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# Natural Deep Eutectic Solvents (NADES) Research Framework: Bibliometric Analysis

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***Authors' contributions***

*This work was carried out in collaboration among all authors. Authors EW and BK designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors LHYA and DVA managed the literature research, performed the bibliometric analysis, and wrote the draft of the manuscript. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aims:** The Natural Deep Eutectic Solvents (NADES) method is an extraction method currently being developed using affordable green solvents with low cytotoxicity. This research aims to (a) identify developments in NADES research, and (b) develop research gaps for NADES for future research.

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**Study Design:** This research was conducted using bibliometric analysis.
**Place and Duration of Study:** Library sources refer to research articles available online that can be accessed via websites or search engines by entering specific keywords related to the topic.
**Methodology:** A research approach using quantitative methods was carried out using bibliometric analysis. Data analysis using bibliometric analysis of "Natural Deep Eutectic Solvents" sourced by article tittle, abstract, and keywords that produced 1,045 Scopus documents.
**Results:** The results show a growing research trend in NADES, but there are still several gaps that need to be addressed as mentioned in the proposed research framework.
**Conclusion:** Future research should focus on more comprehensive comparisons, more detailed method explanations, deeper understanding of molecular mechanisms, and long-term stability evaluations to improve the applicability of NADES in various fields. This paper contributes to the development of NADES.

*Keywords: Alginate extraction; bibliometric; natural deep eutectic solvents; research gap; journal of molecular liquids.*

## 1. INTRODUCTION

In recent years, the exploration of more efficient, sustainable, and environmentally friendly extraction methods has become a major focus in the scientific and industrial worlds. The extraction of natural materials plays a crucial role in producing high-value materials. However, conventional extraction methods often involve the use of chemical solvents that have the potential to negatively impact the environment and human health. Many organic solvents release volatile compounds into the atmosphere, contributing to air pollution and potentially causing respiratory problems among exposed populations [1]. Traditional solvent-based extraction processes require substantial amounts of energy for heating and distillation, leading to higher operational costs and greater carbon footprints such as hexane and chloroform. Additionally, the removal of spent solvents contributes significantly to overall process energy consumption [2].

One of the latest developments that is attracting attention is the use of Natural Deep Eutectic Solvents (NADE) as an alternative in the extraction process of natural ingredients. In view of this, the use of NADES as an alternative solvent offers a promising approach. NADES is an extraction method currently being developed using affordable green solvents with low cytotoxicity [3,4]. According to Lai et al. [5], the NADES method has been proven to be effective in extracting flavonoids, phenolic acids, polyphenols, saponins, etc. from natural ingredients. A review highlighted the potential of NADES in extracting bioactive from agro-food residues, emphasizing their unique properties such as low toxicity and biodegradability [6]. This makes them suitable for applications in the food, nutraceutical, and pharmaceutical industries [6,7,8].

NADES is formed from intermolecular interactions between hydrogen bond donors and acceptors, resulting in a eutectic mixture with a lower melting point than its components. Its preparation can be done by dilution in water with heating and drying, or direct mixing with water and heating. Unlike DES which uses quaternary ammonium salts, NADES uses natural primary metabolites such as sugars, organic acids, amino acids, and choline derivatives [9]. NADES has unique characteristics such as low melting point, minimal volatility, high thermal stability, and tuneable viscosity. Its hydrophobicity is influenced by its composition and interaction with water. With these advantages, NADES is a promising solution for environmentally friendly extraction technology.

Furthermore, the economic feasibility of NADES is bolstered by their ability to be produced from inexpensive, renewable resources, which can lead to significant cost savings in extraction processes. Research [10] showed that NADES pretreatment resulted in lignin solubility of 72-75% and allowed NADES reprocessing cycles up to three times without decreasing efficiency, potentially reducing operational costs and waste. On the other hand, Kumar et al. [11] conducted an economic evaluation of various NADES-based biorefinery design scenarios. The results showed that with a net present value (NPV) of 1.4 million USD, an internal rate of return (IRR) above 100%, and a payback period of less than 2 years, this design showed promising economic feasibility if production scaled up and the NADES recycling method was applied [11].

In the other hand, Alginate is a type of *polysaccharide* found in *Phaeophyceae* cell walls with levels reaching 40% of the total dry weight Abka-Khajouei et al. [12]. Alginate does play an important role in maintaining the structure of algae cell tissue. This polysaccharide compound is a major component of brown algae cell walls and contributes significantly to structural integrity and physiological function of algae [13,14]. On the other hand, alginate, a polysaccharide found in brown algae, has unique properties that make it useful in a variety of industrial applications. Alginate also has good water absorption capacity and can form hydrogels, with properties that can be modified by adding reinforcing materials such as nanoparticles. Its high biocompatibility makes it suitable for biomedical applications, while its modifiability through various strategies such as adding nanoparticles or forming composites allows optimization of performance according to application needs. However, the process of extracting alginate from brown algae often involves complex chemical and physical treatments, which can impact the quality and sustainability of the process. Therefore, the search for more efficient and environmentally friendly extraction methods for alginate is highly relevant.

