Review

Combined Graphene-Based Materials and Deep Eutectic Solvents for Sustainable Sensing Applications

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Combined Graphene-Based Materials and Deep Eutectic Solvents for Sustainable Sensing Applications

Rossella Svigelj [1,*], Rosanna Toniolo [1], Cristina Bertoni [2] and Alessandro Fraleoni Morgera [3,*]

[1] Department of Agrifood, Environmental and Animal Sciences, University of Udine, Udine, Italy
[2] Electrolux Italia SpA - Porcia (Pordenone), Italy
[3] Department of Engineering and Geology - University of Chieti-Pescara, Pescara, Italy
* Correspondence:

Abstract: The recently explored synergistic combination of graphene-based materials and deep eutectic solvents (DESs) is opening novel and effective avenues for developing sensing devices with optimized features. In more detail, remarkable potential in terms of simplicity, sustainability, and cost-effectiveness have been demonstrated for sensors, resulting in the creation of hybrid devices with enhanced signal-to-noise ratio, linearity, and selectivity. Therefore, this review aims to provide a comprehensive overview of the currently available scientific literature discussing investigations and applications of sensors that integrate graphene-based materials and deep eutectic solvents, with an outlook for the most promising developments of this approach.

Keywords: graphene; deep eutectic solvents; sensors; ionic liquids; NADES; nanocomposites

1. Introduction

Sensing strategies are evolving towards technologies more and more focused on ultra-low detection threshold and highly selective devices. These performances can be enabled by nanotechnologies, operated thanks to either lithographically defined, top-down structures [1–3] or chemically/biochemically obtained, bottom-up constructs [4–6]. A kind of bridge between the top-down and the bottom-up approaches can be represented by graphene-based nanostructures. Graphene is a two-dimensional material composed of a single layer of carbon atoms arranged in a hexagonal lattice structure [7]. Andre Geim and Konstantin Novoselov isolated and characterized graphene in 2004, an achievement for which they were awarded the Nobel Prize in Physics in 2010 [8]. A scientific database research carried out in November 2023 using the keyword "graphene" yielded over 203.000 papers, including approximately 10.000 review papers. Leaving aside the peculiar physical properties of the material, on which the reader can find a wealth of information in uncountable excellent reviews (see for example [9–11]), the applications are almost infinite: among some of the most successful and/or investigated ones, it is possible to mention general electronics and optoelectronics [12–15], energy-related applications [16,17], catalysis [18,19], medicine [20–23], mechanical reinforcement of composites [24–27], as well as sensing [28–30].

In this latter field graphene, and even more its derivatives, have shown the ability to detect analytes in both liquid [31,32] and gas phase [33–35], down to extremely low detection limits. In some cases graphene-based species were able to provide limits of detection for liquid phase sensors as low as 52 pg/L for selected molecules [36], while in the gas phase limits of detection down to a few molecules have been repeatedly reported [37]. Regarding gas sensing, high sensitivity to various gases, including ammonia, nitrogen dioxide, and methane have been demonstrated [38–40]. Moreover, graphene evidenced a huge potential for biosensing, demonstrating the ability to detect biomolecules such as DNA, proteins or enzymes with high sensitivity [41]. Indeed, a graphene-based device has been able to detect a single bacteria in 1 μL of liquid [42]. In all the most performing devices, graphene or graphene derivatives have been functionalized with various chemical moieties,

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in order to enhance both selectivity and sensitivity, and a variety of surface modifiers have been used: acids, bases, alcohols, DNA, proteins, oligomers, enzymes and many others[43–45].

A very recent addition to the toolbox of available functional changes to graphene surfaces are Deep Eutectic Solvents (DES), i.e., solvents presenting characteristics similar to those of ionic liquids (ILs). In turn, ILs are organic salts with a low melting point (usually below 100°C), obtained by the combination of an organic cation, commonly imidazolium-based cations, with a diverse array of anions such as Cl^-, BF_4^-, PF_6^-, NTf_2 [46]. This feature allow them to be used in a variety of applications requiring high electrical ionic conductivity and liquid state, like for example Lithium-based batteries [47]. However, ILs are expensive and may pose problems of environmental pollution, due to their high stability and affinity for lipidic membranes, and viable alternatives for these compounds are actively sought for [48]. In recent years, DESs have emerged as a more economical and environmentally friendly potential substitute of ILs [49,50].

DESs join the major advantages of ILs (good electrical conductivity, low volatility) with a high biodegradability, due to their intrinsic chemical structure, and are hence very interesting compounds to be coupled with graphene-based materials for designing novel devices with high performance and environmental sustainability (Figure 1).

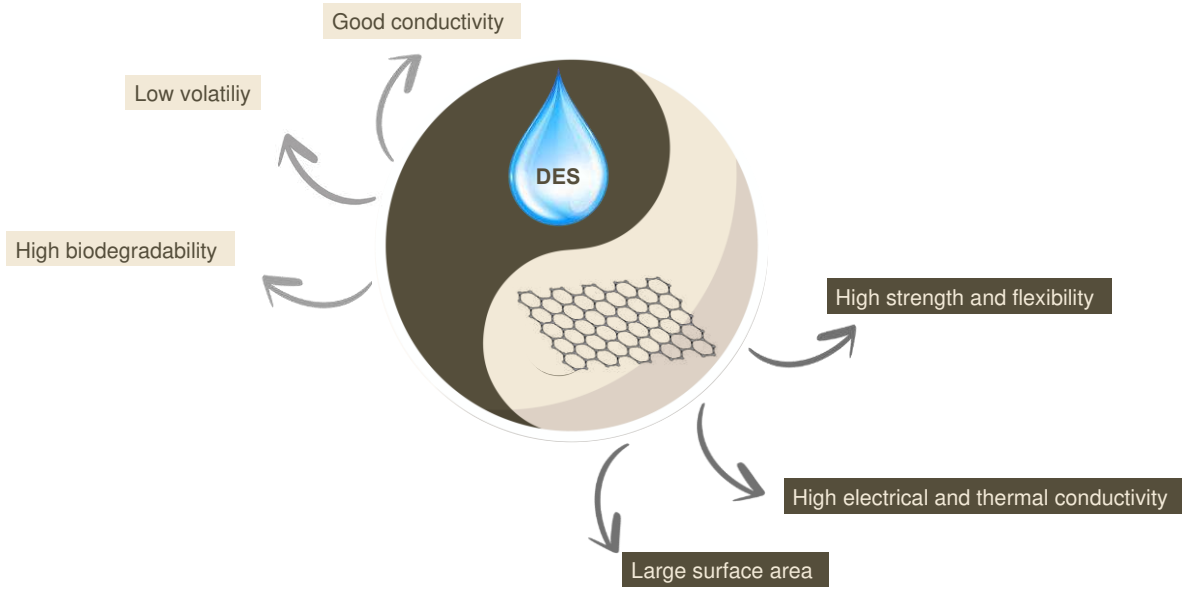

Figure 1. Overview of the ideal coupling of the general characteristics of DESs and graphene-based materials for sensing applications.

DESs are obtained by simply mixing, in appropriate stoichiometric ratios, two components, i.e., a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD) [51]. HBA is usually a high melting point salt such as a halide of tetra-alkylammonium, phosphonium and quaternary ammonium, while HBD is generally chosen in the classes of alcohols, carbohydrates, amines, amides [52]. The mixing in specific stoichiometric ratios of the pure starting compounds, followed by heating, under stirring at temperatures between 50 and 100 ° C for 2-4 h at atmospheric pressure, allows obtaining an homogeneous eutectic liquid mixture, as shown in Figure 2 [53]. This simple procedure guarantees the fast and inexpensive production of eutectic solvents with a high degree of purity that do not require further purification.

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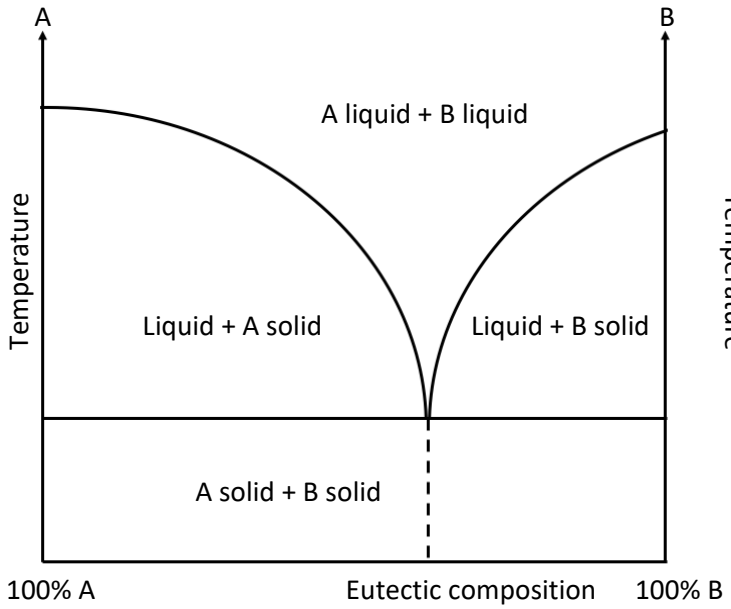

Figure 2. Eutectic phase diagram.

