Green Solvents for the Liquid Phase Exfoliation Production of Graphene: The Promising Case of Cyrene

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The liquid phase exfoliation (LPE) of graphite has allowed to produce graphene materials on a large scale and at a reasonable cost. By this method, stable dispersions, inks and liquid suspensions containing atomic-thick graphene flakes with tailored concentrations can be produced, opening up applications in a wide range of cutting-edge technologies such as functional coatings, printed and flexible electronics, and composites. However, currently established LPE techniques raise several health and environmental risks, since unsafe and toxic solvents (such as NMP, DMF, and DMSO) are often regarded as the most effective liquid media for the process. Therefore, it appears necessary to unlock eco-friendly and sustainable methods for the production of graphene at an industrial scale. This review focuses on the latest developments in terms of green solvents for LPE production of graphene. We highlight the use of a new green solvent, Cyrene, and its performance when compared to conventional solvents.

Keywords: 2D materials, solution processing method, sonication, high-shear mixing, inkjet printing, environmental risks, sustainability

INTRODUCTION

As the archetypal two-dimensional material, graphene has been the proposed material in the last decade for several technologies such as wearable/flexible electronics (Tan et al., 2017), structural and multifunctional nanocomposites (Wang et al., 2021), energy storage (Li and Zhi, 2018), strain sensors (Mehmood et al., 2020), water treatment (Bhol et al., 2021) and biomedical devices (Yang et al., 2013). A scalable mass production of highly pure graphene at low cost is the prerequisite for the commercialization phase. Among the many production methods, liquid phase exfoliation (LPE) allows to obtain liquid dispersions of graphene flakes with high yield. LPE technique was initially reported in 1989 for MoS₂ and WSe₂ (Gutiérrez and Henglein, 1989) and translated to graphene in 2008, demonstrating an affordable production of 2D materials in large quantities (Hernandez et al., 2008). LPE graphene flake dispersions are suitable for several applications, such as flexible, transparent, and printable electronics (Secor et al., 2013; Secor et al., 2015; Li et al., 2018; Shin et al., 2018). Usually, LPE identifies a group of approaches where natural and synthetic bulk materials are directly exfoliated into their corresponding isolated layers in a liquid medium, using the energy provided by different techniques: ultrasonication (Turner et al., 2019), wet ball-milling (Zhao et al., 2010), electrochemical, micro-fluidization (Xu et al., 2018), and high-shear mixing force (Paton et al., 2014), wet-jet milling (Del Rio Castillo et al., 2018) and high-pressure system (using an airless paint sprayer) (Nemala et al., 2018). These approaches can be executed in a variety of liquid solvents, including water (frequently mixed with surfactants), organic solvents, ionic liquids, oils, and salts.
(Xu et al., 2018). The general LPE process consists of three steps: intercalation, exfoliation and separation (Li et al., 2020). The solvent is a crucial factor in the exfoliation process, and to be effective it should fulfil three main requirements: 1) transmit the exfoliating power efficiently, 2) minimize the energy needed to disrupt the van der Waals forces among layers and 3) stabilize the exfoliated layers by providing steric hindrance to prevent re-agglomeration (Banavath et al., 2021). We will start this mini review by giving an overview of the most effective solvents for LPE of graphite. Although commonly used, these solvents entail severe health and environmental risks and should be replaced to reach a sustainable commercialization phase. The search for "green" solvents thus appears pivotal. By analyzing recent literature, we will describe the most representative green options to make stable graphene-based dispersions at high yield. As a case study, we will focus on dihydrollevoglucosenone (trademarked as Cyrene), which can be currently regarded as the most promising green solvent for LPE graphene.