Research on the use of NADES in alginate extraction has emerged as an interesting research topic in response to concerns over the environmental and human health impacts of conventional chemical solvents. NADES has been successfully used for the extraction of polyphenols and bioactive compounds from natural products [15,16,17]. This shows great potential for applications in alginate extraction. The combination of the environmentally friendly solvent properties of NADES and its ability to dissolve polar and non-polar compounds can open new avenues in the alginate extraction process. This research has the potential to not only produce a purer and better-quality final product but also reduce negative impacts on the environment and speed up the extraction process.

The extraction of alginate from natural sources such as *Sargassum polycystum* has become an interesting research topic. Alginate is a biopolymer commonly found in brown algae and has various applications in the food, pharmaceutical, and heavy industries. Research related to alginate extraction using conventional methods has been carried out, but the use of NADES as a more environmentally friendly and effective alternative is starting to gain attention [18,19,20]. There is a study that has explored the use of NADES in the extraction of alginate from *Sargassum polycystum* grown in Vietnam. This study found that the optimal extraction conditions were at a temperature of 60°C, a solvent-to-material ratio of 40/1 (v/w) using Na2CO3 at pH 9, and a single extraction process. The results showed that the highest alginate content obtained was 176.22 mg uronic acid equivalent per gram dry weight, with suitable antioxidant activity [21].

Therefore, the objectives of this study are to (a) identify research developments and trends in NADES, and (b) develop a NADES research gap for future research. This research uses a quantitative research approach from bibliometric analysis. Specifically, the scope of this research is based on the article and review where experts based on their experience in the field of NADES. This research will contribute to the future development of Alginate Extraction and NADES from the research gaps revealed in the research framework. The structure of this paper is as follows. Section 2 explains the background of this research and related research. Section 3 explains the research method. Section 4 data analysis. Section 5 is the final section that summarizes the findings.

## 2. METHODOLOGY

### 2.1 Related Works

The type of research carried out to analyze the NADES literature appears in several terms, such as systematic review, bibliometric analysis, scient metrics, or even traditional literature review. This section allows us to evaluate some previous studies that apply bibliometric analysis to the NADES in general and especially for alginate extraction literature.

The research conducted on Alginate Extraction was entitled "Seaweeds as Promising Resource of Bioactive Compounds: Overview of Novel Extraction Strategies and Design of Tailored Meat Products" by Gullón et al. [22]. In this research, the aspects collected relate to the latest technology used to obtain and isolate bio compounds from seaweed. The use of whole seaweed and its bioactive extracts to develop meat foods that provide health benefits while reducing components considered unhealthy in meat is under review [23,24]. In addition, the prevention of oxidation events is also explained.

However, there are still several challenges regarding the organoleptic and sensory properties of the products produced, which affect consumer acceptance. So, more research is needed to address the gap to enable seaweed-based meat products to be marketed.

Furthermore, in research on NADES in the paper entitled "Green extraction of value-added compounds form microalgae: A Short Review on NADES and Related Pre-treatments" by Mehariya et al. [25]. This research discusses the potential application of NADES for the extraction of intracellular compounds from microalgae biomass and related pre-treatment to increase extraction efficiency. NADES are formed from a mixture of natural components, usually consisting of a hydrogen bond acceptor (HBA) such as choline chloride and a hydrogen bond donor (HBD) such as an organic acid, sugar, or amino acid. The formation of NADES is driven by hydrogen bonding between the components, resulting in a eutectic mixture with a melting point lower than that of the individual components. Key properties of NADES include high biodegradability, low toxicity, biocompatibility, low volatility, and high solubilization capacity [26,27].

## 2.2 Research Question

First, the author considers NADES to be interesting fields for future development. To our knowledge, no bibliometric analysis has been carried out to analyze the Alginate Extraction and NADES literature in the last decade. The following Research Question (RQ) is designed to identify research developments and trends in Alginate Extraction and NADES:

RQ 1 : How many research documents are published by each journal based on the level of relevance to the theme of NADES?
RQ 2 : What is the impact of each journal that publishes papers on the theme of NADES?
RQ 3 : How are growth resources relevant to NADES research?
RQ 4 : How to analyze the thematic map that appears based on the title of the document with the research theme NADES?

The bibliometric analysis in this study followed several basic protocols in the review process [28]. This process is carried out systematically and uses explicit stages so that it can be reproduced by other researchers. Bibliometric analysis can also be carried out with a mind-mapping approach that shows the limits of knowledge [29]. Bibliometric analysis is generally used in various scientific disciplines and focuses on quantitative studies in journal articles, books, or other forms of written publications [30]. In this research, five main steps of bibliometric analysis will be carried out, consisting of determining search keywords, checking initial search results, refining search results, compiling related data, and data analysis.