DESs are highly viscous and dense liquids, with low volatility, high thermal and electrochemical stability, low flammability, good conductivity, and high ability to solvate both organic and inorganic compounds [50,54]. Their significant biodegradability and remarkably low toxicity levels, together with their aforementioned properties, allow to fully qualify them as "green solvents" [55,56]. Moreover, the starting reagents for their production are easily available, which makes them even more attractive compared to classic organic solvents and to ILs.

The density of DESs, due to their molecular organization, is usually greater than that of the starting components. This is due to the fact that when the HBDs and HBAs are mixed, the spaces between the molecules decrease, leading to an increase in the density value (the so-called "hole theory") [57]. Their viscosity is usually high, due to both intermolecular forces, regulated by hydrogen bonds (the starting constituents of the DESs include a high number of hydroxylic groups), Van Der Waals and electrostatic interactions, and the large size of the ions, as well as to the reduced free volume that characterizes the medium [53]. The polarity varies according to the considered type of DES, with the HBAs/HBDs molar ratio having a major influence on this parameter. For example, in the specific case of DES composed of choline chloride (ChCl) and glycerol, an increase in the concentration of ChCl (HBA) corresponds to a linear increase in polarity. Taken all together and coupled to their high conductivity, the aforementioned properties make DESs very interesting systems for electrochemical applications, since they can perform the role of both solvent and electrolyte at the same time [58].

Finally, they can be obtained from fully natural compounds like amino acids, sugars, choline and organic acids, creating a subset of even more environmentally friendly DESs called "Natural Deep Eutectic Solvents" (NADESs) [59], with intermediate properties between those of an aqueous and a lipid medium [60]. Indeed, NADESs are able to solubilize poorly soluble metabolites in water and to contribute to the synthesis of intracellular macromolecules [61]. The presence of these compounds in plants and animals, for example, favors the survival of the considered species, even in conditions of low temperatures or small quantities of water [62].

DESs have found application in many different fields [63], like chemical analysis, as extracting solvents [64], in chromatographic and electrophoretic separations [65], and in the fabrication of electrochemical sensors [66–69]. Their use leads to more effective and selective extractions, thanks to the possibility of modulating their hydrophobic / hydrophilic characteristics. DESs have been used also to extract metals [70], bioactive compounds such as flavonoids [71,72], phenols and polyphenols [73], saponins, anthraquinones and other molecules from natural matrices [74,75], biopolymers such

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as lignin [76], starch [77] and proteins such as gluten from food matrices[78]. In separative techniques, DESs have been used as mobile phase modifiers in liquid chromatography[79]. Finally, in the electroanalytical field they have been used simultaneously as electrolytes and preconcentrating solvents in the development of gas sensors [80,81] and biosensors aimed at determining gluten [82,83].

In this review an overview on the use of DESs in sensing devices based on graphene or graphene derivatives is made;this overview is complemented by a few selected cases of use of ILs instead of DESs, in order to highlight the ongoing transition between ILs and DESs in their use coupled to graphene-based materials. In most cases DESs have been used as solvents for the extraction/pre-concentration of the analyte; only in a few works DESs have been reported as functionalizing groups of the graphene derivative to enhance the sensing performance of the resulting device. An outlook of the possible developments in the field completes the review.

2. Enhancing Sensor Performance through DESs-Graphene Integration

In the following, we have tried to underline the different and multiple aspects in which the combination of DESs and graphene can lead to advantages in the development of sensors and related materials, considering a series of articles in which the distinctive characteristics of DESs have been synergistically combined with those of graphene to yield notable advantages with respect to existing sensors.

In order to have a clear view of the progress enabled by using DESs in this context it is necessary to mention some previous works in which graphene-based materials have been coupled with ILs. For example, Li et al. paired graphene oxide with ionic liquids to create a versatile hydrogel employing an environmentally friendly physical-crosslinking method [84]. In this work, polyvinyl alcohol was chosen to establish a dual network with starch molecules, leveraging its biocompatibility, biodegradability, and mechanical robustness, while the ionic liquid enhanced the chemical network compatibility and further increased its mechanical properties. The incorporated graphene oxide (GO), possessing abundant oxygen-containing groups (hydroxyl group, carboxyl group, and epoxy group), contributed to stabilize the network (Figure 3). The authors hypothesized that the simultaneous incorporation of ionic liquid and GO would synergistically enhance the mechanical performance, conductivity, and anti-freezing properties of the starch-based hydrogel, with the aim of developing soft, multimodal wearable sensors. This novel material was used to create wearable sensors, capable of detecting tensile stress, compression, and temperature (with a sensitivity of 0.71%/°C). Furthermore, this material has proven to have excellent stretchability (657.5 %), strength (0.64 MPa), high conductivity (1.98 $S \cdot m^{-1}$) and good anti-freezing property (<− 20 °C). These sensors were then employed to monitor human motion, pressure, and body temperature.

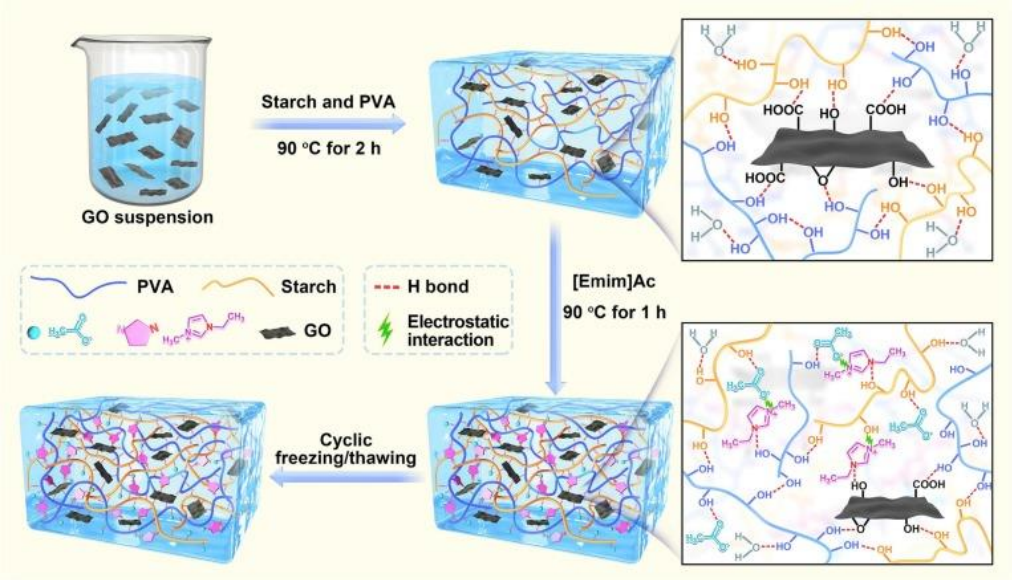

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Figure 3. Illustration of the design strategy and formation mechanism of the starch-based hydrogel described in [84]. Reproduced with permission from Elsevier.

Yonghong et al. utilized graphene quantum dots and an IL to create an electrode for the detection of rutin [85]. With this set-up they noticed an enhancement of the differential pulse voltammetry signal, as well as of both the effective surface area and the conductivity of the sensor, resulted from the synergy between the graphene quantum dots and the ionic liquid. These features allowed them to develop a sensor capable of detecting rutin with a linear response within the concentration range of 5×10^{-9} to 1×10^{-5} mol L^{-1} and a limit of detection (LOD) of 2×10^{-9} mol L^{-1}.

Shabani-Nooshabadi et al. utilized CuO/reduced graphene nanoribbons nanocomposites and an ionic liquid (1-ethyl 3-methyl imidazolinium chloride) to simultaneously detect the biologically active molecules tramadol, olanzapine, and acetaminophen [86]. The incorporation of the IL-incorporating nanocomposite in this novel sensor resulted in an increased surface area, outstanding conductivity, and superior electro-catalytic performance. The sensor demonstrated a linear detection range of 0.08–900 μM and a low detection limit of 0.05 μM specifically for tramadol.

Baizhao and colleagues exploited graphene combined with ILs in a sensor for the determination in liquid phase of sunset yellow, a synthetic dye used in the food industry [87]. The authors used a glassy carbon electrode coated with an ionic liquid-functionalized graphene and a molecularly imprinted polymer (MIP) suspension. They took advantage of the fact that some ILs components can interact with hydrophilic template molecules, preparing IL-based water-compatible MIPs and increasing in this way the ability of the MIPs to recognize hydrophilic analytes. However, MIPs do not always result to be conductive, hence the researchers introduced graphene to improve this aspect. Furthermore, the combination of ILs and graphene led to a more stable composite, with a better electrochemical performance reaching a limit of detection (LOD) of 4 nM.