**TOWARDS GREEN SOLVENTS FOR THE LPE OF GRAPHITE**

An ideal solvent for the exfoliation of graphite into graphene should meet several key requirements. In general, an ideal solvent would allow the complete exfoliation of graphite, leaving no un-exfoliated flakes in the sediment. The Hansen solubility parameters offer a framework to predict if and how a material will disperse in a particular solvent and form a solution (Charles, 2007). The surface tension of the solvent and graphite should ideally match to stabilize the graphene flakes in the dispersion after the exfoliation, preventing their re-agglomeration (Shen et al., 2015). For these reasons, researchers have originally selected solvents that matched as much as possible the Hansen solubility parameters and surface tension value of graphite (Hernandez et al., 2008; Capasso et al., 2015; Shen et al., 2016; Xu et al., 2018). The dynamic viscosity of the solvent is another important parameter in terms of exfoliation efficiency and stability. In principle, a high viscosity would be beneficial for the LPE process, increasing the exfoliation yield and decreasing the defect density and sedimentation rate (Manna et al., 2016; Salavagione et al., 2017; Simfukwe et al., 2017). However, a threshold must be set for practical applications, since an excessive viscosity favors the stable suspension of large agglomerates/particles during the centrifugation step, thus preventing the separation from thinner and lighter flakes (Backes, 2020). As a last consideration, a LPE solvent should feature a low boiling point to allow an easy removal of any solvent residue, which might degrade the properties of graphene (especially in terms of electrical conductivity) (Neill, 2009).

Conventional solvents for the LPE of graphite (surface tension ~55 mN m⁻¹ (Ronacorso et al., 2012)) exhibit a surface tension ranging within 40–50 mN m⁻¹ and Hansen solubility parameters close to those of graphite (δ₀ = 18.0 MPa⁻⁰.⁵, δ₀ = 9.3 MPa⁻⁰.⁵, δ₁₁ = 7.7 MPa⁻⁰.⁵) (Hernandez et al., 2010). Within this range, several highly polar solvents were selected, including N-methylpyrrolidone (NMP), N,N-dimethylformamide (DMF), dimethylsulfoxide (DMSO), N,N-dimethylacetamide (DMAC), and γ-butyrolactone (GBL) (Güler et al., 2021). Non-polar solvents such as ortho-dichlorobenzene (DCB) were also reported to produce homogenous graphene dispersions (Güler et al., 2021). In general, amine-based solvents such as NMP and DMF are the most effective in producing crystalline, oxygen-free graphene flakes (Güler and Sönmez, 2020). Hernandez et al. originally reported the production of stable dispersions of few-layer graphene in NMP (Hernandez et al., 2008; Xu et al., 2018). The initially reported concentration of 0.01 mg mL⁻¹ has been gradually increased above 1 mg mL⁻¹ by several groups with longer sonication times (Khan et al., 2010; Wang et al., 2012; Wu et al., 2014). Successful exfoliation and stable dispersions were also reported in DMF and DMSO, with concentrations similar to those obtained in NMP (Coleman, 2013; Xu et al., 2018; Trusova et al., 2021; Vacacela Gomez et al., 2021). Although the exfoliation is effective, NMP, DMF, and DMSO have high boiling points which cause issues in the removal of solvent residues. More importantly, these solvents present severe health risks. In 2008, NMP and DMF were classified as Substances of Very High Concern. According to the European REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) regulation (Regulation No 1907/2, 2022), several restrictions were applied regarding their use or import to Europe. Same warnings were raised in the USA. DMSO has also recently raised serious safety concerns, after several studies have demonstrated both the toxicity on retinal neuronal cells (Galvao et al., 2014) and the "extreme changes in micro RNAs and alterations in the epigenetic landscape", in both cardiac and hepatic micro-tissues, even for concentrations as low as 0.1% (Verheijen et al., 2019).

