

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

1 **ABSTRACT**

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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.

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 title, 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.

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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 (NADES) 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 [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, [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].

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

69
70 Research on the use of NADES in alginate extraction has emerged as an interesting
71 research topic in response to concerns over the environmental and human health impacts of
72 conventional chemical solvents. NADES has been successfully used for the extraction of
73 polyphenols and bioactive compounds from natural products [15],[16],[17]. This shows great
74 potential for applications in alginate extraction. The combination of the environmentally
75 friendly solvent properties of NADES and its ability to dissolve polar and non-polar
76 compounds can open new avenues in the alginate extraction process. This research has the
77 potential to not only produce a purer and better-quality final product but also reduce negative
78 impacts on the environment and speed up the extraction process.

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

91
92 Therefore, the objectives of this study are to (a) identify research developments and trends
93 in NADES, and (b) develop a NADES research gap for future research. This research uses a
94 quantitative research approach from bibliometric analysis. Specifically, the scope of this
95 research is based on the article and review where experts based on their experience in the
96 field of NADES. This research will contribute to the future development of Alginate Extraction
97 and NADES from the research gaps revealed in the research framework. The structure of
98 this paper is as follows. Section 2 explains the background of this research and related

99 research. Section 3 explains the research method. Section 4 data analysis. Section 5 is the
100 final section that summarizes the findings.

101

102 **2. METHODOLOGY**

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104 **2.1 Related Works**

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

110 The research conducted on Alginate Extraction was entitled "Seaweeds as Promising
111 Resource of Bioactive Compounds: Overview of Novel Extraction Strategies and Design of
112 Tailored Meat Products" by [22]. In this research, the aspects collected relate to the latest
113 technology used to obtain and isolate bio compounds from seaweed. The use of whole
114 seaweed and its bioactive extracts to develop meat foods that provide health benefits while
115 reducing components considered unhealthy in meat is under review [23],[24]. In addition, the
116 prevention of oxidation events is also explained. However, there are still several challenges
117 regarding the organoleptic and sensory properties of the products produced, which affect
118 consumer acceptance. So, more research is needed to address the gap to enable seaweed-
119 based meat products to be marketed.

120 Furthermore, in research on NADES in the paper entitled "Green extraction of value-added
121 compounds form microalgae: A Short Review on NADES and Related Pre-treatments" by
122 [25]. This research discusses the potential application of NADES for the extraction of
123 intracellular compounds from microalgae biomass and related pre-treatment to increase
124 extraction efficiency. NADES are formed from a mixture of natural components, usually
125 consisting of a hydrogen bond acceptor (HBA) such as choline chloride and a hydrogen
126 bond donor (HBD) such as an organic acid, sugar, or amino acid. The formation of NADES
127 is driven by hydrogen bonding between the components, resulting in a eutectic mixture with
128 a melting point lower than that of the individual components. Key properties of NADES
129 include high biodegradability, low toxicity, biocompatibility, low volatility, and high
130 solubilization capacity [26],[27].

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132 **2.2 Research Question**

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

138 RQ 1 : How many research documents are published by each journal based on the level
139 of relevance to the theme of NADES?

140 RQ 2 : What is the impact of each journal that publishes papers on the theme of NADES?

141 RQ 3 : How are growth resources relevant to NADES research?

142 RQ 4 : How to analyze the thematic map that appears based on the title of the document
143 with the research theme NADES?

