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"Exploring sensory potential of NaDES: from synthetic skin to cosmetic applications"

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1. Introduction

Natural Deep Eutectic Solvents (NaDES) are organic solvents formed by combining hydrogen bond acceptors (HBAs) like choline chloride or amino acids, with hydrogen bond donors (HBDs) such as sugars, alcohols, or organic acids in defined molar ratios [1,2]. This combination leads to a marked deviation from ideal mixing behavior, resulting in the formation of a stable eutectic system . NaDES gained attention since 2011 for their ability to solubilize both hydrophilic and lipophilic compounds and facilitate their transport and storage within cells [2,3]. Their non-toxic, biodegradable, non-volatile and thermally stable nature, along with low cost, makes them appealing alternatives to conventional solvents [4]. NaDES are now widely used in food, pharmaceutical, nutraceutical, cosmetic, and green chemistry applications, particularly for extracting and stabilizing phytonutrients from natural by-products [2,5].

In cosmetics, the shift toward greener, sustainable formulations aligned with the UN's 2030 goals has increased interest in NaDES for theirnatural origin, ability to improve solubility and formulation efficiency [6,7]. Their exceptional solubilization properties are crucial for enhancing the delivery of poorly soluble bioactives like antioxidants, vitamins, and plant extracts [8]. NaDES have shown higher extraction efficiency than conventional solvents, for example, extracting flavonoids and carotenoids from marigold with a betaine-based NaDES [9], and stabilizing phycobiliproteins such as phycocyanin and phycoerythrin [10].

Despite their potential, the application of NaDES in cosmetic formulations remains largely underexplored, particularly in relation to sensory attributes [9,11]. Yet, solvents play a crucial role in shaping product texture, spreadability and skin feel [12,13]. This highligts a clear research gap and presents an opportunity to investigate NaDES not merely as extraction media but as functional formulation ingredients in their own right.

This study aims to assess, for the first time, the sensory potential of 11 hydrophilic and lipophilic NaDES, designed through the Smart Selection Strategy, which considers market-specific regulations [14,15] and sustainability metrics like life cycle and cost [16,17]. These NaDES, already shown to be effective in stabilizing compounds from Spirulina, Porphyridium cruentum, and marigold [9,10], will be further investifgated for their impact on key sensory attributes including texture, spreadability and afterfeel, contributing to a deeper understanding of their potential in cosmetic product development.

2. Materials and methods

2.1 Products

In order to evaluate the sensory and physicochemical properties of NaDES compared to standard cosmetic ingredients, 11 NaDES (6 lipophilic and 5 hydrophilic) (Table 1) were prepared by heating and stirring their components until fully mixed. After cooling, they were stored at 20°C.

Table 1. NaDES formulations, nature and their corresponding codes

Corresponding code	Molar ratio	Water amount (% w/w)	NaDES		
			Component 1	Component 2	Component 3
Hydrophilic					
H-BG	1:8	/	Betaine	Glycerol	/
H-BGG	1:4:1	30	Betaine	Glycerol	Glucose
H-PGG	1:4:1	20	Proline	Glycerol	Glucose
H-UG	4:1	/	Urea	Glycerol	/
H-CAG	1:1	20	Citric acid	Glucose	/
Non polar					
NP-C8M	1:1	/	C8	Menthol	/
NP-C8C12	4:1	/	C8	C12	/
NP-C8P 1:2	1:2	/	C8	Propanediol	/
NP-C8P 5:1	5:1	/	C8	Propanediol	/
NP-C12M	1:2	/	C12	Menthol	/
NP-MO	1:1	/	Menthol	Octanediol	/

Their properties were then compared with 6 commonly used cosmetic ingredients from various chemical families (Table 2), enabling a comprehensive analysis of NaDES performance relative to traditional formulations.

