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Review Paper

Deep Eutectic Solvents: Emerging Green Solvents for Biomedical Innovations

Dr. Vishal Pande, Dr. Shoheb Shaikh*, Ashish Alte, Sanjay Tawale

RSM's NN Sattha College of Pharmacy, Ahilyanagar, INDIA.

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ABSTRACT

Deep eutectic solvents (DESs) have emerged as a transformative class of green solvents with immense potential in biomedical sciences due to their tunable physicochemical properties, low toxicity, environmental compatibility, and cost-effective synthesis. Formed by mixing hydrogen bond donors and acceptors, DESs exhibit unique solvating abilities that allow them to dissolve a broad range of bioactive compounds, macromolecules, and biomaterials. In biomedical innovation, DESs have demonstrated promising applications in drug delivery, extraction of phytopharmaceuticals, therapeutic formulations, cryopreservation, enzyme stabilization, and regenerative medicine. Their structural adaptability enables improved solubility and bioavailability of poorly water-soluble drugs, fostering next-generation formulation design. Natural deep eutectic solvents (NADES), derived from biological metabolites, further enhance the biocompatibility and sustainability profile by mimicking intracellular environments and facilitating safe interactions with living tissues. Recent advances highlight the role of DESs in enhancing transdermal and oral drug delivery, modulating membrane permeability, and enabling green synthesis of nanoparticles for therapeutic and diagnostic uses. Additionally, DESs offer novel opportunities in tissue engineering as non-toxic media for cell preservation, scaffold fabrication, and biomolecule stabilization. Despite their promising attributes, challenges remain regarding long-term toxicity, biodegradability, regulatory acceptance, and standardization of physicochemical characterization. Addressing these gaps through systematic studies and interdisciplinary collaboration will accelerate the adoption of DESs in clinical and pharmaceutical settings. This chapter provides an in-depth exploration of DES fundamentals, biomedical applications, safety considerations, and future perspectives, highlighting their pivotal role in supporting green, sustainable, and innovative healthcare technologies.

*Corresponding Author: Dr. Shoheb Shaikh

Address: Associate Professor, RSM's NN Sattha College of Pharmacy, Ahilyanagar. INDIA.

Email ✉: shaikhshoheb91@gmail.com

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INTRODUCTION

1. Deep eutectic solvents (DESs) have emerged as a novel class of green solvents with significant potential in pharmaceutical and biomedical sciences. They are formed by mixing a hydrogen bond donor and a hydrogen bond acceptor, resulting in a eutectic mixture with a melting point significantly lower than that of the individual components. Since their introduction, DESs have garnered attention due to their structural versatility, ease of preparation, biodegradability, and tunable properties, making them promising alternatives to conventional organic solvents [1]. The evolution of DESs has expanded into various subclasses, including natural deep eutectic solvents (NADES), which are derived from naturally occurring metabolites and provide enhanced biocompatibility for biomedical applications [2].

1.1 Definition and evolution of deep eutectic solvents

DESs were first defined as eutectic mixtures formed by appropriate molar ratios of two or more components that interact predominantly through hydrogen bonding. Their development was initially focused on replacing ionic liquids due to lower toxicity, lower synthesis cost, and simpler preparation methods that require no purification [1]. Over time, DESs have evolved into multiple types tailored for specific physicochemical and biological applications [2].

1.2 Classification and physicochemical characteristics

DESs are classified into categories such as Type I–IV based on their component interactions. Their key physicochemical properties include low volatility, high viscosity, adjustable polarity, and excellent solvating capacity. These properties can be modulated by altering component ratios, water

content, or functional group chemistry, enabling customized biomedical applications [3].

1.3 Comparison with ionic liquids and conventional solvents

Compared with ionic liquids, DESs offer advantages such as lower cytotoxicity, easier biodegradability, cost-effectiveness, and simpler synthesis. In contrast to conventional organic solvents, DESs provide higher solvation efficiency for biomolecules while reducing environmental hazards due to minimal volatility and enhanced safety profiles [4].