144 The bibliometric analysis in this study followed several basic protocols in the review process
145 [28]. This process is carried out systematically and uses explicit stages so that it can be
146 reproduced by other researchers. Bibliometric analysis can also be carried out with a mind-
147 mapping approach that shows the limits of knowledge [29]. Bibliometric analysis is generally
148 used in various scientific disciplines and focuses on quantitative studies in journal articles,
149 books, or other forms of written publications [30]. In this research, five main steps of
150 bibliometric analysis will be carried out, consisting of determining search keywords, checking
151 initial search results, refining search results, compiling related data, and data analysis.
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153 **2.3 Data Collection**

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155 This study uses the Scopus database. Scopus has several advantages for bibliometric
156 analysis, such as its broad and multidisciplinary coverage. The quality of Scopus data is also
157 high because it goes through strict selection, so the validity of the analysis results is more
158 guaranteed. Detailed citation data and the ability to perform historical analysis also make it
159 superior in identifying long-term patterns. The article sourced by article title, abstract, and
160 keywords. The keyword "*Natural Deep Eutectic Solvents*" was applied. The period used 2011
161 when the first publication on NADES was published until 2023 when the data collection for
162 this article was first carried out. The criteria taken are journal articles and review journals
163 only. Thus, 1,045 articles and reviews were obtained with the keyword "Natural Deep
164 Eutectic Solvents" from 2011 to 2023. This research is limited to articles indexed in Scopus
165 due to researcher limitations.
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167 **2.4 Data Processing**

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169 The data used is then exported into *.bib* format. R Studio software with bibliometrics
170 packages was used for analysis data. Scopus uses Author ID and Affiliation ID to avoid
171 mistakes in identifying authors or institutions. This reduces the risk of misattribution and
172 ensures more accurate bibliometric analysis. So that data preprocessing does not need to
173 be done much. The analysis used is adjusted to the RQ that has been prepared previously
174 so that the results obtained can answer the RQ that has been proposed
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176 **2.5 Interpretation Result**

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

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189 The search was carried out on December 2023 using keywords in the form of search strings
190 relevant to NADES where keywords were searched based on the title, keywords and
191 abstract of the article. Based on the keywords that have been determined, an article search
192 process is carried out in the electronic database used as a source of information. The
193 electronic database used in this research is Scopus, considering that Scopus is the largest
194 reputable scientific database currently available and provides various journal articles that

195 have gone through a peer-review process [31]. In this way, the quality obtained can be
196 guaranteed.

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198 **4.1 Initial Search Result**

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

203 **Table 1. The term “Natural Deep Eutectic Solvent” appears for the first time in the**
204 **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 <i>Carthamus tinctorius L.</i>	Analytical Chemistry	2013
Egan, P.A., Van Der Kooy, F.	<i>Xanthorrhizol</i> and curcuminoids NADES extraction from <i>C. xanthorrhiza</i>	Chemistry and Biodiversity	2013

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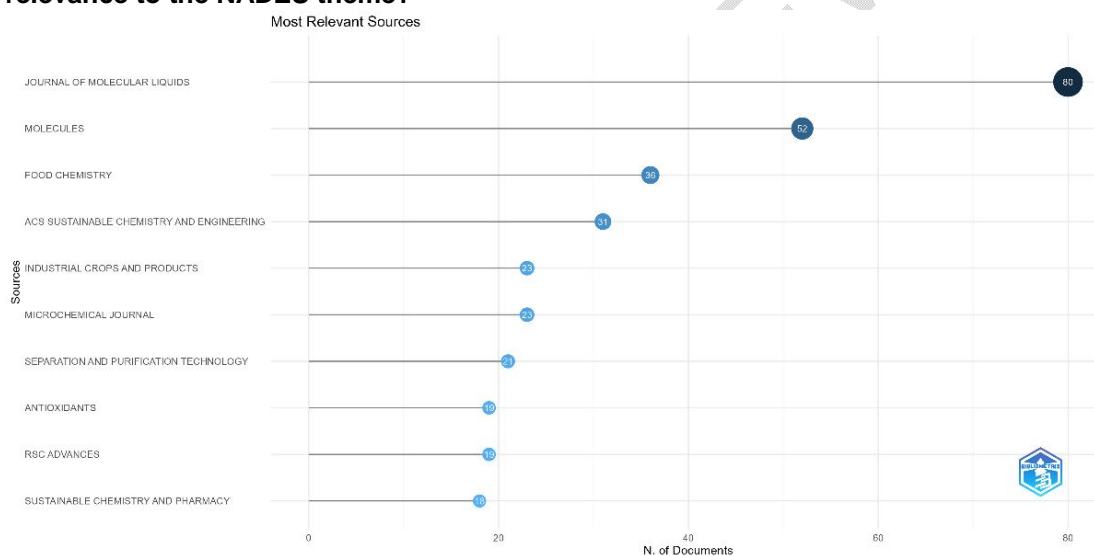
206 Research by [32] showed that NADES can act as an alternative solvent in biochemical and
207 physiological processes of cells, especially in extreme conditions such as drought and high
208 temperatures. Research by [33] discussed the synthesis of 5-arylidene-2-imino-4-
209 thiazolidinones compounds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