Now shifting our focus back to the category of environmentally friendly deep eutectic solvents, in 2015 Hayyan et al. prepared several ammonium- and phosphonium- based DESs, and employed them for the subsequent modification of oxidized graphene [88]. Thanks to the DESs, they obtained different levels of reduction and, in some cases, both functionalization and reduction was achieved. The FTIR analyses showed that their DES 5 (Choline Chloride / Urea, 1:2) was the most affecting agent among the DESs, and five new peaks were detected after treatment, all of which corresponded to peaks in the DES spectrum. The bands between 3326–3186 cm^{-1} represented $-NH_2$ and −NH stretching vibrations, whereas the in-plane stretching of –NH was evident at ~1605 cm^{-1}. These observations indicate that the treatment of graphene with $KMnO_4$ (pH = 0.14) and DES 5 led to changes in the functional groups obtained from DES on the carbon surface. New peaks were observed also in the XRD patterns, suggesting alterations in the crystalline structure of the graphene. This indicates that the treatment with DES led to changes in the arrangement of atoms in the graphene lattice, possibly due to the introduction of functional groups or other chemical modifications. However not all DESs produced new functional groups. The main result obtained after characterizing the material with IR spectra, TGA/DTG, XRD, SEM and TEM was to highlight a change occurred in the surface chemistry of the material, which resulted in a few DES-functionalized graphene oxides (namely, those functionalized with Cholin chloride/urea, N,N-Diethylethanolammonium chloride/ethylene glycol, N,N-Diethylethanolammonium chloride/triethylene glycol) in an improved dispersion and stability in water with respect to the simple oxidized graphene.

Another approach, based on the fabrication of a novel reduced graphene oxide-supported nickel cobaltate nanorods composite (RGO-$NiCo_2O_4$), was proposed by Shao et al., who realized a nonenzymatic electrochemical sensor for glucose [89]. DESs were used to produce the RGO-$NiCo_2O_4$ nanorods composite, which demonstrated good electrocatalytic activity toward glucose oxidation in alkaline solution. DESs allowed also to obtain a large electrocatalytic active area created by small nanoparticles on the surface of the $NiCo_2O_4$ nanorods, in coordination with reduced graphene oxide, which provided in addition an excellent electrical conductivity. The sensor showed a wide linear range between 1 μM and 25 mM, and a detection limit towards glucose of 0.35 μM, all obtained with an eco-friendly method to fabricate the sensing nanocomposite layer.

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In another study, Hu and co-workers synthesized an electrochemically reduced graphene oxide (ERG) on a glassy carbon electrode (ERG/GCE) [90]. Subsequently, a polythionine-methylene blue (PTH-MB) polymer was electropolymerized on the electrode surface in phosphate-buffered saline solution (PBS) with pH 6. The electropolymerization was carried out incorporating a 50% (v/v %) of DES solution containing thionine and methylene blue. These modified electrodes were then evaluated for their performance in the direct electrocatalytic oxidation of NADH, a crucial coenzyme associated with various physiological processes such as cell proliferation, tumor formation, development, ischemia, and certain brain diseases. The sensor exhibited a good linear range spanning from 1.52 μM to 3333.33 μM, accompanied by a notably low detection limit of 0.51 nM.

Again Hu and collaborators proposed a modification of a glassy carbon electrode for the electrocatalytic oxidation of NADH with an approach similar to the previously mentioned one, except for the fact that they used a ternary NADES (choline chloride, malic acid, and H_2O in a molar ratio of 1:1:2, and choline chloride, glucose, H_2O in a molar ratio of 1:1:11) as deep eutectic solvent, see Figure 4 [91]. Excellent electrocatalytic activity was displayed by the sensor functionalized with this combination of materials, with a high degree of reproducibility (the maximum relative standard deviations RSD%, range from 3.65 to 4.32%), a large linear range (0.51–3333.33 μM), a low detection limit (0.159 nM) and good stability (4 weeks). Moreover, the sensing composite material is simple to prepare and responds quickly to NADH (response time 3 s), and the resulting sensor was used to test urine samples, revealing good baseline recovery rates (between 89 and 102% of the original baseline). Using the same electrochemical reduction of GO and electro-polymerization of thionine-methylene blue in NADES electrolyte solution described in the previously commented ref. [90], the authors have effectively proven a straightforward, quick, environmentally friendly technique for the synthesis of nanocomposites. A particular point of interest in this work is that without the use of additional specific reagents and enzymes, the oxidation of NADH occurs at a low potential, preventing poisoning of the electrode surface.

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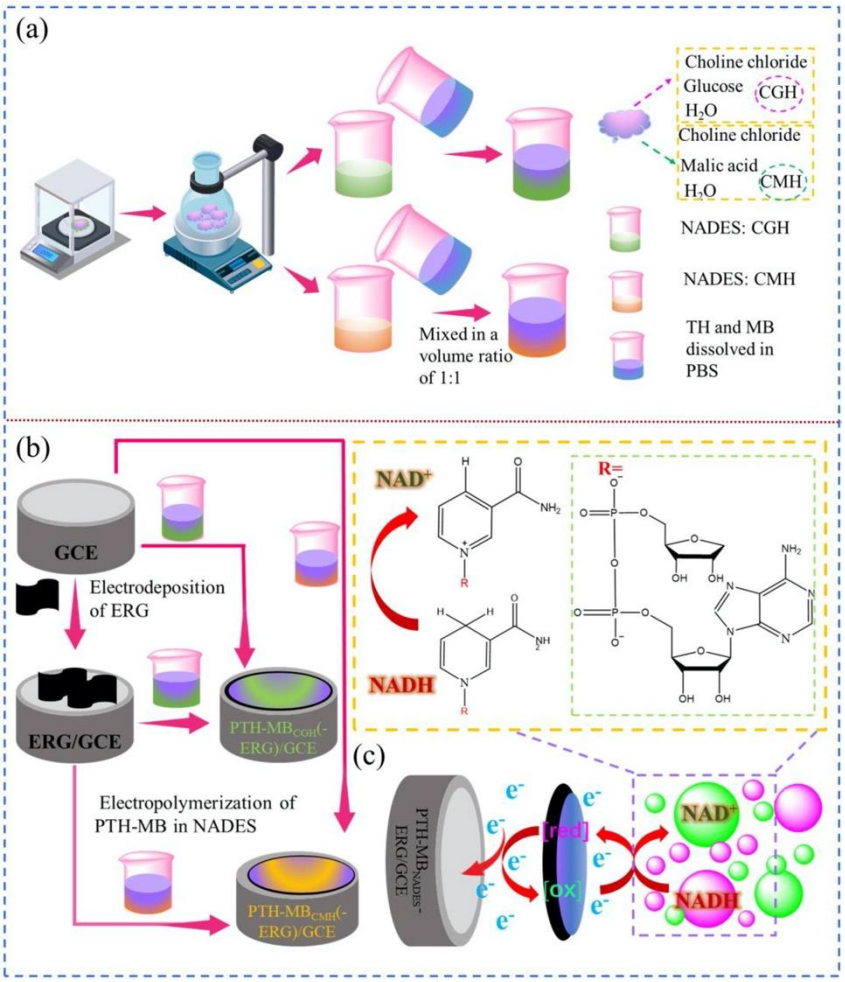

Figure 4. (**a**) Schematic procedure for preparation of NADESs and electropolymerization solutions. (**b**) Fabrication of the PTH-MB$_{NADES}$ and PTH-MB$_{NADES}$-ERG electrodes. (**c**) The proposed NADH measurement mechanism on the proposed electrode [91]. Reproduced with permission from Elsevier.

In another interesting study, Gollas et al. explored the electrochemical behavior of graphene in the deep eutectic solvent choline chloride/ethylene glycol (12CE), and the potential of this couple for electrochemical applications [92]. In more detail, the study measured the graphene potential window in 12CE and estimated the apparent electron transfer kinetics of an outer-sphere redox couple. 12CE electrolyte was also employed to fabricate nanostructured metal (Zn) and metalloid (Ge) hybrids with graphene by electrodeposition. The results show that the two-dimensional nature of graphene critically impacts DES electrochemistry, leading to spatially graded amounts of deposited zinc and graphene degradation during potentiodynamic Zn deposition. The observed lower stability in the cathodic regime was linked to electrochemical formation of radicals during choline reduction, which attacked and degraded the monolayer graphene. However, the degradation and spatial inhomogeneity of deposits could be avoided by potentiostatic deposition at less cathodic potentials, as demonstrated by uniform electrodeposition of germanium. These findings are important for the processing of graphene and related carbon materials in choline chloride-based DESs and for their application in such electrolytes.

Kumar et al. evaluated the behaviour of rhodamine B (RB) in the DES called “Reline” (choline chloride–urea) with or without graphene oxide (GO) [93]. Researchers explored the synergistic effects of GO and DES on photophysical processes by changing solvent nature and GO amounts, finding that the fluorescence of RB can be notably altered (either enhanced or quenched) by the presence of a surfactant or of the GO. The intensity of fluorescence is influenced by RB concentration at the surfaces of the GO or of the Reline layer. The results of this investigation suggest that the basic nature of Reline may produce an RB zwitterion, which can form an ion pair with DES− monomer, leading to

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sizeable fluorescence intensity. The aforementioned behavior hold promises for potential applications in chemical sensors or biotechnology exploiting optical detection means.

In a recent work, Mahyari et al. proposed an aptasensor (i.e., a sensor able to detect aptamers) based on a nanocomposite constituted by gold nanoparticles modified with poly deep eutectic solvent-functionalized graphene oxide, for the detection of C-reactive protein biomarkers [94] (Figure 5). The resulting nano-composite was highly dispersabe and stable in the chosen medium, granting superior functionality and surface charge density for the device. In particular, the sensor demonstrated high sensitivity (LOD = 0.0003ng mL^{-1}), selectivity (tested against interfering agents such alpha-fetoprotein, lysine, and uric acid for which the sensor showed a negligible response), reproducibility (RSD was found to be 4.6%) and stability (the sensor proved to be stable for 10 days), and with a linear range of 0.001-50 ng mL^{-1}. In this strategy the nanocomposite was used as carrier as well as signal enhancer; moreover, this approach provided the clear possibility to be used also for other analytes, upon changing the selected aptamer.

