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Natural Deep Eutectic Solvents (NADES): Green Solvents for Pharmaceutical Applications and Beyond- A Review

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Abstract: *Natural deep eutectic solvents (NADES) are emerging as sustainable, biodegradable, and non-toxic alternatives to conventional organic solvents. Composed of natural components such as sugars, amino acids, and organic acids, they offer tunable physicochemical properties for diverse applications. In pharmaceuticals, NADES enhance drug solubility, stability, and bioavailability. Their green synthesis and compatibility with biological systems make them ideal for eco-friendly processes. This review highlights recent advancements, challenges, and future prospects of NADES in pharmaceutical and related fields.*

Keywords*:* NADES, Green chemistry, Applications, HBD, HAD

I. INTRODUCTION

The term "eutectic", derived from the Greek word meaning "easily melted", refers to a specific mixture of components that, in defined proportions, achieves the lowest possible melting point [1] In materials and solvent chemistry, eutectic systems represent equilibrium mixtures that liquefy at a characteristic eutectic temperature. This review emphasizes the significance of natural product research involving eutectic solvents, particularly focusing on their potential as green and sustainable alternatives within pharmaceutical sciences [1,2].

In recent years, Natural Deep Eutectic Solvents have gained substantial attention across diverse scientific disciplines, including chemistry, environmental science, physics, astronomy, energy research, biological sciences, and pharmaceutical technology[3]. Within the pharmaceutical sector, DES are being extensively investigated for drug formulation and delivery systems, particularly for topical, transdermal, ocular, and oral applications [3,4].

The increasing global demand for sustainable bioprocesses and renewable bioactive compounds has driven the shift toward green extraction methodologies [5]. Guided by the principles of Green Chemistry, current strategies emphasize minimizing solvent consumption, reducing hazardous waste generation, and adopting biodegradable, non-toxic solvent systems for efficient separation and purification of natural analytes [6,7].

Amid current environmental and health challenges, the pharmaceutical and cosmetic industries are undergoing transformation toward greener and safer production processes. Among the most promising innovations are Natural Deep Eutectic Solvents (NADES) a subclass of DES offering low toxicity, high tunability, and excellent biodegradability. Synthetic NADES replicate these natural behaviors and have been successfully applied in cosmetic, pharmaceutical, and food industries, including the extraction of phenolic compounds from plant materials [7].

NADES are typically composed of natural metabolites—sugars, amino acids, and organic acids—forming eutectic mixtures with low melting points[7]. These solvents are biodegradable, customizable, and highly effective for the extraction of flavonoids, alkaloids, and saponins, often yielding better selectivity and extraction efficiency than conventional solvents. Since 2014, NADES have evolved as a distinct group of DES, improving environmental compatibility and reducing toxicity risks.

Recent advances in green chemistry have demonstrated the effectiveness of NADES for valorizing agrifood and horticultural residues, underscoring their potential as eco-friendly, sustainable solvents for the future of pharmaceutical and natural product research
[7].

THEORY of NADES

Natural Deep Eutectic Solvents (NADES), introduced by Choi and Abbott (2011), are formed by combining natural metabolites such as choline chloride, sugars, amino acids, or organic acids. The theory behind NADES is based on strong hydrogen bond interactions between a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA), which disrupt the crystalline structure of individual components and drastically reduce the melting point, creating a stable liquid at room temperature. This phenomenon, supported by differential scanning calorimetry and FTIR spectroscopy, provides experimental proof of extensive H bond formation and molecular rearrangement. The thermodynamic relationship governing melting point depression can be simplified as:

$$\ln(x_A) = \frac{\Delta H_{fus,A}}{R}\left(\frac{1}{T_{fus,A}} - \frac{1}{T}\right)$$

These interactions explain the stability, polarity, and solvation capacity of NADES. Their biodegradability, Tunable properties, and biocompatibility make them superior green solvents for applications in extraction, catalysis, and pharmaceutical sciences (Abbott et al., 2004; Choi et al., 2011).

