Carbon Quantum Dots: Surface Passivation and Functionalization

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Abstract: This review deals with the promising newest carbon-based nanomaterial: Carbon Quantum Dots (CQDs). CQDs demonstrate optoelectronic properties comparable to conventional inorganic semiconductors, however they are environmental friendly and benign. They possess complicated structures, particle sizes up to 10 nm and upon surface passivation and/or functionalization their optoelectronic properties are critically improved and tuned. Although there are a few recent reviews on this topic, the majority of them emphasize on CQDs applications or even the synthetic procedures followed to acquire CQDs. In contrary, this review refers in brief to the aforementioned and focuses on the surface passivation and functionalization routes and therefore the functional groups and heteroatoms used for the development of high quality CQDs. Introduction and doping with appropriate heteroatoms is the key point to tailor made features of CQDs and thus organic chemistry provides the vital background for the essential functionalizations.

Keywords: Carbon quantum dots, surface passivation, organic functionalization, fluorescence, luminescence, optoelectronic properties, synthesis, applications.

1. INTRODUCTION

Graphite, diamonds, activated carbon, charcoal, nanodiamonds, carbon nanotubes, fullerenes, and more recently graphene and carbon quantum dots (CQDs); for sure, carbon always finds its way to be on the spotlight of human’s interest. During the past two decades, various carbon nanostructures have enriched the known allotropes and structures of carbon. The tremendous scientific and research interest on them is reflected by two Nobel Prizes (Chemistry 1996, Physics 2010) and one Kavli Prize (Nanoscience 2008). Nowadays, more than ever, countless worldwide research groups focus on these carbon-based nanomaterials. Bonding and hybridization flexibility of carbon atoms, combined with the extraordinary physicochemical properties of these nanostructures, settle them as ideal candidates for state-of-the-art applications.

CQDs represent at the moment the newest class of carbon-based materials. Xu et al. on their effort to obtain with electrophoresis purified single-walled carbon nanotubes from arc-discharged soot, isolated, detected and thus accidentally discovered CQDs as a byproduct [1], even though it was Riggs’ team that four years earlier had reported strong luminescent soluble carbon nanotubes in a comparable approach by purifying and cutting down nanotubes [2].

From their discovery and up to date, CQDs with critically improved and/or tailored properties have been acquired by numerous research works. The huge number of these reports, along with the growing interest for CQDs has led to a few recent reviews on this topic. However, the majority of them emphasize on CQDs applications or even the synthetic procedures followed to get CQDs [3-13]. In contrary, this review refers in brief to the aforementioned and focuses on the surface passivation and functionalization routes and thus the functional groups and heteroatoms used for the development of high quality CQDs.

On the other hand, organic chemistry is a powerful tool that enables the successful modification of various inorganic substrates and structures, forming hybrids and altering and/or tuning their physicochemical properties. Incorporation of appropriate functional organic groups and heteroatoms leads to desired tailored applicability of the final composites. These features of organic chemistry are greatly exploited in the case of CQDs and this review aims to a comprehensive overview of organic functionalized CQDs.

2. OVERVIEW OF SYNTHETIC METHODS FOR THE PRODUCTION OF CQDS

The very first production of CQDs was achieved in 2004 with arc discharge [1]. In the upcoming years, the potential of additional physical or chemical methods to acquire CQDs was also tested with positive results. In this direction, Sun et al. reported the successful fabrication of colorful photoluminescent CQDs by laser ablation of a mixture from graphite powder and cement [14]. A year after chemical approaches were introduced as Liu and colleagues obtained multicolor fluorescent carbon nanoparticles from the combustion soot of candles (Fig. 1) [15]. At the same time, Zhou’s team prepared blue luminescent carbon nanocrystals in an electrochemical soaking manner [16]. The aforementioned techniques were further enriched later on with diverse approaches; either according to the top-down route for which final materials derive from a process where matter is broken down, or by the bottom-up route where CQDs are synthesized from suitable molecular precursors.

Thus, Bourlinos and his co-workers produced surface functionalized carbogenic quantum dots in a simple one-step chemical way by thermal decomposition of appropriate molecular precursors [17, 18]. Almost simultaneously in 2009, Peng et al. and Liu et al. reported aqueous routes for the preparation of CQDs [19, 20]; the former from carbohydrates based on chemical oxidation with strong acids and the latter with supported synthesis from resols by using silica spheres as carriers. The same year, the first microwave-assisted pyrolytic synthesis of CQDs from a poly(ethylene glycol) (PEG-200) and saccharides mixture was reported by the group of
3. OVERVIEW OF CQDS PROPERTIES AND APPLICATIONS

CQDs possess a series of attributes which set them as potential substitutes of conventional semiconducting quantum dots. First of all, they demonstrate strong photoluminescence which can be controlled and tuned by the nanoparticles’ size. Their fluorescence intensity can be further improved upon surface passivation with the formation of thin insulting capping layer. Since they are carbon-based materials that may as well possess oxygen groups, their surfaces can be easily functionalized with organic molecules, introducing various heteroatoms and tailoring their wavelength emission and consequently their applicability. Their hydrophilicity or hydrophobicity is also adjustable and CQDs can be highly soluble in H\textsubscript{2}O which is usually desirable. As mentioned earlier, CQDs can be acquired from various cost effective raw materials with diverse methods, while they are environmental friendly and benign. Most CQDs display chemical inertness, high stability and resistivity to photobleaching. Last but definitely not least, CQDs own two additional and very important characteristics: low cytotoxicity and excellent biocompatibility that render them superior compared to conventional semiconducting quantum dots and endow them with the potential of biological use [4-6].

