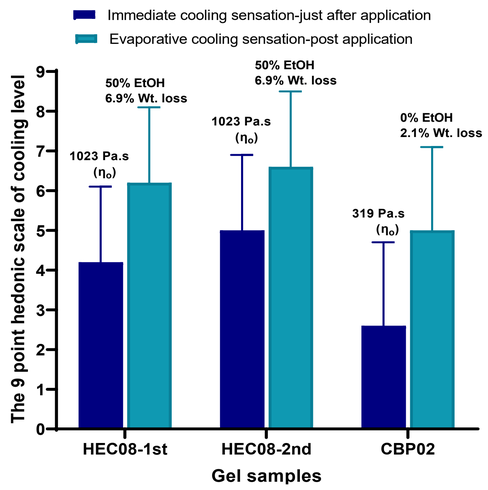


Figure 4: Sensory scores of immediate and evaporative cooling sensation of the HEC08 and CBP02 gels evaluated by human subjects. Data are presented as mean ± standard deviation (SD). The HEC08 gel was blindly replicated and named as HEC08-1st and HEC08-2nd.

Conclusion

This preliminary study demonstrates good correlation between change in skin temperature as recorded by IRT camera and perceptive cooling sensation difference assessed by voluntary subjects (n=5). The obtained results also suggest that the in vitro IRT has potential to predict the intensity of cooling that the subjects assess during human sensory trials.

Learning objectives

Triangular correlational assessment of gel cooling sensation by IRT camera-based technique both in vitro and in vivo, and sensory test with human volunteer (in vivo).

Acknowledgements

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