Review Article

Acupuncture and Herbal Medicine

OPEN

Carbon quantum dot preparation and application to detecting active ingredients in traditional Chinese medicine

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Abstract

Carbon quantum dots (CQDs) are fluorescent carbon nanomaterials that have been applied to biology, medicine, and optoelectronics, owing to their significant advantages such as simple synthesis methods, low cost, and widely available sources of raw synthesis materials. This review summarizes CQD preparation methods, which include hydrothermal and microwave-assisted synthesis methods, as well as separation methods such as centrifugation, dialysis, and filtration. Additionally, we review the application of CQDs in the detection of active ingredients, primarily phenolic compounds, in traditional Chinese medicine. We also discuss the quenching mechanism of CQD fluorescence using the active ingredients of traditional Chinese medicine. Limitations such as insufficient test selectivity, weak fluorescence intensity, and an unclear quantitative relationship between preparation methods and properties should be resolved for the efficient use of CQDs to detect active ingredients in Chinese medicine.

Keywords: Carbon quantum dots, Flavonoids, Fluorescence quenching, Phenolic compounds, Quality control, Traditional Chinese medicine

1 Introduction

Carbon nanomaterials such as carbon nanotubes, nanodiamonds, fullerenes, and carbon quantum dots (CQDs) have recently undergone rapid development. Among these materials, CQDs have received widespread attention globally. The annual number of research papers on CQDs has increased since 2010 (Figure 1), reaching more than 2,000 per year after 2015.

CQDs are zero-dimensional nanomaterials with a size of less than 10 nm, and they typically have photoluminescence capabilities. The fluorescence emission behavior of CQDs may be affected by many properties such as excitation wavelength, ion concentration, pH value, and solution temperature. CQDs have been used in applications such as bioimaging[1–3], nanomedicine[4-5], and drug delivery[6–8], owing to their significant advantage of low toxicity[9].

In addition to the attractive properties of CQDs, the preparation of CQDs also presents the advantages of synthesis methods that are both simple and low cost as well as the wide availability of synthetic raw materials. The following materials can be used to prepare CQDs: compounds such as ethanol, citric acid, and ethylenediamine; foods such as starch, fruit juice, and vegetables[10–12]; natural products such as leaves and grass[13-14]; and human waste such as waste residue and sludge[15–17].

Recently, the quality detection technology for traditional Chinese medicine has developed rapidly. Chromatographic methods are widely used in pharmacopoeia to quantitatively determine the chemical components of traditional Chinese medicine, which provides strong support to control their quality. However, limitations, such as the high cost of detection and long analysis time, still exist. CQDs have already demonstrated good application prospects in food and drug safety and environmental quality monitoring, which provide new pathways for the quality testing of traditional Chinese medicines.

A literature review was conducted to find published papers on CQDs detecting active ingredients in traditional Chinese medicine. A comprehensive systematic literature search was conducted in the Web of Science and CNKI. The literature search covered the period from October 2004 to June 2020. In this review, the recent synthesis and separation methods of CQDs and their application in traditional Chinese medicine quality testing are summarized.

2 CQD synthesis and separation methods

Many methods to synthesize CQDs have been reported. These materials can be prepared *via* laser ablation and hydrothermal methods using macromolecular and small molecular compounds as raw materials, respectively. Table 1 presents the synthesis methods and characteristics of CQDs.

Seventyfour articles were statistically analyzed, and the ratio of the various preparation methods used is shown in Figure 2. Generally, small-molecule compounds have been commonly reported for the synthesis of CQDs, owing to their simple and environmentally friendly synthesis methods and their advantageous properties of uniform

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Acupuncture and Herbal Medicine (2021) 1:2

Received 9 February 2021 / Accepted 6 July 2021

http://dx.doi.org/10.1097/HM9.0000000000000002

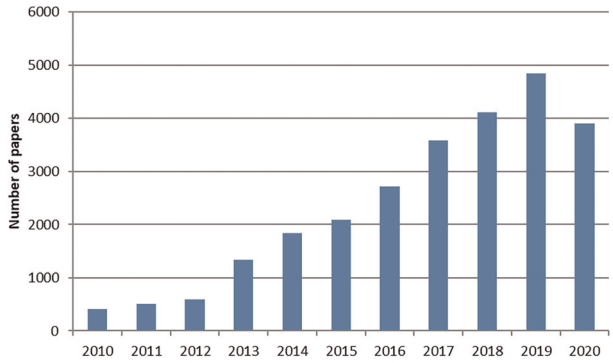


Figure 1. Number of papers on the Web of Science website related to the topic of "carbon quantum dots" for the past 11 years.

size and stability. The hydrothermal method is currently the most widely used synthesis method for the preparation of CQDs. The arc discharge method and laser ablation method are rarely used, owing to their cumbersome processes. Citric acid, ethylenediamine, sugars, and amino acids are the most commonly used raw materials[18–22]. In addition to the hydrothermal method, the microwave-assisted synthesis method is also simple to operate and has been widely used in recent years.

At present, separation and purification methods for CQDs consist of centrifugation, filtration, dialysis, precipitation, extraction, and column chromatography. Table 2 lists the CQD separation and purification methods in the existing literature. Table 2 shows that the individual purification methods that are most frequently used are centrifugation and dialysis. The combinations of centrifugation and filtration with dialysis are the most commonly used separation processes. Ion-exchange resins can often provide better separation effects since CQDs typically have acid/base groups on their surfaces. There are also a few studies in which CQDs are not separated and purified[30,42].

3 Application of CQDs in the detection of active ingredients in traditional Chinese medicine

Currently, CQDs are primarily used to detect flavonoids and phenolic compounds in the field of traditional Chinese medicine. Many phenolic compounds have a linear relationship with the fluorescence quenching of CQDs within a particular concentration range, they can be used for quantitative detection.