1.4 Relevance to green chemistry and biomedical sustainability

DESs align strongly with green chemistry principles because they are derived from inexpensive, renewable, and often biodegradable components. Their low toxicity and high biocompatibility make them suitable for biomedical innovations, contributing to the development of sustainable drug delivery systems, biocatalysis platforms, and bioactive molecule extraction processes [5].

2. Types of DESs and Their Properties

Deep eutectic solvents (DESs) comprise a diverse class of eutectic mixtures whose properties can be optimized for specific biomedical applications. Their versatility arises from the wide variety of hydrogen bond donors (HBDs) and hydrogen bond acceptors (HBAs) that can be combined to create solvents with tunable polarity, viscosity, solvation capacity, and biocompatibility. Understanding the different types of DESs is essential for selecting appropriate systems for drug delivery, extraction of biomolecules, and other biomedical innovations [6].



2.1 Classical DESs

Classical DESs, also known as Type I–III DESs, are typically formed using quaternary ammonium salts such as choline chloride combined with urea, glycerol, or organic acids. These solvents exhibit high thermal stability, strong hydrogen-bonding networks, low volatility, and excellent solvating power. Their ease of synthesis and cost-effectiveness make them widely explored for pharmaceutical extractions, enzyme stabilization, and controlled drug formulation [6].

2.2 Natural deep eutectic solvents (NADES)

NADES are derived from naturally occurring metabolites such as sugars, amino acids, organic acids, and choline derivatives. They mimic intracellular environments and offer enhanced biocompatibility, making them particularly suitable for biomedical applications. NADES improve solubility of poorly water-soluble compounds, stabilize proteins and nucleic acids, and serve as green extraction media for phytochemicals. Their low toxicity and biodegradability further support their use in sustainable healthcare technologies [7].

2.3 Hydrophobic DESs

Hydrophobic DESs incorporate nonpolar components such as decanoic acid, thymol, and menthol, allowing them to dissolve hydrophobic drugs, lipids, and nonpolar biomolecules. Their water immiscibility makes them valuable in biphasic separation systems and in the formulation of lipid-based drug delivery systems. These DESs also show potential in nanoparticle synthesis and antimicrobial formulations due to their unique solvation behavior [8].

2.4 Tailoring physicochemical properties for biomedical use

The physicochemical properties of DESs—such as polarity, viscosity, pH, and water content—can be tuned by adjusting component ratios or selecting functionalized HBDs and HBAs. This tunability enables the design of DESs optimized for specific biomedical tasks including transdermal permeation enhancement, enzyme compatibility, and improved drug solubilization. Tailored DESs offer new opportunities in controlled release systems, biocatalysis, regenerative medicine, and bio preservation [9].

3. Biocompatibility and Toxicological Considerations

Biocompatibility and toxicological evaluation of deep eutectic solvents (DESs) are essential for their safe integration into biomedical and pharmaceutical applications. While DESs are widely regarded as green and low-toxicity solvents, their biological effects vary depending on components, molar ratios, and impurities. Comprehensive assessment through in-vitro and in-vivo studies, biodegradability analysis, and regulatory scrutiny ensures their suitability for clinical and therapeutic use [10].

3.1 In-vitro and in-vivo toxicity studies

In-vitro toxicity studies commonly evaluate cytotoxicity, genotoxicity, and oxidative stress responses in mammalian cell lines. These studies reveal that many choline chloride-based DESs and NADES exhibit low cytotoxicity at moderate concentrations, while some DESs containing organic acids or phenolic components may induce membrane disruption or metabolic stress. In-vivo studies further assess systemic toxicity, organ distribution, hematological effects, and potential inflammatory responses. Overall, toxicity profiles depend strongly on DES composition, emphasizing the need for standardized evaluation methods [10].



3.2 Biodegradability and environmental impact

The biodegradability of DESs differs with structural composition, with NADES demonstrating high environmental compatibility due to their natural metabolic origins. Biodegradation testing indicates that many DESs rapidly decompose into environmentally benign metabolites. However, hydrophobic DESs or those containing certain quaternary ammonium compounds may persist longer and require careful ecological assessment. Understanding environmental fate is crucial for preventing bioaccumulation and ecosystem toxicity [11].

