

# Bioactive Recovery Reimagined: The Role of Microwave Technology and NADES in Green Extraction Science

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## ABSTRACT

Natural Deep Eutectic Solvents (NADES) and Microwave-Assisted Extraction (MAE) have gained increasing attention as sustainable and high-performance alternatives for extracting bioactive compounds from botanical and agro-industrial sources. This review highlights recent progress in integrating MAE with NADES, emphasizing their combined advantages as an environmentally conscious extraction platform. MAE utilizes rapid volumetric heating to promote efficient cell wall rupture and accelerate mass transfer, thereby significantly reducing extraction time, energy input, and solvent consumption. Meanwhile, NADES formed from naturally derived, biodegradable constituents such as sugars, amino acids, and organic acids offer customizable polarity, low toxicity, and enhanced solvation capacity, making them viable substitutes for conventional organic solvents.

To optimize the recovery of key phytochemicals such as phenolics, flavonoids, alkaloids, and polysaccharides, critical operational variables are examined, including microwave power, irradiation time, solvent composition, viscosity, polarity, and hydrogen-bond interactions within NADES matrices. Comparative assessments with traditional extraction methods and other green extraction technologies illustrate both the strengths and limitations of the MAE-NADES system.

In addition, this review discusses current challenges involving viscosity management, solvent recyclability, process scalability, and compliance with regulatory and safety standards. Considerations related to toxicological evaluation and regulatory acceptance are particularly important for applications in food, pharmaceutical, and cosmetic industries.

Overall, the integration of MAE and NADES represents a promising and sustainable extraction strategy aligned with the principles of green chemistry. With continued optimization and validation, this combined approach holds strong

potential for large-scale industrial recovery of high-value bioactive compounds.

**Keywords:** Microwave-Assisted Extraction; Natural Deep Eutectic Solvents; Sustainable Extraction Technologies; Bioactive Compound Recovery; Solvent Recyclability and Toxicological Assessment.

## I. INTRODUCTION

Microwave-assisted extraction (MAE) has emerged as one of the most efficient green extraction technologies for recovering bioactive molecules from natural matrices [1]. Unlike conventional approaches such as Soxhlet extraction, maceration, and refluxing which typically require prolonged processing and large quantities of organic solvents, MAE employs electromagnetic irradiation to rapidly and uniformly heat the solvent and plant material [2]. The underlying mechanism involves ionic conduction and dipole rotation, wherein polar molecules continuously reorient in response to the oscillating electromagnetic field, generating localized thermal energy and molecular friction [3]. This targeted heating promotes efficient rupture of cell walls, enhances mass transfer, and increases solvent penetration, collectively improving extraction yield and selectivity while significantly reducing both energy consumption and solvent use [1]. Owing to its rapid operation, reproducibility, and alignment with green chemistry principles, MAE has been successfully applied to isolate phenolics, flavonoids, alkaloids, essential oils, and polysaccharides from a wide range of botanical materials and agro-industrial residues [4,5].

Parallel to these advancements, Natural Deep Eutectic Solvents (NADES) have gained prominence as a new class of environmentally friendly solvents, contributing notably to the evolution of green extraction practices [6]. NADES are formed by combining two or more naturally occurring constituents commonly sugars, amino acids, organic acids, and choline derivatives which

interact through extensive hydrogen-bond networks to form stable eutectic systems [7]. Their biodegradability, non-volatility, tunable polarity, adjustable viscosity, and strong solvation capabilities make them well-suited for selectively extracting structurally diverse bioactive compounds [8]. Moreover, their inherent low toxicity and ability to stabilize thermolabile molecules position NADES as attractive substitutes for conventional organic solvents [9]. Recent findings further indicate that NADES can enhance extraction efficiency, simplify downstream handling, and improve the storage stability of the resulting extracts [10].