## 2.3 Data Collection

This study uses the Scopus database. Scopus has several advantages for bibliometric analysis, such as its broad and multidisciplinary coverage. The quality of Scopus data is also high because it goes through strict selection, so the validity of the analysis results is more guaranteed. Detailed citation data and the ability to perform historical analysis also make it superior in identifying long-term patterns. The article sourced by article tittle, abstract, and keywords. The keyword *"Natural Deep Eutectic Solvents"* was applied. The period used 2011 when the first publication on NADES was published until 2023 when the data collection for this article was first carried out. The criteria taken are journal articles and review journals only. Thus, 1,045 articles and reviews were obtained with the keyword "Natural Deep Eutectic Solvents" from 2011 to 2023. This research is limited to articles indexed in Scopus due to researcher limitations.

## 2.4 Data Processing

The data used is then exported into *.bib* format. R Studio software with bibliometrics packages was used for analysis data. Scopus uses Author ID and Affiliation ID to avoid mistakes in identifying authors or institutions. This reduces the risk of misattribution and ensures more accurate bibliometric analysis. So that data preprocessing does not need to be done much. The analysis used is adjusted to the RQ that has been prepared previously so that the results obtained can answer the RQ that has been proposed.

## 2.5 Interpretation Result

Interpretation of the results is done, there will be 4 results that need to be interpreted according to the number of RQs. In this interpretation, it not only explains the bibliometric result graph but also adds a review related to the existing articles. on the other hand, interpretation is also done based on the development of publications that match the keywords that have been searched. This study did not filter the language, so there are a few articles that are not in English. On the other hand, this study did not filter the region so there may be different research developments related to NADES in each region.

## 3. RESULTS AND DISCUSSION

The search was carried out on December 2023 using keywords in the form of search strings relevant to NADES where keywords were searched based on the title, keywords and abstract of the article. Based on the keywords that have been determined, an article search process is carried out in the electronic database used as a source of information. The electronic database used in this research is Scopus, considering that Scopus is the largest reputable scientific database currently available and provides various journal articles that have gone through a peer-review process [31]. In this way, the quality obtained can be guaranteed.

### 3.1 Initial Search Result

Initial search results with the keyword NADES produced 1,045 Scopus documents. In searching for articles, the period start from 2011 until 2023. Based on the research results, articles related to the NADES theme were first discovered in 2011, as shown in Table 1.

Research by Choi et al. [32] showed that NADES can act as an alternative solvent in biochemical and physiological processes of cells, especially in extreme conditions such as drought and high temperatures. Research by Mobinikhaledi and Amiri [33] discussed the synthesis of 5-arylidene-2-imino-4-thiazolidinones compounds through a one-pot reaction using natural eutectic solvents (deep eutectic solvents, DES) as catalysts and reaction media. This method was developed as a more environmentally friendly alternative compared to conventional synthesis methods that use hazardous organic solvents. NADES as a potential new medium for green technology. NADES offers an environmentally friendly and effective alternative to conventional solvents in various applications [34]. The use of natural eutectic solvents (NADES) as a new extraction medium for phenolic metabolites from safflower (*Carthamus tinctorius L.*) [35]. Research by Simamora et al. [36] examines the use of natural eutectic solvents (NADES) for the extraction of xanthorrhizol (XTZ) and curcuminoids from Curcuma xanthorrhiza rhizomes. Four types of NADES were prepared and their physicochemical properties, including polarity, viscosity, density, and pH, were characterized. FTIR analysis confirmed the formation of hydrogen bonds between NADES components.

**Table 1. The term “Natural Deep Eutectic Solvent” appears for the first time in the journal**

| Writer | Title | Source | Year of publication |
|---|---|---|---|
| Choi, Y. H., van Spronsen, J., Dai, Y., Verberne, M., Hollmann, F., Arends, I. W., Witkamp, G. J., & Verpoorte, R. | Are Natural Deep Eutectic Solvents the Missing Link in Understanding Cellular Metabolism and Physiology? | Plant Physiology | 2011 |
| Mobinikhaledi & Amiri | Natural eutectic salts catalyzed one-pot synthesis of 5-arylidene-2-imino-4-thiazolidinones | Research on Chemical Intermediates | 2013 |
| Dai, Y., Van Spronsen, J., Witkamp, G. J., Verpoorte, R., & Choi, Y. H. | Natural deep eutectic solvents as new potential media for green technology | Analytica chimica acta | 2013 |
| Dai, Y., Witkamp, G.-J., Verpoorte, R., Choi, Y.H. | Natural Deep Eutectic Solvents as a New Extraction Media for Phenolic Metabolites in Carthamus tinctorius L. | Analytical Chemistry | 2013 |
| Egan, P.A., Van Der Kooy, F. | *Xanthorrhizol* and curcuminoids NADES extraction from *C. xanthorrhiza* | Chemistry and Biodiversity | 2013 |

NADES was first reported and developed by Choi et al. [32]. In the study, Choi et al. developed a series of natural eutectic solvents consisting of primary metabolites commonly found in living cells and named them NADES. NADES was developed as a green solvent to replace organic solvents that are generally toxic, volatile, and harmful to human health and the environment. Initially, the NADES method was applied in the pharmaceutical and health sectors, but currently the application of the NADES method is very broad, including in the food industry for alginate extraction.