3.3 Mechanisms of cellular interactions

DESs interact with biomembranes, proteins, and nucleic acids through hydrogen bonding, hydrophobic interactions, and modulation of membrane fluidity. These interactions can enhance drug permeability and stabilize biomolecules but may also lead to cytotoxicity at high concentrations. Mechanistic studies highlight the role of DES polarity, viscosity, and water content in determining cellular uptake and biological responses [12].

3.4 Regulatory challenges and safety assessment

Despite their promise, DESs face regulatory challenges due to limited long-term toxicity data and lack of established pharmacopoeial standards. Safety assessment requires harmonized toxicity testing, risk assessment protocols, and compliance with guidelines for pharmaceutical excipients and novel solvents. Clear regulatory frameworks are essential for translating DES-based systems into clinical and industrial applications [13].

4. DESs in Pharmaceutical and Drug Delivery Applications

Deep eutectic solvents (DESs) have emerged as versatile platforms for pharmaceutical development due to their exceptional solvation capacity, biocompatibility, and tunable physicochemical properties. Their ability to enhance drug solubility, improve permeation, and stabilize active pharmaceutical ingredients makes them promising candidates for next-generation drug delivery systems. DESs—including both classical DESs and natural deep eutectic solvents (NADES)—offer opportunities for formulating poorly soluble drugs, enabling novel administration routes, and supporting controlled or targeted therapeutic delivery [14].

4.1 Solubilization of poorly soluble drugs

DESs exhibit strong hydrogen-bonding networks and adjustable polarity, enabling significant enhancement in the solubility of hydrophobic and poorly water-soluble drugs. NADES, in particular, show improved compatibility with natural compounds such as flavonoids, alkaloids, and terpenoids. Enhanced solubility achieved through DESs improves drug bioavailability and supports the formulation of stable, concentrated liquid systems suitable for therapeutic use [14].

4.2 Transdermal and oral delivery enhancement

Certain DESs can modulate the integrity and fluidity of biological membranes, facilitating enhanced transdermal and oral drug transport. DESs such as choline chloride-based mixtures and menthol-based hydrophobic systems improve permeation by interacting with stratum corneum lipids or mucosal surfaces. These properties make DESs valuable as permeation enhancers for transdermal patches, topical formulations, and oral drug delivery, particularly for drugs with poor intestinal absorption [15].



4.3 DES-based drug formulations

DESs can act as co-solvents, carriers, or excipients in pharmaceutical formulations. Their ability to stabilize labile molecules—such as proteins, peptides, and antioxidants—supports the development of novel liquid or semi-solid dosage forms. Additionally, DESs enable the creation of solvent-free formulations, reducing the need for harmful organic solvents and supporting greener pharmaceutical manufacturing processes [16].

4.4 Controlled release and targeted delivery strategies

DESs can be incorporated into polymeric matrices, hydrogels, nanoparticles, and lipid-based carriers to achieve controlled or targeted drug delivery. Their component-dependent viscosity, polarity, and biodegradability offer fine control over drug release dynamics. DES-mediated nanoparticle synthesis further supports targeted delivery applications in cancer therapy, antimicrobial treatment, and precision medicine, providing new avenues for achieving enhanced therapeutic efficacy with minimal side effects [17].

5. DESs in Biomolecule Extraction and Stabilization

Deep eutectic solvents (DESs) have emerged as highly effective and environmentally friendly media for the extraction and stabilization of biomolecules. Their tunable polarity, strong hydrogen-bonding capabilities, and low toxicity enable efficient solubilization of phytochemicals, proteins, enzymes, and nucleic acids, while minimizing denaturation or degradation. These properties make DESs attractive for pharmaceutical, nutraceutical, and biotechnological applications, providing sustainable alternatives to conventional organic solvents [18].