Studies on the detection of flavonoids and phenolic compounds using CQDs are listed in Table 3. It can be observed from the table that citric acid is one of the most frequently used synthetic raw materials. Synthesis methods consist of microwave, hydrothermal, and chemical oxidation methods. The most commonly used separation methods are dialysis and dialysis after filtration. The limits of flavonoid detection are lower than 0.3 μM, and those of other phenolic compounds are lower than 5 μM. Detections

Table 1

Synthesis methods and characteristics of CQDs.

Synthesis method	Procedure	Characteristic	Reference
Arc discharge method	First, single-walled carbon nanotubes are extracted from arc discharge soot *via* the preparation electrophoretic method. Second, fluorescent nanoparticles are obtained after purification.	The operation and purification process are complicated, and the quantum yield is low.	[23]
Laser ablation method	A carbon precursor is irradiated with a laser, and the surface of the carbon nanoparticles is modified by different methods to obtain CQDs.	The preparation process requires the use of organic solvents or strong acids. The modification process is relatively complicated and time-consuming. It is also convenient to perform the synthesis and surface modification of fluorescent carbon nanoparticles simultaneously.	[24–28]
Electrochemical method	CQDs are obtained *via* the electrolysis of graphite anodes or other electrolytes.	The method is simple, fast, and low-cost; however, the device is relatively complicated.	[29–32]
Microwave method	A carbon precursor is heated rapidly under microwave conditions to synthesize CQDs.	The method is simple, environmentally friendly, efficient, low-cost, and has a high quantum yield.	[7,17,33–45]
Hydrothermal method	A carbon precursor is placed in a high-temperature and high-pressure sealed container for a long period of time for the reaction to synthesize CQDs.	The synthetic materials are simple. CQDs have the advantages of high water solubility, uniform size. and high quantum yield.	[1–4,6,10–14,16,20–22,46–72]
Pyrolytic method	A carbon precursor is carbonized using external heating to synthesize CQDs.	The method is simple, low-cost, and does not require solvents; however, it presents the disadvantage of requiring long-term high-temperature heating.	[19,73–76]
Chemical oxidation method	A strong oxidant is used to oxidize the carbon precursor, and the reaction generates heat to drive further reactions.	The method is simple, fast, and efficient. However, it is not suitable for the large-scale preparation of CQDs, owing to the large consumption of the oxidant.	[15,77-78]

CQDs: Carbon quantum dots.

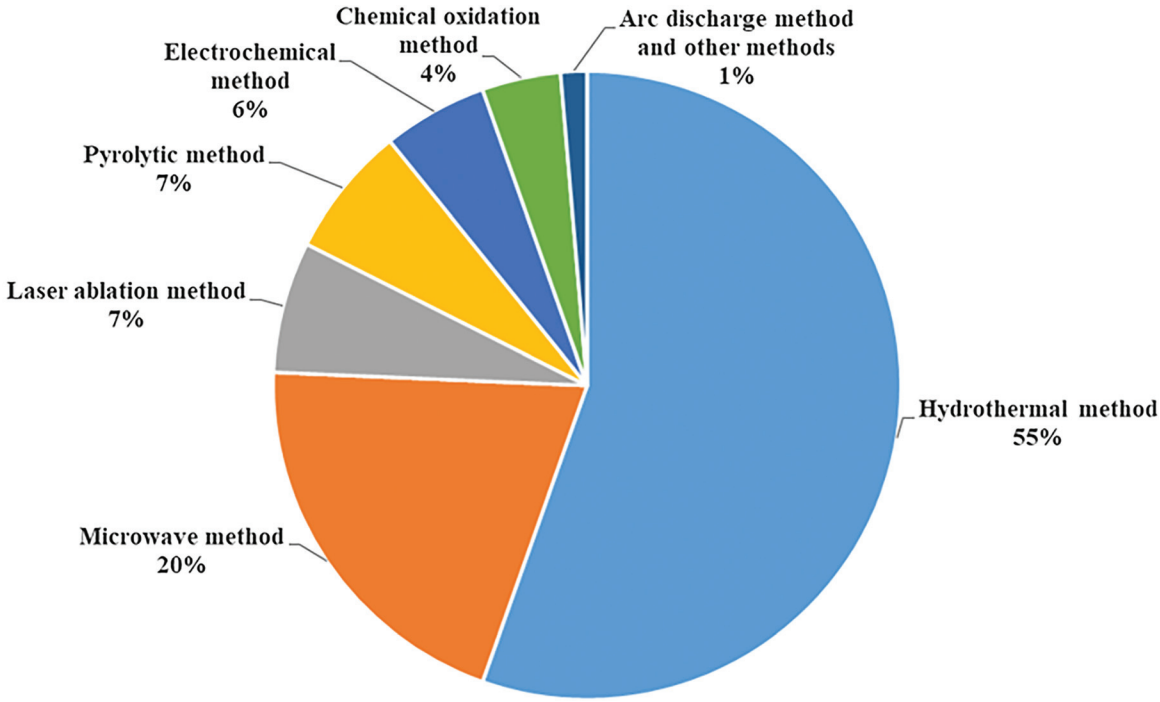


Figure 2. Percentage distribution of various preparation methods.

do not typically experience interference from common ions, sugars, and other compounds. However, the fluorescence of CQDs may be quenched by some heavy metals[21,51,64,72]. He et al.[64] prepared CQDs *via* a one-step hydrothermal synthetic route; these CQDs can specifically interact with Hg^{2+} in an aqueous medium to form aggregates, which facilitated electron transfer from the CQDs to Hg^{2+}. As a result, the fluorescence of the CQDs was efficiently quenched, which made the detection of Hg^{2+} highly sensitive with a quantitation limit of 2.2 nM. Thus, the fluorescence probe established was successfully applied to the quantitative detection of Hg^{2+} in Fufang Shuanghua pills and Changyanning pills.

