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Polyethylene glycol (PEG) derived carbon dots: Preparation and applications

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ABSTRACT

Carbon dots (C-dots), the latest member of the renowned carbon nanomaterials family, have attracted enormous attention for their extraordinary properties. Polyethylene glycol (PEG), as a nontoxic, non-immunogenic and high water soluble polymer, is widely used for the PEGylation of protein/peptide drugs and traditional nanoparticles. Recently, PEG has been heavily investigated regarding their unique capability in enhancing C-dots fluorescence emission, elucidating C-dots formation and photoluminescence mechanism. In this article, we summarized recent excitements of PEGs as passivation agents, solvents/matrices and sole carbon precursors in the synthesis of C-dots. We also discussed the formation mechanism of PEG-derived C-dots as well as their applications in various fields. Current challenges, and perspectives on the future trends of PEG-derived C-dots are also highlighted and discussed.

1. Introduction

Carbon dots (C-dots), also known as carbon quantum dots or carbon nanodots, are among the most studied carbon-based nanomaterials in the last decade. With excellent photoluminescence (PL) and stability, high water dispersion, exceptional biocompatibility and low toxicity as well as rich and tunable surface functionalities, C-dots have attracted enormous interests as a potential nontoxic alternative of traditional semiconductor-based quantum dots. Since their discovery and development in early 2000s [1,2], the past decade has witnessed the tremendous growth of this field, with numerous synthesis methods and applications being established and developed [3–6]. Nowadays, C-dots could be synthesized from essentially any carbon-containing materials or substances, for example, bulk carbon materials [7–9], small organic molecules [10–14], polymers [15,16], biomacromolecules [17,18], food [19–21] as well as bacterial [22] have all been applied for the fabrication of C-dots. With these C-dots, broad applications in various fields such as bioimaging, drug delivery, theranostics design, sensor development, catalysis, optoelectronics, energy harvesting, storage and conversion have been developed [23–27]. Despite the rapid advancements and enormous potentials, further development of C-dots still faces some challenges that cannot be bypassed. First of all, most of the C-dots obtained in current synthesis are generally low in PL quantum yield (QY). Thus, extra and tedious surface passivation with organic molecules, polymers or doping with heteroatoms (i.e., N, S, P) is often required for property tuning [28–31]. Second, the detailed formation mechanism of C-dots, especially for those fabricated in a "bottom-up" manner, has generally not been elucidated. Last, the exact PL mechanism of C-dots is still under debate, which might be due to the diverse synthesis methods and lack of consistence of the reported studies [32,33]. Without a clear understanding of the formation and PL mechanism of C-dots, the ultimate goal of rational design and synthesis of C-dots with desired properties for specific applications would be impossible.

As a result, significant efforts have been devoted to tackle these challenges. Among the various efforts, the use of polymers in the synthesis of C-dots has been promising by providing some alternatives to partly tackle these challenges. In practical applications, polymers have been widely applied to increase PL QYs, enhance emission lifetimes, fine-tune emission wavelengths, advance absorption in specific spectral range as well as tailor other in-general properties by C-dots surface passivation/functionalization and composition [34–36]. Further, well-defined molecular precursors (especially polymers that contain heteroatoms such as S, P, B, and aromatic rings) could endow C-dots with elegant characteristics for special purposes, significantly expanding the realm of C-dots [37,38]. Most importantly, polymers, especially those man-made ones, are designed and synthesized under strict conditions

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with unambiguous and repeating structures. Thus polymers have become preferred carbon precursors for the fabrication of C-dots due to their reproducibility in large-scale production with tunable properties (i.e., polymer chain length, polarity, terminal functionalities, carbon contents, etc.) tailored for specific C-dots fabrications. This is quite significant for continuous and fruitful efforts in figuring out the detailed structure of C-dots as well as their formation and PL mechanism [39–43].

Polyethylene glycol (PEG) is among the most successful polymers as regarding the vital roles they play in C-dots passivation and synthesis. Chemically speaking, PEG is a class of synthetic polymers with a repeating subunit of ethylene glycol ($HO–CH_2–CH_2–OH$), the structure of PEG could be commonly expressed as $H–(O–CH_2–CH_2)_n–OH$. PEG is available in a range of molecular weights (M.W.), depending on the number of the repeating subunits; the M.W. could range from a few hundreds to several hundreds of thousand Daltons. By convention, PEG is referred to materials with a M.W. up to 100,000 Daltons. Due to its superior properties, such as nontoxicity, non-immunogenicity, high water solubility, PEG has been approved by the Food and Drug Administration (FDA), USA, for various biomedical uses. As a result, C-dots derived from PEG are intrinsically less toxic, and with better biocompatibility. Further, because of the excellent passivation ability of PEG, the processes to synthesize C-dots from PEG are easy, self-passivated, and generally benign to the environment. Considering the simple and clear structure of PEG as well as the easy accessibility of series of PEGs in a variety of M.W. with various functions, the formation mechanism of PEG-derived C-dots has been extensively explored and relatively clear compared to other C-dots [44–46]. The formation mechanism has been successfully used to explain and predict various properties (i.e., size, PL emission) of C-dots formed under different conditions. Despite the significant advancements, articles specifically focusing on PEG-related C-dots have been rather limited. In this review paper, we summarized recent advancements of PEGs as passivation agents, solvents/matrices and sole carbon precursors for the synthesis of C-dots. We also discussed the formation mechanism of PEG-derived C-dots as well as their applications in various fields. As such, we believe these findings should bring nontrivial insights to the further development of C-dots and attract general interests from the broader fields of carbon-based nanomaterials.

2. PEG as passivation agent in C-dots synthesis

2.1. PEG for PEGylation

As a versatile material, PEG has been heavily utilized for medical, chemical, biological, commercial, industrial as well as recreational applications [47]. Among the various applications, PEG is best known for its application as PEGylation agent [48]. The idea of conjugating PEG to a protein (or "PEGylation of protein) to enhance protein circulation and activity lifetimes in body was proposed back in the late 1960s [49]. Since then, considering its superior properties (i.e., high water solubility, nontoxicity, non-immunogenicity, non-antigenicity and FDA approval), PEG has played significant roles in drug delivery, enhancing the circulation lifetime and stability of protein and peptide drug molecules. With the introduction of PEG, the drug conjugates generally demonstrate decreased degradation by metabolic enzymes, prolonged residence in body and reduced protein immunogenicity [50].

Later on, PEGylation has been extended to substances/materials other than protein/peptide drug molecules. Early studies demonstrated that PEGylated biomaterial surfaces (either by covalent attachment or noncovalent absorption) could decrease/prevent the adsorption of protein or virus onto the surfaces compared to non-PEGylated surfaces [48], which could significantly increase the bioavailability of biomaterials in body (especially in vascular systems). As the development of nanotechnology, nanoparticles (NPs) are increasingly applied for biomedical purposes such as bioimaging, drug delivery, and theranostic system. As such, the PEGylation of NPs have become the most pursued approach to enhance the biocompatibility, water solubility, decrease enzymatic degradation, and provide non-immunogenicity of NPs [51].

2.2. PEG for C-dots passivation

As witnessed by the numerous research articles and applications of C-dots, there has been increasing interest on C-dots in the past decade [3]. It's worth to mention, the easy access and cheap availability of the starting material and the numerous methods available for C-dots synthesis are among the most important reasons for the continuing, intense public interest on C-dots. Generally speaking, there are mainly two strategies for the synthesis of C-dots, namely "top-down" and "bottom-up" depending on the nature of the starting materials applied. In the early years, "top-down" approach, which involving the breakdown of bulk carbon materials into tiny functionalized carbon nanoparticles (i.e., less than 10 nm) under harsh conditions, has been very popular. On the other hand, "bottom-up" approach, in which C-dots are prepared from organic substances through a "polymerization – carbonization" fashion has attracted much more attention in recent years. In most of the synthesis, surface passivation is necessary to improve the PL property of C-dots. In general, a separate step is often required to carry out the surface passivation of C-dots synthesized by the "top-down" approach; while the passivation of "bottom-up" C-dots could be done in a "one-pot" fashion simultaneously with the synthesis of C-dots [28–31].

It's worth mentioning, surface passivation is different from surface modification. In general, surface modification will cause the change of original physical, chemical and biological characteristics of a material. Meanwhile, surface passivation (also called Atalla passivation) indicates that a material becomes less affected by the environment and preserve some important properties with a "shield". This "shield" can be led by chemical reaction or spontaneous oxidation. To be specific, passivation of C-dots is aimed at improving the PL intensity by forming a thin insulating capping "layer" to prevent the loss of energy generated along with the emission. The selection of passivation agents often focuses on polymers such as PEG or organic molecules that do not contain visible chromophores [31]. Therefore, the surface passivation of C-dots generally only enhances the PL intensity but will not cause the change of emission wavelength. However, due to the introduction of passive agents on the surface, the passivated C-dots could have unique surface chemistry properties such as abundant surface functionalities that may benefit a variety of future applications such as drug delivery.

Inspired by its wide applications in the PEGylation of protein drugs and NPs, PEG has been heavily used as a passivation agent for the passivation of C-dots since 2006 (Table 1). In the groundbreaking report from Sun's group, PEG demonstrated high efficiency in tuning the C-dots properties, especially the enhancement of PL property [2]. Before passivation, there was no detectable PL from the laser-ablated ("top-down" approach) carbon NPs, even after the samples were treated with nitric acid solution under refluxing. Surprisingly, upon the surface passivation of the acid treated C-dots by attaching diamine-terminated PEG (PEG_{1500N}, Fig. 1A), bright and stable PL emissions were detected (Fig. 1B). Mechanistically, the PL of the C-dots was attributed to the presence of the surface energy traps, which was stabilized and became emissive upon surface passivation. In a different study from the same group, the passivation of C-dots by PEG_{1500N} was also demonstrated as the key to enhance the PL [52]. Other groups also re-

Table 1
Selective examples of PEG-passivated C-dots: synthesis and applications.