Table 2. Reference products used for comparative analysis

Supplier	Trade name	INCI name
Wacker (Germany)	Belsil DM 1 Plus	Dimethicone
Aroma zone (France)	Vegetal glycerin	Glycerin
Olvea (France)	Apricot oil	Apricot oil
Aroma zone (France)	Jojoba oil	Jojoba oil
Stéarinerie Dubois (France)	DUB CO	Ethylhexy cocoate
Stéarinerie Dubois (France)	DUB PTO	Pentaerythrityl tetraethyhexanoate

2.2 Linear spreading behavior

Linear spreading behavior was measured using a TA.XT Plus texture analyzer (Stable Micro System, UK) with Texture Exponent software. The friction rig was equipped with an HD6 Helioplate poly(methyl methacrylate) (PMMA) plate and a polypropylene sheet, which mimics human skin's surface energy (39 mN/m). A 200 µL sample of the product was applied to the polypropylene surface, and a PMMA plate was placed on top. The test was performed in triplicate at a speed of 2 mm/s to measure the force needed to spread the product over 120 mm.

2.3 Spontaneous spreading

Spontaneous spreading was measured on the non-biological skin model, Vitroskin® (IMS, USA), which mimics human epidermis in terms of texture, pH, wettability, surface free energy, and ionic strength. Vitroskin® was hydrated 24 hours before use, following IMS's hydration protocol, using a water-glycerin mixture (85.15/14.85 w/w) for 24 hours at 23°C and 50% humidity. After hydration, 10 µL of the product was applied to a 65x65 mm square of Vitroskin® and allowed to rest for 10 minutes. Talc powder was then applied to halt spreading, and the spread area was traced with a permanent marker. The spreading area was measured using ImageJ software, calculating the ratio of the spread area to time and droplet volume. The experiment was performed in duplicate for reliability.

2.4 Stickiness after application (residual film)

To evaluate the residual film left by the products, a Biody Plate #30 artificial skin surface was used with a TA.XT Plus Texture Analyzer (Stable Micro System, UK), equipped with a P/025 spherical stainless steel probe and a 500g load cell. A 35 µL product sample was applied to a 9.6 cm² circular area of the Bioskin® Plate #30, using 10 finger rotations at 90 RPM. After resting for 3 minutes, a force vs. time curve was generated, and the area under the curve was calculated using Texture Exponent software. This area represented the work needed to unstick the probe from the surface.

2.5 Glossiness after application (residual film)

Glossiness was measured immediately after application and 5 minutes later using a Glossimeter (Courage-Khazaka electronic GmbH MPA580, Germany) to observe changes in surface reflectivity. A 30 µL product sample was applied to a 4 cm diameter circular area of the Biody Plate #30, and evenly spread using 20 rotations at 90 RPM.

2.6 Data analysis

Statistical analysis was done using XLSTAT software. One-way ANOVA identified significant differences ($p < 0.001$), and Tukey's test was used for multiple comparisons. Principal Component Analysis (PCA) was performed to analyze variable correlations and highlight significant product differences.

3. Results and discussion

3.1. In-vitro analysis of product performance during rub-out

In vitro instrumental methods validated for their correlation with sensory perception were used to investigate the relationship between physico-chemical properties and skin-feel attributes. Two main techniques were employed: spontaneous spreading on Vitroskin®, which simulates the texture of human skin, and friction measurement using the Biody Plate #30, which mimics the resistance encountered during product application [18–20].