Liu et al.[45] prepared CQDs *via* the microwave method using aspartic acid and urea. Hydroxyl (–OH), carboxyl (–COOH), and amino ($–NH_2$) functional groups existed on the surface of the CQDs with an average diameter of 2.8 nm. Results showed that chlorogenic acid had no quenching effect on the CQDs. Additionally, Zhu et al.[20] prepared CQDs *via* the hydrothermal method using citric acid and L-histidine. Carboxyl and amino functional groups existed on the surface of CQDs with an average diameter of 3.9 nm. In this case, chlorogenic acid had a clear fluorescence quenching effect on the CQDs. Although some CQD functional groups were the same, a considerable difference in the quenching effect was observed, which indicated that the influences of the preparation methods and raw materials on CQD performance were complex.

The structural formulas of the detected compounds are listed in Table 4. All the compounds contain a benzene ring structure and a conjugated system composed of two or more hydroxyl groups or other groups on the same benzene ring. This also indicates that ingredients with a similar chemical structure may be analyzed with CQDs.

Table 2

Separation and purification of CQDs.

Separation and purification methods	Reference
Preparative electrophoresis	[23]
Centrifugation	[3,12,19,24-25,27-28,43,66]
Extraction	[26]
Dialysis	[1,4,22,29,37,39,41,44–46,61–65,71,74,77]
Column chromatography	[21,53-54]
Washing with water	[14]
Filtration	[34,36,40,50,69]
Dialysis after centrifugation	[2,11,13,17,20,35,38,55,59,78]
Dialysis after filtration	[10,47,51,57-58,60,76]
Dialysis after extraction	[49,67]
Filtration and centrifugation	[7,32,61,72]
Dialysis after centrifugation and filtration	[6,15,16,48,52,56,68,73]
Precipitation after centrifugation and filtration	[75]
Dialysis after alcohol precipitation and centrifugation	[31]
Centrifuge, filter, adjust pH, and then centrifuge	[33]
Dialysis after filtration, centrifugation, and extraction	[70]

CQDs: Carbon quantum dots.

4 Fluorescence quenching mechanism of CQDs

There are many mechanisms by which phenolic chemical components quench CQD fluorescence, including the inner filter effect (IFE), static quenching effect, and photoinduced electron transfer.

IFE refers to the absorption of light at both the excitation and emission wavelengths by phosphors or other coexisting substances[79]. The CQDs absorb the excitation or emission light in the detection system when

Table 3

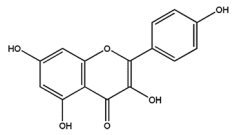
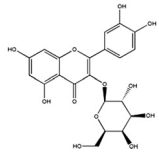
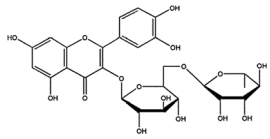
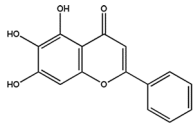
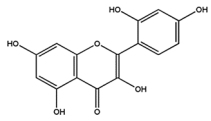
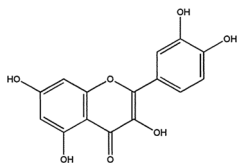
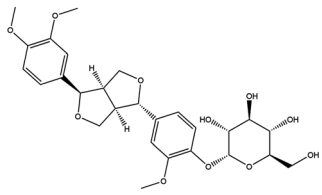
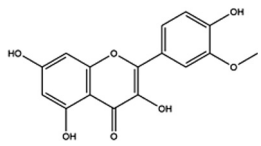
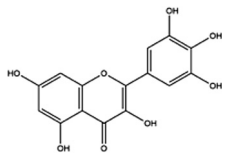
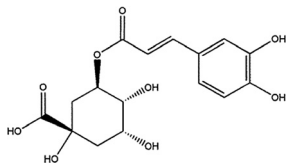
Application of CQDs in the detection of ingredients in Chinese medicines.