Even though many worldwide research groups have been working on CQDs lately, the exact mechanism of photoluminescence is not yet revealed. This is because of the complicity of CQDs’ structure and mainly of their core. For sure, the PL properties are correlated with functionalization and heteroatom doping. Hence, it has been shown that doping with more electronegative elements than C, such as N, drives to blue shift of the photoluminescent emission, while doping with less electronegative atoms as S and Se leads to red shift [55]. It has also been shown that diverse oxygen functionalities or solvents may shift the PL emission wavelength [56]. Recently, there is a trend in CQDs’ publications to finally unravel the origin of their PL properties and not just indistinctly link them with functional groups. Thus, experimental and theoretical analyses associate the sp\textsuperscript{2}-hybridized carbon network with the PL emission at short wavelengths and alternative deactivation pathways with red-shifted PL emissions [57]. In addition, the introduction of oxygen functionalities, and more specifically epoxides and hydroxyls, induces more electronic states between the CQDs’ bandgap causing red shift in the observed PL emission [58].

Concerning CQDs’ applications, it is rational that these revolve around CQDs’ main feature, i.e. strong photoluminescence. Therefore, fundamental applications regard energy and catalysis. More specifically, CQDs have been employed: for photo-reduction and oxidation [59], as electrochemiluminescent reagents [21, 60, 61], as sensors (Fig. 2) [8, 43, 49, 62-73], as photo-electro-catalysts [25, 74-78], for organic photovoltaic devices [79], as detectors [29, 44, 47, 55, 74, 80-87], for light emitting diodes [88-91], for solar cell devices [92], for ink-free printing luminescent patterns [93], for energy transfer [94], etc. However, based as well on their biocompatible nature, CQDs have been extensively used for bioimaging [8-11, 30, 34, 35, 37, 40, 41, 43, 46, 52, 68, 92, 95-118], but also for theranostic photodynamic therapy [119], as antimicrobial agent [28], as gene nanocarriers [112, 120, 121], for cancer therapy [13, 11, 30, 34, 35, 37, 40, 41, 43, 46, 52, 68, 92, 95-118], but also for theranostic photodynamic therapy [119], as antimicrobial agent [28], as gene nanocarriers [112, 120, 121], for cancer therapy [13, 122], in general as drug delivery systems [33, 123, 124], etc.
4. SURFACE PASSIVATION AND FUNCTIONALIZATION OF CQDs

4.1. Surface Passivation of CQDs

It did not take long from CQDs discovery [1] until the crucial and highly beneficial effect of surface passivation was reported by Sun et al. (Fig. 3) [14]. In fact, Sun’s group had previously described the formation of strong luminescent water soluble carbon nanotubes with the use of poly-(propionyl-ethylenimine-co-ethylamine) (PPEI-EI) that bound the nanotubes [2]. Essential linkage for the attachment of the polymer on the carbon nanostructures occurs at surface defect sites [14, 125].

![Image](image_url)

**Fig. (3).** Aqueous solution of the PEG1500N-attached carbon dots (a) excited at 400 nm and photographed through band-pass filters of different wavelengths as indicated, and (b) excited at the indicated wavelengths and photographed directly. Schematic illustration of a carbon dot passivated with PEG1500N (c). (Reproduced with permission from ref. [14]).

Bare surface of CQDs is not just exposed to contaminants but rather defenseless due to carbon and oxygen endogenous nature to react with organic molecules, which may cause the disappearance of the optoelectronic properties of CQDs. Therefore, a protection layer is vital for the stability and long life usage of CQDs. Surface passivation forms a thin insulating capping layer that shields CQDs from the adhesion of impurities and further improves their fluorescence intensity. Various polymers or organic molecules have been and may be used as surface passivation agents as long as they do not contain visible or near-UV chromophores and therefore are non-emissive at visible wavelengths, leaving intact the observed colorful luminescence emissions of the passivated CQDs [14].

In this direction, Sun et al. developed surface passivated CQDs with diamine-terminated oligomeric poly-(ethylene glycol) H2NCH2(CH2CH2O)nCH2CH2CH2NH2 (average n ~ 35, PEG1500N). In a typical reaction, PEG1500N was mixed with acid-treated carbon particles and the mixture was heated at 120 °C for 72 h. After the reaction, the mixture was cooled to room temperature (RT) and dispersed in water. Suspension was centrifuged for 30 min resulting to a colored homogeneous supernatant suspension of PEG1500N-passivated carbon dots. Using the same methodology surface passivated CQDs were also acquired using PPEI-EI with EI fraction ~20% [14]. The aforementioned treatment (120 °C for 72 h) has been applied unchanged or slightly modified in numerous works ever since. In brief, the following passivation agents are used in literature frequently: PEG1500N [14, 20, 53, 59, 76, 90, 96, 97, 126-129], PPEI-EI [14, 90, 95], 4,7,10-trioxa-1,13-tridecanediamine [19, 105, 127], 1-hexadecylamine [89, 130, 131], PEG200 [21, 62, 63], PEG400 [132], PEG8000 [33], PEG1500, PEG2000, PEG3000 and PEG5000 [46], PEG20000 [119], PEIa1000 [109], poly(ethyleneimide)-b-poly(ethylene glycol)-b-poly(ethyleneimide) and 4-arm amine-terminated PEG [98], branched or linear PEI [44, 65, 81, 83, 120, 133], PEG and PEI [115], etc. It is noteworthy that apart from surface passivation, this treatment commonly introduces useful amine groups and therefore also acts as surface functionalization.

4.2. Surface Functionalization of CQDs

Surface functionalization is an intriguing pathway for developing tailor made features on CQDs. The easiest and first applied method for this purpose is the treatment with acid solutions. Refluxing for a few hours with a high concentration nitric acid solution (2-3 N) creates useful surface defects and introduces various oxygen functional groups such as carboxyl, carbonyl, and hydroxyl groups [14, 15, 20]. Nonetheless, acid treatment and in general post-synthetic functionalization, is not the solely approach to insert dopants on CQDs. These can be as well created together with the formation of the CQDs via one-step synthetic procedures by using suitable molecular precursors. In addition, by using alkali environment, reduction agents, acylation (alkanoylation) reactions, carbodiimide chemistry, organosilanes, etc. essential functional groups may be grafted on the surfaces of CQDs. The up to date reported in literature techniques for acquiring functionalized CQDs are summarized in Table 1 and described in detail further below.