Carbon source[a)]	Synthesis method	Passivation parameters Agent[b)]	Approach[d)]	Effects[e)]	C-dots applications	Ref.
Graphite	Laser ablation	PEG_{1500N}	Stepwise	PL↑	Bioimaging	[2,52]
Graphite	Laser ablation	PEG_{200}		PL↑	–	[54]
Graphite	Laser irradiation	PEG_{200N}		PL	–	[56]
GO	Thermal exfoliation	$PEG_{?N}$		PL↑Cytotoxicity↓	Bioimaging	[60]
Resols	Direct heating	PEG_{1500N}		PL↑	Bioimaging	[53]
Starch	Oxidative acid treatment	PEG_{1500N}		Cytotoxicity↓ Size↓; Red→	–	[61]
Cassava peels	Hydrothermal	PEG		PL↑; Red→	–	[62]
GA	Direct heating	$PEG_{?N}$		Cytotoxicity↓	–	[83]
Cigarette ash	Ultrasonication	PEG_{1900S}	One-	PL↑	Bioimaging	[55]
Gluconic acid	Direct heating	PEG_{200} [c)]	pot	Tribological↑	Lubrication	[63]
CA	Hydrothermal	PEG_{2000}		PL↑	Bioimaging	[64]
CA; AA	Microwave	PEG_{8000}		PL↑	–	[65]
Glucose	Microwave	PEG_{600}		Blue→; New PL peak	Memory device	[67]
Glucose	Direct heating; Microwave; Ultrasonication	PEG_{200}		Adsorption↑	Desulfurization	[68]
Chitosan	Hydrothermal; Microwave	PEG_{4000}		PL↑	Bioimaging	[71,72]
Gelatin	Microwave	PEG_{4000}		PL↑	Bioimaging	[73]
Honey	Microwave	PEG_{400}		PL↑; Red→	Bioimaging	[74]
Carob molasses	Hydrothermal	PEG_{15000}		PL↑; H_2O_2 Scavenger; Antioxidant	–	[77]

[a)] GO: graphene oxide; GA: glutamic acid; CA: citric acid; AA: ascorbic acid.
[b)] PEG_{1500N}: polyethylene glycol terminated with $-NH_2$ (M.W., 1500 Daltons); $PEG_{?N}$: polyethylene glycol terminated with $-NH_2$ (M.W. was not mentioned in the reference); PEG_{1900S}: polyethylene glycol terminated with –SH (M.W., 1900 Daltons).
[c)] PEG with M.W. of 200, 600, 1000 and 4000 have been applied for the synthesis of C-dots; however only PEG_{200}-derived C-dots were characterized.
[d)] Stepwise: C-dots synthesis and passivation were done in separate steps; one-pot: C-dots synthesis and passivation were done simultaneously.
[e)] PL↑: enhancement of photoluminescence intensity; Cytotoxicity↓: decrease of cellular toxicity; Size↓: decrease of C-dots size; Red→: red shift of the emission spectra; Tribological↑: enhancement of tribological properties; Blue→: blue shift of the emission spectra; Adsorption⇧: increased adsorption of sulfur thiophenic compounds.

ported that separate steps of surface passivation by PEG are essential for their C-dots to obtain PL emission [53,54]. Interestingly, not all "top-down" C-dots need a separate step of surface passivation (stepwise passivation) in order to attain PL property; "top-down" C-dots that are passivated in a "one-pot" manner has also been reported [55]. Interestingly, Du and co-workers synthesized C-dots by laser irradiation of graphite powders assisted by ultrasound, which emitted no visible light before surface passivation. However, both "one-pot" and stepwise passivation (oxidative acid treatment followed by covalent conjugation of N-terminated PEG) gave very similar, bright blue emissions [56], mechanistically indicating that as long as the passivation could stabilize the surface energy traps, it does not matter whether a "one-pot" or stepwise passivation approach is adopted. Thus, it is reasonable to expect some un-passivated "top-down" C-dots could emit lights as long as they have a certain amount of stable surface energy traps. Indeed, "top-down" C-dots without passivation possessing PL emission property have been reported, although with relatively low quantum yields [8,57–59]. In most of the stepwise passivations, C-dots and PEG are covalently attached (i.e., through amide bond formation between the N-terminated PEG and the surface carboxyls of C-dots) [2,52,53,60,61]; however, noncovalent passivation is also possible [62].

Unlike C-dots synthesized in "top-down" approach, C-dots prepared in "bottom-up" approach are generally passivated in a "one-pot" fashion in which the synthesis and passivation of C-dots are done simultaneously (Table 1). Studies in which C-dots were synthesized from gluconic acid [63], citric acid [64–66], ascorbic acid [65], glucose [67,68], organic dyes [69,70], chitosan [71,72], gelatin [73], and honey [74] as carbon precursors, together with PEGs as passivation agents were all done in this "one-pot" fashion. For example, Gopinath and co-workers investigated the effects of PEG_{4000} passivation on the synthesis of chitosan-based C-dots preparation *via* microwave pyrolysis [71] and hydrothermal reaction [72]. In these two studies, passivation by PEG_{4000} has been shown to significantly enhance the PL of the C-dots compared to the unpassivated counterparts. To rule out the possibility of PEG_{4000} being carbonized, separate blank experiments where PEG_{4000} was subjected to similar microwave/hydrothermal treatments were carried out; the treated PEG_{4000} solution remained clear and showed no PL activity that justified the role of chitosan as sole carbon source for C-dots formation. Similar results were reported in a different study where PEG_{4000} was used for the passivation of gelatin-based C-dots [73]. In these studies, PEG_{4000} showed no detectable degradation or dehydration under the reaction conditions, presumably due to the non-dehydrating nature and high M.W. of PEG_{4000}. However, in a different study where PEG_{2000} was used, the authors believe that PEG_{2000} not only functioned as passivation agent, but also directly involved in the carbonization process as carbon precursor (Fig. 2) [64].

2.3. PEG passivation on C-dots' photoluminescence properties and beyond

As for the PL mechanism of C-dots, there are three predominant theories, namely surface state, molecular state and quantum confinement effect. [32,33,76] Surface state theory states that there exist many electronic states on the surface of C-dots due to a variety of surface functional groups. When C-dots are excited at different wavelengths, electrons in different energy traps on the surface of C-dots will get excited separately by high-energy irradiation. Due to the presence of multiple electronic states (surface states) caused by various surface functionalities, the excited electrons will firstly shift to the energy band of a certain surface state after going through a series of non-irradiative energy emission processes such as vibrational relaxation and then return to the ground state to recombine with the holes while releasing the energy in the form of light. However, the concept of surface states is quite abstract in comparison to molecular state theory. In molecular state theory, people believe there exist many fluorophores on the surface of C-dots and the PL properties of C-dots are largely decided by the PL properties of these fluorophores. However, it is hard to be used to explain the excitation-dependent PL behaviors of C-dots. The last theory, quantum confinement effect points out that the PL property of C-dots is due to their nanoscale size. This theory was a major feature of quantum dots. As an alternative of quan-

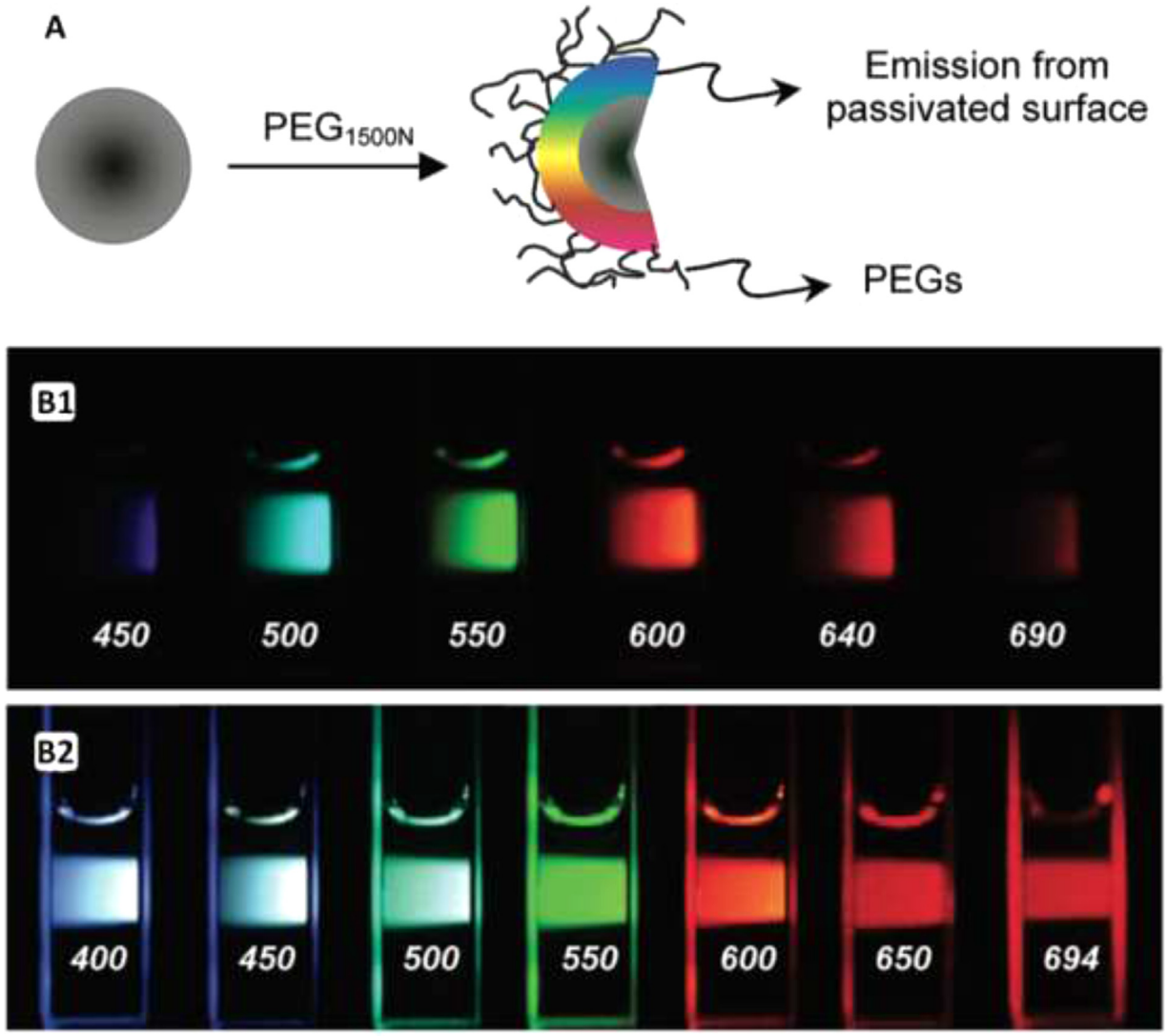

Fig. 1. (A) Covalent passivation of C-dots with PEG_{1500N}. (B) Aqueous solution of the PEG_{1500N}-passivated C-dots (B1) excited at 400 nm and photographed through band-pass filters of different wavelengths as indicated, and (B2) excited at the indicated wavelengths and photographed directly. Reproduced with permission from ref. [2] Copyrights 2006, American Chemical Society.

tum dots, C-dots have a similar core-shell structure, which was validated. Therefore, it is hypothesized C-dots also have quantum confinement effect. Nonetheless, in comparison among the three theories, surface state theory is the most popular one and has been widely used to explain many PL phenomena and unique applications such as photocatalysis [11].