Raw materials for synthesis	Preparation method	Separation and purification method	Quantum yield	Detection object	Linear range	Limit of detection	Selectivity	Reference
Acetic acid, water, and diphosphorus pentoxide	Chemical oxidation	Dialysis	–	Kaempferol in Xindakang tablets and human serum samples	3.5–49 μM	38.4 nM	There was little effect on detection when potential interfering substances existed, such as relevant metal ions, amino acid, and other coexisting substances, which may have existed in the real samples.	[77]
Acetic acid, water, and diphosphorus pentoxide	Chemical oxidation	Dialysis after centrifugation	–	Hyperin in Fufangmuji granules and human serum samples	0.22–55 μM	78.3 nM	There was little effect on detection when potential interfering substances existed, including relevant metal ions, biomolecules, and other coexisting compounds, which may have existed in real samples.	[78]
Trisodium citrate, 11-aminohendecane, and polyethylene glycol 400	Microwave method	Filtration	–	Rutin in buckwheat and quinoa	3–40 μM	2.3 μM	Cu^{2+} and Ag^{+} induced interference effects on detection. However, there was little effect on detection when carbohydrates and amino acids existed.	[40]
Citric acid, ethylenediamine	Pyrolytic method	Centrifugation	–	Rutin, flavonoids in Chinese herbs of Artemisiae Japonicus and *Houttuynia cordata*	1–80 μM	–	–	[19]
Citric acid and N-acetyl-L-cysteine	Hydrothermal method	Dialysis	49%	Baicalein in human serum and *Scutellaria baicalensis*	0.69–70 μM	0.21 μM	There was little effect on detection when different interferents existed.	[22]
Glycine and urea	Microwave method	Dialysis	13%	Morin in human urine samples	0.4–60 μM	0.12 μM	There was little effect on detection when representative metal ions and biomolecules existed.	[41]
β-cyclodextrins	Microwave method	–	–	Quercetin and ginkgo flavonoids	1–800 μM	–	–	[42]
Citric acid and sodium hydroxide	Microwave method	Centrifugation	–	Quercetin	6–100 μM	0.1 μM	–	[43]
L-Aspartic acid and urea	Microwave method	Dialysis	–	Isorhamnetin in ginkgo leaf tablets	0.22–180 nM	1.32 nM	There was little effect on detection when common metal ions and possible components (ferulic acid, rutin, chrysophanol, daidzein) existed in drugs.	[44]
Citric acid, melamine, and formaldehyde	Hydrothermal method	Dialysis	–	Phillyrin in Shuanghuanglian Oral Liquid	0.008–0.03 mg/L	0.036 μg/L	There was little effect on detection when sugars, amino acids, and other inorganic ions existed.	[71]
Aspartic acid and urea	Microwave method	Dialysis	17%	Myricetin in red wine samples and human serum samples	1–80 μM	18.4 nM	There was little effect on detection when common metal ions, amino acids, and other coexisting substances (chlorogenic acid, chrysophanol, rutin, daidzein, and ferulic acid) existed.	[45]
Malic acid and urea	Hydrothermal method	Dialysis after filtration	16.5%	Chlorogenic acid in honeysuckle samples	0.15–60 μM	45 nM	There was little effect on detection when various metal ions, anion, sugar. and amino acids existed.	[57]
Citric acid and L-histidine	Hydrothermal method	Dialysis after centrifugation	22%	Chlorogenic acid in coffee and honeysuckle	1.53–80 μM	0.46 μM	There was little effect on detection when inorganic ions and other molecules existed.	[20]
Ethylenediamine, H_3PO_4, and 4-aminophenylboronic acid	Hydrothermal method	Dialysis after filtration	21.95%	Curcumin in mineral water and tap water	0–1.5 μM	68 nM	There was little effect on detection when various metal ions and biological macromolecules existed.	[58]
Sodium citrate and thiourea	Hydrothermal method	Dialysis after centrifugation	26.9%	Curcumin in urine samples	0.15–18 μM	0.04 μM	There was little effect on detection when some ions and small biological molecules existed.	[59]
Urea and citric acid	Hydrothermal method	Dialysis after filtration	24.3%	Caffeic acid in red wine samples	0.79–100 μM	0.24 μM	There was little effect on detection when some common ions, sugars, and amino acids existed.	[60]
Poly (ethylene glycol) acrylate	Pyrolytic method	Dialysis after filtration	0.3%	Tannic acid in red and white wine samples	0.1–10 mg/L	0.018 mg/L	–	[76]
Glucose and ethylenediamine	Hydrothermal method	Filtration and centrifugation	–	Pyrogallic acid in water samples	4.0–90 μM	3.5 μM	There was little effect on detection when amino acids, phenolic compounds, and some ions existed.	[61]

CQDs: carbon quantum dots.

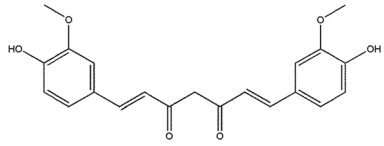
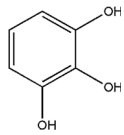
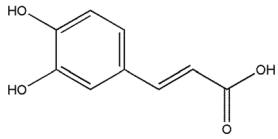
Table 4

Structural formulas of the detected compounds.

Compounds	Category	Structural formulas	Reference
Kaempferol	Flavonoids		[77]
Hyperin	Flavonoids		[78]
Rutin	Flavonoids		[19,40]
Baicalein	Flavonoids		[22]
Morin	Flavonoids		[41]
Quercetin	Flavonoids		[42-43]
Phillyrin	Flavonoids		[71]
Isorhamnetin	Flavonoids		[44]
Myricetin	Flavonoids		[45]
Chlorogenic acid	Phenolic compounds		[57]

(*continued*)

Table 4
(continued).

Compounds	Category	Structural formulas	Reference
Curcumin	Phenolic compounds		[58-59]
Pyrogallic acid	Phenolic compounds		[61]
Caffeic acid	Phenolic compounds		[60]

the absorption spectra of the quencher in the detection system overlap with the excitation or emission spectra of the CQDs; this produces the IFE[80]. Wu et al.[58] observed that CQD fluorescence was almost completely quenched within 1 min after adding curcumin to the system. The CQD emission spectra exhibited a precise overlap with the absorption band of curcumin; thus, curcumin could absorb the CQD emission light[58]. No clear excited-state interaction or electrostatic interaction between curcumin and the CQDs was identified. Consequently, IFE was the only possible dominant reason for CQD fluorescence quenching induced by curcumin[58]. IFE was also identified as the quenching mechanism of chlorogenic acid on CQDs[57].

Static quenching occurs when a non-fluorescent ground-state complex is formed *via* the interaction between CQDs and a quencher[81]. Huang et al.[82] confirmed the static quenching mechanism using the quenching effect of heme on CQDs. The average CQD fluorescence lifetime was approximately constant in the absence or presence of heme, and an ultraviolet absorption peak confirmed that heme and CQDs form a complex, which indicated that the CQD fluorescence quenching mechanism is static quenching[82]. The quenching constants increase with increasing temperature for dynamic quenching; however, static quenching does not have this effect. Therefore, the fluorescence quenching mechanism can be analyzed using the Stern–Volmer equation[83]. Li et al.[61] investigated the quenching effect of pyrogallic acid on CQDs at different temperatures. The use of the Stern–Volmer equation confirmed that the fluorescence quenching mechanism of pyrogallic acid on CQDs is static quenching. Similarly, the mechanism by which baicalein quenches CQD fluorescence is also static quenching[22].

