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Review

New horizons in the extraction of bioactive compounds using deep eutectic solvents: A review

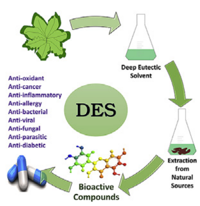
Mohamad Hamdi Zainal-Abidin [a], Maan Hayyan [a, b, *], Adeeb Hayyan [a, b], Natesan Subramanian Jayakumar [a]

[a] University of Malaya Centre for Ionic Liquids (UMCiL), Department of Chemical Engineering, University of Malaya, Kuala Lumpur 50603, Malaysia
[b] Institute of Halal Research University of Malaya (IHRUM), Academy of Islamic Studies, University of Malaya, Kuala Lumpur 50603, Malaysia

HIGHLIGHTS

- Deep eutectic solvents (DES) have drawn significant attention in the last decade.
- DES have distinctive physicochemical properties and chemical characteristics.
- Recently, DES have been introduced as promising extractants for bioactive compounds.
- This is the first comprehensive review aims to cover this research field.
- DESs are expected to play a pivotal role in the extraction of bioactive compounds.

GRAPHICAL ABSTRACT



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ABSTRACT

With the rapid development of ionic liquid analogues, termed ‘deep eutectic solvents’ (DESs), and their application in a wide range of chemical and biochemical processes in the past decade, the extraction of bioactive compounds has attracted significant interest. Recently, numerous studies have explored the extraction of bioactive compounds using DESs from diverse groups of natural sources, including animal and plant sources. This review summarizes the-state-of-the-art effort dedicated to the application of DESs in the extraction of bioactive compounds. The aim of this review also was to introduce conventional and recently-developed extraction techniques, with emphasis on the use of DESs as potential extractants for various bioactive compounds, such as phenolic acid, flavonoids, tanshinone, keratin, tocols, terpenoids, carrageenans, xanthones, isoflavones, α-mangostin, genistin, apigenin, and others. In the near future, DESs are expected to be used extensively for the extraction of bioactive compounds from various sources.

Contents

* Corresponding author. University of Malaya Centre for Ionic Liquids (UMCiL), University of Malaya, Kuala Lumpur 50603, Malaysia.
E-mail addresses: maan_hayyan@yahoo.com, maan.hayyan@gmail.com (M. Hayyan).

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1. Introduction

The growth of the pharmaceutical industry has led to the rapid development of various methods for the extraction and separation of bioactive compounds. Natural bioactive components normally come from secondary metabolites. Although these secondary metabolites are slightly less important than primary metabolites (i.e., nucleic acid, amino acid, sugar) to living organisms, they are essential for several vital mechanisms, such as stress-response and natural defense mechanisms [1]. Natural bioactive components can be obtained from diverse living organisms, such as fungi, plants, algae, fruit, and microbes, but different extraction and separation techniques are required for different bioactive compounds [2], which can be categorized as phenylpropanoids, isoprenoids, alkaloids, flavonoids, and polyketides [3]. To date, 60% of approved anticancer drugs originated from natural bioactive compounds. In addition to their use in the pharmaceutical industry, these bioactive compounds also are used extensively in the production of agrochemicals, nutraceuticals, and cosmetics [1].

There are two main types of extraction and separation techniques, i.e., conventional and modern extraction techniques [1,4]. The conventional methodologies include maceration, percolation, Soxhlet extraction, and solvent extraction [5]. Typically, these methodologies involve long, complicated extraction periods, high cost (due to the volume of solvents required), low yield due to thermal degradation, the use hazardous and flammable solvents, and inadequate disposal and recycling practices for the solvents. The modern techniques include enzyme-assisted extraction, ultrasound-assisted extraction, microwave-assisted extraction, subcritical fluid extraction, supercritical extraction, and high pressure-assisted extraction [4,5]. These extraction methodologies generally have much better efficiency, shorter extraction time, lower cost, and higher purity of the extracted compounds. However, there are several issues associated with both techniques, including the solvents' toxicity, thermal instability, polarity, solubility, and poor selectivity. Other issues include the types and concentrations of the solvents, their moisture content, the recovery of bioactive components from the solvent, and changes in the chemical structures of compounds during extraction due to ionization, hydrolysis, and oxidation [6,7]. Water is the most commonly-used solvent in the pharmaceutical, agricultural, cosmetic, and food industries because its physical and chemical characteristics satisfy most of the obligatory conditions required by the U.S. Food and Drug Administration (FDA) and the European Union [5]. However, water is only effective as an extraction solvent for polar and hydrophilic bioactive compounds; it is less effective for non-polar and hydrophobic compounds. Water-soluble impurities are another major problem that may affect the extraction process [1]. Therefore, there is high demand for a suitable universal solvent for extraction.

Currently, more alternative chemical methods that produce less adverse effects on the environment are being explored to replace the conventional chemical methods. One example is the use of green solvents to replace the traditional hazardous solvents that are used extensively in industry [8]. In this context, ionic liquids (ILs) have gained considerable attention due to their unique physical and chemical characteristics [9,10]. ILs are molten salts that are liquids at temperatures below 100 °C, and they usually consist of bulky and asymmetric organic cations and organic or inorganic anions [4,11]. They have some attractive attributes, such as non-flammability, high thermal stability, chemical stability, and low volatility [12]. Over the last two decades, due to their remarkable capability to dissolve a wide range of bioactive compounds from various biomass matrices [13], there has been a significant increase in the use of ILs as green solvents for the extraction, separation, and purification of natural bioactive compounds [4]. The large numbers of ion combinations that are possible with ILs make it possible to design task-specific solvents [11], which circumvents the limitations of conventional extraction methodologies by providing more effective extraction techniques. However, there are concerns about the application of ILs for the extraction of bioactive compounds that relate to the toxicity of these compounds, their potential effects on health and the environment, and the high cost associated with their synthesis and purification requirements [1,14–17]. Thus, the search for alternative solvents to replace the 'controversial' ILs and other traditional solvents has led to the use of deep eutectic solvents (DESs) for the extraction of bioactive compounds. Thus, increased attention has been focused on the applications of DESs that are viewed as being analogous to ILs. DESs have physicochemical properties that are very similar to those of ILs [18], and they have been reported biodegradable and have lower toxicity and lower cost than ILs [8,18,19]. In recent research, it was reported that the cytotoxic levels of DESs were affected significantly by the hydrogen bond donor that was used [12,20].

Abbott et al. [21] introduced DESs as a system formed from a mixture of two or more Lewis acids and bases or Brønsted-Lowry acids and bases that has the lowest freezing point compared with its starting constituents. The physical structure of some DESs is thought to be similar to that of the ILs. However, DESs, in general, are different in terms of the source of the starting ingredients and