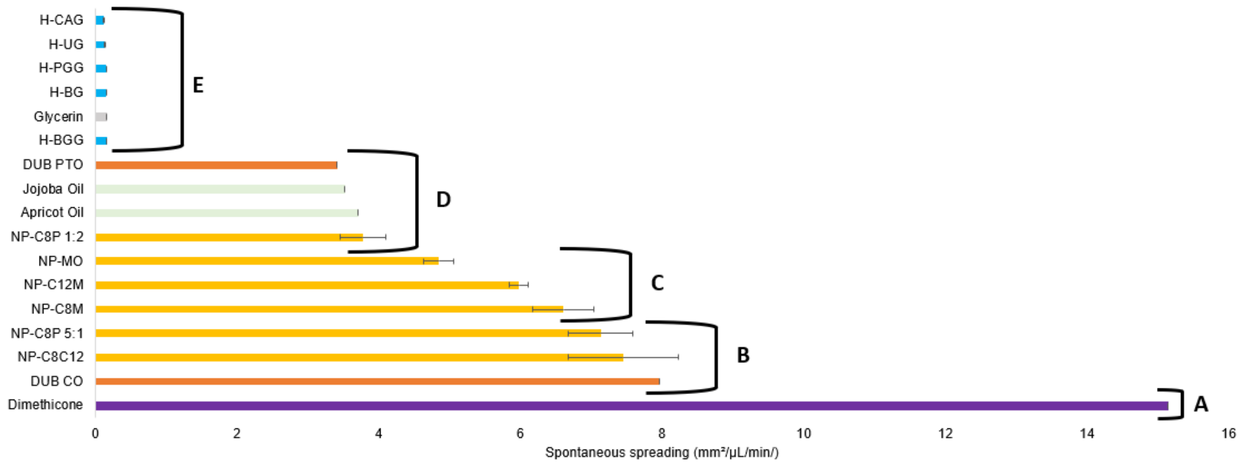

Figure 1. Mean value of spontaneous spreading on Vitroskin® for 11 NaDES and 6 reference products. Results refer to lipophilic NaDES (in yellow), to the hydrophilic NaDES (in blue), to vegetable oils (in green), to esters (in orange), to silicon (in purple) and to polyol (in grey) respectively. a-e Means sharing common superscripts are non-significantly according to Tukey's test (P > 0.01).

Spontaneous spreading evaluates how a sampled product behaves when dispensed on a surface without external application force [28,33], offering insight into a product's natural affinity with the skin, influenced by surface tension and viscosity. Statistical analysis (Tukey test) showed that products formed distinct spreading behavior groups (Figure 1). Hydrophilic NaDES and glycerin exhibited low, non-significantly different spreading values. This limited spreading behavior is consistent with their relatively high viscosity and surface tension, which reduce their ability to flow spontaneously over the substrate. In such systems, cohesive forces within the liquid outweigh adhesive interactions with the surface, leading to a more restricted spreading area. These results align with previous findings on emollients that associate higher viscosity and surface energy with limited spreading, especially in hydrophilic environments[19].

In contrast, lipophilic NaDES exhibited more variable spreading behavior. Certain systems, such as NP-C8C12 and NP-C8P (5:1), performed comparably to benchmark emollients like DUB CO, while NP-C8P (1:2) showed no significant difference from reference oils such as jojoba oil, apricot oil, or DUB PTO. This functional similarity, despite differences in chemical composition and origin, highlights the potential of lipophilic NaDES as versatile alternatives to conventional emollients in cosmetic formulations. Their ability to mimic the spreading behavior of widely used oils suggests promising applicability in tailoring texture and skin-feel across diverse product types.

3.2. Assessment of glossiness and stickiness of the residual film

Table 3. Glossiness: Mean values, standard deviations, and changes observed between application and 5 minutes after application for 11 NaDES and 6 reference formulations. a-d Means sharing common superscripts are non-significantly different as tested by Tukey's test (P > 0.01).