COMPOSITION OF NADES

Natural Deep Eutectic Solvents (NADES) are formed by combining two or more natural components—typically a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA)—in specific molar ratios, resulting in a eutectic mixture with a significantly lower melting point than the individual components. Common constituents include choline chloride, urea, sugars, amino acids, organic acids, and polyols, which are generally safe, biodegradable, and often GRAS-listed (Generally Recognized as Safe).[8]

Alongside these primary metabolites, recent research has uncovered more complex, biosynthetically advanced compounds referred to as specialised metabolites as potential components of NADES. Examples include flavonoids, monoterpenes, phenols, and alkaloids, all of which contribute additional functionality and broaden potential applications. The flexibility of NADES is further emphasized by the wide range of metabolite combinations reported in the literature, with the majority of these mixtures. [9,10]

Component Type	Chemical Nature	Common Examples
Hydrogen bond donor	Molecules with -OH, - COOH, - NH_2 groups	Glucose, Fructose Lactic Acid, Citric Acid, Glycerol, Sorbitol
Hydrogen Bond Acceptors (HBA)	Molecules With Lone Electron Pairs (Salts, Amino Acids)	Choline Chloride, Betaine, Amino Acids (Proline, Lysine), Urea
Salts and Organic Bases	Ionic Compounds and Organic Bases	Choline acetate, ammonium salts, imidazole derivatives

Table 1: Composition of NADES

CHARACTERISTICS of NADES[1,8,9,10]

Natural Deep Eutectic Solvents (NADES) are composed of natural, biodegradable components such as sugars, amino acids, organic acids, and choline derivatives [12]. Owing to their natural origin, NADES are biocompatible, exhibit low toxicity, and possess negligible volatility, reducing air contamination risks [1,13]. Their tunable physicochemical properties viscosity, polarity, and melting point can be adjusted by varying hydrogen bond donors (HBDs) and acceptors (HBAs). A strong hydrogen-bond network results in melting point depression, keeping them liquid at room temperature [1,14]. NADES demonstrate excellent solubilizing power, high thermal stability, recyclability, and wide applicability in pharmaceuticals, cosmetics, food, and biotechnology [1,15].

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Toxicity

NADES are generally considered low-toxic compared to conventional organic solvents and many ionic liquids. Toxicity depends on the choice of components — quaternary ammonium salts (e.g., choline chloride) and natural compounds (e.g., urea, sugars, organic acids) tend to exhibit low cytotoxicity. Some DES with synthetic or halide-based components may show higher toxicity, limiting their biological or pharmaceutical applications. NADES, composed exclusively of natural metabolites (sugars, amino acids, organic acids), typically demonstrate minimal toxicity, making them suitable for food,
pharmaceutical, and cosmetic applications. .[1,14,15]

Biodegradability

Many DES and NADES are readily biodegradable due to their natural and biodegradable constituents. Studies report high biodegradation rates in soil and aquatic environments, especially for NADES. Biodegradability makes them environmentally preferable alternatives to traditional solvents and many ionic
liquids that are persistent and toxic. .[1,14,15]

Sustainability

NADES are considered green solvents due to:
Simple, energy-efficient synthesis (solvent-free, mild heating). Use of renewable, non-toxic natural materials.
Low volatility and reduced environmental emissions. Potential for recycling and reuse.
Their application can reduce reliance on volatile organic compounds and hazardous chemicals, aligning with principles of green chemistry and sustainable development. Challenges remain in scaling up and ensuring complete lifecycle assessments for
commercial use. [1,14,15]