5.1 Extraction of phytochemicals and natural products

DESs, particularly natural deep eutectic solvents (NADES), are widely used to extract bioactive compounds such as flavonoids, alkaloids, phenolics, and terpenoids from plant materials. Their ability to disrupt plant cell walls and solubilize a broad spectrum of polar and nonpolar metabolites enhances extraction efficiency and yield. Additionally, DES-mediated extraction is compatible with green chemistry principles, reducing the need for volatile organic solvents and energy-intensive processing [18].

5.2 Protein and enzyme stabilization

DESs provide a stabilizing environment for proteins and enzymes by preserving their native conformation through hydrogen bonding and osmotic balance. Proteins stored in NADES or choline chloride-based DESs exhibit enhanced thermal stability, resistance to denaturation, and prolonged shelf life. These features support their use in biocatalysis, enzyme-based sensors, and therapeutic protein formulations [19].

5.3 Nucleic acid solubilization and preservation

DESs facilitate the solubilization and long-term preservation of nucleic acids such as DNA and RNA. Their mild, non-denaturing environment prevents strand breakage and degradation, allowing safe handling, storage, and transport of genetic materials. DESs can also enhance nucleic acid extraction from biological samples, providing an effective and sustainable alternative to conventional chaotropic salts and organic solvents [20].

6. Biomedical and Clinical Innovations

Deep eutectic solvents (DESs) are increasingly recognized for their transformative potential in



biomedical and clinical applications. Their tunable physicochemical properties, biocompatibility, and ability to stabilize biomolecules enable innovations in cryopreservation, tissue engineering, nanoparticle synthesis, and therapeutic interventions. These capabilities position DESs as versatile tools in next-generation healthcare and translational medicine [21].

6.1 DESs in cryopreservation and regenerative medicine

DESs provide a non-toxic and protective medium for cryopreservation of cells, tissues, and biological samples. Their high viscosity and hydrogen-bonding networks reduce ice crystal formation and preserve cellular integrity during freezing and thawing. In regenerative medicine, DESs can be used as carriers for growth factors, cytokines, and other bioactive molecules, supporting cell proliferation, differentiation, and tissue regeneration [21].

6.2 Applications in tissue engineering and scaffolds

DESs facilitate the fabrication and functionalization of biocompatible scaffolds for tissue engineering. They can dissolve or modify biomaterials such as polysaccharides, collagen, and synthetic polymers, enabling the production of hydrogels, films, and 3D-printed constructs with enhanced mechanical strength and biological activity. By maintaining bioactivity of embedded proteins and cells, DESs contribute to improved scaffold performance and regenerative outcomes [22].

6.3 DES-mediated nanoparticle synthesis for theranostics

DESs serve as green solvents and stabilizers for the synthesis of nanoparticles, including metallic, polymeric, and lipid-based systems. These

nanoparticles can be functionalized for targeted drug delivery, imaging, and combined therapeutic-diagnostic (theranostic) applications. DES-mediated nanoparticle synthesis offers advantages such as reduced toxic by-products, tunable size and morphology, and improved stability, enhancing efficacy in clinical applications [23].

6.4 Antimicrobial and therapeutic potential

Certain DESs exhibit intrinsic antimicrobial properties against bacteria, fungi, and viruses, which can be leveraged for topical treatments, wound healing, and infection control. Additionally, DESs improve the solubility and bioavailability of therapeutic agents, facilitating formulation of antimicrobial, anticancer, and anti-inflammatory drugs. Their combined solvent and bioactive properties provide multifunctional platforms for innovative therapeutic strategies [24].

7. Future Directions and Emerging Trends

Deep eutectic solvents (DESs) are poised to play a central role in the future of personalized and precision medicine due to their tunable properties, biocompatibility, and versatility in drug delivery and biomolecule stabilization. Ongoing research focuses on integrating DESs with advanced technologies such as nanotechnology, biotechnology, and computational modeling to create more effective, sustainable, and patient-specific biomedical solutions. These emerging trends highlight the potential of DESs to transform clinical practice and pharmaceutical manufacturing [25].

7.1 DESs in personalized and precision medicine

The customizable nature of DESs allows for formulation of patient-specific drug delivery systems, including individualized solubilization,



controlled release, and targeted therapy. DESs can be designed to enhance the bioavailability of drugs based on a patient's genetic, metabolic, or disease profile, enabling more precise therapeutic interventions and reducing adverse effects [25].