		Glossiness value (UA)	
		T=0min	**T=5min**
Blank	Biody	5,3 ± 0,0	
H-BG	Hydrophilic NaDES	14,3 ± 3,3^{b}	10,2 ± 0,7^{c}
H-BGG		12,7± 3,7^{c}	6,9 ± 1,1^{d}
H-PGG		13,6 ± 2,7^{c}	13,6 ± 1,9^{c}
H-UG		24,0 ± 1,4^{b}	23,3 ± 0,0^{b}
H-CAG		37,0 ± 8,0^{a}	43,4 ± 7,7^{a}
NP-C8M	Lipophilic NaDES	22,4 ± 1,6^{b}	10,5 ± 1,3^{d}
NP-C8C12		16,8 ± 3,2^{b}	8,1 ± 1,1^{d}
NP-C8P 1:2		25,3 ± 0,8^{b}	8,4 ± 0,4^{d}
NP-C8P 5:1		13,8 ± 0,9^{c}	4,2 ± 0,1^{d}
NP-C12M		36,5 ± 3,2^{b}	12,8 ± 0,3^{c}
NP-MO		43,6 ± 4,4^{a}	15,0 ± 0,9^{c}
Dimethicone	Silicon	8,4 ± 0,5^{c}	6,5 ± 0,3^{d}
DUB PTO	Ester	49,1 ± 1,6^{a}	20,1 ± 3,0^{b}
DUB CO		20,2 ± 2,6^{b}	16,5 ± 2,1^{c}
Apricot Oil	Vegetable oils	41,1 ± 3,3^{a}	20,6 ± 1,6^{b}
Jojoba Oil		38,7 ± 0,0^{a}	22,4 ± 1,4^{b}
Glycerin	Polyol	26,5 ± 4,2^{b}	18,7 ± 1,0^{b}

Glossiness is a key sensory attribute valued by consumers [21], assessed as the immediate visual effect following application and influenced by product properties like viscosity, refractive index and spreadability. As shown in Table 3, glossiness decreases over time primarily due to evaporation and absorption of volatile components into the substrate. Glossiness decrease is more pronounced in lipophilic NaDES compared to their hydrophilic counterparts, likely due to differences in spreading behavior, volatility and interfacial interactions. After 5 minutes, formulations containing NP-C8M, H-BGG, NP-C8P 1:2, NP-C8C12, and NP-C8P 5:1 exhibit low gloss levels, closely resembling to dimethicone. This suggests a matte finish and lower residual shine, which may be desirable in applications such as mattifying skincare or makeup. In contrast, NP-MO, H-PGG, NP-C12M, and H-BG maintain higher gloss levels, with values comparable to DUB CO, indicating a more luminous or dewy finish. H-UG aligns with reference ingredients like glycerin, DUB PTO, and certain natural oils, offering moderate and balanced gloss levels. Notably, H-CAG stands out with the highest gloss value of all samples tested, reflecting its strong film-forming or surface-coating ability. These results highlight the diversity of visual finish achievable with NaDES and their potential to fine-tune aesthetic properties in cosmetic formulations.