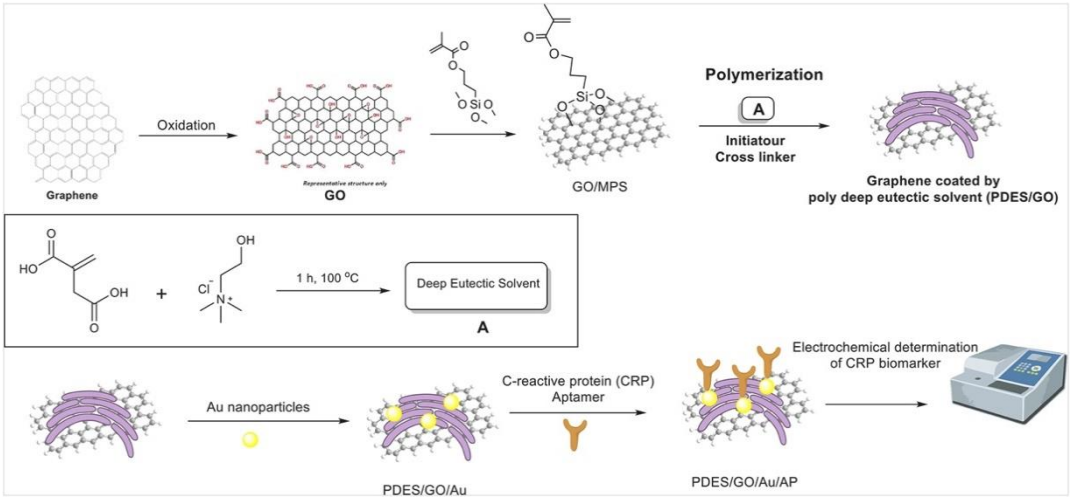

Figure 5. Schematic fabrication process of the C-reactive protein aptasensor based on Graphene Oxide /PolyDES/Au NPs. Reproduced with permission from Elsevier [94].

Recently, Yao et al. proposed the construction of a sensor based on cellulose nano-fiber (CNF)-dispersed graphene (Gr) as a humidity sensing layer [95]. The extraction of CNFs from waste pulp involved a synergistic approach, combining DES treatment with ultrasonication. Graphene powders (10, 20, and 40 mg) were introduced into a solution of CNF with a concentration of 0.1 wt%, followed by ultrasonic treatment for 3 hours. This process resulted in the formation of a well-dispersed suspension of CNF/Gr; the suspension was then easily filtered onto a CNF film to form the sensing element of the humidity sensor (Figure 6). Due to their extended surface, CNFs provided abundant adsorption sites to capture water molecules, and promoted electron transfer from adsorbed water molecules to graphene, further amplifying electrical signals upon a hygroscopic mechanical expansion of the sensing layer under humidity conditions. The sensor provides satisfactory response (45 s) and recovery time (33 s), low hysteresis (4%), wide RH detection range (15–99%), and long-term stability (15 days). Furthermore, it could monitor the humidity of human skin and human breath, indicating a versatile noncontact humidity sensing function by altering its component proportion of CNF-to-Gr on demand.

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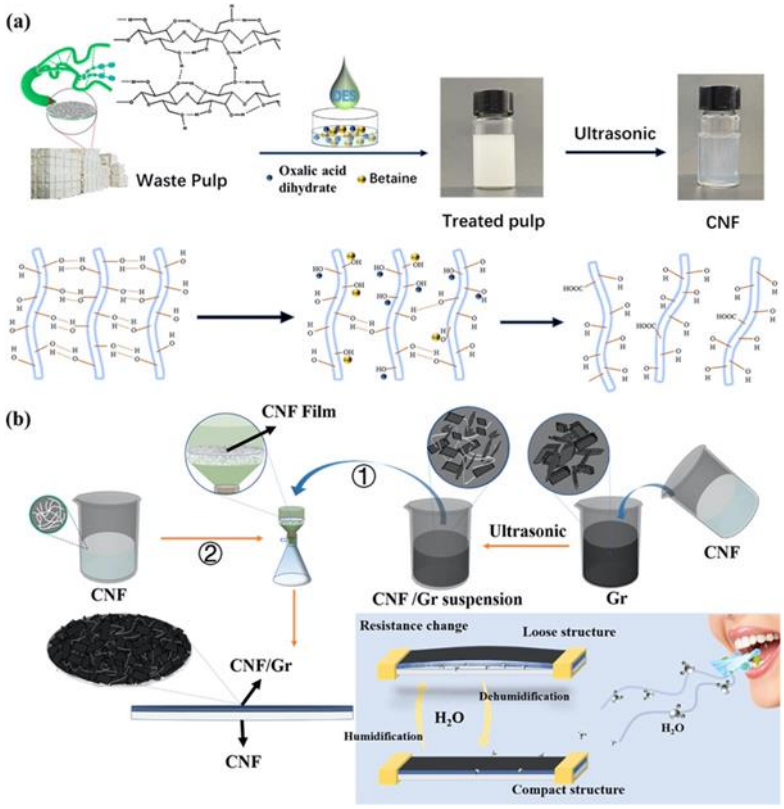

Figure 6. (**a**) Scheme of the extraction process of CNFs from waste pulp. (**b**) Schematic diagram of the preparation of a humidity sensor by employing CNF-dispersed graphene (①) as the humidity sensing layer. The latter was filtered onto the coessential CNF film surface to form the sensor (②). Reprinted (adapted) with permission from American Chemical Society [95].

A recent study by Wan et al. explored the conversion of lignocellulosic biomass into porous graphene using direct laser writing (DLW) and DESs (including choline chloride:oxalic acid, choline chloride:formic acid, and choline chloride:ethylene glycol) [96] (Figure 7). This process has been termed *laser-induced graphene* (LIG). The study found that the cellulose pulp resulting from pretreatment with choline chloride oxalic acid DES was a suitable substrate for LIG formation, and the obtained LIG exhibited a 3D porous structure and high crystallinity. It was suggested that pseudo-lignin from the DES-treated cellulose pulp helped to produce LIG. The LIG-embedded films showed good electrochemical characteristics when utilized to create on-chip supercapacitors and dopamine sensor, with a linear range between 1×10^{-6} to 40×10^{-6} M and a LOD of 0.659×10^{-6} M. Thus, it was demonstrated that DESs can act as enabling auxiliary compounds for the production of lignocellulose-derived porous graphene materials in large quantities, and that these materials could have a wide range of uses for effective, inexpensive and even disposable electronics.

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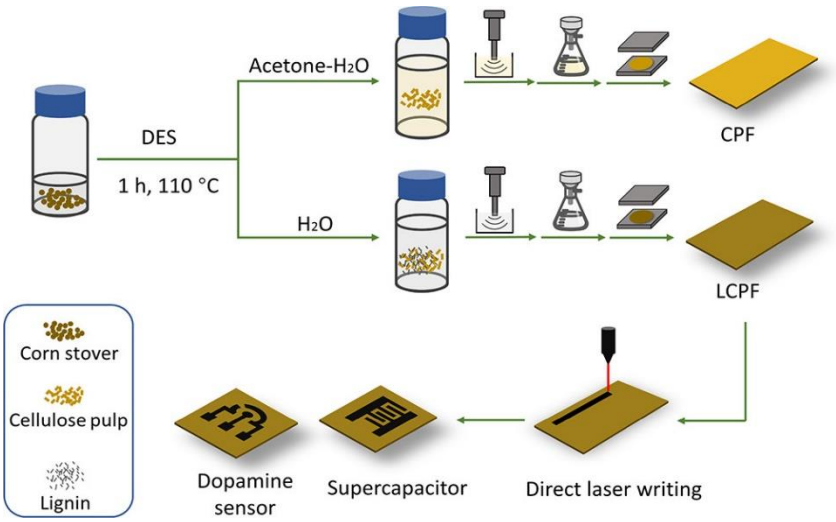

Figure 7. Schematic diagram of fabrication of biomass-based sensors involving the use of DESs. Corn stover is pretreated with a DES followed by addition of an antisolvent (acetone–water mixture or water). The pretreatment slurry is then ultrasonicated and vacuum-filtrated to form wet films. The hot-pressed films are used for direct laser writing to form LIG and further fabricated into on-chip supercapacitors and dopamine sensors. Reprinted with permission from American Chemical Society [96].