**One-step Pyrolysis**

Pioneers in the one-step formation of functionalized CQDs were Bourlinos and his colleagues who managed to prepare both organophilic and hydrophilic carbon nanoparticles [17, 18]. To achieve this, citric acid [HOOCH2CH(OH)COOH] was mixed with different amines (R–NH2) and upon thermal decomposition capped nanoparticles were formed. In this fascinating approach, as citric acid protonates the amines, the relevant ammonium citrate salts are formed through the ionic interaction (–NH4+OOC–). With thermal treatment, the citrate unit serves as the carbon source while the compensating organic ammonium provides the attached surface modifier. This is accomplished as amide linkages (–NHCO–) are created from the thermal dehydration of the ammonium carboxylate moieties (–NH4+OOC–) and bind the organic corona covalently to the core. In the case of octadecyl ammonium (C18H37NH3+), citrate salt, organic nanoparticles are taken, while hydrophilic nanoparticles are obtained with 2-(2-aminoethoxy)-ethanol (OHCH2CH2OCH2CH2NH2). Except one-step functionalization, this methodology results to rather uniform monodisperse nanoparticles due to the low melting point of the specific citrate salts and the surface blocking provided by the organic modifiers [17]. If sodium 11-amino-undecanoate [H2N–(CH2)10COO–] is used as the amine precursor, a carboxyl surface modified carbon-based nanoparticle is acquired, which becomes organophilic if sodium is subsequently exchanged with cetyltrimethylammonium [C16H33N(CH3)3]+ [18]. In all cases, after mixing citric acid with the amines, the surface functionalized carbon dots are obtained after pyrolysis at 300 °C.

Similar procedure was followed later on by Wang et al. whom oil-soluble CQDs exhibited a maximum quantum yield of 53% and
the formation of an amide linker, a quaternary ammonium moiety was grafted on the surface. In following years, as referred in Table 1, numerous works have been based on the one-step pyrolysis or co-pyrolysis of various precursors which in many cases were environmental friendly abundant raw materials. This process led to the simultaneous carbonization towards CQDs and incorporation of functional groups with amines and in general nitrogen containing groups being the most common ones. Nevertheless, even though these works are cited in Table 1 (including the microwave-assisted or hydrothermal treatments), many of those are not described further below unless the applied procedure reports something novel compared to previous works [14, 15, 17, 18, 20, 22, 25, 28, 29, 32, 34, 35, 37–44, 46–51, 54–56, 59, 52, 65–68, 70–75, 77, 79–82, 84–88, 90–94, 101, 102, 104, 106, 110, 112, 114–119, 121, 123, 124, 126, 129–131, 133–145, 148–171].

**Employment of Organic Reactions**

In 2009, Wang et al. employed an already applied reaction for the functionalization of carbon nanotubes to modify CQDs and obtained fluorescent derivatives [59]. After refluxing CQDs with aqueous nitric acid, oxidized CQDs were treated with thionyl chloride. The acyl chloride derivative was then reacted with PEG1500 giving carbon dots with surface-attached modifiers. Hence, the covalent bonding of amines on acyl chlorides is a reaction that can be applied in the case of CQDs too [59]. The acyl chloride mediated was also used by Gupta and colleagues in order to attach aniline and methylene blue on the surfaces of CQDs [79]. Pristine CQDs were treated with nitric acid followed by acylation in the presence of DMF as catalyst, and acylation reaction with either aniline or methylene blue resulted to covalent conjunction through amide groups’ creation. Later on, Anilkumar’s team again grafted PEG1500N after thionyl chloride reaction and proceeded further in crosslinking the CQDs with dimethyl pimelidimide [143]. Recently, Wang’ group managed to attach an imidazole derivative onto the surface of CQDs according to the same principles [144]. At first, amino-modified CQDs were developed by the co-pyrolysis of citric acid and urea, while 1H-imidazole-4-carboxylic acid was reacted with thionyl chloride. Afterwards, the acylation reaction was employed as the acyl chloride derivative of imidazole was reacted with the amino-modified CQDs at 80 °C for 12 h in THF, leading to the covalent conjugation of imidazole (Fig. 4).

Aiming to targeted cancer cell imaging, Li’s team managed to conjugate transferrin on surface passivated CQDs. After being treated with concentrated nitric acid for introducing carboxyl groups and passivated with PEG1500N, or poly(ethylenimide)-b-poly(ethylene glycol)-b-poly(ethylenimide) or a 4-arm amine-terminated PEG, the CQDs were mixed with transferrin in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) which activated the carboxyl groups of transferrin for coupling with the amine groups of the surface passivation agent to give finally covalent amide bonds [98]. In another similar biological molecule attachment, Gonçalves and her co-workers after acid treatment and passivation with PEG200N successfully bound N-acetyl-L-cysteine introducing sulfur atoms in the capping layer of the CQDs [62]. The same group under the same protocol tethered mercaptosuccinic acid importing once again sulfur atoms in the capping layer [145].

EDC chemistry was applied as well by Huang et al. [119]. The carboxyl groups of chlorine e6, also known as talaporfine which is a photosensitizer used in photodynamic therapy, were activated with EDC and N-hydroxysuccinimide ( NHS) in order to react with the amine groups of passivated with PEG2000N CQDs ending to cova-

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### Table 1. Synthetic routes to functionalized CQDs.