As such, passivation by PEG could stabilize the surface energy traps of C-dots and make them emissive [2], thus the fluorescence emission QYs are generally increased upon passivation. Even though PL emission enhancement is most often the point of start when C-dots are passivated, however, the effects of PEG passivation are not limited to PL emission (Table 1). In general, passivation may also influence water solubility, biocompatibility, and other physical (i.e., sizes), chemical as well as biological properties (i.e., toxicity) [61,77,78]. For example, PEG-passivated C-dots, as water-based lubricant additives, demonstrated far superior lubrication effects under four-ball mode and steel/steel contact test compared to PEG or un-passivated C-dots [63]. In the report by Fallah et al., PEG passivation was found to be crucial for the adsorption capability of C-dots for the adsorptive desulfurization of liquid model fuels [68]. Near infrared (NIR) imaging is among the most sought after imaging techniques considering the transparency of NIR light to animal tissues [79,80]. Although much effort has been devoted, studies showing C-dots with NIR emissions are still very limited in literature [10,16,21,81]. Interestingly, passivation of C-dots by PEG has been shown to red shift the emissions of bared C-dots [61,82]. For example, Wu et al. reported a very encouraging study in which the passivation of honey-derived C-dots by polymers could significantly enhance the fluorescence properties. Specifically, C-dots passivated by hyperbranched polymer showed a significant increase in NIR emission (Fig. 3A) compared to PEG (linear polymer) passivated counterpart, presumably because the hyperbranched-polymer-increased surface area significantly amplified the average radiant efficiency [82]. Further, functional PEGs are easily accessible, for example, PEGs with terminal hydroxyl (–OH), thiol (–SH), amine ($–NH_2$), carboxyl (–COOH), methoxyl ($–OCH_3$), as well as cholesterol are all commercially available. The wide availability of commercial PEGs with different terminal functionalities makes the tuning of surface functionalities of PEG modified C-dots very facile. Apart from the above-mentioned benefits, PEGylation has also been shown to be able to decrease the toxicity of C-dots (Fig. 3B) [60,61,83]. Selective examples regarding the synthesis and applications of PEG-passivated C-dots are summarized in Table 1.

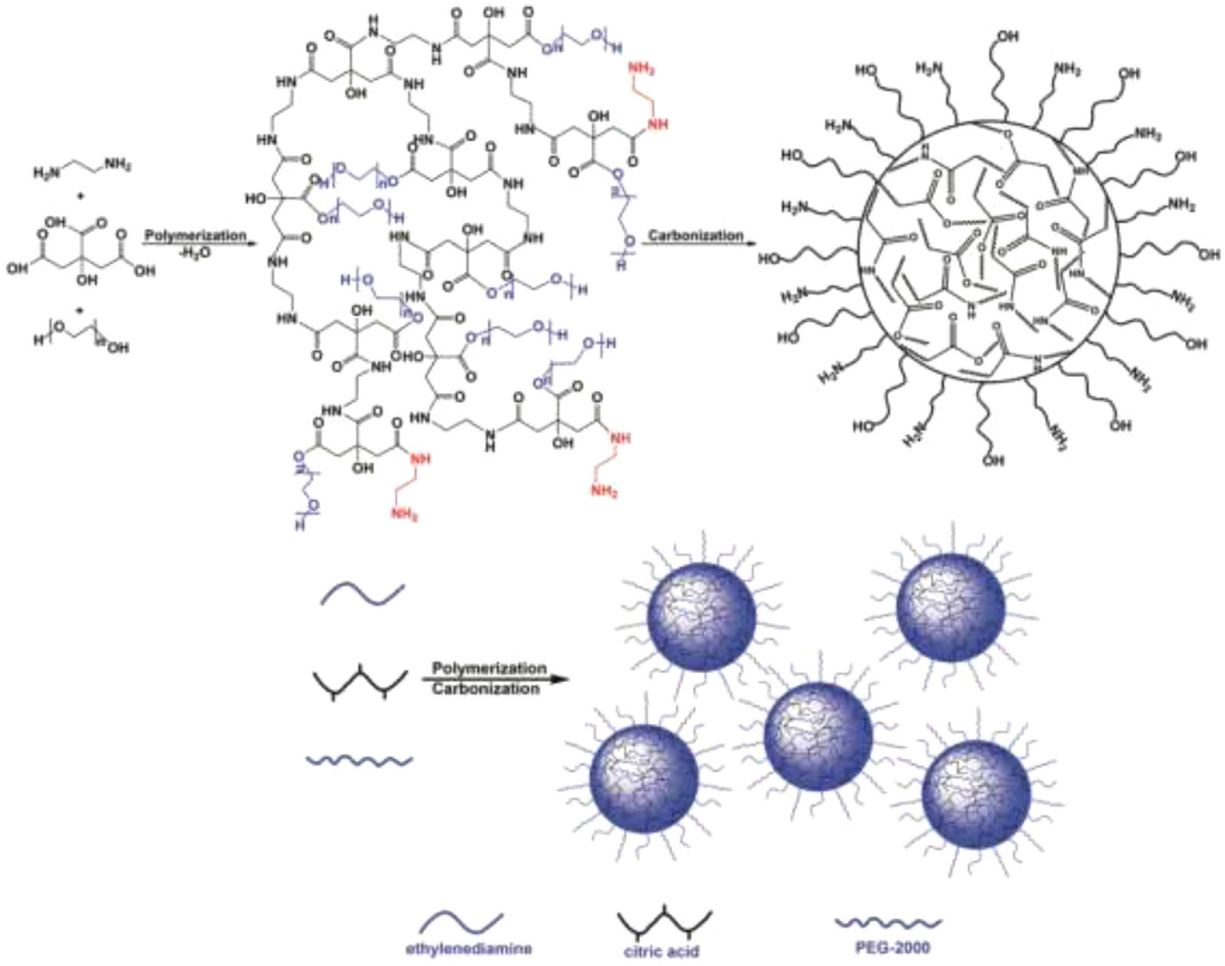

Fig. 2. Schematic illustration showing the possible synthetic mechanism of C-dots passivated by PEG_{2000}. Reproduced with permission from ref. [75] Copyrights 2015, Royal Society of Chemistry.

3. PEG as solvent/matrix in C-dots synthesis

PEG is amphiphilic, and thus soluble in both water and many organic solvents (i.e., CH_3CH_2OH, CH_2Cl_2, CH_3Cl, etc.), making it ideal for reaction medium. Indeed, PEG has been widely used for the synthesis of NPs (especially metal and oxide NPs) in which the superior properties such as high boiling points, good reducing and coordinating abilities, as well as aqueous-comparable metal-salt solubility are fully exploited [51,84]. Inspired by these studies, C-dots preparation using PEG as reaction medium also surfaced in recent years, although far less compared to NPs. For example, Lehmacher and Feldmann reported the synthesis of red emissive C-dots from 1,2,4,5-tetracyanobenzene, in which PEG_{400} was selected as a solvent and also functioned as a surface stabilizer/passivation agent (Fig. 4A) [85]. In a different study, a mixed solvent of PEG_{200} and water was used for the microwave-assisted pyrolysis preparation of C-dots from glucose (Fig. 4B) [86]. PEG has also been used as solvent for C-dots synthesis in a "top-down" approach in which graphite powders were used as carbon precursor (Fig. 4C) [56]. Since homogeneous reactions are generally more efficient than heterogeneous ones, thus in the above-mentioned examples, PEGs were limited to the ones with low M.W. in liquid state. Interestingly, a very recent report has shown that solid PEG could also function as a reaction medium/matrix to assist the synthesis of C-dots [87]. In this study, ethanolamine was first dispersed within PEG_{1000} matrix, and then the composites were thermally treated which gave fluorescent C-dots containing nanocomposites. This solid synthesis approach eliminated the use of toxic chemicals and could be extended to a variety of thermally stable polymers.

4. PEG as carbon precursors for C-dots synthesis

Chemically and structurally speaking, PEGs are good carbon precursors for C-dots synthesis. This is especially true for those with a small M.W. (i.e., less than 800 Daltons) since they not only have a high percentage of carbon, but also is subjected to easy dehydration, polymerization and carbonization. In an early study, Du et al. observed some weak fluorescence emissions from their control experiments in which PEG_{200N} were irradiated by laser, and treated by perchloric acid under heating, respectively. This study may be the first report in literature that C-dots were directly synthesized from PEG as carbon precursor [56]. In the investigations of PEG-assisted synthesis of NPs, Feldmann and co-workers frequently observed relatively intense emissions of blue light in their products which were hard to explain [84]. Enlightened by numerous reports of C-dots related studies, later on, they were able to trace the unexpected fluorescence to C-dots formed from the thermal decomposition of PEGs during NPs synthesis [88]. Inspired by these works, various studies have reported the use of PEGs as direct carbon precursors for the synthesis of C-dots and significant advancements have been achieved.

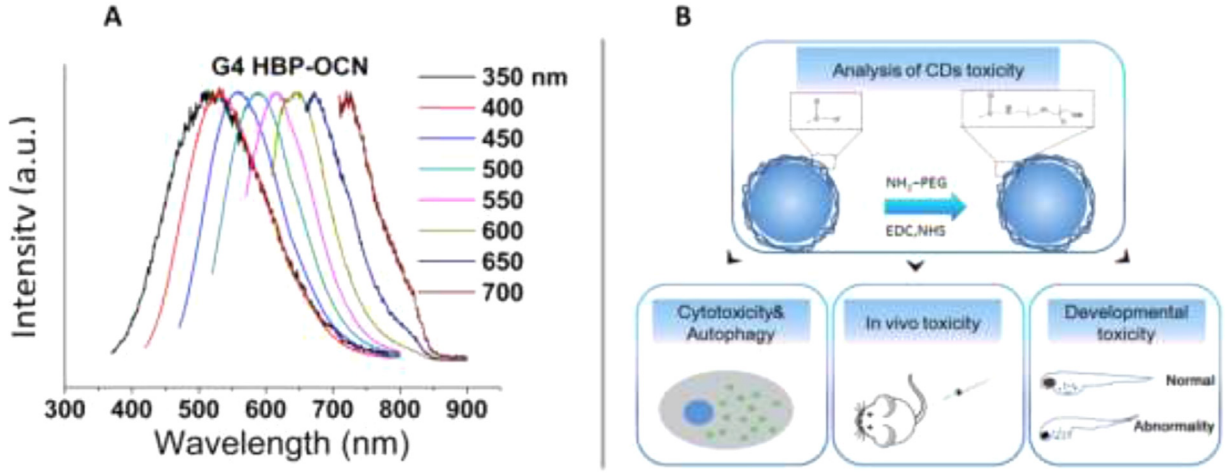

Fig. 3. (A) Normalized emission spectra of hyperbranched polymer passivated C-dots showing the emission spectra extended into the NIR region. Reproduced with permission from ref. [82] Copyrights 2013, Ivyspring International Publisher. (B) Schematic illustration of the *in vitro* and *in vivo* toxicology studies of passivated and un-passivated C-dots. *In vitro* study is for the evaluation of cytotoxicity and cell autophagy, while *in vivo* study is for the assessment of long-term toxicity and developmental toxicity. Reproduced with permission from ref. [83] Copyrights 2015, Royal Society of Chemistry.

