Chapter 6
Trends and Prospects for Deep Eutectic Solvents

6.1 Sustainable Chemistry

The trends regarding the chemical industry for the twenty-first century are along several paths [1]. One trend is the replacement of fossil raw materials (oil, natural gas) or mined minerals with renewable sources, such as biomass or recycled wastes. Sustainable processes for the valorization of waste biomass by its conversion to biofuels (biodiesel) via green processes are currently in the forefront of research. Trends in the minimization of industrial wastes and their treatment for a sustainable environment are also currently of importance [2]. The advent of neoteric solvents has been an important step in this direction, deep eutectic solvents playing a major role in this process. Another trend is the replacement of stoichiometric processes by catalytic ones, in particular, those involving enzymes, and heterogeneous catalysis replacing homogeneous one for the purpose of recycling the catalyst. Deep eutectic solvents are involved in this trend too. The use of mechano-chemistry, ultrasound, and microwaves as energy inputs rather than the application of external heat is another trend used in the synthesis of organic materials [3].

Deep eutectic solvents, also called low-transition temperature mixtures, have been deemed to be "the organic reaction medium of the century" [4]. These solvents may play the role of an active catalyst besides serving as the solvent for the reaction. For example, the deep eutectic solvents formed between choline chloride and zinc chloride or trimethylcyclohexylammonium methanesulfonate and *p*-toluenesulfonic acid use their acidic natures for the catalysis of the esterification of long-chain and aromatic carboxylic acids with alkanols. These are illustrations of one of the many organic reactions that have been and can be carried out in deep eutectic solvents, including alkylation, cyclization, condensation, redox, and organometallic reactions [4]. A large portion of the publications dealing with deep eutectic solvents pertain to a choline salt as one of the components. The application of such salts in organic transformations has been recently reviewed [5], including reactions catalyzed by choline (cholinium) chloride without or with metallic Lewis

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acids or carboxylic acids or by choline hydroxide, or reactions involving oxidizing agents. Such ionic liquids are said to be “the future solvents of the chemical and allied industry” because of their “green” properties. The use of deep eutectic solvents in polymerization reactions has recently been reviewed too [5], noting that a monomeric component of the solvent itself may undergo polymerization, or else the liquid serves just as a solvent for the reaction. As examples, acrylic or methacrylic acid, acting as the hydrogen bond donor of the deep eutectic mixture with choline chloride, can thus be polymerized. Another example is the polymerization of hydroxyethylmethacrylate in the choline chloride/ethylene glycol deep eutectic solvent [6]. These methods of polymerization should become more extensively used because of the “greenness” of the deep eutectic solvents.

Biomass treatment in deep eutectic solvents has come to the forefront of technical innovation along two paths: biocatalysis by such solvents that are compatible with enzymes and biodiesel production from lignocellulose. Enzymes, such as lipases, proteases, epoxide hydrolases, and peroxidases can be used in deep eutectic solvents, such as choline-based ones, or their mixtures with water [6]. Highly polar substrates, such as carbohydrates and nucleosides, can be treated in deep eutectic solvents, in those cases when water cannot be used because it may hydrolyze the products. Pretreatment and saccharification of lignocellulose can thus be carried out in deep eutectic solvents in order to produce biodiesel liquid fuel [7]. The tunability and biodegradability of deep eutectic solvents is stressed in [8], where organocatalysis (basic or acidic) and biotransformations in these solvents are dealt with. “Given their promising features, it may be expected that many applications in these areas will appear in the coming years” is a conclusion of this report. In another recent review [9], the eco-friendly and sustainable aspects of deep eutectic solvents are emphasized and many organic synthetic reactions are described. The recent progress concerning deep eutectic solvents in biocatalysis is discussed in [10], where the understanding of how these solvents affect the biocatalytic reaction is said to lead to new applications.