### 3.2 Statistical Compilation of Data

As previously mentioned, the data collected after searching is stored in the form of a BibTex file. Then the file is processed with the help of Bibliometric software to complete the metadata of the articles obtained such as author's name, title, keywords, abstract, and journal description (journal name, year of publication, volume, issue, pages). The dataset is verified, and necessary information is added when there is incomplete data. Then the search result data is analyzed and classified based on the verified data collection.

#### 3.2.1 How many research documents are published by each journal based on their level of relevance to the NADES theme?

Fig. 1 shows the number of research documents published by each journal based on their level of relevance to the Natural Deep Eutectic Solvent (NADES) theme. This data displays a list of the names of journals that are widely published and the intervals for the number of documents published with a blue bar chart. The darker the blue color indicates the greater the quantity and relevance to the research theme, the number of documents published by all journals ranges from 0 to 80 documents. Journal of Molecular Liquids is a journal in the top position with a total of 80 published documents with a dark blue bar chart compared to the bar charts of other journals. This is because the journal is relevant to the theme discussed.

An example of a journal published by the Journal of Molecular Liquids is the journal entitled "NADES as Potential Solvents for Anthocyanin Pectin Extraction from *Myrciaria cauliflora* fr Product: In Silico and Experimental Approach Solvent Selection" written by Benvenutti et al. [37]. In this research, silico and experimental approaches were combined to select NADES compounds aimed at selective and sequential extraction of anthocyanins and pectin from *Myrciaria cauliflora* products. The results obtained from this research are based on in silico evaluation, NADES and the target compound show amphoteric character which indicates an affinity between the two. Acid-based NADES showed the highest affinity in the H-bond acceptor region, while betaine and water-content NADES showed the best affinity in the H-bond donor region. However, all NADES showed low affinity towards non-polar compounds.