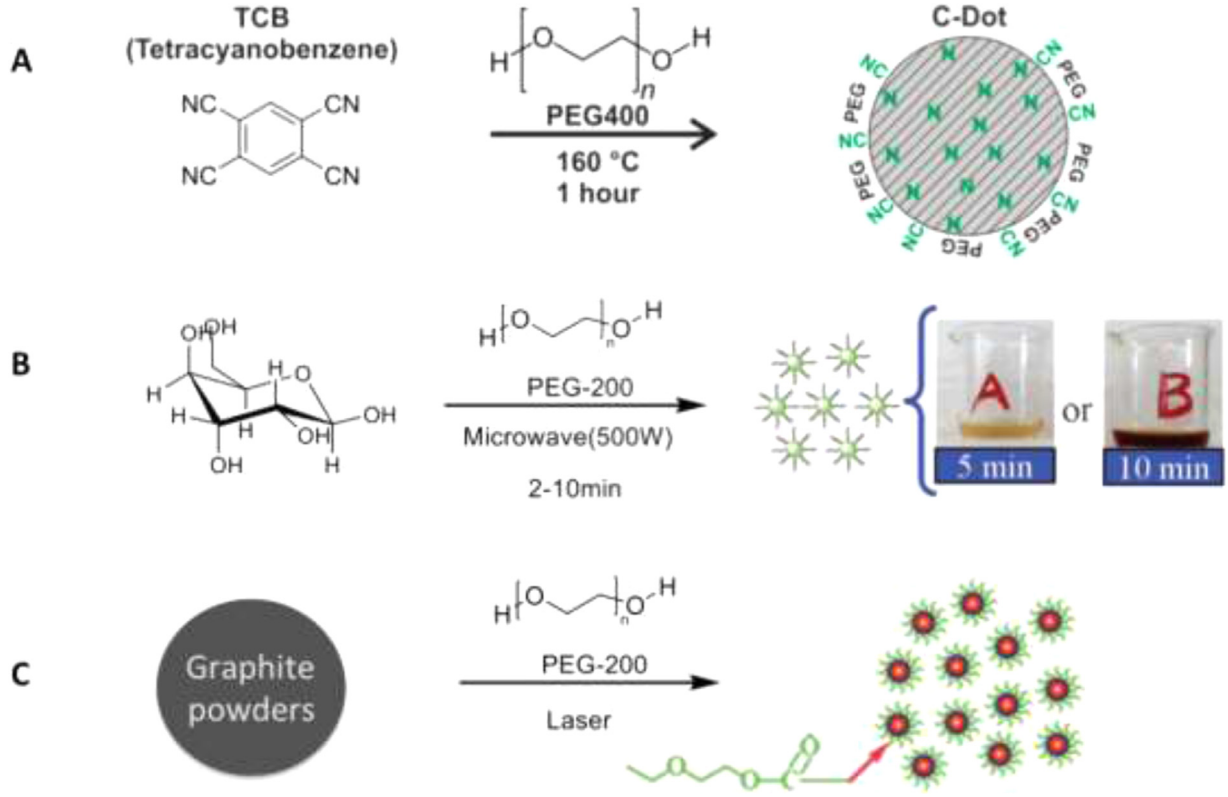

Fig. 4. PEG-mediated synthesis of C-dots: (A) Schematic illustration of the synthesis of C-dots from 1,2,4,5-tetracyanobenzene. Reproduced with permission from ref. [85] Copyrights 2019, by the authors. (B) Schematic illustration of the synthesis of C-dots from glucose. Revised with permission from ref. [86] Copyrights 2009, Royal Society of Chemistry. (C) Schematic illustration of the synthesis of C-dots from graphite powders. Revised with permission from ref. [56] Copyrights 2009, Royal Society of Chemistry.

4.1. Reaction mechanism of PEG-derived C-dots synthesis

All PEG-based C-dots synthesis could be regarded as the "bottom-up" approach, in which most of the reactions go through a "pyrolysis – clustering – carbonization" process. Mechanistically speaking, the pyrolysis step requires high-energy input to initiate, which could be realized by direct heat transfer, microwave, ultrasonication, etc. In this step, PEG chains are broken down and could be oxidized into various fragments (i.e., polymeric radicals, carbonyls, hydroxyls and alkenes) in the presence of oxygen (Fig. 5A). During the clustering step, the alkenes (fragments containing carbon-carbon double bonds) aggregate to form the hydrophobic cores which can grow even larger as more of these electron-rich fragments (i.e., alkenes, even aromatic rings) are produced in a reaction environment where pyrolysis, dehydration and oxidation of PEG are favored. On the other hand, hydrophilic, oxygen-containing fragments (i.e., hydroxyls, carbonyls, ethers) tend to stay around the surface of the cluster to form the

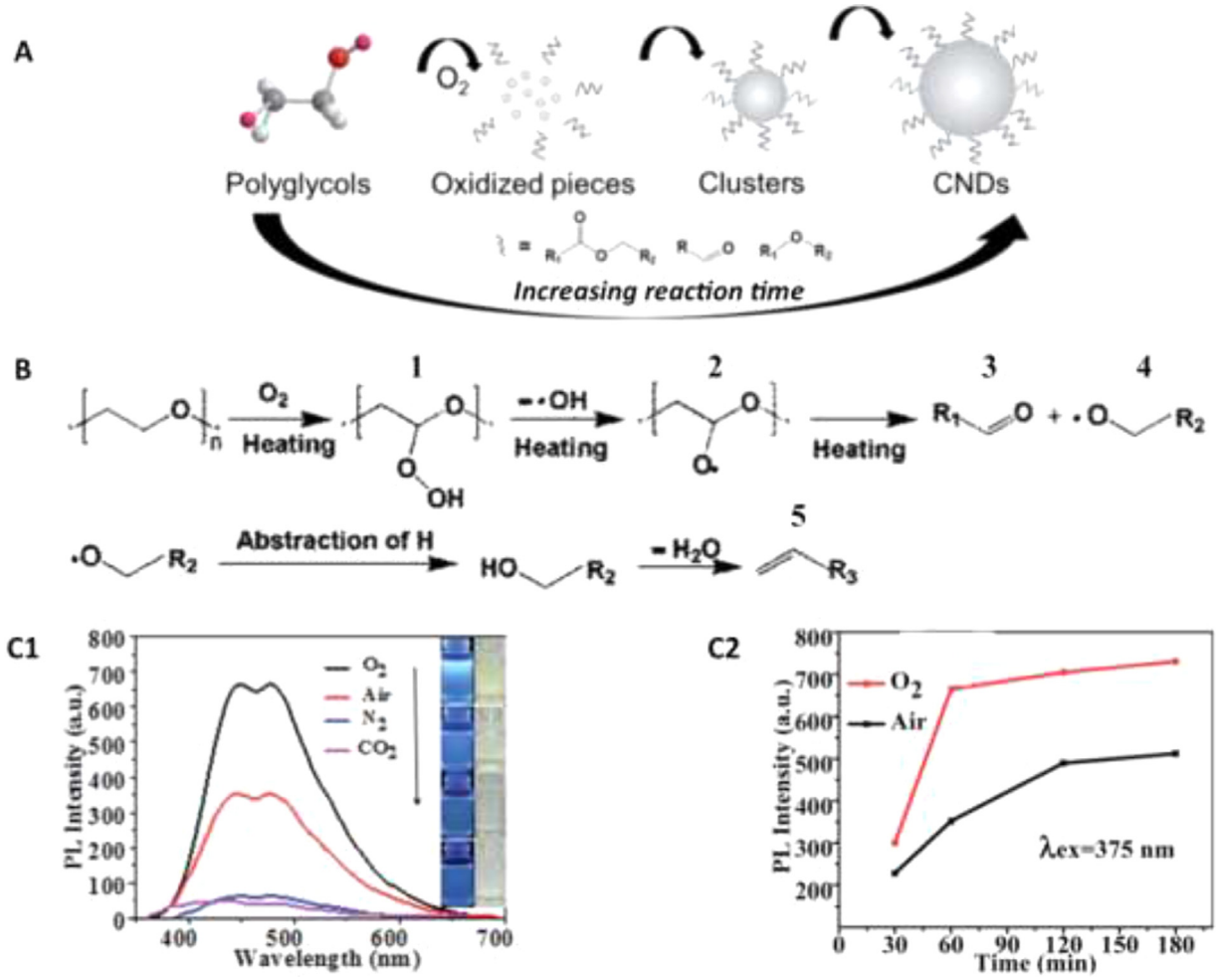

Fig. 5. PEG as carbon precursor for synthesis of C-dots: (A) Schematic illustration of the potential processes for the formation of C-dots. Revised with permission from ref. [44] Copyrights 2014, Royal Society of Chemistry. (B) Schematic illustration of the possible PEG chain cleavage and oxidation mechanism. Revised with permission from ref. [44] Copyrights 2014, Royal Society of Chemistry. (C) PL emission spectra of C-dots synthesized in various gas atmospheres (C1) and fluorescence emission intensity versus reaction time curves of C-dots synthesized at 100 ºC with various different reaction durations (C2). Reproduced with permission from ref. [46] Copyrights 2017, Royal Society of Chemistry.

surface passivation layers. As these processes continue, core-shell structured PEG C-dots with aromatic cores and hydrophilic surfaces will eventually form (Fig. 5A) [44,45]. Specifically, the PEG chain cleavage and oxidation process could be reasonably proposed as follows (Fig. 5B): Carbon radicals are first generated in the reaction, and quickly transform to peroxides 1 in presence of oxygen; then a hydroxyl radical could leave the unstable peroxides to form reactive intermediate 2. Next, C–O bond of 2 is cleaved subsequently to form carbonyl compound 3 and unstable polymeric radical specie 4. Abstraction of hydrogen by 4, followed by a dehydration process (elimination of a water molecule) eventually result in the formation of carbon-carbon double bond (specie 5). As can be seen, oxygen is a key reagent of the oxidation process for the generation of radicals in this mechanism. Indeed, one study has shown under identical conditions, if the reaction was carried out in a nitrogen atmosphere, the formation of PEG-derived C-dots took much more time compared to the counterpart performed in air [44]. Further, reactions carried out in oxygen atmosphere undoubtedly shortened the reaction time, improved the PL intensity and QY significantly, and increased the average fluorescence lifetime (Fig. 5C) [46]. For example, the QY and lifetime of C-dots prepared in air were 5.78% and 2.4 ns, respectively; while they were improved to 7.84% and 3.0 ns, respectively, when the C-dots were synthesized in an pure oxygen atmosphere [46].