PROPERTIES of NADES

Deep eutectic solvents (DESs) can be customized for particular uses, much like ionic liquids (ILs), by selecting suitable combinations of quaternary ammonium salts and various hydrogen bond donors [16]. These solvents can be engineered to exhibit a range of physicochemical characteristics such as viscosity, pH, and freezing point—depending on the intended application. DESs are known for their low vapor pressure, broad liquid-phase temperature range, non-flammability, ease of synthesis and purification, and compatibility with biological systems COOLING
The cooling point of NADES is significantly lower than that of their individual components due to strong hydrogen bonding. This melting/freezing point depression arises from disrupted crystal lattice formation during cooling. [17;19]
NADES often remain liquid at sub-zero temperatures, showing glass transition rather than crystallization.
Cooling rate and component ratio affect whether the system vitrifies or crystallizes. Water content influences the cooling point, often raising it and potentially inducing crystallization. Understanding the cooling behaviour is key for storage, thermal stability, and cryoprotection applications. [17,18,20]

DENSITY

DESs typically have higher densities than water, with most falling within the range of 1.0 to 1.3 g/cm³. However, when metal salts are incorporated, their densities can increase to between 1.3 and 1.6 g/cm³.[21] The molar ratio between the organic salt and the hydrogen bond donor (HBD) also plays a significant role in determining the density of a DES. For example, in a ChCl–glycerol system, increasing the amount of ChCl leads to a decrease in density.[22] A predictive method has been developed to estimate DES density across various temperatures, achieving an accuracy within ±1.9%. This approach also takes into account the influence of the salt-to-HBD molar ratio.[23]

VISCOSITY

DESs typically have high viscosities due to strong hydrogen bonding between their components. Viscosity decreases with increasing temperature as molecular interactions weaken. The molar ratio of salt to HBD significantly affects viscosity; more HBD often increases it.[24] DESs containing glycerol, sugars, or amino acids tend to be more viscous. Adding water or co-solvents can lower viscosity by disrupting hydrogen bonds. Accurate models have been developed to predict viscosity based on temperature and composition.[25]

SURFACE TENSION

Surface tension reflects the strength of cohesive forces among liquid molecules at the interface and is highly influenced by the liquid's composition, temperature, and pressure. Measurements of surface tension at 298.15 K and 101.3 kPa were conducted for three choline chloride-based DESs using levulinic acid, phenol, and ethylene glycol as hydrogen bond donors (HBDs). It was found that the DES containing ethylene glycol exhibited a lower surface tension (45.66 mN/m) compared to pure ethylene glycol (48.90 mN/m), with similar trends observed for the other DESs.[26] Choline chloride acts like a surfactant, reducing cohesive forces at the surface of the DES. In choline chloride–glycerol DESs, surface tension shows a linear decrease with rising temperature. Additionally, increasing choline chloride concentration lowers the surface tension by disrupting the strong hydrogen bonding network of glycerol.[22]

pH

pH is a crucial factor in designing DESs, as these solvents are mixtures of Lewis or Brønsted acids and bases. The pH depends on the relative acidity of the cationic and anionic components within the DES. For example, DESs made from choline chloride and D-glucose at various molar ratios generally exhibit neutral pH values around 7 at room temperature. The pH of a 1:1 choline chloride–D-glucose DES remains stable between 25°C and 45°C but drops to between 6.0 and 6.6 when the temperature reaches 50°C.[27] Studies on seventeen different DESs show that pH tends to decrease as temperature increases. Furthermore, the pH varies considerably depending on the type of hydrogen bond donor (HBD) used in the DES formulation.[28]

HYDROPHILICITY/HYDROPHOBICITY

Deep eutectic solvents (DESs) are typically composed of ionic compounds and are therefore hydrophilic. However, hydrophobic DESs, which do not mix with water, are essential for applications like selective solvent extraction.[29] The first hydrophobic DESs were created using quaternary ammonium salts and decanoic acid, effectively extracting volatile fatty acids from water. Additionally, DESs made from lidocaine and decanoic acid have been used to remove alkali and transition metal ions from aqueous solutions.[30] Hydrophobic DESs derived from natural sources such as DL- menthol combined with organic acids like pyruvic, lactic, acetic, and lauric acid have also been developed. Their structures and purities were confirmed using NMR and FTIR spectroscopy. These DESs have been successfully used to extract biomolecules including tryptophan, isophthalic acid, vanillin, and caffeine from water, leveraging their hydrophobic nature.[31]

PREPARATION of NADES:

Deep eutectic solvents (DESs) were synthesized using a simple, solvent-free method involving the combination of a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD) in appropriate molar ratios. Typically, choline chloride was used as the HBA, while urea, glycerol, or ethylene glycol served as the HBD, depending on the target DES system.