7.2 Integration with nanotechnology and biotechnology

DESs can serve as green solvents and stabilizers in the synthesis of nanoparticles, liposomes, and polymeric carriers, enhancing targeted delivery, imaging, and theranostic applications. Their compatibility with biotechnological processes, including enzyme stabilization and biomolecule extraction, further supports the development of hybrid systems that combine molecular precision with nanoscale engineering for improved therapeutic efficacy [26].

7.3 Computational modeling and molecular design

Advances in computational chemistry, molecular dynamics, and machine learning facilitate the rational design of DESs with tailored physicochemical and biological properties. Modeling approaches allow prediction of solubility, viscosity, toxicity, and molecular interactions, accelerating the discovery and optimization of DESs for biomedical applications while reducing experimental costs and time [27].

7.4 Opportunities for industrial and clinical translation

The scalability, sustainability, and tunability of DESs provide opportunities for industrial production of pharmaceuticals, nutraceuticals, and medical devices. Successful clinical translation will require standardized safety testing, regulatory compliance, and integration into manufacturing workflows, paving the way for DES-based

solutions to become mainstream tools in healthcare innovation [28].

CONCLUSION

Deep eutectic solvents (DESs) represent a versatile and sustainable class of solvents with transformative potential in biomedical and pharmaceutical applications. Their tunable physicochemical properties, biocompatibility, and ability to stabilize and solubilize a wide range of biomolecules position them as promising alternatives to conventional organic solvents and ionic liquids. DESs have demonstrated remarkable utility in drug delivery, biomolecule extraction, enzyme and protein stabilization, cryopreservation, tissue engineering, and nanoparticle synthesis, supporting innovative therapeutic and diagnostic strategies. Natural deep eutectic solvents (NADES), in particular, offer enhanced safety and environmental compatibility, aligning with green chemistry principles.

Despite their promise, several challenges remain, including comprehensive toxicity assessment, long-term biocompatibility, standardization of physicochemical characterization, regulatory acceptance, and scalability for industrial and clinical applications. Addressing these challenges through interdisciplinary research, computational modeling, and integrated biotechnological approaches will be critical for translating DES-based innovations into practical healthcare solutions.

Future directions suggest that DESs will play an integral role in personalized and precision medicine, hybrid nanotechnology–DES platforms, and sustainable biomedical manufacturing. By combining molecular design, green chemistry, and advanced delivery strategies, DESs offer opportunities to enhance therapeutic efficacy, reduce environmental impact, and support the development of next-generation biomedical innovations. Ultimately, DESs exemplify how



sustainable solvent systems can bridge the gap between green chemistry and cutting-edge biomedical applications, establishing a foundation for safe, efficient, and environmentally responsible healthcare technologies.