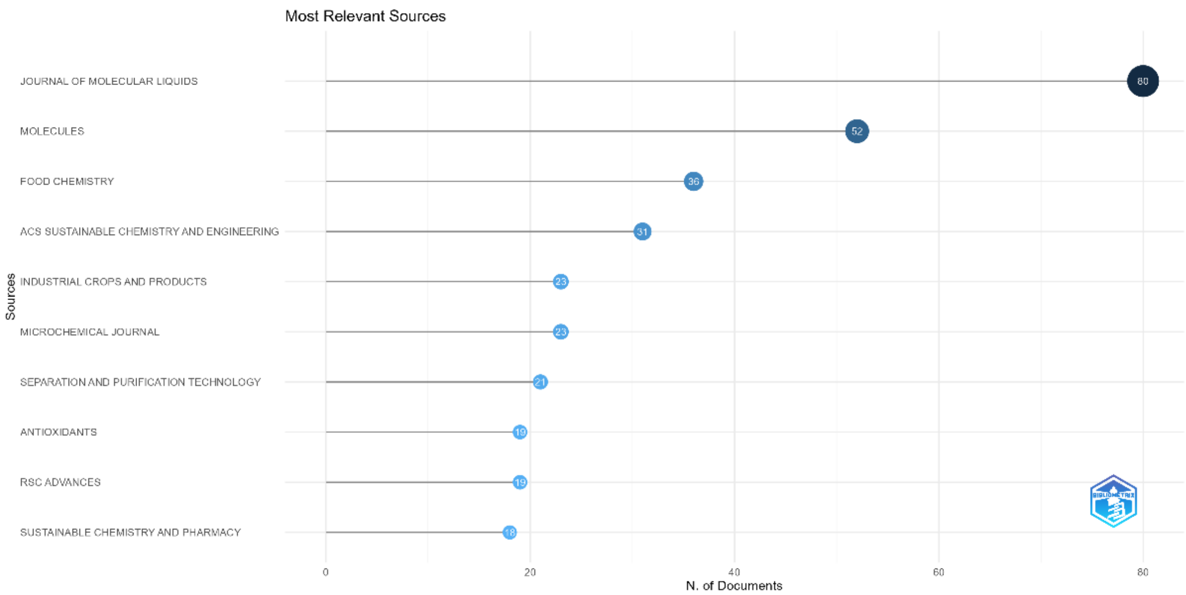


**Fig. 1. Most relevant source Natural Deep Eutectic Solvent (NADES)**

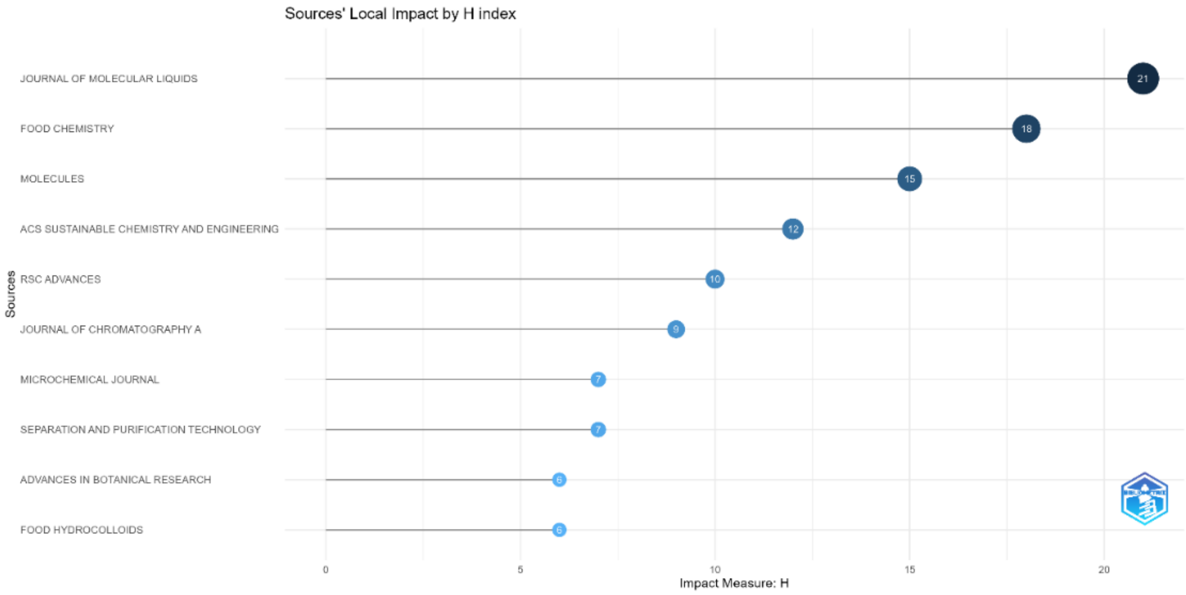


**Fig. 2. Source impact Natural Deep Eutectic Solvent (NADES)**

### 3.2.2 What is the impact of each journal that publishes papers on the NADES theme?

Journal calculations are not only based on the quantity produced or its relevance. However, this research was also carried out based on the impact produced by each journal that published papers on the theme of Natural Deep Eutectic Solvent (NADES) by calculating the H-index of the journal which is depicted in the blue bar diagram. Apart from showing the H-Index value obtained, the diagram above also illustrates the impact produced by the journal through the blue color displayed. The darker the blue color on the graph, the greater the impact generated by the journal. The journal H-Index interval in this study ranged from 0.0 to 21.0. Fig. 2 shows the Journal of Molecular Liquids is in the top position with an H-index of 21.0 which is marked in dark blue. Furthermore, Food Chemistry is in second place with an H-index of 18.0. Meanwhile, in journals with an H-index of 6.0, there are 2 journals marked in light blue on the diagram, which indicates the low impact of these journals.

The journal with the highest impact is the Journal of Molecular Liquids. Journal of Molecular Liquids is an international journal that focuses on fundamental aspects of structure, interactions, and dynamic processes in simple, molecular, and complex fluids. This journal is published by Elsevier. This journal aims to publish scientific research, theory, and application development from various fields of inquiry regarding chemistry, physics, and materials. The most cited article about Natural Deep Eutectic Solvent (NADES) was entitled “Properties and thermal behaviour of natural deep eutectic solvents” by Craveiro et al. [38]. The study investigated the properties and thermal behaviour of NADES based on choline chloride, organic acids, amino acids and sugars. Key properties examined included density, thermal behaviour, conductivity and polarity. The paper provides a comprehensive characterization of various NADES systems, offering insights into their thermal behaviour and physicochemical properties that are important for their development as sustainable solvents.

### 3.2.3 How is the growth of sources relevant to NADES research?

This research also discusses the development of journals which are sources of research with the theme of Natural Deep Eutectic Solvent (NADES). Fig. 3 shows the annual growth curve for each journal from 2011 to 2023 so that we can get an idea of whether the journal experienced an increase or decrease in the curve line during the research period, especially in the publication of papers with the theme Natural Deep Eutectic Solvent (NADES). This curve illustrates that research with the theme of Natural Deep Eutectic Solvent (NADES) tends to experience increasing growth in publications each year.