In this context, current solvents for LPE graphene appear as a limiting factor in the long-term development and sustainability of the production. Safety concerns also demand the need for impractical and expensive equipment (e.g., safety equipment, fume-hoods, exhausts, etc.), with a direct impact on the production cost. In order to scale-up the process and approach an industrial production, the identification of environmentally safe solvents that do not raise health risks is thus imperative. These solvents should be efficient for the exfoliation process, while having a moderate cost. A low boiling point is also a desired feature. Such characteristics would at once minimize the ecological impact and lower the production complexity and cost of the production of graphene. Capello et al. proposed a framework for a comprehensive assessment of how “green” a solvent is (Capello et al., 2007). The authors used a complementary, multi-criteria evaluation: They combined EHS (environment, health and safety) considerations on the inherent hazards of a solvent, and a LCA (life-cycle-assessment) that quantifies the energy use connected to solvent production and disposal/treatment as waste (Capello et al., 2007). According to this definition, low-boiling-point solvents such as acetone and isopropyl alcohol (61°C and 56°C, respectively) can be considered green alternatives (Capello et al., 2007). They have been previously used to disperse graphene at low concentration (few μg mL⁻¹)
FIGURE 1 | The application of solvent selection criteria for optimizing graphene dispersions. (A) Illustration of the solvent selection steps applied for the computational screening of suitable solvents. (B) Graphene dispersion concentration as a function of (i) dispersive, \( \delta_D \) (ii) polar, \( \delta_P \) and (iii), hydrogen-bonding, \( \delta_H \) Hansen solubility parameters, with the dashed red line being indicative of ideal graphene properties. NMP, DMF and DCB are shown as reference. (C) Hansen solubility map showing the similarity of the final bio-based solvent candidates (and NMP) to graphene in terms of their polarity. The Hansen radius (Ra) is the radius of the sphere in the Hansen space, where each axis corresponds to one solubility parameter. (D) Principle Component Analysis (PCA) bi-plot for candidate solvents (including NMP, DCB and DMF for reference) with vectors indicating surface tension, kinematic viscosity (KV) are and Hansen radius (Ra). Reproduced with permission from Ref (Salavagione et al., 2017). Copyright © The Royal Society of Chemistry 2017.
(Hernandez et al., 2010). However, these solvents have low flash points (12–13°C), which raise safety concerns for industrial use. Cyclohexanone and cyclopentanone have also been previously proposed as green and bio-based LPE solvents, but they present similar issues (flash point of 44°C and 31°C, respectively) (Hernandez et al., 2010).

Other green alternatives are represented by aqueous media with surfactants (e.g., sodium dodecylbenzenesulfonate (Lotya et al., 2009), sodium cholate, (Green and Hersam, 2009), and sodium deoxycholate (Hasan et al., 2010)), and/or polymers (e.g., Pluronic® (Seo et al., 2011)) useful to overcome surface tension mismatch (water has a surface tension of 72 mN m⁻¹). Surfactant-assisted exfoliation in aqueous media is one of the most suitable alternatives to achieve high-quality graphene at high concentrations (Zhang et al., 2018). Green et al. prepared stable dispersions of graphene using sodium cholate (SC) as a surfactant in aqueous medium, yet achieving a low concentration (10 μg ml⁻¹) (Green and Hersam, 2009). In an analogous study, dispersions in water and SC were prepared by tip-sonication up to 7 mg/ml concentration using longer exfoliation times (96 h) and dispersions in water and SC were prepared by tip-sonication up to 7 mg/ml concentration using longer exfoliation times (96 h) and dispersions in water and SC were prepared by tip-sonication up to 7 mg/ml concentration using longer exfoliation times (96 h) and dispersions in water and SC were prepared by tip-sonication up to 7 mg/ml concentration using longer exfoliation times (96 h) and dispersions in water and SC were prepared by tip-sonication up to 7 mg/ml concentration using longer exfoliation times (96 h) and dispersions in water and SC were prepared by tip-sonication up to 7 mg/ml concentration using longer exfoliation times (96 h) and dispersions in water and SC were prepared by tip-sonication up to 7 mg/ml concentration using longer exfoliation times (96 h) and dispersions in water and SC were prepared by tip-sonication up to 7 mg/ml concentration using longer exfo...
which are usually responsible for end-of-life pollution issues. When incinerated, Cyrene yields only carbon dioxide and water as byproducts: This is a major difference over NMP, which liberates NOx when decomposed. Also, Cyrene has very low acute and aquatic toxicity with LD₅₀ (lethal dose, 50%) and EC₅₀ (effective concentration, 50%) values of >2000 mg kg⁻¹ and >100 mg L⁻¹, respectively. Overall, Cyrene is biodegradable and not mutagenic. Although it has a rather high boiling point (227°C), its low flash point (108°C, lower than several oxygenated solvents, such as alcohols and ketones) makes it safe to handle.