4.2. Synthesis methods of PEG-derived C-dots

As can be seen from the mechanism discussed above, PEG-based C-dots synthesis generally go through a “pyrolysis – clustering – carbonization” process, thus methods that could assist this process such as direct heating, hydrothermal, microwave, ultrasonication, electrolysis as well as oxides and base treatments have all been reported (Table 2). Direct heating (i.e., mantle heating or refluxing) is the most widely used method in organic synthesis and also quite popular in “bottom-up” preparation of C-dots. The direct heating of PEG_{400} to produce C-dots has been successful [44,89,90]. In Wu and co-workers study, PEG_{400} was heated at 160 ºC for different durations (0.5, 2 and 6 h), and it was found that the reaction time played a key role in the formation of C-dots. As the heating time increased, the C-dots gained larger size and their emission also red shifted (Fig. 6A) [44]. In a different report, Feldmann and co-workers, on the other hand, investigated the temperature effects on the synthesis of C-dots from PEG_{400}. Their study revealed that PEG_{400} heated at relatively low temperature (i.e., 160 ºC) for one hour only produced C-dots with very weak blue emission (Fig. 6B1). When the temperature increased to 230 ºC, C-dots with max intensity were formed and significantly red shifted that the C-dots could cover the complete optical spectrum (400–700 nm,

Table 2
Selective examples of PEG-derived C-dots: synthesis, property and applications.

Carbon source[a)]	Synthesis method	C-dots properties Size distribution (nm)	Emission maximum (nm)	QY (%)	C-dots applications	Ref.
PEG_{400}	Direct heating	2.3; 4.7[b)]	450; 500	2.5; 3.6	Bioimaging	[44]
		3–5	440; 450; 615	50; 75	–	[89, 90]
$PEG_{400, 1500, 6000}$	Hydrothermal	2–4	435	3.5	Bioimaging	[91]
PEG_{2000}		1–5.4	455	43	–	[92]
PEG_{200}	Microwave	3.5–5.5	470	16	Bioimaging	[94]
		<5	430	–	Biosensing	[96]
		1–3	470	–	NP synthesis	[95]
PEG_{400}		–	470	7.8	–	[46]
PEG_{400}	Ultrasonication	2–9	460	16	–	[103]
		6; 10[b)]	460; 480	16	Catalysis	[119–122]
		4–8	470	–	Antiparasite	[104]
		2–10	460	–	Neural growth	[105]
		3–8	510	–	Anode material	[106]
		4–9	470	16	Lubricant	[127]
$PEG_{200, 600, 800}$	Electrolysis	4.5–7	485	38; 36; 32	Biosensing	[111]
PEG_{200}	Green synthesis	1–5	500	0.69	Bioimaging	[113]
PEG_{400}		2.3; 4.1[b)]	490–700[c)]	–	Ion sensing	[45]
PEG_{400}		<10	410	18.4	Thermosensing	[112]

[a)] PEG_{400}: polyethylene glycol (M.W., 400 Daltons).
[b)] Average size, instead of size distribution, is presented.
[c)] The emission maximums of C-dots could shift from 490 to 700 nm depending on the reaction conditions.

Fig. 6B3). Further study showed that at 230 ºC, the reaction time only had a marginal effect on the formation of C-dots [89].

According to the C-dots formation mechanism discussed (Fig. 5), the two observations above could be well explained. When heated at low temperature (160 ºC) [44], the cleavage and oxidation of PEG_{400} was relatively slow, thus the formation of electron-rich fragments (i.e., carbon-carbon double bonds, aromatic compounds) and the clustering process were slow. As a result, longer reaction time would allow this process to accumulate and eventually produce C-dots with larger sizes (i.e., containing larger conjugated structures), and thus emitted light with longer wavelength. As the heating temperature gradually elevated (i.e., to 230 ºC) [89], the rate of cleavage and oxidation of PEG_{400} was significantly increased, and more (enhanced fluorescence intensity) and larger (red shifted emission) C-dots formed in a short amount of time, thus the reaction time did not play an important role any more. However, at even higher temperatures (i.e., above 230 ºC), the cleavage and oxidation of PEG_{400} became much more fast and less controlled, thus less C-dots formed and the ones formed were generally in bad quality in terms of their fluorescence intensity, particle size, size distribution and agglomeration. Interestingly, in both of these two studies, additives such as organic compound [44] or rare earth metal ions [89] were able to tune the C-dots emission properties, shifting the emission into the red region.

Hydrothermal treatment is another regularly applied method in the synthesis of C-dots, in which the desired temperature and pressure of reaction medium could be easily obtained by tuning the reaction temperature and solvents adopted. Thus it is also frequently used for the PEG-derived C-dots synthesis. For example, Lu and co-workers fabricated C-dots by simple hydrothermal treatment of aqueous solution of PEGs (PEG_{400}, PEG_{1500} and PEG_{6000}) at 120 ºC for 72 h. The as-prepared C-dots had diameters in the range of 2–4 nm, and the ones derived from PEG of larger M.W. presented larger sizes as well as wider size distribution. Interestingly, the C-dots demonstrated very similar PL properties in which high photostability in different pH (3–7) and NaCl aqueous solutions (0–2.0 M) were observed [91]. In a different study, where PEG_{2000} as carbon precursor, ionic liquid as surface modifier and HCl as reaction accelerator, bright C-dots were fabricated by treating the mixture in Teflon stainless steel autoclave (200 °C for 12 h) [92]. Prominently, acid had a significant effect on the PL intensity of the C-dots: QYs of C-dots were enhanced as the increase of acid concentration, and a QY of 43% was obtained at optimum condition (Fig. 7A). This phenomenon was attributed to the ability of acid in the modification of the surface groups of C-dots according to the authors' mechanism investigation.

Microwave assisted pyrolysis is an excellent alternative to direct heating and hydrothermal treatment for C-dots synthesis, best known for its extremely fast heating and superior ability in controlling nucleation of NPs [93]. As a result, microwave assisted synthesis of C-dots from PEGs has also been attempted. For example, simple irradiation of aqueous PEG_{200} solution by domestic microwave (900 W for 10 min) could generate C-dots whose PL emissions could tolerate a wide range of pH (3–8) [94]. Interestingly, the addition of additive amount of phosphoric acid could significantly accelerate the reaction and C-dots could be synthesized in less than one minute (750 W for 55–57 s) [95]. Further investigation shown that water was not necessary in the synthesis of C-dots from PEG_{200}; as a matter of fact, the absorbance and emission intensity of obtained C-dots could be increased about 30% while maintaining the λ_{max} and λ_{em} unchanged if water was excluded from the reaction [96]. Unfortunately, efforts to fabricate C-dots from PEG with M.W. higher than 600 Daltons have failed [94]. As two of the most important parameters in microwave-assisted reactions, the microwave power and time duration effects on C-dots properties were carefully evaluated [46,94–96]. Interestingly, a similar trend was observed: the increase of power or irradiation time resulted in the enhancement of the fluorescence intensities of the produced C-dots at the beginning; however, after a certain range, further increasing of power or irradiation time adversely affected the emission intensities (Fig. 7B, C and D). Based on the C-dots formation mechanism depicted above (Fig. 5), these phenomena could be well explained. When low power was applied, the cleavage and oxidation of PEG was relatively slow, thus the formation of electron-rich fragments, the clustering process and the nucleation of C-dots were slow. As a result, increasing the radiation power or time would increase the number of C-dots formed which would have a positive effect on the fluorescence emission intensity. However, at a certain point, when the irradiation power was too high or the irradiation time was too long, the cleavage and oxidation of PEG became much more fast and less controlled and over carbonization could be an issue. In those circumstances, less C-dots formed and the ones formed were generally in bad quality in terms of the fluorescence intensity.