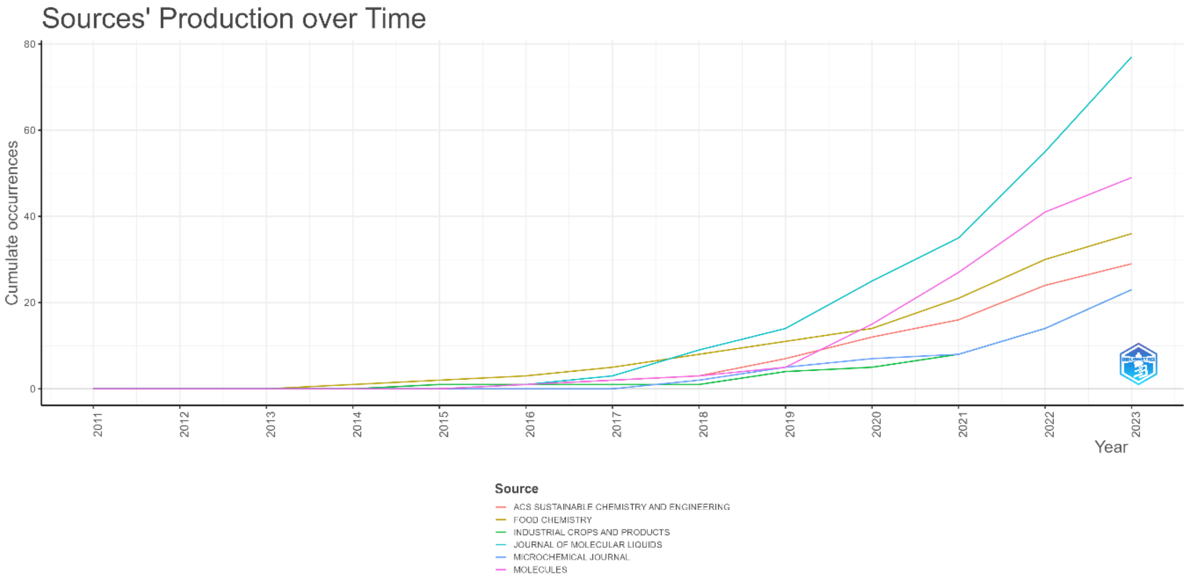


**Fig. 3. Source Growth Natural Deep Eutectic Solvent (NADES)**

From the curve above it can also be seen that the Journal of Molecular Liquids is in the first place, experiencing significant growth from 2013 to 2023, and has the potential to continue to grow in the following years. In 2011, NADES emerged as part of the broader group of Deep Eutectic Solvents (DES), focusing on the use of natural components [39]. Starting from this, NADES was recognized as a promising environmentally friendly solvent for the extraction of compounds from plant materials [40]. From 2013, the primary focus was on understanding the basic properties of NADES and their potential in fields like green chemistry and extraction processes, especially for bioactive compounds from plants. By the mid-2010s, research expanded to investigate NADES for food preservation, cosmetics, pharmaceuticals, and biotechnology, due to their ability to enhance solubility, reduce toxicity, and improve extraction efficiency [41,42]. The year 2014 marked the beginning of a significant increase in research on NADES. The number of publications on NADES has increased rapidly since 2014.

By 2020, the versatility of NADES had been widely explored, especially in the extraction of antioxidants, phenolic compounds, and proteins from food waste. The solvents were increasingly used in industrial applications such as biorefineries and cryopreservation. The development of NADES in 2020 such as,

1) Bioactive Compound Extraction

NADES proved effective in extracting antioxidants, phenolic compounds, and proteins from food waste and plant materials. Examples include the extraction of phenolic compounds from olive pomace, phlorotannins from seaweed, and bioactives from microalgae [43]. In the other hand, NADES has shown great potential in the extraction of various bioactive compounds, including anthocyanins. A study in 2023 showed that lactic acid (LA)-based NADES is highly polar and can increase the solubility of anthocyanins. In addition, ethylene glycol (EG) and butanediol (BDO)-based NADES are also effective in extracting anthocyanins with high monomeric anthocyanin content [44].

2) Lignin Isolation

NADES has been used as an environmentally friendly alternative for lignin isolation from agricultural waste. A study in 2023 showed that NADES was effective in extracting lignin from various biomass sources [45].

Recent research, around 2022-2023, further expanded NADES applications to areas like drug delivery systems and nanotechnology. Advances in the preparation techniques have made them more cost-effective and adaptable for specialized uses [46,47]. The development of NADES in 2022-2023 such as,

1) Drug Delivery Systems

NADES have been explored for improving drug bioavailability and absorption in pharmaceutical applications. They are being used to enhance the stability and oral bioavailability of some Chinese herbal medicines, thereby improving their therapeutic effects. NADES have shown potential in transdermal drug delivery systems (TDDS) by enhancing the percutaneous absorption of both small molecules and macromolecular drugs like proteins and small interfering RNAs [48].

2) Nanotechnology

Recent reviews highlight the application of NADES in nanotechnology. NADES are being combined with nanomaterial-based drug delivery systems to improve the safety and therapeutic efficacy of encapsulated drugs [49].

In the other hand, for food industry sectors, NADES have recently been explored for use in creating edible films. These films are made from biocompatible and biodegradable components, offering an eco-friendly alternative to traditional plastic-based food packaging. The NADES-based films are primarily used to enhance food preservation by forming protective barriers that can inhibit the growth of microorganisms, reduce oxidation, and improve the retention of food moisture [31,47]. The composition of NADES allows for flexibility in the development of films with desired properties such as water resistance, mechanical strength, and thermal stability. These properties can be adjusted by selecting specific hydrogen bond donors and acceptors during the formulation of the solvent. For example, NADES made from choline chloride and glycerol, or organic acids has shown potential in producing edible films with excellent antioxidant and antimicrobial activity, which can extend the shelf life of perishable food products [46,50].

In the other hand, development in creating eco-friendly active food packaging by utilizing anthocyanins extracted with NADES written by Velásquez et al. [51]. The study aimed to efficiently extract these compounds using ultrasound-assisted methods combined with specially designed NADES. The study tested several NADES formulations (such as those based on glycerol, choline chloride, and organic acids) for extracting anthocyanins from *Luma chequen* berries. These solvents proved effective, with anthocyanin yields ranging from 81.1 to 327.6 mg cyanidin 3-glucoside equivalents per 100 g of dry berry weight. Extracts from the NADES were incorporated into edible films made from carrageenan, which exhibited significant antioxidant and antibacterial activities. The films showed promise in enhancing food preservation, with inhibition of bacterial strains like *E. coli* and *S. aureus*.