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

228 229 4.2 Statistical Compilation of Data

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

237 238 How many research documents are published by each journal based on their level of 239 relevance to the NADES theme?

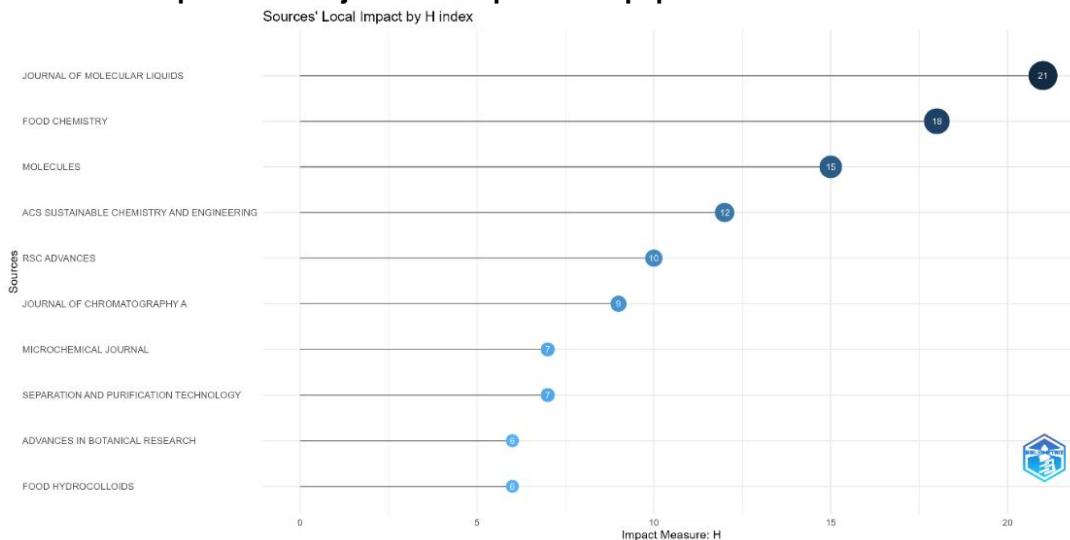


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241 **Fig. 1. Most Relevant Source Natural Deep Eutectic Solvent (NADES)**

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

251
252 An example of a journal published by the Journal of Molecular Liquids is the journal entitled
253 "NADES as Potential Solvents for Anthocyanin Pectin Extraction from *Myrciariacauliflora*fr
254 Product: In Silico and Experimental Approach Solvent Selection" written by [37]. In this
255 research, silico and experimental approaches were combined to select NADES compounds
256 aimed at selective and sequential extraction of anthocyanins and pectin from

257 *Myrciariacauliflora* products. The results obtained from this research are based on in silico
 258 evaluation, NADES and the target compound show amphoteric character which indicates an
 259 affinity between the two. Acid-based NADES showed the highest affinity in the H-bond
 260 acceptor region, while betaine and water-content NADES showed the best affinity in the H-
 261 bond donor region. However, all NADES showed low affinity towards non-polar compounds.
 262 **What is the impact of each journal that publishes papers on the NADES theme?**



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Fig. 2. Source Impact Natural Deep Eutectic Solvent (NADES)