Photoinduced electron transfer can be explained as the electron transfer between the CQDs (electron donor or electron receptor) and quencher (electron receptor or electron donor), which forms cation radicals and anion radicals, respectively[81]. Ahmed et al.[76] proposed a possible mechanism for CQD quenching using tannic acid that may be attributed to an electron transfer process from the photoexcited CQDs to the aromatic groups in tannic acid. The CQDs may be wrapped by tannic acid-mimicking dendrimers, which allows an effective non-radiative energy transfer process. Similarly, Liu et al.[78] also confirmed this photoinduced electron transfer *via* the fluorescence quenching effect of hyperoside on the prepared CQDs.

5 Summary and outlook

Compared with conventional methods for the quantitative detection of flavonoids and other phenolic compounds, methods based on CQD fluorescence quenching sensors provide many analytical advantages, such as simple operation, environmentally friendly synthesis, rapid detection, and low cost. However, there are still several limitations regarding these methods that need to be mitigated.

First, the detection selectivity requires improvement.

The complex components of Chinese medicinal material extracts and Chinese medicine preparations interfere with the specific detection of CQDs, owing to their similar chemical structures and physical and chemical properties. Additionally, there may be substances, such as heavy metal ions (Hg^{2+}, Cu^{2+}, and Fe^{3+}) and pesticide residues, in Chinese medicinal materials that also quench CQD fluorescence[51,72]. These factors may lead to false-positive test results. Therefore, low selectivity limits the application of CQDs to the detection of active ingredients in traditional Chinese medicine. Surface passivation and doping with heteroatoms and nitrogen have a significant influence on the fluorescence performance of CQDs[84]. We intend to improve the synthesis method and doping with different heteroatoms to increase the fluorescence properties and detection selectivity of CQDs.

Second, the fluorescence intensity of CQDs is low.

Although the methods to detect phenolic compounds based on CQDs have been applied to the detection of active ingredients in traditional Chinese medicine, their sensitivity is still lower than that of high-performance liquid chromatography (using both ultraviolet and mass spectrometry). Future research efforts should be directed toward significantly enhancing the fluorescence yield and

fluorescence intensity of CQDs to improve the sensitivity of CQD detection. Therefore, the optical properties and luminescence mechanism of CQDs should be thoroughly studied to optimize the synthesis and modification methods of CQDs.

Third, the quantitative relationship between the preparation methods and the performance of CQDs is unclear.

The structure and properties of the obtained CQDs are significantly different, owing to the variety of raw materials and preparation methods used. However, the relationship between the structure and properties of CQDs is rarely discussed. A possible reason is that the prepared CQDs comprised a mixture, and their structure was not completely identified in most published studies. To the best of our knowledge, there is no study that compares the performance of CQDs prepared with the same raw materials but using different methods. Presently, it is still difficult to design a synthesis route according to the nature of the detection object. We recommend the systematic study and identification of the quantitative relationship between the synthesis conditions and CQD performance so that suitable raw materials and reasonable synthetic routes can be selected as required.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

The study was supported by the National S&T Major Project of China (2018ZX09201011-003) and the National Project for Standardization of Chinese Materia Medica (ZYBZH-C-GD-04).

Author contributions

Thanks for the investigation, conceptualization and writing original draft of Bo Liu, the investigation and conceptualization of Shangxin Guo, project administration,the writing review and editing of Xiaohui Fan, the supervision, funding acquisition, project administration, validation, writing review and editing of Xingchu Gong.

Ethical Approval of Studies and Informed Consent

Not applicable.

Acknowledgments

None.

References

[1] Niu WJ, Li Y, Zhu RH, et al. Ethylenediamine-assisted hydrothermal synthesis of nitrogen-doped carbon quantum dots as fluorescent probes for sensitive biosensing and bioimaging. *Sensor Actuat B Chem* 2015;218(8):229–236.

[2] Wu FS, Su HF, Wang K, et al. Facile synthesis of N-rich carbon quantum dots from porphyrins as efficient probes for bioimaging and biosensing in living cells. *Int J Nanomedicine* 2017;12(8):7375–7391.

[3] Singh V, Rawat KS, Mishra S, et al. Biocompatible fluorescent carbon quantum dots prepared from beetroot extract for in vivo live imaging in C-elegans and BALB/c mice. *J Mater Chem B* 2018;6 (20):3366–3371.

[4] Zhang M, Wang WT, Zhou NL, et al. Near-infrared light triggered photo-therapy, in combination with chemotherapy using magneto-fluorescent carbon quantum dots for effective cancer treating. *Carbon* 2017;118(7):752–764.

[5] Lu SM, Li GL, Lyu ZX, et al. Facile and ultrasensitive fluorescence sensor platform for tumor invasive biomaker beta-glucuronidase detection and inhibitor evaluation with carbon quantum dots based on inner-filter effect. *Biosens Bioelectron* 2016;85(12):358–362.

[6] Zhang M, Wang J, Wang WT, et al. Magnetofluorescent photothermal micelles packaged with GdN@CQDs as photothermal and chemical dual-modal therapeutic agents. *Chem Eng J* 2017;330 (12):442–452.

[7] Chiu SH, Gedda G, Girma WM, et al. Rapid fabrication of carbon quantum dots as multifunctional nanovehicles for dual-modal targeted imaging and chemotherapy. *Acta Biomat* 2016;46 (12):151–164.

[8] Zhang YQ, Ma DK, Zhang YG, et al. N-doped carbon quantum dots for TiO_2-based photocatalysts and dye-sensitized solar cells. *Nano Energy* 2013;2(5):545–552.

[9] Kong WQ, Liu J, Liu RH, et al. Quantitative and real-time effects of carbon quantum dots on single living HeLa cell membrane permeability. *Nanoscale* 2014;6(10):5116–5120.