#### 3.2.4 How do I analyze the thematic map that appears based on the title of the document with the NADES research theme?

This research will also analyze the thematic maps that appear based on density and centrality which are analyzed based on the title of the document with the research theme Natural Deep Eutectic Solvent (NADES) which is divided into 4 quadrants as illustrated in Fig. 4. These results were obtained from a semi-automatic algorithm by reviewing titles of all references that are the object of research. The upper left quadrant is a highly developed and isolated theme. This quadrant shows themes that are specific and rarely researched, but have high development, as indicated by high density but low centrality. While the bottom left quadrant is a theme that is developing or declining, this quadrant shows themes that have been used for a long time but are experiencing an increasing or decreasing trend with low density and centrality. The themes in this quadrant are deep eutectic solvents, solvents, and eutectics. Looking at developments with the Natural Deep Eutectic Solvent (NADES) sub-theme in recent years, the trend of words in this quadrant has increased.

Meanwhile, the upper right quadrant is a motor theme or driving theme which is characterized by high density and centrality, so it needs to be developed and is important to study in further research. Themes that appear in this quadrant are Solvent, Article, and Chemistry. Finally, the lower right quadrant is the basic theme and transverse themes which are characterized by high centrality but low density. These themes are important to include in research because they are general topics that are commonly used. Therefore, there are still many opportunities to develop the Natural Deep Eutectic Solvent (NADES) method.

### 3.3 Research Gap

The development of this research framework is based on several recent and important studies in the field, which were discovered from the results of bibliometric analysis. Table 2 presents the initial research framework in the form of a table of potential future research needs and gaps.