<table>
<thead>
<tr>
<th>Synthetic Route</th>
<th>Functional Group</th>
<th>Ref.</th>
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<tbody>
<tr>
<td>Acid treatment</td>
<td>Carboxyls, arbonyls, hydroxyls</td>
<td>[14, 15, 20] and many other beyond</td>
</tr>
<tr>
<td>One-step pyrolysis</td>
<td>Varied, depended on precursor used</td>
<td>[17, 18, 42, 46, 56, 65-67, 72, 80, 81, 86, 88, 101, 110, 123, 130, 133-142]</td>
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<tr>
<td>Acylation (alkanoylation)</td>
<td>Varied, depended on molecule used</td>
<td>[59, 79, 90, 143, 144]</td>
</tr>
<tr>
<td>Carbodiimide chemistry</td>
<td>Varied, depended on molecule used</td>
<td>[49, 62, 87, 98, 101, 119, 124, 145-147]</td>
</tr>
<tr>
<td>Organosilanes</td>
<td>Depended on organosilane used</td>
<td>[91, 114, 117, 148, 149]</td>
</tr>
<tr>
<td>Solvothermal</td>
<td>Amines, boron-containing</td>
<td>[106, 159]</td>
</tr>
<tr>
<td>Alkali treatment</td>
<td>Oxygen-bearing</td>
<td>[75]</td>
</tr>
<tr>
<td>Metal attachment</td>
<td>Varied metals</td>
<td>[126, 129]</td>
</tr>
<tr>
<td>Post reduction</td>
<td>Hydroxyls, hydrazides, alkyl</td>
<td>[104, 160-163]</td>
</tr>
<tr>
<td>Oxidation (plus ammonia)</td>
<td>Amines</td>
<td>[28]</td>
</tr>
<tr>
<td>Ultrasonication (plus ammonia)</td>
<td>Nitrogen-bearing groups</td>
<td>[25]</td>
</tr>
<tr>
<td>Other</td>
<td>Varied</td>
<td>[22, 29, 39, 43, 50, 54, 74, 77, 82, 85, 92-94, 102, 112, 131, 164-171]</td>
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lently grafted chlorine e6 through amide bonds. Additionally, Zhang’s team achieved to fabricate quinoline derivative-functionalized carbon dots [49]. CQDs were prepared at 160 °C from citric acid and branched PEI, while carbodiimide chemistry was employed to covalently conjugate a quinoline derivative onto the surface of the CQDs. The same principals, i.e. carbodiimide reactions, were employed for the covalent conjugation of glutamic acid and ciprofloxacin on amino-functionalized CQDs prior formed by the co-pyrolysis of citric acid, glycerin, and PEG diamine at 250 °C for 5 h [146]. In 2015, another work by Wang and co-workers was based on EDC chemistry [87]. Carboxyl-modified CQDs were produced from citric acid and ethylenediamine under hydrothermal conditions at 200 °C for 5 h. Then, in the presence of EDC and NHS the carboxyl groups were activated and linked covalently to a 10D amino-modified aptamer of Salmonella typhi-murium after reacting for 1 h with gentle stirring in darkness.

The same synthetic route, EDC/NHS coupling chemistry, was followed by Yang et al. who reported the covalent attachment of a nuclear localization signal (NLS) peptide onto the surface of amino-functionalized CQDs [147]. Pristine N-doped CQDs were fabricated hydrothermally at 60 °C for 8 h from citric acid, PEG2000, and ethylenediamine. The conjugation with the simian virus 40 large T-antigen NLS was achieved with a 48 h long reaction at room temperature in darkness.

Completing the description of reports that lay on EDC chemistry, Yang’s group managed to tether a photoactive diazido PtIV complex on CQDs [124]. Initially, carboxyl-functionalized CQDs were produced from activated carbon by refluxing under oxidative acidic conditions. Then, the Pt IV-azide was conjugated via amide bonding between its amino-pyridine groups and the carboxyl groups of CQDs based on EDC coupling. Finally, surplus carboxyl surface groups were treated with an excess amount of ethylenediamine and material was reacted with folic acid (Fig. 5).

Organosilanes

Since organosilanes represent a significant class of functional compounds, their usage in modifying CQDs it was just a matter of time. Hence, in 2011 Wang et al. presented the first organosilane-
functionalized CQDs via one-step synthetic route [148]. The group prepared highly luminescent CQDs through the pyrolysis of anhydrous citric acid in N-(β-aminomethyl)-γ-aminopropylmethyl-dimethoxysilane (AEAPMS) at 240 °C for 1 min. The fast procedure resulted to ultrasmall CQDs of about 0.9 nm with high quantum yield of up to 47%. CQDs were further processed, whereas the silane presence or its substitution by other silanes deeply expands the variety of the functional groups that can be covalently attached on the surfaces of CQDs and/or the reactions that can be made in additional steps (Fig. 6). Recently, Huang and colleagues employed (3-aminopropyl)triethoxysilane (APS) and applied a one-step simultaneous preparation, passivation, and functionalization of CQDs [114]. Glycerol was used as carbon source and it was reacted with APS at 200 °C for 30 min in a microwave, with the formed CQDs bearing silicate and amine surface functional groups.

The same year, Wen et al. mixed 3-(2-aminoethylamino)propyltrimethoxysilane and graphene oxide with ethanol and treated the suspension hydrothermally at 150 °C for 10 h to obtain once again organosilane-surface functionalized CQDs [117]. In 2015, Wang’s team carbonized citric acid at 150 °C for 4 h under solvothermal conditions in AEAPMS [149]. Their findings revealed that the organosilane was anchored by both sides onto the CQDs’ surfaces, leading to dual long chain surface functional groups with either –NH$_2$ or –Si(OCH$_3$)$_3$ as terminal moieties. In advance, Wang et al. achieved the embedment of water-soluble nitrogen/sulfur-co-doped carbon dots into a polyhedral oligomeric silsesquioxane (POSS) matrix [91]. The N,S-co-doped CQDs were prepared from citric acid and L-cysteine upon hydrothermal treatment as described further below in the co-doped CQDs section [150], while the water-soluble octa(tetramethylammonium)-functionalized POSS was used. Hybrid material in powder form emerged by simple mixing of aqueous solutions of CQDs and POSS, followed by solvent slow evaporation at 30 °C for 24 h.

**Fig. (6).** Schematic illustration for the preparation of photoluminescent CQDs, surface-functionalized with an organosilane via one-step process, and further production of flexible CQD film and CQDs/silica particles. (Reproduced with permission from ref. [148]).