[10] Qiang R, Yang S, Hou K, et al. Synthesis of carbon quantum dots with green luminescence from potato starch. *New J Chem* 2019;43 (27):10826–10833.

[11] Alam AM, Park BY, Ghouri ZK, et al. Synthesis of carbon quantum dots from cabbage with down- and up-conversion photoluminescence properties: excellent imaging agent for biomedical applications. *Green Chem* 2015;17(7):3791–3797.

[12] Mehta VN, Jha S, Kailasa SK. One-pot green synthesis of carbon dots by using Saccharum officinarum juice for fluorescent imaging of bacteria (*Escherichia coli*) and yeast (*Saccharomyces cerevisiae*) cells. *Mater Sci Eng C Mater Biol Appl* 2014;38(9):20–27.

[13] Yadav PK, Singh VK, Chandra S, et al. Green synthesis of fluorescent carbon quantum dots from *Azadirachta indica* leaves and their peroxidase-mimetic activity for the detection of H_2O_2 and ascorbic acid in common fresh fruits. *ACS Biomater Sci Eng* 2019;5 (2):623–632.

[14] Sabet M, Mahdavi K. Green synthesis of high photoluminescence nitrogen-doped carbon quantum dots from grass via a simple hydrothermal method for removing organic and inorganic water pollutions. *Appl Surf Sci* 2019;436(1):283–291.

[15] Gunjal DB, Gurav YM, Gore AH, et al. Nitrogen doped waste tea residue derived carbon dots for selective quantification of tetracycline in urine and pharmaceutical samples and yeast cell imaging application. *Opt Mater* 2019;98(12):109484.

[16] Wang CJ, Shi HX, Yang M, et al. Facile synthesis of novel carbon quantum dots from biomass waste for highly sensitive detection of iron ions. *Mater Res Bull* 2020;124(4):110730.1–110730.8.

[17] Hu YP, Gao ZJ. Sewage sludge in microwave oven: a sustainable synthetic approach toward carbon dots for fluorescent sensing of para-Nitrophenol. *J Hazard Mater* 2020;382(1):121048.

[18] Wang BB, Jin JC, Xu ZQ, et al. Single-step synthesis of highly photoluminescent carbon dots for rapid detection of Hg^{2+} with excellent sensitivity. *J Colloid Interface Sci* 2019;551(9):101–110.

[19] Shang J, Zhang HR. Preparation of nitrogen doped carbon quantum dots and flavonoids analysis in Chinese herbal medicine. *Shandong Chem Ind* 2018;47(1):61–63.

[20] Han Z, He L, Pan S, et al. Hydrothermal synthesis of carbon dots and their application for detection of chlorogenic acid. *Luminescence* 2020;35(7):989–997.

[21] Liang JY, Han L, Liu SG, et al. Carbon dots-based fluorescent turn off/on sensor for highly selective and sensitive detection of Hg^{2+} and biothiols. *Spectrochim Acta A* 2019;222(80):117260.

[22] Zhang J, Nan D, Pan S, et al. *N.S* co-doped carbon dots as a dual-functional fluorescent sensor for sensitive detection of baicalein and temperature. *Spectrochim Acta A* 2019;221(11):117161.

[23] Xu XY, Ray R, Gu YL, et al. Electrophoretic analysis and purification of fluorescent single-walled carbon nanotube fragments. *J Am Chem Soc* 2004;126(40):12736–12737.

[24] Sun Y-P, Zhou B, Lin Y, et al. Quantum-sized carbon dots for bright and colorful photoluminescence. *J Am Chem Soc* 2006;128 (24):7756–7757.

[25] Hu SL, Niu KY, Sun J, et al. One-step synthesis of fluorescent carbon nanoparticles by laser irradiation. *J Mater Chem* 2009;19 (4):484–488.

[26] Goncalves H, Jorge PAS, Fernandes JRA, et al. Hg(II) sensing based on functionalized carbon dots obtained by direct laser ablation. *Sensor Actuat B Chem* 2010;145(2):702–707.