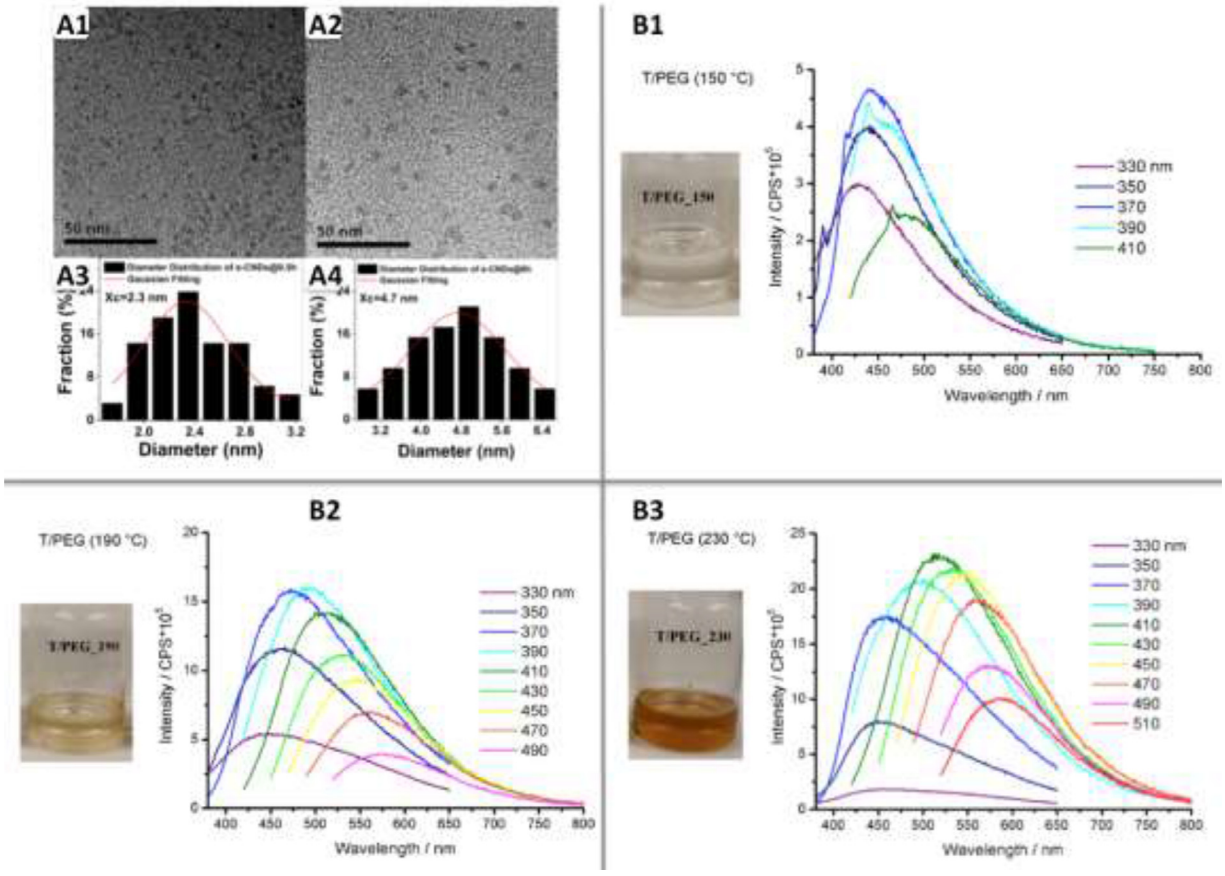

Fig. 6. (A) Effect of reaction time on the synthesis of C-dots from PEG_{400}: TEM image (A1) and diameter distribution (A3) of C-dots prepared after heating at 160 °C for 0.5 h; TEM image (A2) and diameter distribution (A4) of C-dots produced after heating at 160 °C for 6 h. Revised with permission from ref. [44] Copyrights 2014, Royal Society of Chemistry. (B) Effect of temperature (150, 190, 230 °C) on the synthesis of C-dots from PEG_{400}: (B1) Photo (left) and emission spectra (right) of C-dots produced by refluxing PEG_{400} at 150 °C for 1 h; (B2) Photo (left) and emission spectra (right) of C-dots produced by refluxing PEG_{400} at 190 °C for 1 h; (B3) Photo (left) and emission spectra (right) of C-dots produced by refluxing PEG_{400} at 230 °C for 1 h. Revised with permission from ref. [89] Copyrights 2014, Royal Society of Chemistry.

During ultrasonic treatment of liquids, numerous tiny local spots of extremely high temperature (e.g. 5500 °C) and pressure (e.g. several thousand atmospheres) could be induced by the cavitation process *via* the formation, growing and collapsing of gas bubbles [97]. As a result, these local harsh conditions have been widely used for organic synthesis, NPs and C-dots fabrication [98–102]. Recently, Gedanken and co-workers reported the synthesis of C-dots *via* direct ultrasonic treatment of PEG_{400}. In this study, it was revealed that the sonication amplitude and duration, as well as the temperature of PEG_{400} all had some effects on the formation and fluorescence of C-dots. Unfortunately, attempts to fabricate C-dots from PEG with higher M.W. (2000, 3000 and 6000 Daltons) did not succeed [103]. With this methodology, the same group further fabricated gallium-doped C-dots (Ga@C-dots) [104], gallium-doped C-dots on Ga NPs (Ga@C-dots@GaNPs) [105], as well as tin-doped C-dots (Sn@C-dots) and tin-doped C-dots on tin NPs (Sn@C-dots@SnNPs) [106]. These materials have been found very useful in various applications. Electrochemical exfoliation of bulk carbon materials (i.e., graphite) has proved itself a powerful and reliable "top-down" methodology for the synthesis of C-dots [107–110]. Inspired by these studies, electrolysis assisted synthesis of C-dots from PEG with different M.W. (200, 600 and 800 Daltons) has also been reported [111].

While the methods (i.e., conventional heating, microwave pyrolysis, hydrothermal, ultrasonic and electrolysis treatments) discussed above are highly useful in fabricating C-dots, they are not energy-efficient and may not be environment-friendly enough from the viewpoint of green chemistry. Thus attempts to prepare C-dots from PEG using methods that do not require external energy input, complicated operations and sophisticated instruments have been reported. In these innovations, self-generated heat arisen from the chemical and/or physical changes of reagents (such as P_2O_5 [112], concentrated NaOH solutions [45,113]) is enough to sustain the energy required for the formation of C-dots, and thus external energy is not required. For example, C-dots could be facilely fabricated by mixing PEG_{400} and NaOH solution for 10 mins at room temperature [45]. Encouragingly, the size and maximum emission wavelength of the resulted C-dots could be easily tuned by varying the concentrations of NaOH solution (Fig. 7E), which could be explained by the C-dots formation mechanism discussed previously (Fig. 5). Briefly, higher concentration of NaOH could expedite the pyrolysis and oxidative degradation of PEG_{400}, thus the clustering, and C-dots formation. As a result, C-dots with larger size were fabricated, and their emissions were red shifted [45].

4.3. Applications of PEG-derived C-dots

Thanks to their superior PL property, excellent biocompatibility, rich and tunable surface functionalities, and facile synthesis; PEG-derived C-dots have realized broad applications in various fields such as bioimaging, biosensing, biomedical, catalysis, and energy storage (Table 2).

4.3.1. PEG-derived C-dots for Bioimaging

PEG-derived C-dots are generally low cytotoxic, have excellent PL stability that can bear various pH and long exposure to excitation, and thus they have been widely used for cell imaging

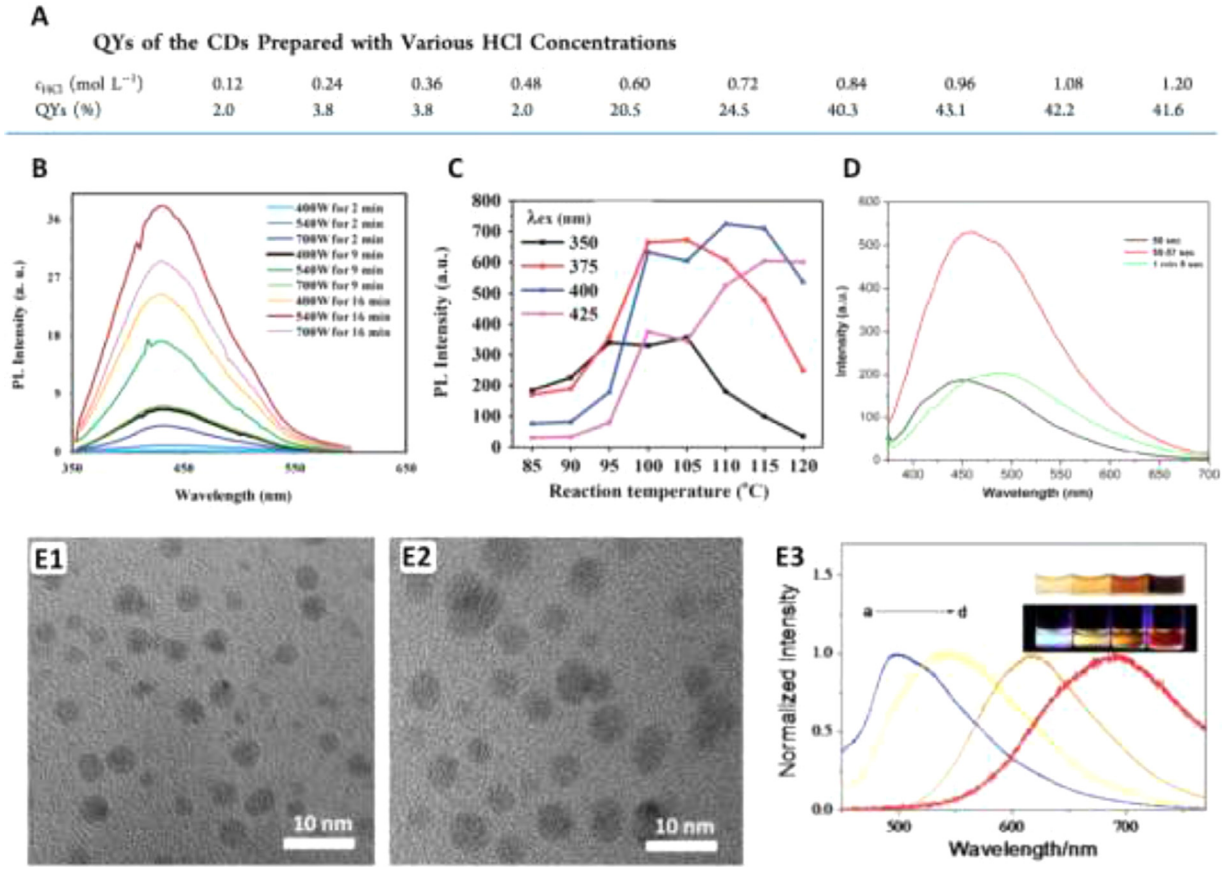

Fig. 7. (A) Table showing the QYs of C-dots fabricated from PEG_{2000} *via* hydrothermal with various concentrations of HCl. Reproduced with permission from ref. [92] Copyrights 2017, American Chemical Society. (B) Fluorescence emission spectrum of C-dots synthesized from PEG_{200} *via* microwave-assisted pyrolysis with various conditions. Reproduced with permission from ref. [96] Copyrights 2014, Royal Society of Chemistry. (C) PL intensity-reaction temperature curve of C-dots, C-dots were synthesized from PEG_{400}, which was heated with a 500 W microwave irradiation to reach different temperatures and maintained for 60 mins. Reproduced with permission from ref. [46] Copyrights 2017, Royal Society of Chemistry. (D) Fluorescence spectra of C-dots prepared from PEG_{200}, PVA and phosphoric acid *via* microwave-assisted pyrolysis with different irradiation time interval. Reproduced with permission from ref. [95] Copyrights 2011, Royal Society of Chemistry. (E) Effect of NaOH concentration on the synthesis of C-dots from PEG_{400}: (E1) TEM image of C-dots prepared by treating PEG_{400} with 0.5 mol/L of NaOH, C-dots average diameter 2.3 nm; (E2) TEM image of C-dots prepared by treating PEG_{400} with 1.77 mol/L of NaOH, C-dots average diameter 4.1 nm; (E3) PL emission spectra of C-dots prepared by treating PEG_{400} with different concentration of NaOH. Concentrations of NaOH from a to d are 0.34, 0.51, 0.97 and 1.77 mol/L, respectively. Inset is photographs of C-dots solutions taken under sunlight (top), and 405 nm UV light (bottom). Reproduced with permission from ref. [45] Copyrights 2017, Springer Science.