**Procedures for Doped with Further than Nitrogen Heteroatoms and Co-doped CQDs**

In 2013, the first sulfur-doped CQDs were reported by Chandra et al. [92]. For this, thiomalic acid was refluxed for 4 h at 90 °C together with a small amount of concentrated sulfuric acid. Solvent extraction with dichloromethane and ammonium hydroxide addition followed, and finally the S-doped CQDs were formed after the polymerization of the precursor. Malic and succinic acids were also used instead of thiomalic acid in order to evaluate the applicability of the methodology which resulted to high sulfur content as verified by EDX analysis (atomic weight ratio C/S = 5.57/1). Sulfur-doped CQDs were also produced by Kwon and co-workers [131]. Glucose was used as carbon source and thioglycolic acid as sulfur source. Bis(2-ethylhexyl) sulfosuccinate sodium salt (AOT), water, and decane were used to form a water-in-oil reverse micelles microemulsion solution, whereas hexadecylamine was used as passivation agent. Final materials came from the pyrolysis at 160 °C for 2 h of a mixture of the aforementioned chemicals, while the initial concentration of thioglycolic acid and its ratio to glucose displayed a direct proportion to the sulfur content of the S-doped CQDs. Waste frying oil was used by Hu et al. and once again S-doped CQDs were obtained [54]. In a simple and fast reaction, waste frying oil was treated with concentrated sulfuric acid at 100 °C for just 5 min and S- doped CQDs were formed. XPS and FT-IR spectroscopies revealed not only the core doping with thiophene-S groups but also the functionalization of the surfaces with sulfonate groups.

In advance, Dong’s team presented the formation of nitrogen and sulfur co-doped CQDs upon hydrothermal treatment of appropriate precursors [150]. The group prepared simple oxygen containing CQDs by heating citric acid monohydrate in an autoclave at 200 °C for 3 h. When glycine was added in the mixture, the same treatment led to the synthesis of nitrogen-doped CQDs. Finally, and as expected, when L-cysteine replaced glycine, CQDs with both nitrogen- and sulfur-bearing groups were acquired. Sulfur- and nitrogen-co-doped CQDs were also developed by Sun and colleagues [39]. Human hair fibers were etched with sulfuric acid and carbonized after heating at various temperatures. Diverse bonding configurations were formed originating from thiophenes, sulfates, and sulfonates for S and pyridinic and pyrrolic groups for N. Experimental findings indicate that higher reaction temperature favors the fabrication of smaller sized doped CQDs with enhanced sulfur content. Sulfur/nitrogen co-doped is also the case of the CQDs prepared by Huang and co-workers shortly after [35]. Hydrothermal treatment of gentamycin sulfate at 200 °C for 1.5 h resulted to a narrow size distribution of nanoparticles with an average diameter of 2.8 ± 0.7 nm. Final CQDs possessed varied kinds of amine and sulfonate groups as confirmed by XPS analysis. In addition, Hu et al. fabricated N and S co-doped CQDs with the microwave-assisted co-carbonization of rice and N-acetyl-L-cysteine [42]. The process resulted in the formation of N,S,C-dots covered with carboxylic acid, amido and alkyl sulfide moieties as verified by FT-IR and XPS spectroscopies. The N,S,C-dots exhibited tunable and enhanced fluorescence compared to undoped C-dots (derived by the sole pyrolysis of rice) (Fig. 7). Moreover, Wang and co-workers reported a solvent-free synthesis of nitrogen and sulfur co-doped CQDs with the hydrothermal treatment of glutathione at 260 °C for 1 h [47]. The products demonstrated a 16.1% nitrogen and 2.0% sulfur content whereas amine as well as both thiophene-S and sulfide groups were detected implying that the carbon dots’ surfaces were successfully functionalized with both heteroatom-based groups.
and boric acid (H3BO3) were treated hydrothermally at variable temperatures from 150 up to 400 °C for 2.5 h with the final bare CQDs having boron and nitrogen functional groups but carboxyl surface groups as well. EDC/NHS chemistry was further applied for the passivation of the carbon dots with various passivating agents. A year later, Barman et al. in a similar way prepared boron/nitrogen but also phosphorus/nitrogen co-doped CQDs [153]. Citric acid and diethylammonium were pyrolytically decomposed by hydrothermal treatment at 170 °C for 1 h to form N-doped CQDs. Orthophosphoric acid in the case of P and boric acid in the case of B were added in the reaction mixture to obtain the co-doped products. Phenylboronic acid was employed by Shen and Xia as the sole precursor for the formation of boron-doped CQDs [70]. CQDs were prepared hydrothermally at 160 °C for 8 h and apart from the incorporation of boron atoms in the core of the nanoparticles, XPS and FT-IR spectroscopies verified the successful surface functionalization with boronic groups. Analogous boron groups were detected in the doped CQDs acquired by Fan et al. with the electrolysis of a graphite rod in a borax aqueous solution [170], while Shan’s group incorporated boron (5.9 wt.%) into CQDs by the solvothermal treatment of hydroquinone and BBr3 [159]. Finally, boron/nitrogen co-doped CQDs were synthesized recently by Bourlinos and his colleagues microwave-assisted from citric acid, boric acid, and urea [50].

On the other hand, Yang et al. produced the first selenium-doped CQDs [55]. Initially, carbon nanoparticles of an average size 30-50 nm were obtained from Chinese ink upon refluxing for 6 h with HCl aqueous solution, and afterwards were oxidized with a mixture of HNO3, H2SO4, and NaClO3 for 1 h at 5 °C and 5 h at 15 °C. Following, NaHSe was added to an aqueous solution of the oxidized CQDs and the mixture was treated hydrothermally at 240 °C for 12 h. With the same methodology and by using NaHS instead of NaHSe, S-doped CQDs may be acquired, whereas if oxidized CQDs were dispersed in DMF/H2O (9:1), N-doped CQDs were formed. In all cases, heavy doped (above 10 at.% for heteroatoms) CQDs were obtained and various groups were formed as C-N-C, N-(C), S=O, C-S, Se-Se, and H-Se-C linkages. The high atomic ratios of heteroatoms and the existence of H-Se-C linkages and oxidized S=O groups imply that doping probably was not constricted in the core of the CQDs but in addition functionalized their surfaces too. Furthermore, the findings of the work correlated the electronegativity of the doping heteroatoms with the emitted wavelength of the relevant doped CQDs as blue shift of the fluorescence spectrum was observed for the N-doped CQDs while S or Se doping induces red shift (Fig. 8).