The components were accurately weighed according to the desired molar ratio (commonly 1:1, 1:2, or 1:3) and transferred to a clean, dry glass beaker. The mixture was then gently heated on a magnetic stirrer hotplate at a temperature between 60 °C and 100 °C while continuously stirring. Heating was continued until a clear, homogeneous liquid was formed, indicating the successful formation of the DES through extensive hydrogen bonding interactions between the components.

After synthesis, the mixture was allowed to cool to room temperature. The resulting DES was stored in an airtight container to avoid moisture absorption, especially for hygroscopic formulations. Where low water content was required, the DES was further dried under vacuum or in a desiccator. No chemical reaction or external solvent was involved in this process, making it a green, efficient, and sustainable method. The prepared DES was further subjected to characterization and application-specific testing as required. [1,32]

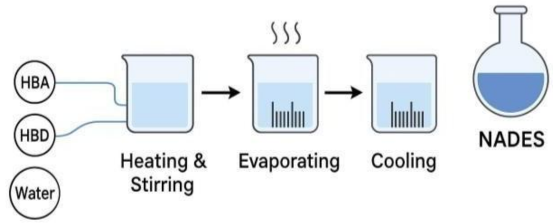

Fig. No.1 PREPARATION of NADES[32]

APPLICATION of NADES

Pharmaceuticals and Medical Research

Natural Deep Eutectic Solvents (NADES) enhance the solubility of poorly water-soluble drugs, providing a green and biocompatible platform for pharmaceutical applications [33]. Composed of natural metabolites like choline chloride with urea or organic acids, NADES improve solubility for APIs including NSAIDs such as aspirin, ibuprofen, ketoprofen, and naproxen. Solubility depends on component molar ratios and water content, allowing Tunable drug delivery. For example, acetaminophen solubility increases nearly fortyfold in NADES with malonic acid at elevated temperatures [34]. This improvement arises from favorable enthalpic interactions within the solvent. NADES serve as co- solvents, stabilizing drugs and offering sustainable, efficient alternatives for formulations and therapeutic applications [35].

Separation Processes and Gas Capture

NADES serve as environmentally friendly solvents for separation and gas capture due to biodegradability, low toxicity, and tunable solvation properties [36]. In separations, NADES based on natural metabolites such as choline chloride with sugars, acids, or polyols efficiently extract bioactive compounds, metal ions, and volatile molecules [37]. Hydrophobic NADES, combining fatty acids with natural HBDs, improve extraction of non-polar analytes [38]. For gas capture, NADES act as non-volatile, thermally stable solvents for CO_2 absorption through reversible hydrogen bonding [39]. CO_2 uptake depends on NADES composition, molar ratio, temperature, and pressure. Choline chloride based NADES show enhanced CO_2 capture at elevated pressures, offering sustainable carbon capture strategies
[40.41].

Biocatalysis and Organic Chemistry

NADES provide enzyme-compatible, tunable solvents for biocatalysis and organic synthesis [42]. Unlike conventional polar solvents, NADES preserve enzyme structure, enabling efficient catalysis in transesterification, esterification, and epoxide hydrolysis. Choline chloride-based NADES with urea or glycerol maintain high enzyme stability, achieving up to 90% yield in lipase-catalyzed reactions. NADES also improve regioselectivity in hydrolase-catalyzed processes [43]. Additionally, they act as solvents and reactants in multicomponent reactions, producing DHPMs and quinazoline derivatives with high efficiency. NADES enable rapid, selective reductions of carbonyl compounds using $NaBH_4$ while remaining biodegradable and non- volatile, providing a sustainable platform for green organic transformations [43,44].