[44,91,94,113]. While the internalization of most C-dots in cells are non-specific; reports have shown that some of the C-dots could target specific regions of cells, realizing cellular-compartment specific bioimaging. For example, C-dots prepared from PEG_{400} *via* direct heating were mainly localized in the cytoplasm regions; [44] while another C-dots were mainly internalized around cytoplasm, labeling only cell membrane and nucleus (Fig. 8A) [91]. Owing to the rich and tunable surface functionalities of C-dots, the specificity of C-dots towards the different regions of cells could be easily manipulated by functionalizing C-dots with a special ligand. For instance, goat antimouse IgG functionalized C-dots successfully labeled and imaged the microtubules of lung cancer cells (Fig. 8B) [44]. Up-conversion (including two-photon) PL imaging is much sought after imaging technique due to its deep penetration and benign property to biotissues as well as the minimum background tissue autofluorescence interference [114,115]. Encouragingly, PEG-derived C-dots with two-photon, or up-conversion PL property have both been reported [91,92].

4.3.2. PEG-derived C-dots for Biosensing

The PL intensity of C-dots could be easily affected by various factors such as the presence of metal ions, small organic molecules or biomacromolecules (i.e., enzymes) as well as the change in the solution conditions (i.e., temperature or pH variations). This phenomenon has been frequently exploited to design and develop C-dots based biosensors. In these systems, one strategy involves the establishment of standard calibration curves based on the quenching (or enhancement) of C-dots fluorescence in the presence of the analytes, thereby the concentrations of analytes in real samples could be determined. Such strategy has been successfully applied for the detection of metronidazole (fluorescence quenching) and Fe^{2+} (fluorescence enhancement) [45,96]. Another strategy, on the other hand, is developed from a conceptually different fluorescence assay which is based on inner filter effect (IFE) [111]. In this assay, combination of PEG-derived C-dots and tyrosinase (TYR) were applied as effective biosensor for the detection of levodopa. Levodopa, employed as a substrate of TYR, has no interference on the excitation of C-dots. However, levodopachrome, which was the product of the catalytic oxidation of levodopa by TYR (Fig. 9A), has a maximum UV absorbance around 500 nm (Fig. 9B). The UV absorbance of levodopachrome significantly overlapped with the emission of C-dots (Fig. 9C), which could quench the fluorescence of C-dots. The degree of the fluorescence quenching of C-dots in this assay was then used to assess the concentration of the substrate, levodopa (Fig. 9D). Since the PL intensity of some C-dots are closely impacted by temperature, biosensors that are capable of indicating minor temperature changes *via* fluorescence change is possible [112].

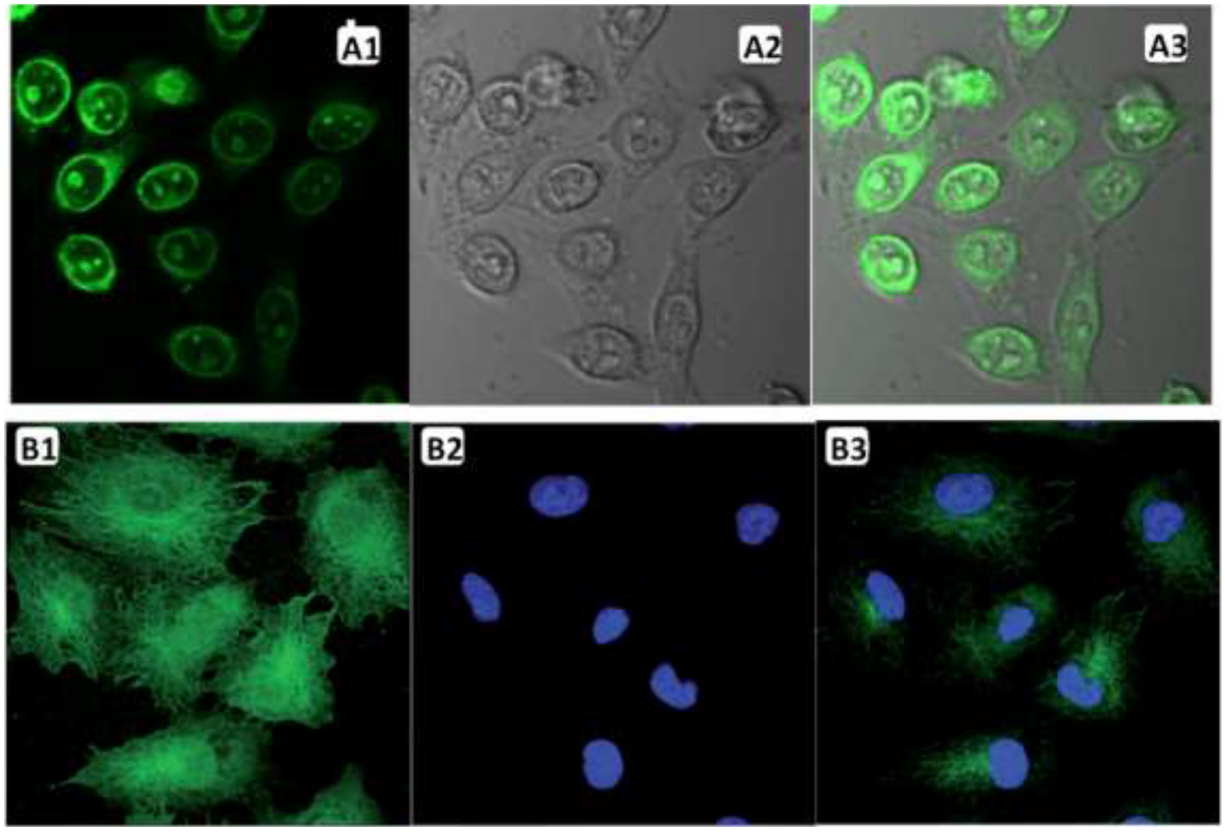

Fig. 8. (A) Two-photon cellular imaging using PEG_{400} derived C-dots under (A1) 800 nm excitation showing the labeling of cell membranes and nucleus and (A2) bright field; (A3) overlaid image of (A1) and (A2). Revised with permission [91]. Copyrights 2014, Elsevier. (B) Immunofluorescent cell images: (B1) targeted imaging of cell microtubules using goat antimouse IgG-modified C-dots (excitation: 488 nm detection window: 510–560 nm); (B2) distinctively labeled nuclei by DAPI (excitation: 405 nm, detection window: 420–490 nm); (B3) merged image of (B1) and (B2). Revised with permission from ref. [44] Copyrights 2014, Royal Society of Chemistry.

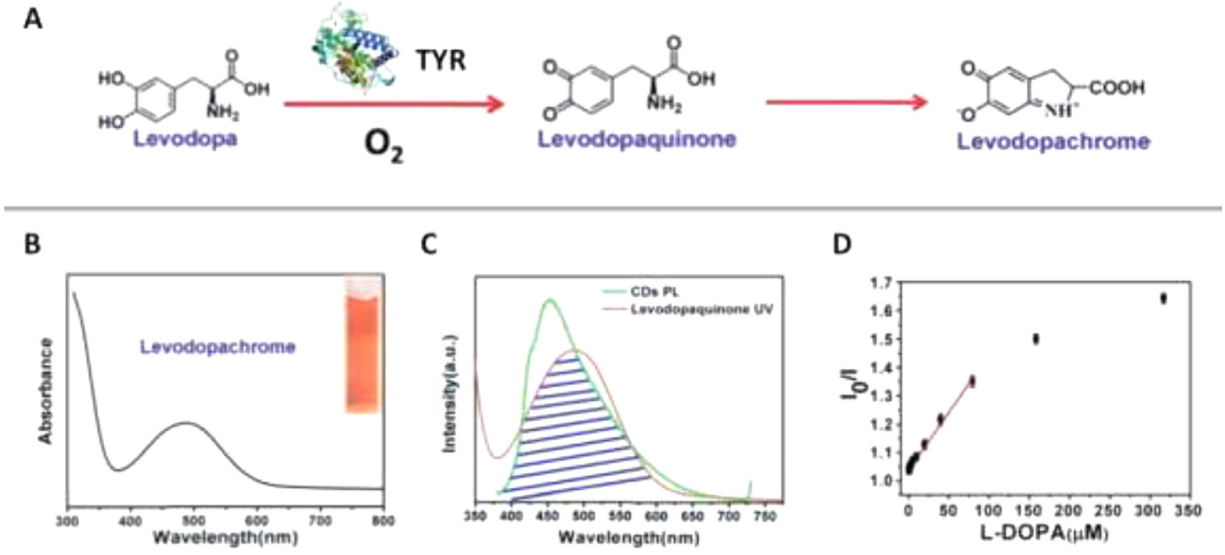

Fig. 9. C-dots based biosensor for the detection of levodopa based on inner filter effect: (A) Schematic illustration of detection mechanism of levodopa. (B) Absorption spectrum of levodopachrome, with the maximum absorption around 500 nm (inset is the photograph under visible light). (C) Superposed spectra of levodopachrome UV–vis absorption and C-dots PL emission. (D) The calibration curve showing the quenching degree of C-dots fluorescence (I_0/I) vs. the concentrations of levodopa. Revised with permission from ref. [111] Copyrights 2015, Royal Society of Chemistry.

4.3.3. PEG-derived C-dots for Biomedicine

Besides bioimaging and biosensing, PEG-derived C-dots have also been used for other bio-related applications [104,105, 116]. For instance, sonochemically prepared C-dots from PEG have shown excellent anti-Leishmaniasis potential: these C-dots exhibited better activity against both Leishmania species than the commercial counterpart; while they were virtually nontoxic as demonstrated in both *in vitro* and *in vivo* studies [104]. In a different study, Ga@C-dots@GaNPs-coated glass substrate has demonstrated excellent capability in promoting neutral growth [105].