Fig. (7). (A) UV-vis absorption spectra of (a) undoped C-dots and (b) N,S-C-dots. Spectra are offset for ease of comparison. (B) and (C) are PL spectra at different λex 300–500 nm of undoped C-dots and N,S-C-dots, respectively. The insets display the images of undoped C-dots and N,S-C-dots under daylight and UV irradiation. (Reproduced with permission from ref. [42]).

Jahan and co-workers developed on the other hand boron/nitrogen co-doped CQDs [152]. N-(4-hydroxyphenyl)glycine and boron/nitrogen co-doped CQDs [152. N-(4-hydroxyphenyl)glycine and boric acid (H3BO3) were treated hydrothermally at variable temperatures from 150 up to 400 °C for 2.5 h with the final bare CQDs having boron and nitrogen functional groups but carboxyl surface groups as well. EDC/NHS chemistry was further applied for the passivation of the carbon dots with various passivating agents. A year later, Barman et al. in a similar way prepared boron/nitrogen but also phosphorus/nitrogen co-doped CQDs [153]. Citric acid and diethylammonium were pyrolytically decomposed by hydrothermal treatment at 170 °C for 1 h to form N-doped CQDs. Orthophosphoric acid in the case of P and boric acid in the case of B were added in the reaction mixture to obtain the co-doped products. Phenylboronic acid was employed by Shen and Xia as the sole precursor for the formation of boron-doped CQDs [70]. CQDs were prepared hydrothermally at 160 °C for 8 h and apart from the incorporation of boron atoms in the core of the nanoparticles, XPS and FT-IR spectroscopies verified the successful surface functionalization with boronic groups. Analogous boron groups were detected in the doped CQDs acquired by Fan et al. with the electrolysis of a graphite rod in a borax aqueous solution [170], while Shan’s group incorporated boron (5.9 wt.%) into CQDs by the solvothermal treatment of hydroquinone and BBr3 [159]. Finally, boron/nitrogen co-doped CQDs were synthesized recently by Bourlinos and his colleagues microwave-assisted from citric acid, boric acid, and urea [50].

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![Fig. (8). The relationship between the electronegativity of heteroatoms and the λem of relevant doped CQDs. (Reproduced with permission from ref. [55]).](image_url)
Alternative Routes and Recent Advances on One-step Pyrolysis and Hydrothermal Treatment Approaches

Jiang and co-workers described an alternative one-step methodology for developing amino-functionalized CQDs [22]. Synthesis was realized inside a submerged-arc plasma reactor by using benzene as carbon source and ethylenediamine as modifying agent. Plasma generated highly reactive free radical sites that interacted with amines and resulted to final materials with primary amine functionalities.

In a different approach, Anilkumar and colleagues oxidized the surfaces of CQDs with nitric acid, dispersed the oxidized CQDs in DMF and added Zn(OOCCH$_3$)$_2$·2H$_2$O under vigorous stirring. Zinc cations were attracted by the negative charge of the surface oxygen functionalities and after slow dropwise addition of an aqueous Na$_2$S solution, ZnS nanoparticles were formed on a fraction of the CQDs’ surfaces [129], relatively to the way Sun’s group had developed previously ZnS-doped carbon nanoparticles [126].

On the other hand, Li et al. did not go with the flow and used alkali conditions to formulate high quality CQDs with stable photoluminescence and a quantum yield of about 12% (Fig. 9) [75]. CQDs were synthesized electrochemically with a relatively low sodium hydroxide concentration (0.05-0.1 N). Nonetheless, as in the case of acid treatment, the produced CQDs also possess oxygen functionalities at their surfaces as carboxyl, carbonyl, and hydroxyl groups.

In a short time period, Liu’s team reported a series of synthetic processes for nitrogen-doped CQDs [29, 74, 165, 166]. At first, the carbon nitride dots as named by the group due to their nitrogen content, were synthesized with the co-polymerization of carbon tetrachloride and 1,2-ethylenediamine either at 80 °C for 60 min, or microwave-assisted for 3.5 min, or solvothermally at 150 °C for 120 min [165]. Subsequently, CQDs were produced by microwave irradiation of N,N-dimethylformamide assisted by acids as chlorosulfonic acid, H$_2$SO$_4$, HCl, or HNO$_3$ [166]. Then, the same acids were used to support the CQDs formation with microwave heat-treatment of various organic amines such as dimethyamline, ethylenimine or tripropylamine [74]. Finally, a diverse approach was followed in their last work, where the hydrothermal treatment of grass at 180 °C was employed [29]. In all cases, fluorescent CQDs with various nitrogen-containing groups were formed; implying that proper selection of the precursors or applied technique can lead to tuned fluorescent CQDs.

Whereas acid treatment is regularly applied for oxidizing pristine CQDs introducing surface oxygen functional groups, Zheng et al. steppped further and performed in addition reduction with sodium borohydride [160]. The reduced CQDs contained also oxygen functionalities only this time there were formed significantly more hydroxyls compared to other groups and to oxidized CQDs. As a result the acid-treated oxidized CQDs exhibited green luminescence attributed to surface energy traps with low quantum yield, while in contrary the reduced CQDs displayed blue luminescence attributed to zig-zag sites with high quantum yield. As confirmed by their results, the enhanced luminescence of the reduced CQDs originated by the high concentration of the surface hydroxyl groups which are known electron-donors. Another conventional reductant, hydrazine hydrate, was employed by Zhang and co-workers for grafting nitrogen-containing groups on the surfaces of CQDs [104]. The group prepared CQDs with the electrolysis of graphite rods in NaOH aqueous solution, followed by reduction treatment with hydrazine hydrate for about 500 min. XPS spectroscopy besides the expected decrease of oxygen-bearing groups revealed the formation of hydrazide groups (O=C–NH–NH$_2$).