The integration of MAE with NADES represents a synergistic advancement in sustainable extraction technology. MAE provides rapid, uniform energy transfer that mitigates the viscosity-related mass-transfer limitations of NADES, while NADES serve as safe, renewable, and selective solvent media consistent with the principles of green chemistry and circular resource utilization [11]. Together, this hybrid approach facilitates high-efficiency recovery of valuable phytochemicals with reduced environmental impact [10]. This review, therefore, examines the theoretical basis, optimization parameters, and operational performance of the MAE-NADES system, with an emphasis on its industrial relevance. Furthermore, it addresses current developments in NADES recycling, safety and toxicological evaluation, cost considerations, and future research directions aimed at establishing MAE-NADES integration as a standard platform for sustainable bioactive compound extraction.

## BACKGROUND OF MICROWAVE THEORY

Microwaves are electromagnetic waves characterized by non-ionizing radiation. Their frequency ranges from 300 MHz to 300 GHz, and their wavelength spans from 1 mm to 1 m [12]. The interaction of microwaves with analyte molecules involves two converging mechanisms: dipole rotation and ionic conduction (in the solvent and sample). Ionic conduction occurs due to the electrophoretic migration of ions when an electromagnetic field is applied. The collisions of these ions with other molecules create resistive heating [13]. Dipole rotation pertains to the oscillating motion of polar molecules that possess dipole moments, which attempt to align themselves with the electric field. This rapid reorientation generates internal molecular friction, resulting in heat production [14]. The induced heating of water

within plant matrices can lead to vaporization within the cells, potentially causing the rupture of cell walls or plasma membranes [2]. The compounds that are extracted subsequently dissolve in a suitable solvent, facilitating their separation from the remaining plant material [15]. The dielectric characteristics determine the amount of energy is absorbed as well as transmitted through a material when it is exposed to microwaves [16]. The dielectric loss factor ( $\epsilon''$ ), which measures the transformation of electromagnetic energy into thermal energy, and the dielectric capacity to become polarized in an electromagnetic field, are examples of its dielectric characteristics. The dissipation factor, loss tangent, or dielectric loss to constant ratio is defined as follows:

$$\text{Tan}\delta = \epsilon'' / \epsilon'$$

Tan $\delta$  represents a descriptive dielectric parameter that can be used as an indication of the material's general capability to absorb microwave energy and to convert the absorbed energy into heat [17].

The power of the microwave irradiation has a major impact on the extraction yield during MAE operation, high irradiation accelerates mass transfer and raises the temperature of the extraction solvent and sample matrix. The microwave irradiation period is also an important factor since, at a certain point, it is evident that the extraction yield increases with increasing duration. To obtain a higher yield while conserving solvent, energy, and time, one to three extraction cycles are sufficient [18]. These parameters of microwave irradiation play a significant role.

## MICROWAVE ASSISTED EXTRACTION

As interest in green technology grows, MAE emerges as a highly feasible method and has become an essential technique for extracting valuable compounds from plant materials [3]. The MAE approach employs electromagnetic irradiation (microwave) to efficiently heat the solid-liquid mixture, resulting in the destruction of tissues and cells, hence facilitating the release of target substances from the sample into the solvent as shown in Fig.1 [19]. MAE has been considered a valuable alternative to traditional methods for the extraction of a variety of biologically active compounds from raw plants and animals.

The main advantages of MAE are shorter extraction times and higher extraction yields. Water is typically used as a solvent in place of traditional organic solvents, which optimizes the procedure

[20]. Further, effective extraction from various biological materials can be accomplished by enhancing and optimizing MAE's extraction parameters (solvent type, microwave strength, microwave irradiation period, etc.). The following references have extensive information about the way these parameters affect MAE [21-23].

#### Effect of Power

Cell structure may be destroyed by microwave radiation, allowing the active ingredient to dissolve into the sample. The interaction between the electromagnetic field and the sample molecules improved as microwave power increased, leading to an increase in recovery efficiency. Higher microwave power, however, may cause some active components to deteriorate due to heat [24]. In a study, power levels ranging from 180 W to 800 W were tested, with extraction time and liquid-to-solid ratio fixed at 10 seconds and 20 mL/g, respectively. The highest yields of 20.6 mg/g DW (Madecassoside) and 11.9 mg/g DW (Asiaticoside) were achieved at 600 W, indicating an optimal balance between energy input and compound stability. While increasing power generally enhanced extraction by promoting rapid heating and improved mass transfer, a further increase to 800 W led to a slight decline in yield, likely due to thermal degradation of the target compounds. This highlights that beyond a certain threshold, excessive microwave energy can negatively impact thermolabile constituents. The study emphasizes that 600 W is the ideal power setting for maximizing glycoside yield in NADES-MAE systems without compromising compound integrity [25].