Here, Fotouhi et al. proposed the development of an electrochemical sensor designed for the precise analysis of paracetamol and 4-aminophenol with enhanced sensitivity [97]. The sensor was fabricated by electro-polymerizing L-arginine onto the surface of a glassy carbon electrode modified with a nanocomposite consisting of graphene quantum dots, a deep eutectic solvent (choline chloride – urea, 1:2), and carboxyl functionalized multiwall carbon nanotubes, as shown in Figure 8. The sensor exhibited excellent performance for the analytical monitoring of paracetamol and 4-aminophenol, with wide linear dynamic ranges (from 0.030 to 110 mmol L^{-1} and 0.050 to 100 mmol L^{-1}) and a LoD of 0.010 mmol L^{-1} and 0.017 mmol L^{-1} respectively. The practical applicability of the sensor was explored by the determination of both compounds in human fluid samples, with recoveries between 97 and 102 % of the baseline. The article also discusses the advantages of electrochemical methods and polymer-modified electrodes, as well as the properties and applications of graphene quantum dots, sensing element of the multiwall carbon nanotubes, and deep eutectic solvents.

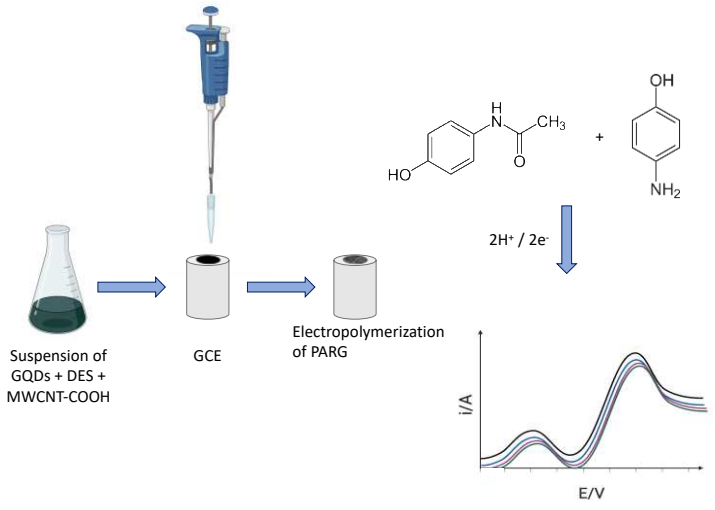

Figure 8. Schematic illustration of the preparation of electrodes for the detection in liquid phase of paracetamol and 4-aminophenol. Adapted with permission from RSC [97].

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More recently, a new method to immobilize MIPs on the surface of reduced graphene oxide (rGO) through covalent bonding has been proposed by Cao and colleagues [98]. The surface of rGO was modified with maleic anhydride via a Diels−Alder reaction, via a DES-based solution prepared using $ZnCl_2$ and choline chloride. Next, 3-propyl-1-vinylimidazolium molecular units were anchored and polymerized in the presence of ethylene glycol dimethacrylate (EGDMA) using chloramphenicol (CAP) as the template. The effect of the molar ratio of individual precursors on the adsorption capacity of synthesized materials was investigated, and an electrochemical sensor for CAP detection was fabricated. The covalent bonding of MIP units enhanced the sensitivity of the sensor with a LOD of 0.204 μM and a linear range 0.2-4.0 μM. The authors selected p-nitrophenol and thiamphenicol as interferent molecules to assess the selectivity of MIP-rGO towards CAP. They demonstrated the high sensitivity and selectivity of MIP-rGO through a relatively low current intensities in the presence of interference molecules. This synthesis strategy involves the covalent binding of MIP on rGO materials via click chemistry facilitated by DESs, under sonication power, excluding harmful solvents and energy-intensive processes, underlining the potential of this approach for fabricating highly sustainable and environmentally friendly devices.

With regard to NADES, an electrochemical sensor for the detection of oleuropein based on the use of this class of solvents and graphene was proposed by Silva et al. [99]. The methodology involved the use of Graphene Oxide Pencil Graphite Electrode (GOPGE) in combination with a buffer modified with a NADES, containing 10% (v/v) of Lactic acid, Glucose and H_2O (LGH). This combination resulted in a signal enhancement of 5.3 times higher than the bare electrode with unmodified buffer. The electrochemical behavior of oleuropein was then evaluated using differential pulse voltammetry. The proposed electrochemical sensor was successfully applied to the determination of oleuropein in an olive leaf extract prepared by ultrasound-assisted extraction, with satisfactory linear range between 0.10 and 37 μM and a LOD of 30 nM.

3. Conclusions and Outlook

The combined use of graphene-based materials and DESs as a “composite” to realize sensing layers is still in its infancy, as the first examples of this approach date back to the mid-2010s. Nonetheless, since then, some examples of effective sensing devices pairing this two classes of materials have been reported, leading to interesting results in terms of remarkable linearity ranges (spanning over more than three orders of magnitude), very low LODs (down to tens of nM) and satisfactory selectivities (at least in the few reports that dealt with this parameter).

The most interesting aspects of pairing a well-known high-performing semiconductor/conductor, such as graphene-related moieties, with DESs pertain, for sure, to the unlimited possibilities of tailoring the sensing layers. This opens up numerous opportunities for the development of selective and performing sensors. A second point worth noting is that the synthesis of DESs is straightforward and inexpensive, which can play an important role in the practical utilization of these materials.

Additionally, the remarkable chemical versatility of DESs broadens their applicability in sensing by enabling the preconcentration of analytes from a mixture through straightforward extraction operations. This aspect, frequently overlooked, facilitates the analysis of low quantities of analyte with minimal efforts in terms of device complexity. Moreover, the overall environmental sustainability of DESs, especially when derived from naturally occurring substances (NADESs), enhances their appeal for envisioned mass applications such as disposable or wearable sensors.

To fulfill this vision, however, a few problems must still be addressed. First, a significant challenge is related to the high viscosity of DESs, which limits mass diffusion (hence the speed of response and in some cases the cyclability of the devices, also creating hurdles to reach low Limits of Detection). This issue can be partially solved by limiting the concentration of DESs in the graphene-derived material/DESs mixture. However, it is also chemically feasible to design specific mixtures with lower viscosity than those currently employed.

Another presently unresolved issue is the limited solubility of graphene and its derivatives in these solvents. This limitation might restrict the presence of the electronic/ionic conductor in the

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heterogeneous sensing layer, potentially diminishing the overall sensor performance. However, this challenge can be addressed or mitigated again through a thoughtful chemical design of the used compounds.

Finally, the shelf life of mixed DESs/graphene-derived materials could be limited, due to issues related to phase separation or degradation of the DESs. In this case the possible solutions involve again a clever chemical design, or a focus on disposable/prepared on the fly devices.

In perspective, the majority of the current practical challenges associated with DESs/graphene-based materials can be solved in a relatively easy way by means of rational design of the chemical compounds, allowing a more extensive applicative research in this very young field (that, we must remember, is less than ten years old). Smart design of the sensing devices, including highly nanostructured sensing surfaces, porous layers, and flow devices, has the potential to proficiently address challenges and achieve superior performance in liquid phase-based and gas analysis. Integrating these strategies with lab-on-a-chip and microfluidics could ideally bridge existing gaps.

A growing community of scientists is gathering around this new field, and the results of their work will be likely visible and impacting sensing strategies already in a few years from now, especially in the fields of food and biomedical industry, in which this technology has already been tested and found extremely useful.

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References

1. Craighead, H.G. Nanoelectromechanical Systems. Science 2000, 290, 1532–1535, doi:10.1126/science.290.5496.1532.
2. Arafat, M.M.; Dinan, B.; Akbar, S.A.; Haseeb, A.S.M.A. Gas Sensors Based on One Dimensional Nanostructured Metal-Oxides: A Review. Sensors (Basel) 2012, 12, 7207–7258, doi:10.3390/s120607207.
3. Kasani, S.; Curtin, K.; Wu, N. A Review of 2D and 3D Plasmonic Nanostructure Array Patterns: Fabrication, Light Management and Sensing Applications. 2019, 8, 2065–2089, doi:10.1515/nanoph-2019-0158.
4. Mandler, D.; Turyan, I. Applications of Self-Assembled Monolayers in Electroanalytical Chemistry. Electroanalysis 1996, 8, 207–213, doi:10.1002/elan.1140080302.
5. Castellana, E.T.; Cremer, P.S. Solid Supported Lipid Bilayers: From Biophysical Studies to Sensor Design. Surf Sci Rep 2006, 61, 429–444, doi:10.1016/j.surfrep.2006.06.001.
6. Liu, D.; Lu, K.; Poon, C.; Lin, W. Metal–Organic Frameworks as Sensory Materials and Imaging Agents. Inorg. Chem. 2014, 53, 1916–1924, doi:10.1021/ic402194c.
7. Allen, M.J.; Tung, V.C.; Kaner, R.B. Honeycomb Carbon: A Review of Graphene. Chem. Rev. 2010, 110, 132–145, doi:10.1021/cr900070d.
8. Mbayachi, V.B.; Ndayiragije, E.; Sammani, T.; Taj, S.; Mbuta, E.R.; khan, A. ullah Graphene Synthesis, Characterization and Its Applications: A Review. Results in Chemistry 2021, 3, 100163, doi:10.1016/j.rechem.2021.100163.
9. Novoselov, K.S.; Geim, A.K.; Morozov, S.V.; Jiang, D.; Katsnelson, M.I.; Grigorieva, I.V.; Dubonos, S.V.; Firsov, A.A. Two-Dimensional Gas of Massless Dirac Fermions in Graphene. Nature 2005, 438, 197–200, doi:10.1038/nature04233.
10. Geim, A.K.; Novoselov, K.S. The Rise of Graphene. Nature Materials 2007, 6, 183–191, doi:10.1038/nmat1849.
11. Geim, A.K.; Grigorieva, I.V. Van Der Waals Heterostructures. Nature 2013, 499, 419–425, doi:10.1038/nature12385.