[27] Nguyen V, Yan LH, Si JH, et al. Femtosecond laser-assisted synthesis of highly photoluminescent carbon nanodots for Fe^{3+} detection with high sensitivity and selectivity. *Opt Mater Express* 2016;6(2):312–320.
[28] Ren X, Zhang F, Guo BP, et al. Synthesis of N-doped micropore carbon quantum dots with high quantum yield and dual-wavelength photoluminescence emission from biomass for cellular imaging. *Nanomaterials* 2019;9(4):495.
[29] Hou YX, Lu QJ, Deng JH, et al. One-pot electrochemical synthesis of functionalized fluorescent carbon dots and their selective sensing for mercury ion. *Anal Chim Acta* 2015;866(3):69–74.
[30] Yao S, Hu YF, Li GK. A one-step sonoelectrochemical preparation method of pure blue fluorescent carbon nanoparticles under a high intensity electric field. *Carbon* 2014;66(66):77–83.
[31] Patra S, Roy E, Madhuri R, et al. Economic and ecofriendly synthesis of biocompatible heteroatom doped carbon nanodots for graphene oxide assay and live cell imaging. *ACS Sustain Chem Eng* 2016;4(3):1463–1473.
[32] Liu RH, Huang H, Li HT, et al. Metal nanoparticle/carbon quantum dot composite as a photocatalyst for high-efficiency cyclohexane oxidation. *ACS Catal* 2014;4(1):328–336.
[33] Lopez C, Zougagh M, Algarra M, et al. Microwave-assisted synthesis of carbon dots and its potential as analysis of four heterocyclic aromatic amines. *Talanta* 2015;132(1):845–850.
[34] Wang L, Bi YD, Hou J, et al. Facile, green and clean one-step synthesis of carbon dots from wool: application as a sensor for glyphosate detection based on the inner filter effect. *Talanta* 2016; 160(11):268–275.
[35] Huang QT, Li Q, Chen YF, et al. High quantum yield nitrogen-doped carbon dots: green synthesis and application as "off-on" fluorescent sensors for the determination of Fe^{3+} and adenosine triphosphate in biological samples. *Sensor Actuat B Chem* 2018;276(12):82–88.
[36] Li HY, Xu Y, Ding J, et al. Microwave-assisted synthesis of highly luminescent N- and S-co-doped carbon dots as a ratiometric fluorescent probe for levofloxacin. *Microchim Acta* 2018;185(2):7.
[37] Konar S, Kumar BNP, Mahto MK, et al. N-doped carbon dot as fluorescent probe for detection of cysteamine and multicolor cell imaging. *Sensor Actuat B Chem* 2019;286(5):77–85.
[38] Edison T, Atchudan R, Sethuraman MG, et al. Microwave assisted green synthesis of fluorescent N-doped carbon dots: cytotoxicity and bio-imaging applications. *J Photochem Photobiol B* 2016;161 (8):154–161.
[39] Ding YY, Gong XJ, Liu Y, et al. Facile preparation of bright orange fluorescent carbon dots and the constructed biosensing platform for the detection of pH in living cells. *Talanta* 2018;189(11):8–15.
[40] Song ZY, Fu YJ, Liang YT, et al. Determination of rutin based on fluorescence quenching of carbon quantum dots. *Guangzhou Chem Ind* 2019;47(4):98–100.
[41] Liu LZ, Mi Z, Hu Q, et al. Green synthesis of fluorescent carbon dots as an effective fluorescence probe for morin detection. *Anal Methods* 2019;11(3):353–358.
[42] Li CS, Liu ZM, Zhang HR. Microwave synthesis of carbon quantum dots and its fluorescence quenching by quercetin. *Shandong Chem Ind* 2018;47(3):14–15.
[43] Wu Y, Zhang HR. One step synthesis of carbonate quantum dots by microwave and its analytical application. *Chem Ind Times* 2018;32 (1):5–8.
[44] Li HH, Liu LZ, Feng F. Facile synthesis of fluorescence carbon quantum dots and their application in detection of isorhamnetin in medicines. *J Instrum Anal* 2020;39(4):514–519.
[45] Liu L, Mi Z, Guo Z, et al. A label-free fluorescent sensor based on carbon quantum dots with enhanced sensitive for the determination of myricetin in real samples. *Microchem J* 2020;157(9):104956.
[46] Guo Y, Wang Z, Shao H, et al. Hydrothermal synthesis of highly fluorescent carbon nanoparticles from sodium citrate and their use for the detection of mercury ions. *Carbon* 2013;52(2):583–589.
[47] Shen T, Wang Q, Guo Z, et al. Hydrothermal synthesis of carbon quantum dots using different precursors and their combination with TiO(2) for enhanced photocatalytic activity. *Ceram Int* 2018;44 (10):11828–11834.
[48] Liu W, Diao HP, Chang HH, et al. Green synthesis of carbon dots from rose-heart radish and application for Fe^{3+} detection and cell imaging. *Sensor Actuat B Chem* 2017;241(4):190–198.
[49] Zhang B, Liu C-Y, Liu Y. A novel one-step approach to synthesize fluorescent carbon nanoparticles. *Eur J Inorg Chem* 2010;(28):4411–4414.
[50] Atchudan R, Edison TNJI, Aseer KR, et al. Highly fluorescent nitrogen-doped carbon dots derived from *Phyllanthus acidus* utilized as a fluorescent probe for label-free selective detection of Fe^{3+} ions, live cell imaging and fluorescent ink. *Biosens Bioelectron* 2018;99(1):303–311.
[51] Shangguan J, Huang J, He D, et al. Highly Fe^{3+}-selective fluorescent nanoprobe based on ultrabright N/P codoped carbon dots and its application in biological samples. *Anal Chem* 2017;89(14):7477–7484.
[52] Wang L, Li BQ, Xu F, et al. High-yield synthesis of strong photoluminescent N-doped carbon nanodots derived from hydro-soluble chitosan for mercury ion sensing *via* smartphone APP. *Biosens Bioelectron* 2016;79(4):1–8.
[53] Huang K, He Q, Sun RS, et al. Preparation and application of carbon dots derived from cherry blossom flowers. *Chem Phys Lett* 2019;731(9):136586.
[54] Dordevic L, Arcudi F, Prato M. Preparation, functionalization and characterization of engineered carbon nanodots. *Nat Protoc* 2019;14(10):2931–2953.
[55] Hua XW, Bao YW, Wu FG. Fluorescent carbon quantum dots with intrinsic nucleolus-targeting capability for nucleolus imaging and enhanced cytosolic and nuclear drug delivery. *ACS Appl Mater Interfaces* 2018;10(13):10664–10677.
[56] Shen J, Shang SM, Chen XY, et al. Highly fluorescent N, S-co-doped carbon dots and their potential applications as antioxidants and sensitive probes for Cr (VI) detection. *Sensor Actuat B Chem* 2017;248(9):92–100.
[57] Yang H, Yang L, Yuan YS, et al. A portable synthesis of water-soluble carbon dots for highly sensitive and selective detection of chlorogenic acid based on inner filter effect. *Spectrochim Acta A Mol Biomol Spectrosc* 2018;189(1):139–146.
[58] Wu B, Liu X, Shi X, et al. Highly photoluminescent and temperature-sensitive P, N, B-co-doped carbon quantum dots and their highly sensitive recognition for curcumin. *RSC Adv* 2019;9 (15):8340–8349.
[59] Han Z, Zhang H, He L, et al. One-pot hydrothermal synthesis of nitrogen and sulfur co-doped carbon dots and their application for sensitive detection of curcumin and temperature. *Microchem J* 2019;146(5):300–308.
[60] Sun QQ, Long YW, Li HX, et al. Fluorescent carbon dots as cost-effective and facile probes for caffeic acid sensing *via* a fluorescence quenching process. *J Fluoresc* 2018;28(2):523–531.
[61] Li MX, Li YX, Zhang Y, et al. Determination of pyrogallic acid in amino-functional carbon quantum dots fluorescence quenching. *Chin J Lumin* 2017;(1):117–123.
[62] Ni PJ, Dai HC, Li Z, et al. Carbon dots based fluorescent sensor for sensitive determination of hydroquinone. *Talanta* 2015;144(11): 258–262.
[63] Wu XL, Song Y, Yan X, et al. Carbon quantum dots as fluorescence resonance energy transfer sensors for organophosphate pesticides determination. *Biosens Bioelectron* 2017;94(8):292–297.
[64] He JH, Cheng YY, Yang T, et al. Functional preserving carbon dots-based fluorescent probe for mercury (II) ions sensing in herbal medicines *via* coordination and electron transfer. *Anal Chim Acta* 2018;1035(9):203–210.
[65] Li NL, Jia LP, Ma RN, et al. A novel sandwiched electrochemiluminescence immunosensor for the detection of carcinoembryonic antigen based on carbon quantum dots and signal amplification. *Biosens Bioelectron* 2017;89(12):453–460.
[66] Jahanbakhshi M, Habibi B. A novel and facile synthesis of carbon quantum dots *via* salep hydrothermal treatment as the silver nanoparticles support: application to electroanalytical determination of H_2O_2 in fetal bovine serum. *Biosens Bioelectron* 2016;81(3):143–150.
[67] Ke J, Li XY, Zhao QD, et al. Upconversion carbon quantum dots as visible light responsive component for efficient enhancement of photocatalytic performance. *J Colloid Interface Sci* 2017;496 (6):425–433.
[68] Zhang Y, Xiao YT, Zhang YJ, et al. Carbon quantum dots as fluorescence turn-off-on probe for detecting Fe^{3+} and ascorbic acid. *J Nanosci Nanotechnol* 2020;20(6):3340–3347.
[69] Yang XP, Xu J, Luo N, et al. N,Cl co-doped fluorescent carbon dots as nanoprobe for detection of tartrazine in beverages. *Food Chem* 2020;310(4):125832.
[70] Al-Hashimi B, Omer KM, Rahman HS. Inner filter effect (IFE) as a simple and selective sensing platform for detection of tetracycline using milk-based nitrogen-doped carbon nanodots as fluorescence probe. *Arab J Chem* 2020;13(4):5151–5159.
[71] Liu YX, Wang WK, Tian Q, et al. Construction and application of a fluorescence sensor for forsythin. *Chin J Anal Lab* 2020;39 (4):438–442.
[72] Liu YS, Zhao YA, Zhang YY. One-step green synthesized fluorescent carbon nanodots from bamboo leaves for copper(II) ion detection. *Sensor Actuat B Chem* 2014;196(6):647–652.