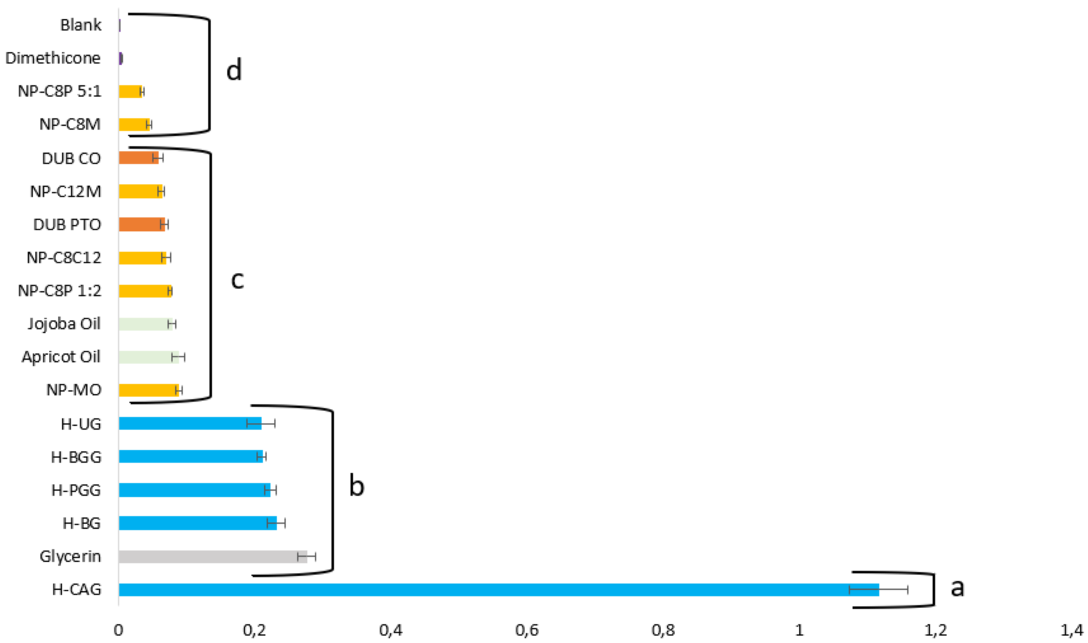

Figure 2. Mean and Standard Deviation of Stickiness on Bioskin After Application of 11 NaDES and 6 Reference Compounds. Results refer to lipophilic NaDES (in yellow), to the hydrophilic NaDES (in blue), to vegetable oils (in green), to esters (in orange), to silicon (in purple) and to polyol (in grey) respectively. a-d Means sharing common superscripts are non-significantly different *according to* Tukey's test (P > 0.01).

Stickiness plays a critical role in the overall skin feel of a cosmetic product, with lower stickiness typically enhancing comfort during and after application [13]. Among the NaDES tested, H-CAG NaDES staands out with the highest stickiness value (Figure 2), characterized by a tacky finish that may limit its sensory acceptability. Other hydrophilic NaDES exhibit stickiness levels comparable to glycerin, suggesting a familiar sensory profile within aqueous systems. In contrast, lipophilic NaDES such as NP-C8C12 and NP-C12M demonstrate low stickiness, behaving similarly to traditional emollients. Notably, NP-C8P 5:1 and NP-C8M show stickiness values equivalent to dimethicone, indicating they are effectively non-sticky. This near-silicone-like performance, combined with their natural origin, reinforces the potential of selected NaDES as viable, biodegradable alternatives to silicones, especially in formulations where a light, non-tacky skin finish is desired.

4. Conclusion

This study provides an innovative evaluation of NaDES for cosmetic applications through physicochemical analyses and *in vitro* sensory tests. Results revealed distinct behaviors between hydrophilic and lipophilic NaDES. Several lipophilic NaDES demonstrated sensory behaviors closely resembling those of benchmark emollients. For instance, NaDES such as NP-C8C12 and NP-C8P (5:1) exhibited high spontaneous spreading and low stickiness, similar to reference oils like jojoba and apricot oil. In contrast, hydrophilic NaDES, particularly those structurally or functionally aligned with glycerin, showed higher stickiness and reduced spreading capacity, consistent with the behavior of glycerin itself. H-CAG stood out as a unique case, combining high stickiness with limited spreading, a profile that may be advantageous in applications requiring localized adhesion or film formation, such as makeup or hair styling products. These similarities with well-established formulation ingredients underscore the relevance of NaDES as versatile and sensorially compatible alternatives in cosmetic product design.

The observed differences in spreading, stickiness, and gloss behavior between lipophilic and hydrophilic NaDES suggest distinct modes of action that could be relevant for various cosmetic applications. Lipophilic NaDES, characterized by their high spreading ability and low stickiness, may contribute to improved film uniformity and more efficient delivery of ingredients at the skin surface. In contrast, the higher stickiness and lower spreading capacity of hydrophilic NaDES could support prolonged surface retention and potential hydrating effects. Additionally, lipophilic NaDES showed a more rapid reduction in gloss over time, whereas hydrophilic NaDES maintained a shinier appearance post-application, indicating differences in film behavior that may influence consumer perception and product positioning.

This study highlights the sensory versatility of NaDES, not as replacements for specific ingredients, but as complementary materials. Some NaDES, such as NP-C8C12 and NP-C8M, may serve as alternatives to ingredients like dimethicone, aligning with sustainability goals. The findings encourage further research into NaDES' integration into cosmetics, particularly in emulsions, to explore their stability and sensory enhancement potential.

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