12. Akinwande, D.; Petrone, N.; Hone, J. Two-Dimensional Flexible Nanoelectronics. Nature Communications 2014, 5, 5678, doi:10.1038/ncomms6678.
13. Fiori, G.; Bonaccorso, F.; Iannaccone, G.; Palacios, T.; Neumaier, D.; Seabaugh, A.; Banerjee, S.K.; Colombo, L. Electronics Based on Two-Dimensional Materials. Nature Nanotechnology 2014, 9, 768–779, doi:10.1038/nnano.2014.207.
14. Wang, C.; Xia, K.; Wang, H.; Liang, X.; Yin, Z.; Zhang, Y. Advanced Carbon for Flexible and Wearable Electronics. Advanced Materials 2019, 31, 1801072, doi:10.1002/adma.201801072.
15. Zheng, X.T.; Ananthanarayanan, A.; Luo, K.Q.; Chen, P. Glowing Graphene Quantum Dots and Carbon Dots: Properties, Syntheses, and Biological Applications. Small 2015, 11, 1620–1636, doi:10.1002/smll.201402648.
16. Bonaccorso, F.; Colombo, L.; Yu, G.; Stoller, M.; Tozzini, V.; Ferrari, A.C.; Ruoff, R.S.; Pellegrini, V. Graphene, Related Two-Dimensional Crystals, and Hybrid Systems for Energy Conversion and Storage. Science 2015, 347, 1246501, doi:10.1126/science.1246501.
17. Jiang, H.; Lee, P.S.; Li, C. 3D Carbon Based Nanostructures for Advanced Supercapacitors. Energy Environ. Sci. 2013, 6, 41–53, doi:10.1039/C2EE23284G.
18. Deng, D.; Novoselov, K.S.; Fu, Q.; Zheng, N.; Tian, Z.; Bao, X. Catalysis with Two-Dimensional Materials and Their Heterostructures. Nat Nanotechnol 2016, 11, 218–230, doi:10.1038/nnano.2015.340.
19. Jin, H.; Guo, C.; Liu, X.; Liu, J.; Vasileff, A.; Jiao, Y.; Zheng, Y.; Qiao, S.-Z. Emerging Two-Dimensional Nanomaterials for Electrocatalysis. Chem Rev 2018, 118, 6337–6408, doi:10.1021/acs.chemrev.7b00689.
20. Karimi, M.; Ghasemi, A.; Sahandi Zangabad, P.; Rahighi, R.; Moosavi Basri, S.M.; Mirshekari, H.; Amiri, M.; Shafaei Pishabad, Z.; Aslani, A.; Bozorgomid, M.; et al. Smart Micro/Nanoparticles in Stimulus-Responsive Drug/Gene Delivery Systems. Chem Soc Rev 2016, 45, 1457–1501, doi:10.1039/c5cs00798d.
21. Biju, V. Chemical Modifications and Bioconjugate Reactions of Nanomaterials for Sensing, Imaging, Drug Delivery and Therapy. Chem. Soc. Rev. 2014, 43, 744–764, doi:10.1039/C3CS60273G.
22. Hong, G.; Diao, S.; Antaris, A.L.; Dai, H. Carbon Nanomaterials for Biological Imaging and Nanomedicinal Therapy. Chem Rev 2015, 115, 10816–10906, doi:10.1021/acs.chemrev.5b00008.
23. Goenka, S.; Sant, V.; Sant, S. Graphene-Based Nanomaterials for Drug Delivery and Tissue Engineering. J Control Release 2014, 173, 75–88, doi:10.1016/j.jconrel.2013.10.017.
24. Mittal, G.; Dhand, V.; Rhee, K.Y.; Park, S.-J.; Lee, W.R. A Review on Carbon Nanotubes and Graphene as Fillers in Reinforced Polymer Nanocomposites. Journal of Industrial and Engineering Chemistry 2015, 21, 11–25, doi:10.1016/j.jiec.2014.03.022.
25. Berman, D.; Erdemir, A.; Sumant, A.V. Graphene: A New Emerging Lubricant. Materials Today 2014, 17, 31–42, doi:10.1016/j.mattod.2013.12.003.
26. Stankovich, S.; Dikin, D.A.; Dommett, G.H.B.; Kohlhaas, K.M.; Zimney, E.J.; Stach, E.A.; Piner, R.D.; Nguyen, S.T.; Ruoff, R.S. Graphene-Based Composite Materials. Nature 2006, 442, 282–286, doi:10.1038/nature04969.
27. Papageorgiou, D.G.; Kinloch, I.A.; Young, R.J. Mechanical Properties of Graphene and Graphene-Based Nanocomposites. Progress in Materials Science 2017, 90, 75–127, doi:10.1016/j.pmatsci.2017.07.004.
28. Joshi, N.; Hayasaka, T.; Liu, Y.; Liu, H.; Oliveira, O.N.J.; Lin, L. A Review on Chemiresistive Room Temperature Gas Sensors Based on Metal Oxide Nanostructures, Graphene and 2D Transition Metal Dichalcogenides. Mikrochim Acta 2018, 185, 213, doi:10.1007/s00604-018-2750-5.
29. Krishnan, S.K.; Singh, E.; Singh, P.; Meyyappan, M.; Nalwa, H.S. A Review on Graphene-Based Nanocomposites for Electrochemical and Fluorescent Biosensors. RSC Adv. 2019, 9, 8778–8881, doi:10.1039/C8RA09577A.
30. Nag, A.; Mitra, A.; Mukhopadhyay, S.C. Graphene and Its Sensor-Based Applications: A Review. Sensors and Actuators A: Physical 2018, 270, 177–194, doi:10.1016/j.sna.2017.12.028.
31. Pumera, M.; Ambrosi, A.; Bonanni, A.; Chng, E.L.K.; Poh, H.L. Graphene for Electrochemical Sensing and Biosensing. TrAC Trends in Analytical Chemistry 2010, 29, 954–965, doi:10.1016/j.trac.2010.05.011.
32. Xu, J.; Wang, Y.; Hu, S. Nanocomposites of Graphene and Graphene Oxides: Synthesis, Molecular Functionalization and Application in Electrochemical Sensors and Biosensors. A Review. Microchimica Acta 2017, 184, 1–44, doi:10.1007/s00604-016-2007-0.
33. Yuan, W.; Shi, G. Graphene-Based Gas Sensors. J. Mater. Chem. A 2013, 1, 10078–10091, doi:10.1039/C3TA11774J.
34. Ratinac, K.R.; Yang, W.; Ringer, S.P.; Braet, F. Toward Ubiquitous Environmental Gas Sensors—Capitalizing on the Promise of Graphene. Environ. Sci. Technol. 2010, 44, 1167–1176, doi:10.1021/es902659d.
35. Ji, Q.; Honma, I.; Paek, S.-M.; Akada, M.; Hill, J.P.; Vinu, A.; Ariga, K. Layer-by-Layer Films of Graphene and Ionic Liquids for Highly Selective Gas Sensing. Angew Chem Int Ed Engl 2010, 49, 9737–9739, doi:10.1002/anie.201004929.
36. Mehta, J.; Vinayak, P.; Tuteja, S.K.; Chhabra, V.A.; Bhardwaj, N.; Paul, A.K.; Kim, K.-H.; Deep, A. Graphene Modified Screen Printed Immunosensor for Highly Sensitive Detection of Parathion. Biosens Bioelectron 2016, 83, 339–346, doi:10.1016/j.bios.2016.04.058.