[73] Dager A, Uchida T, Maekawa T, et al. Synthesis and characterization of mono-disperse carbon quantum dots from fennel seeds: photoluminescence analysis using machine learning. *Sci Rep* 2019;9(9):14004.
[74] Hao J, Li LY, Zhao WW, et al. Synthesis and application of CCQDs as a novel type of environmentally friendly scale inhibitor. *ACS Appl Mater Interfaces* 2019;11(9):9277–9282.
[75] Jiao XY, Li LS, Qin S, et al. The synthesis of fluorescent carbon dots from mango peel and their multiple applications. *Colloids Surf A Physicochem Eng Asp* 2019;577(9):306–314.
[76] Ahmed GHG, Laino RB, Calzon JAG, et al. Fluorescent carbon nanodots for sensitive and selective detection of tannic acid in wines. *Talanta* 2015;132(1):252–257.
[77] Liu L, Feng F, Paau MC, et al. Sensitive determination of kaempferol using carbon dots as a fluorescence probe. *Talanta* 2015;144(11):390–397.
[78] Liu L, Mi Z, Hu Q, et al. One-step synthesis of fluorescent carbon dots for sensitive and selective detection of hyperin. *Talanta* 2018;186(8):315–321.
[79] Larsson T, Wedborg M, Turner D. Correction of inner-filter effect in fluorescence excitation-emission matrix spectrometry using Raman scatter. *Anal Chim Acta* 2007;583(2):357–363.
[80] Li GL, Fu HL, Chen XJ, et al. Facile and sensitive fluorescence sensing of alkaline phosphatase activity with photoluminescent carbon dots based on inner filter effect. *Anal Chem* 2016;88(5):2720–2726.
[81] Zu FL, Yan FY, Bai ZJ, et al. The quenching of the fluorescence of carbon dots: a review on mechanisms and applications. *Microchim Acta* 2017;184(7):1899–1914.
[82] Huang S, Wang LM, Huang CS, et al. A carbon dots based fluorescent probe for selective and sensitive detection of hemoglobin. *Sensor Actuat B Chem* 2015;221(12):1215–1222.
[83] Yang H, Long YW, Li HX, et al. Carbon dots synthesized by hydrothermal process *via* sodium citrate and NH_4HCO_3 for sensitive detection of temperature and sunset yellow. *J Colloid Interface Sci* 2018;516(4):192–201.
[84] Lim SY, Shen W, Gao ZQ. Carbon quantum dots and their applications. *Chem Soc Rev* 2015;44(1):362–381.

How to cite this article: Liu B, Guo SX, Fan XH, Gong XC. Carbon quantum dot preparation and application to detecting active ingredients in traditional Chinese medicine. Acupunct Herb Med. 2021;1(2):81–89. doi: 10.1097/HM9.0000000000000002