Synthesis of Metal Nanoparticles

NADES act as eco-friendly, surfactant-free media for controlled synthesis of metal nanoparticles with tunable shapes and enhanced properties [45]. Gold nanoparticles with star-shaped morphologies and platinum nanocrystals with high catalytic activity have been synthesized using choline chloride–urea NADES. These solvents facilitate uniform nanoparticle growth and prevent aggregation. NADES also stabilize nanomaterials like carbon nanotubes and silver composites, enhancing dispersion and functional performance [46]. Their biodegradable, non-volatile nature makes NADES ideal for sustainable nanotechnology, catalysis, and material science applications. By avoiding toxic organic

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solvents or surfactants, NADES offer environmentally safe, reproducible approaches for nanoparticle preparation with precise size and morphology control.[46,47]

Biological Applications

NADES have extensive applications in biology and biomedicine due to biocompatibility, low toxicity, and unique physicochemical properties [48]. They stabilize proteins, inhibit amyloid fibril formation, enhance drug delivery, and improve enzyme activity. Choline-based NADES enhance skin penetration of agents like hyaluronic acid, increasing bioavailability without toxicity. NADES mixtures such as choline–leucovorin enable oral insulin delivery through micelles or microemulsions, improving intestinal absorption. They also boost enzyme-catalyzed reactions, enhancing enantioselectivity and catalytic efficiency in lipase-mediated processes [49] These features make NADES versatile green solvents for pharmaceuticals, biocatalysis, protein chemistry, and broader biomedical applications, combining safety with high performance.[50]

Metallurgy and Electrodeposition:

NADES provide green alternatives in metallurgy and electrodeposition due to low toxicity, biodegradability, and high metal ion solubility [51]. They support metal extraction, plating, and electropolishing with tunable hydrogen bonding networks that stabilize metal ions, enhancing deposition efficiency. NADES improve surface finish and reduce harmful byproducts compared to conventional electrolytes [52]. Choline chloride-based NADES facilitate electroplating of metals like copper and nickel while maintaining thermal and chemical stability. Their non volatile, recyclable nature allows safer industrial operations, aligning with sustainable development goals [53]. These solvents thus offer efficient, environmentally friendly routes for metal recovery, electrodeposition, and surface treatment applications. Extraction Media NADES are highly effective in metal extraction due to their ability to dissolve metal ions and form stable complexes [54,55]. They selectively recover valuable metals such as copper, nickel, zinc, and precious metals from ores, industrial waste, and electronic scrap. For example, choline chloride–ethylene glycol–urea NADES efficiently extract lead and zinc from electric arc furnace dust while leaving iron and aluminum oxides behind. This selective extraction reduces impurities and improves recovery efficiency. NADES and RTILs provide sustainable, low-toxicity alternatives to volatile organic solvents in metallurgical and recycling processes, contributing to greener, environmentally responsible metal recovery technologies[56].

EXTRACTION OF NATURAL PRODUCTS

Natural deep eutectic solvents (NADES) have emerged as innovative, eco-friendly media for the extraction of bioactive compounds from various natural sources. Composed of naturally derived components such as sugars, amino acids, and organic acids, NADES are biodegradable, non-toxic, and sustainable solvents that effectively dissolve a wide range of phytochemicals. Their tunable polarity and strong hydrogen bonding network enhance the solubility and stability of target compounds, leading to improved extraction efficiency compared to conventional organic solvents. NADES also offer the advantage of low volatility, which reduces solvent loss and exposure risks during the extraction process, making it safer and more cost effective.[57] Recent studies have demonstrated successful extraction of compounds like curcumin, resveratrol, and caffeine using NADES, highlighting their versatility across different plant matrices. Furthermore, NADES can be easily prepared from inexpensive and renewable natural components, supporting green chemistry principles. Although challenges remain in the recovery and recyclability of NADES post-extraction, ongoing research aims to address these issues to enable broader industrial application. Overall, NADES present a promising sustainable alternative for natural product extraction, aligning with the growing demand for environmentally responsible and efficient extraction technologies.[58]