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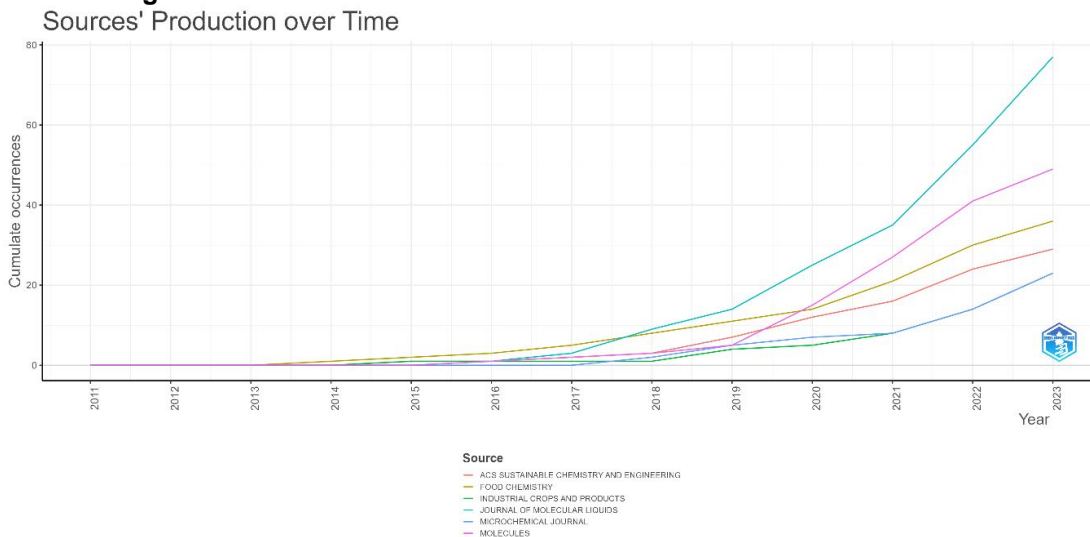
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Journal calculations are not only based on the quantity produced or its relevance. However, this research was also carried out based on the impact produced by each journal that published papers on the theme of Natural Deep Eutectic Solvent (NADES) 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. Figure 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 [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.

291 **How is the growth of sources relevant to NADES research?**



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

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

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

316
317 By 2020, the versatility of NADES had been widely explored, especially in the extraction of
318 antioxidants, phenolic compounds, and proteins from food waste. The solvents were
319 increasingly used in industrial applications such as biorefineries and cryopreservation. The
320 development of NADES in 2020 such as,

- 321 1) Bioactive Compound Extraction
322 NADES proved effective in extracting antioxidants, phenolic compounds, and proteins
323 from food waste and plant materials. Examples include the extraction of phenolic
324 compounds from olive pomace, phlorotannins from seaweed, and bioactives from
325 microalgae [43]. In the other hand, NADES has shown great potential in the extraction
326 of various bioactive compounds, including anthocyanins. A study in 2023 showed that
327 lactic acid (LA)-based NADES is highly polar and can increase the solubility of

328 anthocyanins. In addition, ethylene glycol (EG) and butanediol (BDO)-based NADES
329 are also effective in extracting anthocyanins with high monomeric anthocyanin content
330 [44].

