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IN VITRO ASSESSMENT OF COOLING POTENTIAL OF THE TOPICAL GEL SYSTEM AND INFLUENCE OF INACTIVE INGREDIENTS

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PURPOSE

The purpose of the study was to explore an infrared thermal imaging (IRT)-based technique for in vitro assessment of the cooling potential of topical gel formulations containing hydroxyethyl cellulose (HEC), isopropyl alcohol (IPA), and propylene glycol (PG) at varying concentrations and comprehend the influence of each inactive excipient.

METHOD(S)

- Twelve different gel formulations were prepared with various concentrations of HEC (1 to 5%), IPA (20-50%), and PG (15-50%) (Table 1).

Table 1. Composition of hydroxyethyl cellulose (HEC) based gel formulations.

Ingredients (%, w/w)	F01	F02	F03	F04	F05	F06	F07	F08	F09	F10	F11	F12
HEC	**1**	**2.2**	**3**	**5**	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2
Iso-propyl alcohol	20	20	20	20	**25**	**30**	**45**	**50**	20	20	20	20
Propylene glycol	15	15	15	15	15	15	15	15	**20**	**30**	**40**	**50**
2-Phenoxyethanol	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	63.2	62	61.2	59.2	57	52	37	32	57	47	37	27

- As shown in Figure 1, a piece of excised human skin was placed on a temperature-controlled plate and the skin temperature was maintained at 32 °C. 100 µL of each gel formulation stored at room temperature (24-25 °C) was dispensed and spread on the skin inside a rubber ring of 1.64 cm^2 area.
- The temperature dynamics of the area of interest were recorded at specific time intervals from 0 min (immediately after sample application) to 60 min of duration using IRT.
- Reference skin temperature (T_R≈32 °C) was recorded from a location where gels were not applied (red circular areas in Figure 1).
- The decrease in temperature following the application of gel was calculated by subtracting the temperature of gel (T_S) (blue circular area) values from the reference values (red circular areas).
- The temperature difference (**$\Delta T=T_R-T_S$**) thus obtained was referred to as **the cooling potential** of the gel.
- The implied role of gel viscosity and solvent evaporation was understood through evaluating the correlation of ΔT with the zero-shear viscosity (η_0) and rate of evaporation (ROE) measured at 32 °C.
- Data were statistically analysed using Tukey's pairwise comparison in one-way ANOVA at 95% confidence interval.

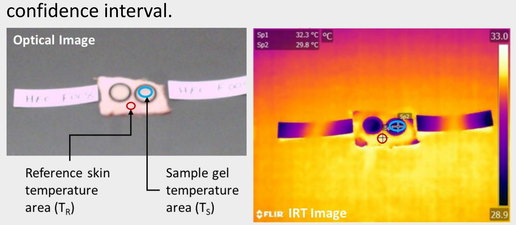

Figure 1. Illustration of in vitro study design to assess the temperature differences between reference skin temperature (red circle) and sample gel temperature (blue circle) using infrared thermal imaging (IRT). The grey circles show the area of the topical application.

RESULT(S)

- The immediate ΔT (at t=0) of the formulations ranged from 5.44 - 8.95° C (Figure 2).
- The temperature differences were elevated with the increase in HEC concentration (F01-F04) (Figure 2A), elucidating an enhanced cooling effect which showed a positive correlation with the viscosity (η_0) (Figure 3A). Difference between 1% HEC (F01) and 5% HEC (F04) remained significant ($p<0.05$) throughout 60 minutes of duration.
- At constant HEC concentration, increasing IPA content from 20% to 50% (F02, F05-F08) demonstrated a consistent increase in ΔT of the gels (Figure 2B). F08 (50% IPA) exhibited significantly higher ($p<0.05$) ΔT compared to F02 (20% IPA) throughout 60 minutes of duration.
- The gels with 20% (F09) and 30% (F10) PG had higher impact on decreasing the skin temperature compared to the gels with 40% (F11) and 50% (F12) PG (Figure 2C).
- Over 60 minutes duration, the ΔT was reduced by up to 6.4° C and based on the average data, the decline was maximum for IPA variants (5.75-6.4° C) (Figure 2B) as compared to HEC (4.15-5° C) (Figure 2A) and PG (4.55-5.35° C) (Figure 2C) variants.
- The IPA variants also showed relatively higher initial ROE (up to 10 min duration) (Figure 3B) which is likely to be a major contributing factor in induced cooling potential (evaporative cooling).
- With increasing HEC and PG concentrations, the ROE was greatly constrained throughout the 60 min period. It is expected that after one hour, the ΔT for F04, F07, F08, F09, and F10 is sustained among the formulations.
- In low HEC and high PG variants, relatively low ΔT was ascribed to the potentially faster rate of thermal equilibration between the gels and the skin temperature due to lower gel viscosity (<200 Pa·s).

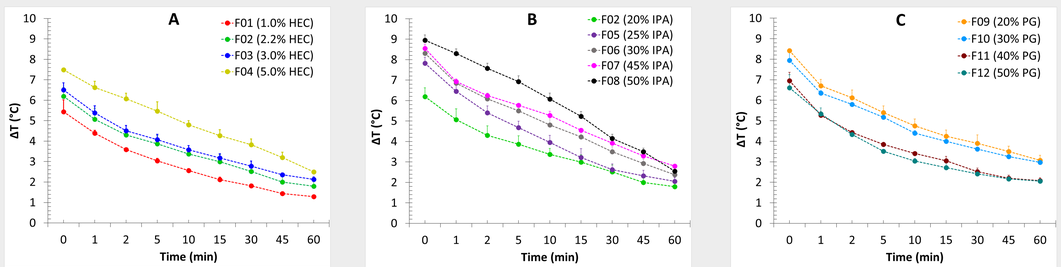

Figure 2. Mean temperature difference (**$\Delta T=T_R-T_S$**) observed for A) HEC, B) IPA, and C) PG variant formulations over 60 minutes. Data plotted as mean (n=3) with standard error of the mean.

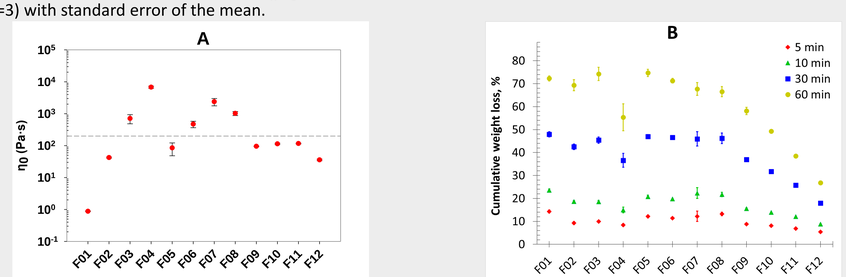

Figure 3. Zero-shear viscosity (η_0) (A) and evaporative weight loss (B) of HEC gel formulations. Reference line in plot A is placed at 200 Pa·s. Data represent mean (n=3) with standard error of the mean.

CONCLUSION(S)

1. The study highlights the use of IRT-based technique for in vitro assessment of cooling potential of the gel (measured as ΔT), following topical application on the skin.
2. The evaluation of HEC gels showed that ΔT was greatly influenced by increase in the IPA concentrations, which is the most evaporative component in these formulations.
3. The increase in concentration of the gelling agent, HEC, also showed enhancement of cooling potential, implying the significance of gel viscosity in thermal dynamics.

FUNDING/GRANT/ENCORE/REFERENCE OR OTHER USE

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