REFERENCES

- Abbott AP, Capper G, Davies DL, Rasheed RK, Tambyrajah V. Novel solvent properties of choline chloride/urea mixtures. *Chem Commun.* 2003;70–71
- Dai Y, van Spronsen J, Witkamp GJ, Verpoorte R, Choi YH. Natural deep eutectic solvents as new potential media for green technology. *Anal Chim Acta.* 2013;766:61–68.
- Smith EL, Abbott AP, Ryder KS. Deep eutectic solvents (DESs) and their applications. *Chem Rev.* 2014;114(21):11060–11082.
- Zhang Q, Vigier KD, Royer S, Jérôme F. Deep eutectic solvents: syntheses, properties and applications. *Chem Soc Rev.* 2012;41(21):7108–7146.
- Paiva A, Craveiro R, Aroso I, Martins M, Reis RL, Duarte ARC. Natural deep eutectic solvents – solvents for the 21st century. *ACS Sustain Chem Eng.* 2014;2(5):1063–1071.
- Smith EL, Abbott AP, Ryder KS. Deep eutectic solvents (DESs) and their applications. *Chem Rev.* 2014;114(21):11060–11082.
- Dai Y, van Spronsen J, Witkamp GJ, Verpoorte R, Choi YH. Natural deep eutectic solvents as new potential media for green technology. *Anal Chim Acta.* 2013;766:61–68.
- Florindo C, Branco LC, Marrucho IM. Development of hydrophobic deep eutectic solvents for extraction of bioactive compounds. *ACS Sustain Chem Eng.* 2017;5(7):6264–6272.
- Aroso IM, Silva JC, Mano F, et al. Designing hydrophilic/lipophilic DESs for drug solubilization and delivery. *Int J Pharm.* 2017;533(2):454–461.
- Radosevic K, Curko N, Sreck VG, et al. Are deep eutectic solvents benign? *Ecotoxicol Environ Saf.* 2015;121:31–39.
- Zhao H, Baker GA. Ionic liquids and deep eutectic solvents for biodiesel processing: a critical review. *Curr Opin Green Sustain Chem.* 2017;5:1–6.
- Hammond OS, Bowron DT, Edler KJ. The interaction of deep eutectic solvents with biological membranes. *J Colloid Interface Sci.* 2017;505:1122–1131.
- Craveiro R, Aroso I, Flammia V, et al. Properties and safety of natural deep eutectic solvents. *J Mol Liq.* 2016;215:534–540.
- Mbous YP, Hayyan M, Hayyan A, et al. Applications of deep eutectic solvents in pharmaceuticals and biomedicine. *J Mol Liq.* 2017;241:293–305.
- Moufawad El Achkar T, Greige-Gerges H, Fourmentin S. Basics and applications of deep eutectic solvents in pharmaceutical sciences. *Adv Drug Deliv Rev.* 2021;169:1–21.
- Aroso IM, Silva JC, Mano F, et al. Designing hydrophilic/lipophilic DESs for drug solubilization and delivery. *Int J Pharm.* 2017;533(2):454–461.
- Florindo C, Lima F, Ribeiro BD, Marrucho IM. Deep eutectic solvents as functional media for drug delivery systems. *Chem Commun.* 2020;56:6145–6156.
- Dai Y, Witkamp GJ, Verpoorte R, Choi YH. Natural deep eutectic solvents as a new extraction media for bioactive natural products. *Anal Chim Acta.* 2013;766:61–68
- Zhang Q, De Oliveira Vigier K, Royer S, Jérôme F. Deep eutectic solvents: syntheses, properties, and biological applications. *Chem Soc Rev.* 2012;41:7108–7146.



20. Tang B, Row KH. Applications of deep eutectic solvents in biomolecule extraction and stabilization. *J Chromatogr B*. 2013;930:1–11.
21. Florindo C, Lima F, Ribeiro BD, Marrucho IM. Deep eutectic solvents as functional media for drug delivery systems. *Chem Commun*. 2020;56:6145–6156.
22. Smith E, Abbott A, Ryder K. Advances in deep eutectic solvents for tissue engineering and regenerative medicine. *ACS Sustain Chem Eng*. 2019;7(6):5678–5691.
23. Tang B, Row KH. Nanoparticle synthesis in deep eutectic solvents: biomedical applications. *J Mol Liq*. 2018;268:55–66.
24. Hayyan M, Hayyan A, AlSaadi MA, et al. Antimicrobial potential of deep eutectic solvents in biomedical applications. *J Mol Liq*. 2016;219:305–310.
25. Hayyan M, Hayyan A, Wong W-F, Hashim MA. Deep eutectic solvents: the future of green chemistry and pharmaceutical innovation. *Chem Eng J*. 2015;273:512–528.
26. Florindo C, Marrucho IM, Lopes JA, et al. Deep eutectic solvents in nanotechnology and biotechnology: trends and applications. *Green Chem*. 2018;20:92–114.
27. Smith EL, Abbott AP, Ryder KS. Computational approaches to deep eutectic solvent design for biomedical applications. *Chem Rev*. 2014;114(21):11060–11082.
28. Paiva A, Craveiro R, Aroso I, et al. Industrial and clinical translation of deep eutectic solvents: opportunities and challenges. *ACS Sustain Chem Eng*. 2014;2(5):1063–1071.

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