37. Schedin, F.; Geim, A.K.; Morozov, S.V.; Hill, E.W.; Blake, P.; Katsnelson, M.I.; Novoselov, K.S. Detection of Individual Gas Molecules Adsorbed on Graphene. Nat Mater 2007, 6, 652–655, doi:10.1038/nmat1967.
38. Basu, S.; Bhattacharyya, P. Recent Developments on Graphene and Graphene Oxide Based Solid State Gas Sensors. Sensors and Actuators B: Chemical 2012, 173, 1–21, doi:10.1016/j.snb.2012.07.092.
39. Demon, S.Z.N.; Kamisan, A.I.; Abdullah, N.; Noor, S.A.M.; Khim, O.K.; Kasim, N.A.M.; Yahya, M.Z.A.; Manaf, N.A.A.; Azmi, A.F.M.; Halim, N.A. Graphene-Based Materials in Gas Sensor Applications: A Review. Sensors and Materials 2020, 32, 759, doi:10.18494/SAM.2020.2492.
40. Alzate-Carvajal, N.; Luican-Mayer, A. Functionalized Graphene Surfaces for Selective Gas Sensing. ACS Omega 2020, 5, 21320–21329, doi:10.1021/acsomega.0c02861.
41. Kuila, T.; Bose, S.; Khanra, P.; Mishra, A.K.; Kim, N.H.; Lee, J.H. Recent Advances in Graphene-Based Biosensors. Biosensors and Bioelectronics 2011, 26, 4637–4648, doi:10.1016/j.bios.2011.05.039.
42. Thakur, B.; Zhou, G.; Chang, J.; Pu, H.; Jin, B.; Sui, X.; Yuan, X.; Yang, C.-H.; Magruder, M.; Chen, J. Rapid Detection of Single E. Coli Bacteria Using a Graphene-Based Field-Effect Transistor Device. Biosens Bioelectron 2018, 110, 16–22, doi:10.1016/j.bios.2018.03.014.
43. Georgakilas, V.; Otyepka, M.; Bourlinos, A.B.; Chandra, V.; Kim, N.; Kemp, K.C.; Hobza, P.; Zboril, R.; Kim, K.S. Functionalization of Graphene: Covalent and Non-Covalent Approaches, Derivatives and Applications. Chem. Rev. 2012, 112, 6156–6214, doi:10.1021/cr3000412.
44. Kumar, S.; Bukkitgar, S.D.; Singh, S.; Pratibha; Singh, V.; Reddy, K.R.; Shetti, N.P.; Venkata Reddy, Ch.; Sadhu, V.; Naveen, S. Electrochemical Sensors and Biosensors Based on Graphene Functionalized with Metal Oxide Nanostructures for Healthcare Applications. ChemistrySelect 2019, 4, 5322–5337, doi:10.1002/slct.201803871.
45. Maio, A.; Pibiri, I.; Morreale, M.; Mantia, F.P.; Scaffaro, R. An Overview of Functionalized Graphene Nanomaterials for Advanced Applications. Nanomaterials 2021, 11, doi:10.3390/nano11071717.
46. Galiński, M.; Lewandowski, A.; Stępniak, I. Ionic Liquids as Electrolytes. Electrochimica Acta 2006, 51, 5567–5580, doi:10.1016/j.electacta.2006.03.016.
47. Tang, X.; Lv, S.; Jiang, K.; Zhou, G.; Liu, X. Recent Development of Ionic Liquid-Based Electrolytes in Lithium-Ion Batteries. Journal of Power Sources 2022, 542, 231792, doi:10.1016/j.jpowsour.2022.231792.
48. Maculewicz, J.; Świacka, K.; Stepnowski, P.; Dołżonek, J.; Białk-Bielińska, A. Ionic Liquids as Potentially Hazardous Pollutants: Evidences of Their Presence in the Environment and Recent Analytical Developments. Journal of Hazardous Materials 2022, 437, 129353, doi:10.1016/j.jhazmat.2022.129353.
49. Mannu, A.; Blangetti, M.; Baldino, S.; Prandi, C. Promising Technological and Industrial Applications of Deep Eutectic Systems. Materials 2021, 14, 2494, doi:10.3390/ma14102494.
50. Smith, E.L.; Abbott, A.P.; Ryder, K.S. Deep Eutectic Solvents (DESs) and Their Applications. Chem. Rev. 2014, 114, 11060–11082, doi:10.1021/cr300162p.
51. Abbott, A.P.; Boothby, D.; Capper, G.; Davies, D.L.; Rasheed, R.K. Deep Eutectic Solvents Formed between Choline Chloride and Carboxylic Acids: Versatile Alternatives to Ionic Liquids. J Am Chem Soc 2004, 126, 9142–9147, doi:10.1021/ja048266j.
52. Chandran, K.; Kait, C.F.; Wilfred, C.D.; Zaid, H.F.M. A Review on Deep Eutectic Solvents: Physiochemical Properties and Its Application as an Absorbent for Sulfur Dioxide. Journal of Molecular Liquids 2021, 338, 117021, doi:10.1016/j.molliq.2021.117021.
53. Zhang, Q.; De Oliveira Vigier, K.; Royer, S.; Jerome, F. Deep Eutectic Solvents: Syntheses, Properties and Applications. Chem Soc Rev 2012, 41, 7108–7146, doi:10.1039/c2cs35178a.
54. Omar, K.A.; Sadeghi, R. Physicochemical Properties of Deep Eutectic Solvents: A Review. Journal of Molecular Liquids 2022, 360, 119524, doi:10.1016/j.molliq.2022.119524.
55. Yu, D.; Xue, Z.; Mu, T. Eutectics: Formation, Properties, and Applications. Chem. Soc. Rev. 2021, 10.1039.D1CS00404B, doi:10.1039/D1CS00404B.
56. Rodríguez-Ramos, R.; Santana-Mayor, Á.; Socas-Rodríguez, B.; Rodríguez-Delgado, M.Á. Recent Applications of Deep Eutectic Solvents in Environmental Analysis. Applied Sciences 2021, 11, 4779, doi:10.3390/app11114779.
57. Abbott, A.P.; Capper, G.; Gray, S. Design of Improved Deep Eutectic Solvents Using Hole Theory. Chem. Eur. J. of Chem. Phys. 2006, 7, 803–806, doi:10.1002/cphc.200500489.
58. Li, Q.; Jiang, J.; Li, G.; Zhao, W.; Zhao, X.; Mu, T. The Electrochemical Stability of Ionic Liquids and Deep Eutectic Solvents. Science China Chemistry 2016, 59, 571–577, doi:10.1007/s11426-016-5566-3.
59. Vanda, H.; Dai, Y.; Wilson, E.G.; Verpoorte, R.; Choi, Y.H. Green Solvents from Ionic Liquids and Deep Eutectic Solvents to Natural Deep Eutectic Solvents. Comptes Rendus Chimie 2018, 21, 628–638.
60. 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, 766, 61–68, doi:10.1016/j.aca.2012.12.019.
61. Liu, Y.; Friesen, J.B.; McAlpine, J.B.; Lankin, D.C.; Chen, S.-N.; Pauli, G.F. Natural Deep Eutectic Solvents: Properties, Applications, and Perspectives. Journal of natural products 2018, 81, 679–690.