#### Effect of irradiation time:

The influence of extraction durations of 10, 15, and 20 minutes on total phenolic content (TPC) was assessed in the study. From 10 to 15 minutes, TPC values increased, indicating improved mass transfer and decreased solvent viscosity, both of which facilitate analyte diffusion into the solvent system. TPC decreased when the extraction period was increased to 20 minutes, most likely as a result of heat-sensitive polyphenolic compounds degrading thermally under extended high-power microwave irradiation. This trend highlights how crucial time optimization is for striking a balance between compound stability and effective solute recovery. The results showed that 15 minutes was the ideal extraction duration, guaranteeing the highest phenolic yield

without sacrificing the target compounds' structural integrity [26].

#### Effect of Liquid-Solid Ratio:

A crucial factor affecting extraction performance in NADES-based systems is the liquid-to-solid ratio (LSR), which establishes the mass transfer rate and concentration gradient between the solvent and matrix [10]. Increasing the LSR initially improved yield in the extraction of acetyl-11-keto- $\beta$ -boswellic acid (AKBA) from frankincense resin because it increased the driving force for mass transfer, which made it easier for AKBA to be released into the NADES phase. All NADES formulations showed a decrease in AKBA production, nevertheless, when the LSR surpassed 60:1 or 70:1. This implies that high solvent volumes might dilute the system without yielding advantages from extraction that are proportionate. Additionally, from an economic and sustainability perspective, excessively high LSRs can lead to solvent waste and reduced scalability, particularly when the limiting reason is diffusion from the inside of the solid matrix rather than solvent supply. Thus, improving LSR is crucial for large-scale extraction operations to preserve affordability and social responsibility in addition to enhancing compound recovery [27].

#### Effect of pH

The durability and recovery of polyphenolic chemicals from plant materials are significantly influenced by the pH of the extraction environment. Using UV spectroscopy, the stability and yield of the polyphenol extraction process from *Pithecellobium dulce* fruit peels were assessed across a pH range of 4 to 11. Alkaline settings between pH 8.5 and 9.3 improved polyphenol extraction without degradation, according to the data. This is probably because basic solvents and the several structurally varied antioxidants in the plant matrix interact more. However, a significant drop in TPC was noted at pH values higher than 9.3, which was explained by the extract's monomeric and polymeric subunits interacting and aggregating, which decreased its solubility [23].

#### NADES (NATURAL DEEP EUTECTIC SOLVENTS)

In many analytical applications over the past few years, the use of conventional organic solvents has been overruled by ionic liquids (ILs) and deep eutectic solvents (DES) [28]. ILs are thought to be less sustainable and more harmful

than DESs [29]. DES have numerous of important benefits, including being less harmful, more biodegradable, quicker to make, and more affordable than ILs [30]. DES's qualities may be readily adjusted by selecting different components and modifying their ratios, making incredibly adaptable [31]. These advantages have led to an increase in interest in DESs in both business and research. These days, they are extensively employed in fields such as organic production, biocatalysis, extraction and dissolving procedures, etc... [32,33].

The family of DES known as NADES is derived from natural substances. NADES was the term given by Choi [34]. They are referred to as "natural" because the main components they contain are sugars, organic acids and bases, and amino acids that are made by plants naturally and utilized to survive. Among the DES family, NADES is therefore a more ecologically harmless and biocompatible choice [35]. Usually, a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA) are combined to create NADES. Strong hydrogen bonds are formed during the interaction between these constituents, upsetting the individual compounds' initial crystalline structures. The mixture's melting point thus drops significantly, turning into a liquid at or close to room temperature [36]. Non-toxic quaternary ammonium salts or amino acids are often used HBAs in NADES and organic acids or carbohydrates serve as HBDs. The common HBAs and HBDs in creation of NADES are listed in Fig.2 Relying on the molecular environment, functional groups including alcohols, amines, aldehydes, ketones, and carboxylic acids can function as both donors and acceptors of hydrogen bonds [37]. Several advantages of NADES are that they are environmentally friendly, biodegradable and exhibit low toxicity, thus being appropriate for applications in the food, pharmaceutical and cosmetic industries. On top of that, extracts obtained through the use of NADES frequently do not need further purification, given their application and safety. Also, bioactives stored in NADES may have an extended shelf-life or stability and their bioactivity could be preserved or improved [38].

