Natural Deep Eutectic Solvents (NADES)

NADES are a new generation of green, non-flammable solvents that emerge as an efficient alternative to conventional hazardous solvents due to their toxicity and high environmental impact. NADES are obtained by combining two or more pure components, where one acts as a hydrogen bond acceptor (HBA) and the other as a hydrogen bond donor (HBD) (Villa et al., 2024). This results in a melting point significantly lower than that of the individual components (Hikmawanti et al., 2021).
NADES are considered “natural” because their components are primary metabolites found in nature, such as sugars, alcohols, organic acids, and amino acids. Their GRAS status (Generally Recognized As Safe) makes them suitable for food applications, which extends to their use in cosmetic products (Cannavacciuolo et al., 2022).

Applications of NADES in Cosmetics

They are used in cosmetic formulations with multiple advantages aligned with the principles of green chemistry, such as sustainability and safety, since they are natural in origin, biodegradable, and non-toxic (Villa et al., 2024).
Many of the individual components of NADES—such as organic acids, sugars, alcohols, and amino acids—are already widely used ingredients in cosmetics and pharmaceuticals, which further enhances the natural profile of formulations.
One of the main benefits of NADES is the possibility of directly incorporating the extract into all kinds of topical formulations (cosmetic and pharmaceutical) without drastically altering the product’s properties.
NADES have consistently demonstrated the ability to improve the performance and stability of plant extracts compared to conventional organic solvents (Hikmawanti et al., 2021). They also exhibit strong solubilizing power for lipophilic molecules, making them particularly valuable for poorly water-soluble bioactive compounds.

Examples of NADES Applications in Bioactive Compound Extraction

- Anti-aging applications: Aerial parts of Searsia tripartita were used to extract naringenin with antioxidant and enzyme-inhibiting activity (tyrosinase, collagenase, elastase, hyaluronidase), all linked to skin aging. This was achieved using a NADES combination of formic acid and choline chloride (Villa et al., 2024).

- Skin-brightening applications: Flowers of Ixora javanica were used to extract flavonoids and anthocyanins with antioxidant activity and skin-lightening potential. The extracts demonstrated superior anti-tyrosinase activity when prepared with a NADES mixture of choline chloride and propylene glycol (Villa et al., 2024).

- Antioxidant applications: Ginger was used to extract gingerols for their antioxidant properties. This was achieved using NADES combinations such as betaine–1,3-butanediol, L-carnitine–triethylene glycol, and L-carnitine–1,3-butanediol (Hikmawanti et al., 2021).

- Circular economy applications: Valuable cosmetic ingredients can be obtained from waste using NADES. For example, tomato pomace extracts showed enhanced antioxidant activity and antifungal effects against Candida albicans (Villa et al., 2024).

- Sustainable raw materials: Cork bark extracts prepared with NADES improved antioxidant activity and showed no cytotoxicity on keratinocytes when incorporated into commercial products (Villa et al., 2024).

Beyond extraction, NADES are also used in the development of active delivery systems.
For instance, NADES based on malonic acid and choline chloride have been studied for formulating tadalafil (TDF) and lidocaine (LCD) for burn treatment, showing wound-healing potential and antimicrobial activity (Villa et al., 2024).
NADES can also be transformed into eutectogels (by gelling with agents such as xanthan gum), which are highly biodegradable, thermally stable, and suitable for the controlled release of active ingredients (Villa et al., 2024).

Chlorogenic Acids

Chlorogenic acids (CGA) are a class of polyphenolic compounds found in many plants, most commonly in green (unroasted) coffee beans.
The CGA family includes several members such as 1L-(−)-quinic acid, caffeic acid (CA), and ferulic acid, among others (Nguyen et al., 2024).
CGAs are natural bioactive substances with multiple functions, including anti-inflammatory and antioxidant properties, which are fundamental in skin care. Their protective skin effects have been demonstrated against UV-induced photoaging, by promoting flap survival, improving skin barrier function, mitigating cutaneous pathologies, and suppressing melanogenesis (Nguyen et al., 2024).
They effectively scavenge free radicals and excessive reactive oxygen species (ROS) at the cellular level (Nguyen et al., 2024).
CGAs also promote the synthesis of collagen and elastin fibers in skin fibroblasts. Treatments with CGAs have been shown to enhance biosynthesis and secretion of collagen in human dermal fibroblasts (HDFs), especially type I collagen (Nguyen et al., 2024), and to attenuate the reduction of fibronectin after UVA exposure (Ruscinc et al., 2024). They also inhibit the activity of enzymes linked to skin aging, such as collagenase (MMP-1), elastase, and matrix metalloproteinases (MMP-3, MMP-9). Collagenase inhibition helps limit skin sagging and loss of elasticity (Saewan et al., 2023).

CGA efficiently absorbs UVB light (280–320 nm), with a peak around 325 nm. Pretreatment with CGA can prevent or mitigate DNA damage and apoptosis induced by UVB exposure (Cha et al., 2014).
Additionally, CGAs exhibit anti-inflammatory activity, helping mitigate pathological skin conditions associated with inflammation (Nguyen et al., 2024).

Specific Dermatological Applications

- Acne: CGAs show activity against acne vulgaris by alleviating *P. acnes*-induced skin lesions through suppression of NF-κB signaling (anti-inflammatory) and inhibition of lipogenesis.

- Skin brightening (anti-melanogenesis): CGAs have the potential to act as anti-hyperpigmentation agents by inhibiting tyrosinase activity (Nguyen et al., 2024).

- Barrier function: CGAs restore the epidermal skin barrier by upregulating key genes such as filaggrin and involucrin in epidermal keratinocytes (Ruscinc et al., 2024).

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