In advance, Linehan and Doyle prepared lipophilic CQDs by using lithium aluminum hydride (LiAlH$_4$) for the essential reduction [162]. Carbon tetrachloride was dissolved within the hydrophilic interior of a tetraoctyl ammonium bromide reverse micelle and it was reduced with LiAlH$_4$ to form hydrogen-terminated CQDs confined within the micelle interior. The surface of the as-

Fig. (9). a) Typical sized CQDs optical images illuminated under white (left; daylight lamp) and UV light (right; 365 nm); b) PL spectra of typical sized CQDs: the red, black, green, and blue lines are the PL spectra for blue-, green-, yellow-, and red-emission CQDs, respectively; c) relationship between the CQDs size and the PL properties; d) HOMO-LUMO gap dependence on the size of the graphene fragments. (Reproduced with permission from ref. [75]).
synthesized CQDs was then modified with dodecane using a platinum-catalyzed process to form C–C bonds, leading to chemically passivated CQDs and minimizing their oxidation. The procedure resulted in highly monodisperse dodecane-capped CQDs with an average diameter of 1.5 ± 0.3 nm. The same synthetic procedure was followed for the production of amine-terminated CQDs by simply substituting dodecane with allylamine, resulting in dispersible in polar solvents CQDs with blue luminescence and a quantum yield of 25% [163].

Contrariwise, Jiang and colleagues used a highly oxidizing agent, namely hydrogen peroxide, to acquire CQDs from graphene oxide (GO). GO was further oxidized and fragmented by H₂O₂ while ammonia was added in the reaction pot so as to introduce amine surface groups. The reaction was carried out for 24 h at 80 °C and resulted in N-doped CQDs with exceptionally high nitrogen content of above 15% as confirmed by XPS analysis. Amide bonds were formed while protonated amines and various oxygen functional groups decorated the CQDs’ surfaces [28]. Ammonia as modifying agent and nitrogen source was also used by Ma and co-workers [25]. The group presented a novel method for the one-pot synthesis of water-dispersible CQDs with the ultrasonic treatment. The group prepared a series of CQDs with tunable photoluminescence throughout the entire visible spectrum when excited by white light [58]. CQDs were formed by the pyrolysis at 180 °C of either citric acid or ethylene glycol mixed in both cases with ethylenediamine end-capped polyethyleneimine. Accordingly, CQDs with main PL emission peaks at 530-550 nm were acquired. If a reducing agent, i.e. NaBH₄, was added in the starting reaction system of citric acid, the formed CQDs exhibited blueshifted PL emissions from violet to yellow, depended on the amount of NaBH₄ added. In contrast, if a dehydrating agent, i.e. H₃PO₄, was added in the ethylene glycol system, the PL emissions were redshifted from yellow to red. The final CQDs displayed an excitation-independent PL emission which was directly correlated to the oxygen and nitrogen containing groups of the CQDs. Thus, nitrogen content decreases, while oxygen’s increases with redshifted PL emission. In addition, the insertion of oxygen functionalities introduces more electronic states between the bandgap leading this way to redshift and decreased quantum yields. Overall, experimental proofs confirmed theoretical calculations and showed that CQDs that emitted from blue to red light possessed gradually more epoxide and hydroxyl groups and less C=O and C-N bonds in this direction, i.e. redshifting.

Once again in literature, the low carbonization temperature of citric acid was exploited by Dong et al. and it was used as carbon source in a one-step synthesis of passivated/functionalized CQDs [65, 81, 83]. For this reason branched polyethyleneimine (BPEI) was used as carbon source in a one-step synthesis of passivated/functionalized CQDs [65, 81, 83]. For this reason branched polyethyleneimine (BPEI) was also used having the dual role of passivation and functionalization. Synthesis was performed at 200 °C so as BPEI did not degenerate and due to the high amine content of BPEI, the final CQDs correspondingly possessed many amine surface functional groups. By taking advantage of these groups, Dong’s team utilized the resulting CQDs as chemical sensors and copper ions detector. On the other hand, Han et al. managed to graft polyethyleneimine on the surfaces of glucose derived CQDs with a simple reaction at 80 °C for 3 h, with the final functionalized CQDs bearing amine surface groups as confirmed by FT-IR spectroscopy [102]. In addition, Gao and colleagues by using microwaves achieved the preparation of polyamidoamine dendrimers capped-carbon dots [66]. Citric acid was co-polymerized together with polyamidoamine in a microwave oven reaction at 170 °C for 20 min resulting to the amine derivative CQDs. Microwave-assisted and amine-bearing were also the CQDs developed by Qu et al. [136] and Niu et al. [67]. In both cases, citric acid and urea were heated for a few minutes in a domestic microwave device producing N-doped CQDs.

The one-step pyrolysis was adopted by Guo and co-workers too [88]. By pyrolyzing the photonic crystal poly(styrene-co-
glycidylmethacrylate) (PS-co-PGMA) at 200, 300, and 400 °C they managed to acquire CQDs with tunable blue, orange or white photoluminescence emission (Fig. 10). The as-prepared CQDs demonstrated high quantum yields of up to 47% and high solubility in water and organic solvents. Further analysis with characterization techniques revealed that all three types of CQDs possessed carbonyl, hydroxyl but also carboxyl surface groups.