Choline chloride (ChCl) is the most employed proton acceptor in the majority of those NADES formulations targeting polyphenols [39]. In the context of proton donors, a diversity of compounds has been tested, such as glycerol, lactic acid, urea, glucose, etc... [6]. In NADES

combinations, water is another often utilized component, typically ranging from 10% to 30% [40]. Using two different donors in ternary mixes is another option [41]. ChCl has lately been replaced by betaine as the HBA in the production of NADES. Because of its low toxicity and great biodegradability of betaine, a byproduct of sugar manufacturing and derived from renewable resources offers benefits over ChCl. Organic compounds have been successfully extracted from plant materials using betaine-based NADES [42]. There are five documented ways to prepare NADES. These include microwave, ultrasonication, freeze-drying, vacuum evaporation, and thermal mixing [43].

#### CONSTRAINTS AND OBSTACLES OF NATURAL DEEP EUTECTIC SOLVENTS

Despite the widespread use of NADES, it is important to remember that the primary drawbacks of employing NADES in the extraction process are some of its characteristics, such as their low vapour pressure, density, and viscosity, which may cause issues in the industry's implementation [44]. The viscosities of several NADES are noticeably greater than those of traditional solvents. This restricts mass and energy transmission, which may impair scalability and reaction [45]. To get around these issues and maximize extraction in an industrial context, water or a carefully regulated temperature rise would be used to stop the decomposition of the desired chemicals [44]. For example, Urea Glycerin (UG) (1:3) viscosity decreased 5 times when temperature was increased and decreased from  $885.43 \pm 7.02$  to  $17.34 \pm 1.14$  mPa·s with water dilution. In the same trend, other NADES, such as Betaine-Lactic acid (BLA), Citric acid-Glucose (GCAH) and Proline-Citric acid (PCAH) also present a significant reduction in viscosity under the same conditions. Simultaneously, electrical conductivity, which is important for the improvement in the extraction of polar compounds, was also found to be negatively correlated with viscosity. At lower viscosity, higher conductivity values were found such as the one observed for the Betaine-Glycerol (BGH), which increased from 0.0072 to 2.1798 mS/cm<sup>3</sup> with decreasing viscosity [46].

#### RECOVERY OF THE BIOACTIVE COMPOUNDS USING NADES

MAE has been seen as a useful alternative to traditional techniques for obtaining a variety of

physiologically active compounds from unprocessed plants and animals[20].

The significance of integrating MAE and NADES so is highlighted in studies, as microwave dielectric heating can reduce mass transfer limitations and disrupt plant cell walls, while NADES improve selectivity, yield, and environmental profiles to align with green chemistry principles and show considerable potential for industrial-scale extraction of bioactive compounds [47]. In order to extract a variety of bioactive chemicals from different plant materials and agro-industrial by-products, MAE, has been widely used. Depending on the matrix and solvent utilized, they can comprise not just flavonoids and phenolic acids but also alkaloids, terpenoids, saponins, tannins, essential oils, polysaccharides, anthocyanins, and even proteins and vitamins [48].

In recent years NADES have been attracting a lot of attention as green efficient alternatives to traditional organic solvents for the extraction of bioactive compounds from plants, fruits and agro-industrial residues [49]. NADES are formed by mixing naturally occurring compounds such as sugars, amino acids, organic acids, and polyols, and have low toxicity, are biodegradable, and have a good extraction capacity [50]. These compounds have unique physicochemical properties, particularly strong hydrogen-bonding networks and allow selective solubilization of a wide variety of phytochemicals such as flavonoids, phenolic acids, alkaloids, and anthocyanins [9].