Biomass valorization into valuable chemicals is attracting much attention in recent years, and deep eutectic solvents play a leading role in this direction. Biodiesel, a liquid fuel resulting from the transesterification of vegetable oils or animal fats in deep eutectic solvents has gained tremendous attention in recent years [11]. These solvents act also as cosolvents, catalysts, and extracting agents, and choline chloride/zinc chloride is an example of a solvent and acid catalyst. Lipase is an active enzyme for biodiesel production in, e.g., choline chloride/glycerol solvent, and this solvent is also effective for the extraction of glycerol from crude biodiesel. The recycling of the deep eutectic solvents is also dealt with in this review [11]. Lignocellulosic biomass is a source of lignin that can be valorized and the biomass can be pretreated and fractionated into its components (cellulose, hemicellulose, and lignin) in these solvents [12]. Starch is relatively soluble in some deep eutectic solvents, e.g., choline chloride/malic acid and lignin is quite soluble in certain deep eutectic solvents (e.g., betaine/lactic acid), but cellulose is hardly soluble in deep eutectic solvents so that the biomass can be fractionated. Degradation of the cellulose to 5-hydroxymethylfurfural (HMF) is a target of an application described in detail [12].

On a quite different level is the relation of natural deep eutectic solvents to biochemical and physiological processes. Such solvents (NADES) can act as cryoprotective agents, preventing the formation of ice crystals in cells. In some insects and even in a vertebrate living thing (frog), their intervention is useful. An example is the combination urea/glucose/amino acids in frogs [13]. The formation of non-water-soluble compounds, such as rutin, quercetin, cinnamic acid, carthamin, taxol, ginkgolide B, and 1,8-dihydroxyanthaquinone in plants has been explained by the role that natural deep eutectic solvents play in their formation and transport [14]. This unexpected activity/stability is explained by the large and strong hydrogen bond network formed in such solvent mixtures. These eutectic mixtures may also explain the holding of water in plants against its evaporation in very arid areas. Molecularly imprinted polymers (MIPs) are of increasing interest due to their specific binding sites and molecular recognition ability. Their production in deep eutectic solvents has been compared with that in room temperature ionic liquids in [15].

The use of deep eutectic solvents for biocatalysis has recently been reviewed [16]. These solvents may have a significant effect on selectivity, stability, and activity of enzymes through their H-bond basicity, ion kosmotropicity, amphiphilicity, hydrophobicity, polarity, and viscosity. “In particular, the combination of reaction and separation will be of interest in the future as here the potential of deep eutectic solvents can be exploited to full extent.” Deep eutectic solvents “have been used as media, solvents/cosolvents or as catalysts for various biological processes, it seems clear that they possess enormous potential for beneficial applications in the future” [17]. This quote is taken from a recent review of the applications in biotechnology and bioengineering—promises and challenges, where, however, it is stressed that the safety (toxicity) concern of these mixtures must be sufficiently addressed.

6.2 Materials and Nanotechnology

The many applications described in Sect. 4.4 point to the expected development foreseen for the use of deep eutectic solvents in the field of nanotechnology. Novel materials or materials with novel properties produced in deep eutectic solvents for their use in heterogeneous catalytic activities are one aspect of the emerging trends. These new nanomaterials, gold nanowire networks, are good candidates for future applications in catalysis [18]. The high viscosity of the Ethaline deep eutectic solvent helps the synthesis of gold nanofoams, “a synthetic strategy that may open a new avenue to the DES-assisted synthesis of inorganic nanofoams and functional devices” [19]. Turning from metals to oxides, it was suggested that “as a burgeoning field, the development of DESs assisted routes for the synthesis of TiO_2 nanomaterials offers both opportunities and challenges for future developments in nanomaterials synthesis." [20]. Iron oxides as "green materials for the photo-electrochemical splitting of water", produced by a microwave-assisted solvothermal methodology in Reline [21] are another example of prospective uses of deep eutectic solvents. Formation of "functional materials, including noble metals, porous carbonaceous materials, transition metal compounds" in deep eutectic solvents (DES) should "inspire scientists to use DES as a powerful tool to push the frontiers of materials, energy and environmental science" is proposed in [22].

Another trend in the use of deep eutectic solvents for the production of nanomaterials is the all-in-one-pot synthetic methods. The choline chloride/$CaCl_2 \cdot 6H_2O$ reaction medium provided "calcium-active sites, and electrosteric stabilization required for formation and growth control of fluoroapatite nanoparticles … introducing and developing a simple, rapid, and sustainable method toward green and economical synthesis of fluoroapatite nanobiomaterials" [23]. In a one-step process, pyrolysis of a mixture of seaweed granules and choline chloride/$FeCl_3$ deep eutectic solvent was employed as a source of iron, as a template, and as a catalyst for the production of Fe_3O_4/Fe-doped graphene nanosheets [24].