62. Choi, Y.H.; van Spronsen, J.; Dai, Y.; Verberne, M.; Hollmann, F.; Arends, I.W.C.E.; Witkamp, G.-J.; Verpoorte, R. Are Natural Deep Eutectic Solvents the Missing Link in Understanding Cellular Metabolism and Physiology? Plant Physiol 2011, 156, 1701–1705, doi:10.1104/pp.111.178426.
63. Hansen, B.B.; Spittle, S.; Chen, B.; Poe, D.; Zhang, Y.; Klein, J.M.; Horton, A.; Adhikari, L.; Zelovich, T.; Doherty, B.W.; et al. Deep Eutectic Solvents: A Review of Fundamentals and Applications. Chem. Rev. 2020, acs.chemrev.0c00385, doi:10.1021/acs.chemrev.0c00385.
64. Abolghasemi, M.M.; Piryaei, M.; Imani, R.M. Deep Eutectic Solvents as Extraction Phase in Head-Space Single-Drop Microextraction for Determination of Pesticides in Fruit Juice and Vegetable Samples. Microchemical Journal 2020, 158, 105041, doi:10.1016/j.microc.2020.105041.
65. Cai, T. Application of Deep Eutectic Solvents in Chromatography: A Review. Trends in Analytical Chemistry 2019, 9.
66. Kalambate, P.K.; Rao, Z.; Dhanjai; Wu, J.; Shen, Y.; Boddula, R.; Huang, Y. Electrochemical (Bio) Sensors Go Green. Biosensors and Bioelectronics 2020, 163, 112270, doi:10.1016/j.bios.2020.112270.
67. Svigelj, R.; Dossi, N.; Grazioli, C.; Toniolo, R. Deep Eutectic Solvents (DESs) and Their Application in Biosensor Development. Sensors 2021, 21, 4263, doi:10.3390/s21134263.
68. Abbott, A.P. Deep Eutectic Solvents and Their Application in Electrochemistry. Current Opinion in Green and Sustainable Chemistry 2022, 36, 100649, doi:10.1016/j.cogsc.2022.100649.
69. Brett, C.M.A. Deep Eutectic Solvents and Applications in Electrochemical Sensing. Current Opinion in Electrochemistry 2018, 10, 143–148, doi:10.1016/j.coelec.2018.05.016.
70. Zante, G.; Boltoeva, M. Review on Hydrometallurgical Recovery of Metals with Deep Eutectic Solvents. Sustainable Chemistry 2020, 1, 238–255, doi:10.3390/suschem1030016.
71. Bi, W.; Tian, M.; Row, K.H. Evaluation of Alcohol-Based Deep Eutectic Solvent in Extraction and Determination of Flavonoids with Response Surface Methodology Optimization. Journal of Chromatography A 2013, 1285, 22–30.
72. Lomba, L.; García, C.B.; Ribate, M.P.; Giner, B.; Zuriaga, E. Applications of Deep Eutectic Solvents Related to Health, Synthesis, and Extraction of Natural Based Chemicals. Applied Sciences 2021, 11, 10156, doi:10.3390/app112110156.
73. García, A.; Rodríguez-Juan, E.; Rodríguez-Gutiérrez, G.; Rios, J.J.; Fernández-Bolaños, J. Extraction of Phenolic Compounds from Virgin Olive Oil by Deep Eutectic Solvents (DESs). Food Chemistry 2016, 197, 554–561, doi:10.1016/j.foodchem.2015.10.131.
74. Duan, L.; Dou, L.-L.; Guo, L.; Li, P.; Liu, E.-H. Comprehensive Evaluation of Deep Eutectic Solvents in Extraction of Bioactive Natural Products. ACS Sustainable Chemistry & Engineering 2016, 4, 2405–2411.
75. Jablonský, M.; Majová, V.; Šima, J.; Hroboňová, K.; Lomenová, A. Involvement of Deep Eutectic Solvents in Extraction by Molecularly Imprinted Polymers—A Minireview. Crystals 2020, 10, 217, doi:10.3390/cryst10030217.
76. Tian, D.; Chandra, R.P.; Lee, J.-S.; Lu, C.; Saddler, J.N. A Comparison of Various Lignin-Extraction Methods to Enhance the Accessibility and Ease of Enzymatic Hydrolysis of the Cellulosic Component of Steam-Pretreated Poplar. Biotechnology for Biofuels 2017, 10, 157, doi:10.1186/s13068-017-0846-5.
77. Zdanowicz, M.; Spychaj, T.; Mąka, H. Imidazole-Based Deep Eutectic Solvents for Starch Dissolution and Plasticization. Carbohydrate Polymers 2016, 140, 416–423, doi:10.1016/j.carbpol.2015.12.036.
78. Svigelj, R.; Bortolomeazzi, R.; Dossi, N.; Giacomino, A.; Bontempelli, G.; Toniolo, R. An Effective Gluten Extraction Method Exploiting Pure Choline Chloride-Based Deep Eutectic Solvents (ChCl-DESs). Food Anal. Methods 2017, 10, 4079–4085, doi:10.1007/s12161-017-0979-y.
79. Tan, T.; Zhang, M.; Wan, Y.; Qiu, H. Utilization of Deep Eutectic Solvents as Novel Mobile Phase Additives for Improving the Separation of Bioactive Quaternary Alkaloids. Talanta 2016, 149, 85–90, doi:10.1016/j.talanta.2015.11.041.
80. Toniolo, R.; Dossi, N.; Giannilivigni, E.; Fattori, A.; Svigelj, R.; Bontempelli, G.; Giacomino, A.; Daniele, S. Modified Screen Printed Electrode Suitable for Electrochemical Measurements in Gas Phase. Anal. Chem. 2020, 92, 3689–3696, doi:10.1021/acs.analchem.9b04818.
81. Zuliani, I.; Fattori, A.; Svigelj, R.; Dossi, N.; Grazioli, C.; Bontempelli, G.; Toniolo, R. Amperometric Detection of Ethanol Vapors by Screen Printed Electrodes Modified by Paper Crowns Soaked with Room Temperature Ionic Liquids. Electroanalysis 2022, elan.202200150, doi:10.1002/elan.202200150.
82. Svigelj, R.; Dossi, N.; Pizzolato, S.; Toniolo, R.; Miranda-Castro, R.; de-los-Santos-Álvarez, N.; Lobo-Castañón, M.J. Truncated Aptamers as Selective Receptors in a Gluten Sensor Supporting Direct Measurement in a Deep Eutectic Solvent. Biosensors and Bioelectronics 2020, 165, 112339, doi:10.1016/j.bios.2020.112339.
83. Svigelj, R.; Dossi, N.; Grazioli, C.; Toniolo, R. Paper-Based Aptamer-Antibody Biosensor for Gluten Detection in a Deep Eutectic Solvent (DES). Anal Bioanal Chem 2021, doi:10.1007/s00216-021-03653-5.
84. Li, X.; Zhang, S.; Li, X.; Lu, L.; Cui, B.; Yuan, C.; Guo, L.; Yu, B.; Chai, Q. Starch/Polyvinyl Alcohol with Ionic Liquid/Graphene Oxide Enabled Highly Tough, Conductive and Freezing-Resistance Hydrogels for

Multimodal Wearable Sensors. Carbohydrate Polymers 2023, 320, 121262, doi:10.1016/j.carbpol.2023.121262.
85. Liu, X.; Qiao, W.; Chang, M.; Wang, Y.; Li, Y. Development of Rutin Sensor Based on Graphene Quantum Dots@nano-Carbon Ionic Liquid Electrode. Ionics 2023, 29, 3385–3392, doi:10.1007/s11581-023-04993-1.
86. Shahinfard, H.; Shabani-Nooshabadi, M.; Reisi-Vanani, A.; Darabi, R. Electrochemical Sensor Based on CuO/Reduced Graphene Nanoribbons and Ionic Liquid for Simultaneous Determination of Tramadol, Olanzapine and Acetaminophen. Carbon Lett. 2023, 33, 1433–1444, doi:10.1007/s42823-023-00512-4.
87. Zhao, L.; Zhao, F.; Zeng, B. Preparation and Application of Sunset Yellow Imprinted Ionic Liquid Polymer − Ionic Liquid Functionalized Graphene Composite Film Coated Glassy Carbon Electrodes. Electrochimica Acta 2014, 115, 247–254, doi:10.1016/j.electacta.2013.10.181.
88. Hayyan, M.; Abo-Hamad, A.; AlSaadi, M.A.; Hashim, M.A. Functionalization of Graphene Using Deep Eutectic Solvents. Nanoscale Res Lett 2015, 10, 324, doi:10.1186/s11671-015-1004-2.
89. Ni, Y.; Xu, J.; Liu, H.; Shao, S. Fabrication of RGO-NiCo2O4 Nanorods Composite from Deep Eutectic Solvents for Nonenzymatic Amperometric Sensing of Glucose. Talanta 2018, 185, 335–343, doi:10.1016/j.talanta.2018.03.097.
90. Ding, M.; Niu, H.; Zhang, N.; Hou, T.; Guan, P.; Hu, X. Facile Fabrication of Electrochemically Reduced Graphene Oxide/Polythionine-Methylene Blue and Its Use as a Platform for Detection of Nicotinamide Adenine Dinucleotide in the Artificial Urine Sample. Electrochimica Acta 2022, 425, 140715, doi:10.1016/j.electacta.2022.140715.
91. Ding, M.; Hou, T.; Niu, H.; Zhang, N.; Guan, P.; Hu, X. Electrocatalytic Oxidation of NADH at Graphene-Modified Electrodes Based on Electropolymerized Poly(Thionine-Methylene Blue) Films from Nature Deep Eutectic Solvents. Journal of Electroanalytical Chemistry 2022, 920, 116602, doi:10.1016/j.jelechem.2022.116602.
92. Fuchs, D.; Bayer, B.C.; Gupta, T.; Szabo, G.L.; Wilhelm, R.A.; Eder, D.; Meyer, J.C.; Steiner, S.; Gollas, B. Electrochemical Behavior of Graphene in a Deep Eutectic Solvent. ACS Appl. Mater. Interfaces 2020, 12, 40937–40948, doi:10.1021/acsami.0c11467.
93. Chavda, V.; Hirpara, D.; Kumar, S. GO/Ionic Surfactant Inspired Photophysical Modulation of Rhodamine B in Reline with or without Additives. Journal of Molecular Liquids 2022, 368, 120614, doi:10.1016/j.molliq.2022.120614.
94. Mahyari, M.; Hooshmand, S.E.; Sepahvand, H.; Gholami, S.; Rezayan, A.H.; Zarei, M.A. Gold Nanoparticles Anchored onto Covalent Poly Deep Eutectic Solvent Functionalized Graphene: An Electrochemical Aptasensor for the Detection of C-Reactive Protein. Materials Chemistry and Physics 2021, 269, 124730, doi:10.1016/j.matchemphys.2021.124730.
95. Gong, L.; Fu, H.; Liu, L.; Li, Z.; Guo, J.; Cao, Z.; Yao, J. Construction and Performance of a Nanocellulose–Graphene-Based Humidity Sensor with a Fast Response and Excellent Stability. ACS Appl. Polym. Mater. 2022, 4, 3656–3666, doi:10.1021/acsapm.2c00188.
96. Zhang, H.; Sun, Y.; Li, Q.; Wan, C. Upgrading Lignocellulose to Porous Graphene Enabled by Deep Eutectic Solvent Pretreatment: Insights into the Role of Lignin and Pseudo-Lignin. ACS Sustainable Chem. Eng. 2022, 10, 11501–11511, doi:10.1021/acssuschemeng.2c02586.
97. Arab, N.; Fotouhi, L.; Salis, A.; Dorraji, P.S. An Amplified Electrochemical Sensor Employing a Polymeric Film and Graphene Quantum Dots/Multiwall Carbon Nanotubes in a Deep Eutectic Solvent for Sensitive Analysis of Paracetamol and 4-Aminophenol. New J. Chem. 2020, 44, 15742–15751, doi:10.1039/D0NJ03371E.
98. Nguyen, T.N.T.; Thi Pham, N.; Ngo, D.-H.; Kumar, S.; Cao, X.T. Covalently Functionalized Graphene with Molecularly Imprinted Polymers for Selective Adsorption and Electrochemical Detection of Chloramphenicol. ACS Omega 2023, 8, 25385–25391, doi:10.1021/acsomega.3c02839.
99. Gomez, F.J.V.; Spisso, A.; Fernanda Silva, M. Pencil Graphite Electrodes for Improved Electrochemical Detection of Oleuropein by the Combination of Natural Deep Eutectic Solvents and Graphene Oxide. Electrophoresis 2017, 38, 2704–2711, doi:10.1002/elps.201700173.