To improve extraction performance and processing efficiency, NADES have been combined with other advanced extraction technologies, most notably MAE [51]. Advantages of MAE include attention to solvent, shorter extraction times and improved yields, and faster heating, among additional benefits [1]. NADES combined with MAE enables not only faster-extraction kinetics, but when utilizing thermolabile and/or sensitive structural bioactive compounds to be the extraction method of choice in green chemical procedures [52].

### NADES RECOVERY AND REUSE

Although NADES have a sustainable advantage over conventional volatile organic solvents, recycling them can be challenging due to their strong hydrogen bonding interactions with target chemicals and low vapor pressure [63]. In order to make industrial extraction and synthesis processes more economically and environmentally sustainable, recycling of NADES is essential [43].

NADES exhibit a problem since they are non-volatile, in contrast to traditional organic solvents that are readily recyclable by distillation. Alternative techniques have been developed to get around this, including liquid-liquid extraction, adsorption chromatography, and anti-solvent precipitation [63]. Because NADES are soluble in water and many target chemicals are not, water addition is one of the most used methods among them [43]. As a result, products might precipitate and subsequently be filtered to separate them. In order to avoid the requirement for chromatographic purification, Nejrroti Set al.[64], for instance, successfully reused NADES throughout four cycles, with yields dropping from 97% to 65%. For the synthesis of imines and bisamides using  $\text{ChCl/urea}$ , Singh K et al.[65] reported a comparable method that produced effective catalyst and product recovery across several cycles. It has been shown that liquid-liquid extraction using ethyl acetate or chromatographic resins such as Diaion HP-20 works well when precipitation is not practical, especially when dealing with water-soluble metabolites. Short-path distillation, membrane filtering, crystallization, and centrifugal partition chromatography are other techniques that have been documented; some of them have achieved >90% NADES recovery. Nevertheless, a lot of these methods need large amounts of energy and solvent, which emphasizes the necessity of customizing the recovery strategy to the target molecule, NADES composition, and industrial setting.

In a biorefinery setting, the study emphasizes the successful recovery and repurposing of NADES after lignin separation [66]. Following biomass pretreatment, rotary vacuum evaporation was used at 60°C to separate the NADES reagent, which consists of lactic acid and choline chloride, from the remaining liquid. The recyclability of the system was demonstrated by the subsequent usage of the recovered NADES and water in the second cycle of biomass pretreatment and lignin precipitation. A Karl Fischer Titrator was used to assess the water content of the recovered NADES, and HPLC quantification of its main components was used to calculate the recovery percentage. Successful pooling of recovered NADES with fermentation liquids for ongoing cycles comprising biomass pretreatment, lignin extraction, xylan recovery, and solvent recycling was demonstrated by further integration into a biorefinery system. This supports NADES's position as a green, recyclable solvent platform in

sustainable biomass processing by proving that solvent recovery and reuse are feasible in a closed-loop system [67].

The extremely low vapor pressure of NADES makes it extremely difficult to extract rutin from them. A rutin recovery rate of 95.1% was made possible by water acting as the most effective anti-solvent, according to the authors' evaluation of choline chloride: glycerol (ChGly) as the extraction medium in this study. NMR spectroscopy was used to further purify and structurally analyze the rutin after recovery, resulting in a maximum of  $0.75 \pm 0.06\%$  (dry basis). The study's focus on NADES's recyclability was significant because it had not before been widely discussed. Following the separation of rutin, water was removed from the ChGly system under vacuum for two hours at  $90^{\circ}\text{C}$ , enabling the solvent to be recycled and utilized again. After three consecutive cycles of recycling, the extraction efficiency of ChGly maintained 92%, 87%, and 81% of its initial performance, respectively. This proves that NADESs may be effectively recovered and repurposed using an easy-to-use, environmentally benign technique, avoiding hazardous chemicals and promoting the creation of sustainable phytochemical extraction methods [68].