CHALLENGES AND LIMITATION OF NADES

One major limitation of Natural Deep Eutectic Solvents (NADES) is their high viscosity, resulting from extensive hydrogen bonding and van der Waals interactions [59]. This viscosity reduces metabolite diffusion, increasing extraction times and sometimes decreasing solubility of target compounds. In organic synthesis, it hinders mass and energy transfer, lowering reaction yields. To address this, adding water or glycerol and gentle heating can weaken intermolecular forces while preserving the solvent's supramolecular structure [60]. Approximately 25% water content often optimizes extraction efficiency, as demonstrated in carthamin extraction from Carthamus tinctorius L.. For less polar compounds, apolar NADES with lower viscosity are preferred.

Physical methods such as ultrasonic waves, microwave irradiation, or bead beating improve dispersion and enhance mass transfer in viscous NADES. Studies show these techniques increase yields of proteins, lipids, and carbohydrates from biomass while reducing extraction time [61]. Scaling up NADES-based processes remains challenging due to handling difficulties in large reactors, affecting mixing, pumping, and mass transfer. Companies like Gattefossé have developed patented extraction processes using sugar, polyol, and water mixtures, e.g., a fructose/glycerol/water (1:1:5) blend, to reduce viscosity and enable efficient plant extractions from Aesculus hippocastanum and Withania somnifera [62].

Other NADES formulations, such as betaine combined with glycol, polyols, or sugars, improve solubility and handling for stilbenoids [63]. Limitations include restricted availability and specific physicochemical properties of components, affecting scalability. Product isolation is complicated by low volatility; unlike organic solvents, NADES often require precipitation with water or direct formulation [64]. Ensuring non-toxicity in formulations is essential [65]. While NADES can act as cosolvents, stabilizers, or analytical additives, their high viscosity and complex interactions require careful optimization. Small amounts improve chromatography resolution, but concentration and compatibility must be fine-tuned for practical applications [66].

FUTURE PERSPECTIVES

The promising results from the use of Natural Deep Eutectic Solvents (NADES) in the formulation of Terbinafine Hydrochloride highlight their significant potential in advancing green pharmaceutical technologies. However, the current application remains largely at the exploratory or laboratory scale, and several opportunities exist for future development and optimization.

In Vivo and Clinical Evaluation:

While in vitro studies may confirm enhanced solubility, stability, and antifungal activity, the next critical step is to validate these results through in vivo pharmacokinetic and pharmacodynamic studies. Investigating skin permeation profiles, systemic absorption (if relevant), and therapeutic efficacy in appropriate animal models or clinical settings would be essential to establish NADES-based Terbinafine formulations as viable alternatives to conventional products.

Long-Term Stability and Shelf-Life Studies:

Although NADES are known to improve drug stability by providing a hydrogen-bond-rich microenvironment, their long- term effects on the chemical integrity of Terbinafine Hydrochloride under various storage conditions (temperature, humidity, light) require thorough investigation. Establishing robust stability data will be necessary to meet regulatory standards.

Mechanistic Understanding of Drug–NADES Interactions:

A deeper molecular-level understanding of how NADES interact with Terbinafine—particularly through techniques like FTIR, NMR, molecular dynamics simulations, and DSC—could guide the rational design of eutectic systems tailored for specific drug molecules. This would allow better prediction of solubility, release, and stability profiles.

Development of Multi-Component Delivery Systems: Future research could explore integrating NADES into advanced drug delivery platforms such as nano-emulsions, microneedles, hydrogels, or transdermal patches to further enhance delivery efficiency. NADES may serve as both solvent and functional excipient in such hybrid systems.