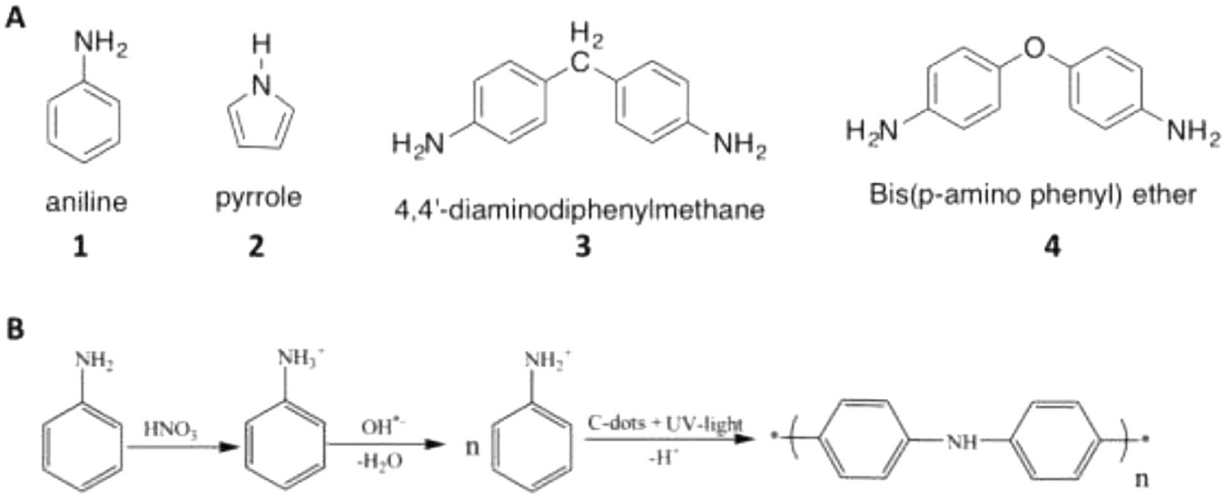

Fig. 10. PEG-derived C-dots catalyzed polymerization reactions: (A) Chemical structures of monomers used in the PEG-derived C-dots initiated polymerization reactions. (B) Schematic representation of the reaction mechanism of C-dots catalyzed aniline polymerization. Revised with permission from ref. [119] Copyrights 2018, Royal Society of Chemistry and the center National de la Recherche Scientifique.

4.3.4. PEG-derived C-dots for Catalysis

Thanks to their nanoscale sizes, C-dots generally have a very high surface-to-volume ratio, which is very advantageous in catalysis. Furthermore, C-dots are known for their rich and versatile surface functionalities, rendering them with organic molecule-like catalysis capabilities. As a result, C-dots have been widely explored for their applications in synthesis and catalysis [117,118]. As for PEG-derived C-dots, their applications for catalysis have been reported only recently. Gedanken's group prepared C-dots from PEG_{400} *via* ultrasonic treatment and successfully applied them in the catalysis of polymer synthesis. With the catalysis of C-dots, polyanilines, polypyrroles, and poly(4,4′-diaminodiphenylmethane) as well as poly(Bis(p-amino phenyl)ether were successfully synthesized from their respective monomers aniline, pyrrole, 4,4′-diaminodiphenylmethane, and Bis(p-amino phenyl) ether (Fig. 10A, substrates 1, 2, 3 and 4, respectively) [119–121]. Furthermore, C-dots were also able to catalyze copolymerization reactions. Heteropolymers such as poly(pyrrole-co-aniline) (the copolymer of substrates 1 and 2, Fig. 10A), poly (Bis(p-aminophenyl)ether-co-aniline) (the copolymer of substrates 1 and 4, Fig. 10A) and poly (Bis(p-aminophenyl)ether-co-pyrrole) (the copolymer of substrates 2 and 4, Fig. 10A) have all been successfully synthesized [121, 122]. In those reactions, C-dots were believed to produce free radicals (i.e., OH radical) to initiate the polymerization process under UV-light (Fig. 10B) [119]. Applications of the polymer products for organic dye absorption, and antibacterial activity have been investigated [120,123–126]. Taking advantages of their excellent reduction and stabilization abilities, PEG-derived C-dots have also been successfully applied as excellent catalysts to synthesize AuNPs and AgNPs [95].

4.3.5. PEG-derived C-dots for other applications

Apart from their applications in bioimaging, biosensing and catalysis, PEG-derived C-dots have also found mechanic, petrol industry, and energy-related applications. For instance, C-dots synthesized from PEG have shown desired tribological properties with excellent anti-wear and extreme-pressure performances, rendering them as potential lubricants [127]. In another study, PEG_{200} C-dots have shown great promise in the selective adsorption and removal of sulfur compounds from model liquid fuels [68]. Further, tin-modified PEG C-dots have proven to be as promising anode materials for Li-ion batteries [106]. Selective examples regarding the synthesis, property and application of PEG-derived C-dots are summarized in Table 2.

5. Challenges of PEG-derived C-dots

Current challenges concerning the PEG-derived C-dots include short maximum emission and low QYs. In order to improve the short maximum emission wavelength, several strategies could be adopted including selection of proper co-reactants and solvents. For instance, it is frequently reported that long-emissive C-dots have been acquired with 1,2-phenylenediamine (OPD) or 1,4-phenylenediamine (PPD) as precursors [10]. In order to elongate the emission wavelength of PEG-derived C-dots, OPD or PPD might be considered as co-reactants that could also serve as N-dopant to improve the fluorescence QYs. Furthermore, solvent effects have been revealed on the preparation of long-emissive C-dots. Ding et al. applied different solvents for the preparation of C-dots with OPD as the precursor and achieved different PL characteristics [128]. Thus, proper exploitation of solvent effects might also be helpful for pushing wavelength of PEG-derived C-dots into the red region. As for the future opportunities of long-emissive PEG-derived C-dots, considering the advantages of PEG-derived C-dots, the long emission will benefit the use of C-dots in the applications of bioimaging to reduce the interference of autofluorescence of biological tissues or organs. In addition, the long emission can be used to trigger photodynamic and photothermal therapies for the treatment of oncology and microbes.

Another challenge of PEG-derived C-dots is their QYs are relatively low (Table 2). To discuss the potential cause of relatively low QYs of PEG-derived C-dots, we will first brief the PL mechanism of C-dots. The predominant theory is surface state theory which indicates electrons in different energy traps on the surface of C-dots will get excited by high-energy irradiation and then returns to ground state by releasing the energy in the form of light. However, due to the presence of multiple electronic states (surface states) caused by various surface functionalities, the excited electrons will firstly shift to the energy band of a certain surface state after going through a series of non-irradiative energy emission processes such as vibrational relaxation and then return to the ground state [11]. Even though PEG is often used as an effective passivation agent, when it is used as a precursor, PEG will undergo the same process as most precursors by "bottom-up" approach, namely carbonization. Arbitrary carbonization can damage the structure of

PEG and cause plenty of complex surface states on the PEG-derived C-dots with many non-irradiative emission processes so that the irradiative emission will be largely reduced. From another point of view, some researchers support a molecular state theory regarding the PL mechanism of C-dots [129]. In this case, C-dots derived from PEG won't have high fluorescence QYs because of the lack of fluorophores considering the lack of aromatic or π-π^* conjugate structures in PEG. Therefore, the QYs of PEG-derived C-dots are relatively low.

There are various strategies that could potentially increase the QYs of PEG-derived C-dots. One of such is to add heteroatoms such as N, S and P [28]. Among them, N-dopants have been widely used in the preparation of highly photoluminescent C-dots and to date, the highest QY of 93.3% has been achieved [130]. With heteroatoms introduced to the structure of C-dots, the increasing lone pair electrons on the surface of C-dots can be excited along with the enhancement of PL emission intensity [131]. However, the addition of heteroatoms could also generate more electronic states [132]. Therefore, together with the increase of QYs, the PL emission might be affected by the heteroatoms. Furthermore, the PL behaviors of C-dots can be well tuned by altering the reaction parameters such as the form of input energy, temperature, time, pH and solvent applied during the synthetic process of C-dots. Even though same precursors were applied to synthesize C-dots, the QYs can be different with different forms of energy input. For instance, Zhou et al. obtained one type of "yellow" C-dots from ultrasonication method while three types of C-dots from microwave oven using the same amount of citric acid, 1,2-phenylenediamine as precursor with water as solvent [11,133]. The QY of C-dots (39.2%) from microwave oven is higher than that from ultrasonication approach (<10%). Additionally, Zhou et al. have also studied the thermal effect on the QYs of C-dots [134], and it was observed that higher temperature would benefit the improvement of QYs. However, too much carbonization at 180 °C reduced the QYs, which is the same case for PEG-derived C-dots. Regarding the effect of reaction time, Papaioannou et al. reported that QYs increased with the extended reaction time. ([135]) In terms of the influence of pH on the synthesis of C-dots as well as their optical properties, Zheng et al. stated that the PL behaviors of C-dots is due to their structures, which can be changed in different pH environments, and alkaline environment might be beneficial for the increase of QYs [130]. Meanwhile, the solvent effect is closely related to the dehydrating ability and solubility of C-dots precursors in different solvents as well as the boiling point, polarity, protic, and non-protic properties of different solvents themselves. And higher dehydrating ability and solubility are beneficial for the formation of C-dots and their optical properties. All the above-mentioned approaches could be used to fine-tune the properties of PEG-derived C-dots and potentially increase their QYs.

6. Conclusion

In this review, we first looked back the classic applications of PEGs in drug delivery and NPs PEGylation. Then we introduced recent advancements of PEGs as passivation agents in the synthesis and fine-tuning of C-dots. The applications of PEGs as solvent and/or matrix for C-dots preparation were also discussed. Last, the use of PEGs as sole carbon precursors for the synthesis of C-dots was summarized, in which the reaction mechanism, various types of synthesis methods as well as the applications of PEG-derived C-dots were carefully discussed. Considering their chemical stability, biological compatibility, rich and tunable surface functionalities, and low-cost accessibility; PEG-derived C-dots have garnered significant interests from various fields. Nevertheless, there are still much more efforts need to be done in order to realize the full potential of PEG-derived C-dots. Firstly, current studies mainly focus on the fabrication and characterization of C-dots from PEG, while their applications have been less investigated. To recognize the importance of PEG-derived C-dots in the carbon-based nanomaterials family, their applications (especially in the biomedical fields) should be given same efforts, if not more, as their synthesis and characterization. Secondly, polymers have proven to be very effective in tuning and improving C-dots chemical, physical and biological properties [35,39,40], those successful experiences should be closely referred to when use PEG to functionalize C-dots and tune their properties. Lastly, unlike other "bottom-up" C-dots preparations, the mechanism of PEG-based C-dots synthesis have been relatively clear; [44–46] thus it's worth spending more efforts to use PEG as a model to study the general mechanism of C-dots formation and PL. As our understanding towards C-dots formation deepens, the rational design of C-dots with desired properties (i.e., specific sizes, surface functionalities, PL, etc.) may become possible eventually. As such, we anticipate much more efforts will be continually devoted to PEG-related C-dots synthesis and exciting applications will be developed.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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