The prospects for using deep eutectic solvents in analogy with the already established use of room temperature ionic liquids in nanotechnology have been summarized a few years ago in [25].

Eutectogels (ETGs) have recently been introduced as a new class of solid composite electrolytes and been prepared easily via a sol–gel route in the deep eutectic solvent constituted by lithium bis(trifluoromethane)sulfonamide with *N*-methylacetamide. These solid composite electrolytes demonstrate an acceptable thermal and electrochemical stability and high ionic conductivity at room temperature. The Li/$LiFePO_4$ half cells assembled with ETGs deliver a stable and reversible specific capacity for over 60 cycles. There are good prospects for the application of ETGs in lithium ion or metal batteries, hence opening up new horizons toward safer, cheaper and more performant devices [26]. A ternary mixture of 2:3:1 choline chloride/urea/glycerol has been used to form a novel gel polymer electrolyte from phthaloylated starch that forms a bioelectrolyte with appreciable conductivity [27].

6.3 Analytical Chemistry, Sorption and Extraction

There are many prospects for natural deep eutectic solvents in analytical chemistry, where they may be used for sample preparation as solvents, as extracting agents, or as reaction media [28], and may further be used in liquid chromatography. Gluten may be extracted from foods for its subsequent determination by using natural deep eutectic solvents, such as the water-diluted citric acid/fructose combination with sonification [29]. Environmentally friendly and nonpolluting solvent pretreatment of palm oil samples for polyphenol analysis using choline chloride based deep eutectic solvents [30] and speciation, pre-concentration and determination of selenium (IV) and (VI) species in water and food samples with choline chloride/phenol

[31] are other examples of the emerging use of such solvents in analytical chemistry. The present applications of deep eutectic solvents in analytical chemistry and trends in these applications are reviewed in [32].

Indirect applications of deep eutectic solvents for a sustainable environment, which may show trends in future applications, are illustrated by the use of such solvents for the preparation of efficient sponges for selective removal of oils from water. Hydrophobic, super-absorbing aerogels result from cellulose nanofibrils pretreated by Reline and then silylated, which have the desired properties [33].

Deep eutectic solvents were expected to play a major role in the extraction of bioactive compounds from various sources for analytical purposes [34]. An overview as well as challenges and opportunities regarding the application of deep eutectic solvents for the extraction of phenolic compounds extraction are presented in [35].

The capture of carbon dioxide in deep eutectic solvents as alternatives to the capture in organic amines or in room temperature ionic liquids is gaining attention. It is possible to develop novel deep eutectic solvents with promising absorption capacity, but more studies are needed to determine the absorption mechanism and to clarify how these sorbents can be adjusted and fine-tuned to be best tailored as optimized media for carbon dioxide capture [36].

6.4 Unconventional Deep Eutectic Solvents

Most of the studies regarding the use of deep eutectic solvents heretofore have used conventional combinations of a hydrogen bond accepting salt (such as choline chloride, tetrabutylammonium chloride, or methyltriphenylphosphonium bromide) and an organic hydrogen bond donating agent (such as urea, ethylene glycol, glycerol, or malonic acid), and some such solvents are commercially available (Reline, Ethaline, Glyceline, Maline). Their applications have been described in Chaps. 4 and 5, and trends regarding these applications are presented above.

More recently, nonconventional deep eutectic solvents that need not be ionic have been added to the tool kit of reaction media and extractants. These include natural deep eutectic solvents (NADES) based on zwitterionic amino acids (betaine, proline), solvents based on lidocaine, menthol, or glucose with carboxylic acids, or mixtures of long-chain carboxylic acids. Deep eutectic solvents based on water as the hydrogen bond donating agents with *N*-alkyl heterocyclic salts or with inorganic salt hydrates as the accepting agents have also been introduced, and their applications are promising but still pending.

However, a deep eutectic solvent based on betaine with polypropylene glycol 400 has recently been introduced for aqueous biphasic extraction systems used in pigment partitioning [37]. The use of the deep eutectic solvent formed by menthol with dodecanoic acid for the extraction of the lower alkanols from aqueous solutions has recently been proposed [38]. Deep eutectic solvents comprising mixtures of two long-chain carboxylic acids have recently been promoted as hydrophobic extracting agents [39].

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