Toxicological and Regulatory Assessment:

Although NADES are typically composed of GRAS (Generally Recognized As Safe) substances, the toxicological behavior of the eutectic mixture itself may differ from its individual components. Systematic toxicology and skin irritation/sensitization studies are essential for regulatory approval, especially for topical pharmaceutical applications

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Personalized Medicine and Customizable Formulations:
NADES allow for high flexibility in component selection, offering the potential for patient-specific or disease-targeted formulations. Future work could focus on customizing NADES compositions based on individual patient needs, disease severity, or delivery site.

Scale-Up and Industrial Feasibility:
Translating lab-scale NADES formulations to commercial-scale production will require studies on scalability, batch-to-batch reproducibility, cost analysis, and compatibility with existing pharmaceutical manufacturing infrastructure. Identifying efficient methods for NADES recovery or recycling may also enhance sustainability and economic viability.
Exploration of Other Antifungal Agents:
Beyond Terbinafine, similar strategies could be applied to other poorly soluble antifungal agents such as Itraconazole, Griseofulvin, or Ketoconazole. This may lead to a broader platform of NADES-based antifungal formulations with superior performance

DISCUSSION
Natural Deep Eutectic Solvents (NADES) are emerging as sustainable, versatile, and multifunctional green solvents with substantial potential in pharmaceutical sciences. Their biodegradability, low toxicity, and ease of preparation from natural components make them environmentally friendly and industrially attractive. NADES act not only as solvents but also as catalysts and reagents, enabling greener synthesis processes with enhanced efficiency and reusability. In extraction and formulation, they improve solubility, stability, and bioavailability of a wide range of active pharmaceutical ingredients, including poorly soluble drugs, proteins, and nucleic acids. The development of Therapeutic Deep Eutectic Systems (THEDES) represents an innovative approach by integrating APIs directly into the solvent matrix. Moreover, NADES contribute to nanotechnology and biotechnology applications through nanoparticle stabilization and enzyme activity enhancement. Despite these advantages, challenges such as high viscosity, limited toxicological data, and underdeveloped regulatory pathways remain. Addressing these limitations through further research and large-scale production optimization will be essential for fully realizing their commercial and sustainable potential. Overall, NADES offer a green, efficient platform that bridges environmental benefits with enhanced pharmaceutical functionality.

II. CONCLUSION

Natural Deep Eutectic Solvents (NADES) represent a promising class of green solvents with significant potential in pharmaceutical and biotechnological applications. Their biodegradability, low toxicity, tunable properties, and multifunctionality make them ideal alternatives to conventional organic solvents. NADES enhance solubility, stability, and bioavailability of drugs, enable efficient extraction processes, and support nanotechnology and enzyme-catalyzed reactions. The development of Therapeutic Deep Eutectic Systems further demonstrates their innovative role in drug delivery. Despite challenges such as high viscosity and limited regulatory guidance, ongoing research into safety, scalability, and formulation optimization will enable NADES to become integral to sustainable and efficient pharmaceutical development.
Natural Deep Eutectic Solvents (NADES) represent a versatile and sustainable class of green solvents with significant potential in pharmaceutical sciences. Their ease of preparation, biodegradability, low toxicity, and tunable polarity make them excellent alternatives to conventional organic solvents. NADES serve multiple roles, acting as solvents, catalysts, and reagents in synthesis, often reusable across cycles. They enhance extraction efficiency for both polar and non-polar compounds and can be employed directly or as pre-treatment solvents.
In pharmaceutical formulations, NADES improve the solubility, stability, and bioavailability of a wide range of active pharmaceutical ingredients, including small molecules, proteins, and nucleic acids. Some NADES components function as active pharmaceutical ingredients themselves, forming therapeutic deep eutectic systems (THEDES). Additionally, NADES contribute to nanotechnology by stabilizing nanoparticles and controlling particle formation.

Their unique properties also support biotechnological applications, such as enzyme stabilization and substrate solubilization. Overall, NADES embody a green chemistry approach that combines environmental benefits with enhanced pharmaceutical functionality. To fully realize their commercial potential, further research into their toxicology, regulatory acceptance, and large-scale production is essential. With these advancements, NADES are poised to become integral tools in sustainable pharmaceutical development.

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