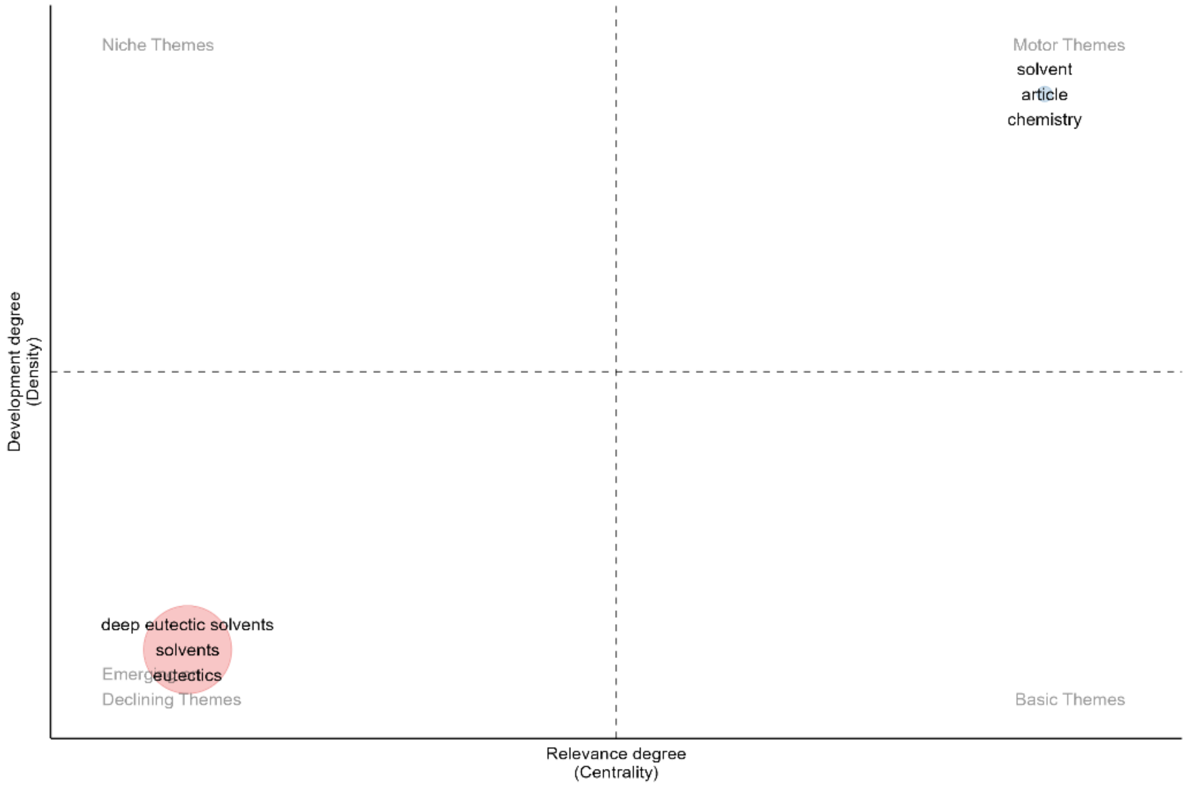


**Fig. 4. Thematic Map Natural Deep Eutectic Solvent (NADES)**

**Table 2. Preliminary research gap**

| Reference | Current latest research | Future needs and gaps |
|---|---|---|
| Boiteux et al. [52] | This research may focus on certain types of bioactive coatings or post-harvest control applications. The results may not be generalizable to other types of coatings or applications. | Further research is needed to compare the effectiveness of different types of coatings. |
| Saffarionpour [53] | This study does not provide information regarding analysis of experimental methods, results, or statistical analysis used in the research. This makes it difficult to assess the robustness and reliability of the findings. | In further research, it is necessary to explain the methods used in the research. |
| Kartini et al. [54] | The study does not delve deeply into the molecular mechanisms behind the superior extraction performance of NADES. Additionally, comparative analysis with existing solvents beyond environmental benefits could strengthen the study. | Further research needs to investigate the molecular mechanism of NADES extraction performance. |
| Kowalonek et al. [55] | The article does not provide data on the long-term stability of the films, which is crucial for commercial applications. The research is limited to chokeberry and lemon balm and may not apply to other plant extracts or broader food packaging uses. | Future research should conduct experiments so that edible film provides long-term stability and is applied to other products. |
| Obluchinskaya et al. [56] | The study does not mention replication or sample sizes, limiting statistical power. Long-term stability of extracts in NADES was not evaluated. | Future research should conduct experiments so that edible film provides long-term stability and redesign the experimental. |

Based on the results in Table 2, Current research in the field of bioactive coatings and post-harvest control applications shows several limitations and opportunities for further development. Although some studies have shown promising results, there are still gaps that need to be addressed in future research.

One of the main limitations is the lack of comparison of effectiveness between different types of coatings. Current research tends to focus on a specific type of coating or application, making it difficult to generalize the results. In addition, some studies do not provide sufficient information on the experimental methods, results, and statistical analyses used, which limits the assessment of the reliability of the findings.

In the context of the use of NADES, further research is needed to investigate the molecular mechanisms behind the superior extraction performance. Comparative studies with existing solvents, beyond environmental benefits, can also strengthen research in this area. Review by Al Hassan et al. [57] showed that Ionic Liquids (ILs) and Natural Deep Eutectic Solvents (NADES) are environmentally friendly solvents that are safer than traditional solvents due to their non-flammable, non-toxic, and biodegradable properties. Although NADES have higher vapor pressure and lower heat stability than ILs, which limits their resistance to extreme temperatures, ILs are effective in removing organic pollutants from wastewater. On the other hand, NADES are superior in terms of low production cost, chemical resistance to water, and ease of synthesis with high purity.

The long-term stability of edible films is a crucial aspect that needs further investigation, especially for commercial applications. Current research is limited to specific plant extracts and may not be applicable to broader use in food packaging. In addition, some studies do not mention replication or sample size, which limits the statistical power of the results.

To address this gap, future research needs to focus on comparing the effectiveness of different coating types, elucidating more detailed research methods, investigating the molecular mechanism of NADES, and evaluating the long-term stability of edible films. In addition, more robust experimental designs with adequate sample sizes and proper replication are needed to improve the reliability and applicability of research results in this area.

## 4. CONCLUSION

This research uses quantitative methods using bibliometric data analysis. Data analysis using bibliometric analysis of NADES produced 1,045 Scopus documents start form 2011 until 2023 for article and review. Quantitative data obtained based on bibliometric analysis has revealed trends and developments in NADES research. In research with the theme NADES, the Journal of Molecular Liquids is the journal in the top position with a total of 80 published documents and continues to develop every year. Journal of Molecular Liquids, a high-impact journal, focuses on fundamental aspects of structure, interactions, and dynamic processes in simple and complex molecular fluids with an H-index of 21.0. The growth trend of NADES publications tends to increase every year, with Journal of Molecular Liquids leading significant growth from 2013 to 2023. NADES research has been growing rapidly since 2011, with increasingly broad and diverse applications, especially in the fields of bioactive compound extraction, pharmaceuticals, and food technology. There are still many opportunities for the development of NADES methods, given their position in the thematic map.

Although recent studies have shown promising results, significant gaps still need to be addressed. Future research should focus on more comprehensive comparisons, more detailed method explanations, deeper understanding of molecular mechanisms, and long-term stability evaluations to improve the applicability of NADES in various fields. Future research needs to focus on several key aspects. First, a comprehensive comparative study is needed to assess the effectiveness of different types of coatings. Second, a more detailed explanation of the research methodology should be a priority. Third, an in-depth exploration of the molecular mechanism of NADES is essential for better understanding. Fourth, a comprehensive evaluation of the long-term durability of edible films should be conducted. In addition, to improve the reliability and relevance of research results in this area, a more robust experimental design with adequate sample size and proper replication is essential. with adequate sample size and proper replication. On the other hand, because this research is limited to Scopus indexed journals, future reviews can add other reputable international journal sources such as WOS or PubMed.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc have been used during writing or editing of this manuscript.

**Details of the AI usage are given below:**

1. Perplexity AI Pro (How has NADES developed since 2011 until now?)

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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