A one-step route was also followed by Zhang et al. [167]. By carbonizing at a relatively low temperature carbon tetrachloride in the presence of sodium amide (NaNH2) as a dechlorination reagent carbonizing at a relatively low temperature carbon tetrachloride in the presence of sodium amide (NaNH2) as a dechlorination reagent and nitrogen source, a nitrogen-doped CQDs material was obtained, exhibiting nitrogen atoms in a graphite-like structure, pyridinic-like N, pyrrolic-like N, and N–H groups. Hydrothermal treatment was also the case of the surfactant-derived amphiphilic CQDs fabricated by Kozák et al. [151]. A basic aqueous solution of the cationic surfactant cetylpyridinium chloride monohydrate was heated at 150 °C for 2 h in a Teflon-lined stainless steel autoclave under hydrothermal conditions ending up to the formation CQDs that possessed various nitrogen containing functional groups as N-H and C=N. In a different approach, dimethylamines were grafted on graphene oxide-derived CQDs as described by Liu et al. [106]. Using N,N-dimethylformamide as solvent and nitrogen source, strong two-photon-induced fluorescent N-doped CQDs were fabricated solvothermally at 200 °C for 4.5 h which proved to be both photostable and biocompatible. In a comprehensive work by Qu and co-workers later on, a systematic study of the formation mechanism and optimization for obtaining highly luminescent N-doped CQDs was performed [154]. The group used citric acid as carbon source to form CQDs hydrothermally at 160 °C for 4 h, and employed various precursors as nitrogen source for doping and functionalization. Urea, hexamethylenetetramine, diethylamine, ethanolamine, and ethylenediamine were tested with the latter exhibiting the highest reported photoluminescence quantum yield of 94% for N-doped CQDs.

Recently, Chen et al. prepared CQDs with surface carboxyl and amine groups upon the hydrothermal treatment of ethylenediaminetetraacetic acid as carbon source and triethylenetetramine as passivation agent [155]. Both precursors served also as ligands to coordinate with Tb3+ ions and chelate them, thus further modifying the surface of the formed CQDs. In advance, Hou and co-workers treated hydrothermally at 200 °C for 5 h citric acid and L-tyrosine methyl ester hydrochloride [156], and via polymerization, carbonization and amidation reactions, managed to fabricate CQDs that bear tyrosinate groups on their surfaces.

Contrariwise, Liu’s group followed a noncovalent functionalization route for modifying the surface of as-prepared CQDs [157]. Initially, CQDs were developed by the microwave-assisted hydrothermal carbonization of a glucose and poly(acrylate sodium) mixture; and then, folic acid was attached on the surface via hydrogen-bond interactions. Lou et al. described lately the formation of supra-structures from CQDs based on self-assembly [93]. Nitrogen-doped CQDs were fabricated from citric acid and urea, and further on, the amide surface groups were partially reacted with 1-bromo-dodecane. The incomplete reaction led to amphiphatic CQDs with both hydrophilic amide and hydrophobic dodecyl surface groups. As a result, these CQDs can self-assemble towards supra-CD systems in the form of agglomerates through amphiphilic interactions in toluene exhibiting quenched luminescence.

Lastly, in a totally different, from the aforementioned, approach for surface functionalization, Cheng et al. employed polymer sci-
ence chemistry for acquiring modified CQDs for biological applications [112]. The surface functionalized CQDs were prepared via surface-initiated atom transfer radical polymerization (ATRP) of a polycation-b-polysulfobetaine block copolymer, namely poly[2-(dimethylamino)ethyl methacrylate]-b-poly[N-(3-(methacryloylamo) propyl)-N,N-dimethyl-N-(3-sulfopropyl)] ammonium hydroxide]. The final dots possessed graft polymer chains that acted as DNA condensing agents and protective layers from undesired interactions.

Advantages and Disadvantages of Applied Methodologies

The diversity of the applied methodologies for the production of CQDs offers researchers a variety of possible routes aiming the best and desired properties for their CQDs. An ideal procedure would use low-cost abundant raw materials, would be easy, reproducible and cost-effective, fabricating stable CQDs with high quantum yields and excitation-independent PL emission, able to be tailored made, with controllable and narrow size distribution and handy surface functionalization and doping. Apparently, none of the existing approaches gathers altogether the aforementioned advantages. Thus, acid or alkali treatment or in general post-synthetic oxidation or reduction might be easy but the same time costly, not reproducible with low control of the surface functionalization. One-step pyrolysis is again easy but in most cases the photoluminescence and physicochemical (such as size) properties of the obtained CQDs are not predefined as desired but rather their PL emission and properties guide the researchers to find real-world applications. Microwave-assisted, hydrothermal and solvothermal routes offer a true convenience regarding the time needed for preparing CQDs but possess the same disadvantages one-step pyrolysis has. Finally, organic surface functionalization with appropriate molecules and organosilanes may tune significant properties as PL emission wavelength, surface charge, electrongerativity, hydrophilicity, etc. but on the other hand might be expensive and as a post-synthetic method it leaves intact the core of the CQDs and probably much of their PL properties and cannot control core’s size which means that it should be combined with a synthetic method that controls the abovementioned. Therefore, an advanced approach aiming to high quality CQDs should comprise advantages of probably a hydrothermal or microwave-assisted one-step pyrolysis of appropriate precursors and a post-synthetic organic surface functionalization.

CONCLUSIONS AND PERSPECTIVES

Surface passivation and functionalization of CQDs over the past years has expanded their applicability. Introduction and doping with appropriate heteroatoms is the key point to tailor made features of CQDs and thus organic chemistry provides the vital background for the essential functionalizations. Recently, the significance of CQDs’ doping has received the attention that it deserves; however, there are yet some aspects to be addressed. More important is that the CQDs’ structure and specifically the dopants-bearing groups are not predefined when doping comes of a one-step pyrolysis of proper precursors that is the most common approach, but rather varied dopant-containing groups are formed which in advance may not functionalize the surfaces but just dope the CQDs’ core. On the other hand, since organic chemistry is a powerful tool that enables the successful modification of various structures (among them and CQDs), functionalization and doping of CQDs seems still a virgin field and there are many reactions/modifications that can be made. Attachment of organometallic compounds and consequently of noble metallic centers such as Au and Pt or transition metals as Cu, Fe and Zn may enhance or reveal new catalytic, sensing or other properties. In addition, covalent bonding of biomolecules or crucial trace elements like N, S and P may create new prospects in bioimaging and biological delivery systems.

CONFLICT OF INTEREST

The author confirms that this article content has no conflict of interest.

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