Salavagione et al. first demonstrate the preparation of LPE graphene in Cyrene. After 2 h of bath sonication, the dispersion showed a final concentration ~0.7 mg ml⁻¹, with a very high yield (~48%). These values are larger than those obtained by most conventional organic solvents, also requiring more complex LPE procedures (Lavin-Lopez et al., 2016). In their analysis, 92.5% of the dispersed flakes were few-layer (more than 10), 75% within five layers, and 7.5% monolayer (final average of 4.5 layers). In similar bath sonication experiments, Gharib et al. obtained a 6 times higher concentration with respect to NMP and DMF (Gharib et al., 2017). Tkachev et al. proposed the preparation of a graphene-based ink in Cyrene by a combination of two LPE methods (i.e., tip-sonication and high-shear mixing). The authors produced highly concentrated dispersions (up to 3.70 g L⁻¹) of few-layer graphene flakes (three to five layers) with mean lateral size of ~200 nm (Tkachev, 2021). Pan et al. developed an environmentally friendly, sustainable, low-cost graphene-based ink in Cyrene with concentration up to 10 mg ml⁻¹, by using sonication assisted exfoliation. The authors added cellulose acetate butyrate (CAB) as a stabilizing agent to achieve even a higher concentrated ink (70 mg ml⁻¹) (Pan et al., 2018) of multilayer graphene flakes (thickness ~5 nm) with lateral size of a few μm.

In terms of applications, Pan et al. screen-printed electrodes from graphene inks in Cyrene and NMP. They obtained analogous sheet resistance values (~1 Ω sq⁻¹) using inks produced with significantly different sonication times (8 h for Cyrene vs. 48 h for NMP). The electrical conductivity of dried and compressed graphene laminates from Cyrene ink (8 h sonication) was 7.13 × 10⁴ S m⁻¹. These results pave the way to low-cost, screen-printable graphene-based wearables for Internet of Things applications, such as healthcare and wellbeing monitoring (Pan et al., 2018). Tkachev et al. prepared graphene-based inks in Cyrene to spray-coat flexible semi-transparent electrodes with high optical transmittance (78%) and low sheet resistance (290 Ω sq⁻¹). They embedded such electrodes in a working prototype of a multi-touch screen with a high signal-to-noise ratio (14 dB). These results illustrate a potential pathway toward the integration of LPE-graphene in commercial flexible electronics (Tkachev, 2021). Hassan et al. proposed a green ink combining Cyrene and ethyl cellulose (polymeric binder that helps lowering sheet resistance by enhancing connectivity and filling the gaps). They used it to fabricate (by 3D extrusion printing) low-cost
patterned electrodes for volatile organic compounds detection fabricated. The devices showed a resistivity as low as 70 Ω cm and high sensitivity to organic compounds (i.e., acetone, ethanol, and methanol). In particular, the device showed a high sensitivity towards ethanol (Hassan et al., 2021). These case study results suggest that Cyrene based graphene inks are more stable and suitable than the currently employed solvents for commercial applications, without any toxicity issues.

CONCLUSION

In summary, there is an urgent need of replacing conventional solvents like NMP and DMF for the liquid phase production of graphene, in order to reduce health and environmental issues and enable a sustainable industrial production. We have presented the most viable “green” solvents in the field, comparing their different properties and their effectiveness (in terms of concentration and yield) as exfoliation media. Among the possible options, Cyrene appears as the most promising green solvent for LPE techniques. The performance of Cyrene for the exfoliation of graphite was analyzed, also focusing on research literature reporting graphene-based devices prepared using this solvent. This mini-review sheds light on a sustainable solution processing methods for graphene, but the findings could be translated to other layered 2D materials, such as hBN, transition metal dichalcogenides and MXenes.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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