331 2) Lignin Isolation

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

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

340 1) Drug Delivery Systems

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

347 2) Nanotechnology

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

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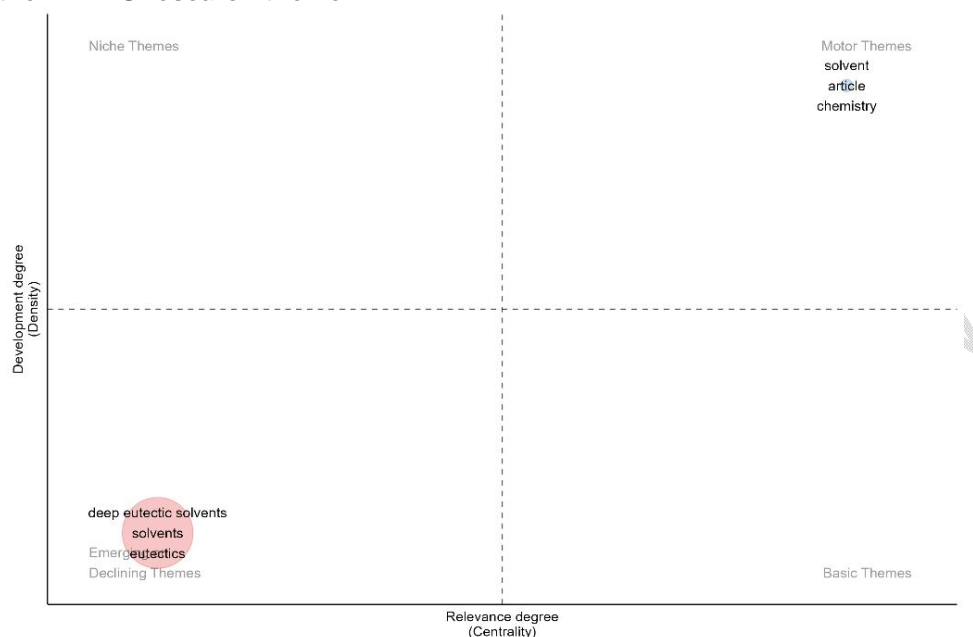
352 In the other hand, for food industry sectors, NADES have recently been explored for use in
353 creating edible films. These films are made from biocompatible and biodegradable
354 components, offering an eco-friendly alternative to traditional plastic-based food packaging.
355 The NADES-based films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

364

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

375

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



378
379 **Fig.4. Thematic Map Natural Deep Eutectic Solvent (NADES)**
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381 This research will also analyze the thematic maps that appear based on density and
382 centrality which are analyzed based on the title of the document with the research theme
383 Natural Deep Eutectic Solvent (NADES) which is divided into 4 quadrants as illustrated in
384 Figure 4. These results were obtained from a semi-automatic algorithm by reviewing titles of
385 all references that are the object of research. The upper left quadrant is a highly developed
386 and isolated theme. This quadrant shows themes that are specific and rarely researched, but
387 have high development, as indicated by high density but low centrality. While the bottom left
388 quadrant is a theme that is developing or declining, this quadrant shows themes that have
389 been used for a long time but are experiencing an increasing or decreasing trend with low
390 density and centrality. The themes in this quadrant are deep eutectic solvents, solvents, and
391 eutectics. Looking at developments with the Natural Deep Eutectic Solvent (NADES) sub-
392 theme in recent years, the trend of words in this quadrant has increased.

393
394 Meanwhile, the upper right quadrant is a motor theme or driving theme which is
395 characterized by high density and centrality, so it needs to be developed and is important to
396 study in further research. Themes that appear in this quadrant are Solvent, Article, and
397 Chemistry. Finally, the lower right quadrant is the basic theme and transverse themes which
398 are characterized by high centrality but low density. These themes are important to include in
399 research because they are general topics that are commonly used. Therefore, there are still
400 many opportunities to develop the Natural Deep Eutectic Solvent (NADES) method.

401 402 **4.3 Research Gap** 403

404 The development of this research framework is based on several recent and important
405 studies in the field, which were discovered from the results of bibliometric analysis. Table 3
406 presents the initial research framework in the form of a table of potential future research
407 needs and gaps.
408

Table 2. Preliminary Research Gap

Reference	Current Latest Research	Future Needs and Gaps
Boiteux <i>et al.</i> , [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 <i>et al.</i> , [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.
Kowaloneket <i>al.</i> , [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 <i>et al.</i> , [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.

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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 [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

429 temperatures, ILs are effective in removing organic pollutants from wastewater. On the other
430 hand, NADES are superior in terms of low production cost, chemical resistance to water, and
431 ease of synthesis with high purity.

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

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

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446 4. CONCLUSION

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

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

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