Likewise, following anthocyanin extraction, choline chloride: citric acid (ChCit) was effectively recycled by diluting the extract with more than 50% water (v/v), which broke the NADES structure and improved chemical release. With NMR analysis verifying the chemical integrity of the recovered solvent, this technique allowed for a NADES recycling yield of up to 96.8%. ChCit recycling efficiency remained high at 77.91% even at pilot size, indicating scalability. All of these research supports the use of NADES in more environmentally friendly, circular bio-extraction systems by demonstrating that straightforward techniques like vacuum evaporation and water dilution may facilitate efficient NADES recovery and reuse [69].

#### TOXICOLOGICAL EFFECT OF NADES

When NADES are being used in industry and commerce, their toxicological evaluation is a crucial factor to take into account. Comprehensive toxicity data is still scarce and dispersed throughout the literature, even though they are categorized as green solvents. The lack of a defined technique to assess or compare toxicity measurements across various DES formulations makes this difficult. Interestingly, concentration-dependent antibacterial

activity is exhibited by numerous NADES, which, depending on the intended use, may be advantageous or harmful. For example, cytotoxicity may be undesirable for use in pharmaceuticals and food, but it shows promise in cancer treatments. Context-specific toxicity studies are crucial as a result. Mammalian toxicity assessment may also be avoided if a NADES is only used for extraction and does not come into close contact with people or animals [70].

Despite the fact that NADES are often made from bio-based and GRAS-listed ingredients, a comprehensive assessment is necessary to ensure their safety [71]. Importantly, synergistic or antagonistic interactions can cause the final eutectic mixture's toxicity to differ greatly from that of its constituent parts. NADES have been categorized into toxicity groups by recent in-silico toxicity evaluations, such as those using quantitative structure-toxicity relationship (QSTR) models; nonetheless, model differences should be interpreted with caution [63]. Likewise, depending on the methods used, in vitro research yields contradictory results. For example, de Morais Pet al.[72] found that the acid alone was more hazardous than its eutectic form, whereas Radosevic Ket al. [73] revealed that organic acid-based NADES had strong antibacterial activity. This disparity draws attention to methodological flaws, such as how viscosity affects antibiogram results, which could not accurately represent cytotoxicity. Furthermore, investigations on cancer cell lines and microorganisms have demonstrated that pH has a substantial impact on toxicity [74,75,50]. Crucially, in vitro and in vivo results are not always consistent. Mbous YPV[76] demonstrated that NADES with higher in vitro EC50 values had increased in vivo toxicity, mostly as a result of absorption difficulties associated to viscosity. Regulatory scrutiny is growing, for example, EU Regulation 1223/2009 forbids the use of ChCl in cosmetics due to its irritating qualities; betaine is suggested as a safer substitute. Likewise, with high exposures, volatile NADES derived from monoterpenes (such as thymol and menthol) may present acute or long-term hazards [63]. Ultimately, even though NADES are thought to be less harmful than traditional solvents, their safe and broad use especially in the food, cosmetic, and pharmaceutical industries require standardized procedures, mechanistic research, and application-specific toxicological data [77].

### **COST EFFECTIVENESS OF NADES**

NADES are cost-effective because of their simple manufacture, low cost, biodegradable components, and removal of expensive downstream purification processes [78]. For the extraction of propolis, NADES present a viable substitute for traditional organic solvents like ethanol. Due to their task-specific design, solvation power for certain bioactives may be optimized by customizing parameters including pH, viscosity, and polarity. Despite the fact that NADES frequently have a greater viscosity, this drawback may be managed inexpensively by diluting them with water, a cheap and safe co-solvent. Crucially, NADES-based extracts frequently behave better over time, negating the requirement for packaging or storage. By lowering processing time and energy consumption, NADES dramatically improve extraction efficiency when used in conjunction with high-energy extraction techniques like MAE or ultrasound-assisted extraction (UAE) [79].

The manufacturing of NADES is far less expensive than that of conventional organic solvents since it doesn't require any specific reagents, chemical reactions, or energy-intensive purifying processes [80]. Their strong chemical and thermal resilience also makes it possible to reuse them again, which further reduces operating costs when combined with recycling techniques like membrane filtering or anti-solvent precipitation [81]. Furthermore, in culinary, cosmetic, or nutraceutical applications, NADES can be used without being extracted from the final extracts, obviating the need for expensive downstream processing. They use less energy because they are compatible with green extraction technologies like UAE and MAE, which increase efficiency and shorten extraction times. Because of these characteristics, NADES is a sustainable and affordable substitute for volatile organic solvents, especially in large-scale bioprocessing and the extraction of natural products [43].

### **FUTURE PERSPECTIVES OF NADES**

Future research and use of NADES will be greatly aided by addressing significant issues with scalability, cost-effectiveness, and regulatory approval [82]. Despite being hailed for their environmentally friendly origin, low toxicity, biodegradability, and adaptability, problems including high viscosity, poor recycling efficiency, and a lack of standardized production procedures continue to prevent NADES from being widely used in industry [83]. The improvement of NADES

formulation for particular applications such as balancing solvent strength, stability, and viscosity, while reducing energy and raw material costs must be the top priority of future research [84]. Furthermore, in order to ascertain if NADES can really compete with conventional solvents on a commercial scale, thorough techno-economic and life cycle evaluations (LCA) are desperately needed [85]. Improving cost-efficiency will need developments in recovery and reuse technologies, such as membrane filtering, anti-solvent tactics, or intelligent process integration [86]. Combined with *in silico* predictive modeling, the creation of task-specific NADES (TS-NADES) for extraction, catalysis or formulation would allow for quicker and more cost-effective solvent design [87,88]. Although NADES has a bright future overall, achieving their full potential in sustainable industrial processes would need multidisciplinary cooperation, investment in scale-up technologies, and targeted research on striking a balance between price and performance [82]. The development of flexible and dynamic solvent systems will influence the future course of DES and NADES research in extraction [89]. Using switchable eutectic solvents, which react to external stimuli like temperature, pH, or polarity changes to enable the selective extraction and recovery of target chemicals, is one such potential avenue [90]. Process efficiency might be greatly increased by this flexibility, particularly for substances that need exact extraction conditions, such as carotenoids and anthocyanins [91]. A disruptive alternative to conventional preparation, *in-situ* creation of eutectic solvents directly inside the sample matrix eliminates the requirement for pre-synthesis and saves preparation time and resources [92].

The use of DES/NADES in biocatalytic systems, where the solvents serve as both an active substrate and a media, is another interesting avenue that enhances stereoselective enzymatic conversions [93]. In addition to encouraging solvent economy, its dual functionality supports atomic efficiency and green chemistry concepts [63]. Last but not least, the advent of computational solvent screening tools such as COSMO-RS has created new avenues for data-driven solvent selection by enabling scientists to quickly model and forecast solvent-solute interactions in a variety of eutectic mixtures, reducing the need for trial-and-error testing [94]. With these developments, static solvent systems have given way to intelligent, responsive, and computationally designed eutectic formulations that can adjust to

the various needs of contemporary extraction methods.

## II. CONCLUSION

A revolutionary breakthrough toward the effective and sustainable recovery of bioactive chemicals from natural resources has been achieved with the combination of NADES and MAE. Rapid dielectric heating made possible by MAE improves solvent penetration and cell disruption, cutting down on extraction time and energy consumption while increasing yield. Simultaneously, NADES, which are made up of biodegradable and biocompatible components, provide a flexible and safe solvent solution that can solubilize a variety of phytochemicals. Together, these two strategies successfully get beyond the limitations of traditional extraction techniques while adhering to the circular economy and green chemistry tenets. However, problems including high viscosity, limited recyclability, and process scalability need more study before they may be adopted in industry. To maximize performance and economic viability, more research into task-specific NADES formulations, recovery techniques, and computational modeling of solvent-solute interactions is necessary. In conclusion, the MAE-NADES system offers a flexible and promising platform for the large-scale extraction of natural bioactives, paving the way for future processing in the food, pharmaceutical, and cosmetic sectors that is safer, cleaner, and uses less resources.

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The authors declare that they have no competing interests.

### Ethical Approval

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### Informed Consent

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### Data Availability

Not Applicable

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