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# CARBON DOTS AS TARGETED DELIVERY FOR ANTICANCER THERAPY: A REVIEW

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## ABSTRACT

Carbon dots are the new class of small nanoparticles with a particle size of less than 10nm used for the treatment of various cancers like breast cancer, liver cancer, skin cancer, prostate cancer etc. In recent years, $CD_S$ are used for the attachment of several drugs and/or ligands due to its ability to act on the targeting site. Low dimensional (<10nm) quantum dots have received great attention for potential use in biomedical applications (diagnosis and therapy) for which large nanoparticles (>10nm) are not suitable. We explored the biological activity of these $CD_S$ in different applications namely bioimaging, biosensors, optronics, apoptosis of cancer cells. The $CD_S$ are synthesized by using different techniques and investigated by spectral methods. The cytotoxic effect of $CD_S$ on cancer cells compared with a standard drug, showing significant results. These $CD_S$ exhibits strong fluorescence with maximum around 670nm. To further understand the role of CDs towards cytotoxicity, confocal or fluorescence microscopy and flow cytometry analysis were carried out. These $CD_S$ shows increased cancer therapy efficiency through the localization of much higher concentration of drugs in the nuclei of tumour cells and induce a high rate of apoptosis.

**Keywords: Carbon Dots ($CD_s$), Fluorescence, Spectral Analysis, Cytotoxicity, Apoptosis**

## INTRODUCTION

Cancer is the foremost public health issue and second leading cause of mortality worldwide. Over 10 million new patients are diagnosed with cancer annually with over 6 million associated deaths, responding roughly 12% worldwide mortality. The occurrence of new cancer cases is expected to grow about 70% over the next two decades and estimated to reach over 15 million new cases diagnosed annually by the year 2020 **[1, 2]**. Particularly, breast cancer is the second most common causing death in woman both in developed and developing countries **[2, 3]**. Carbon quantum dots are a new class of fluorescent carbon nano materials having a particle size in the range of ~2-10nm and also called as carbogenic nanoparticles, carbon nanoparticles ($CNP_S$), carbon dots ($CD_S$) or carbon nanodots ($CND_S$). Recent developments in the bionanomedicine make it a promising route to tackle the cancer through selective therapy using low–dimension nanoparticles as drug delivery vehicles. For instance, target drug embedded nanoparticles vehicles selectively identify the tumor cells and deliver the drugs without affecting the healthy cells i.e., it can penetrate the cancer cell and effectively deliver the drug.

Fluorescent carbon dots ($CQD_S$) were accidentally discovered in 2004 by Xu *et al*, while purifying single walled carbon nanotubes derived from the arc-discharge method. Shortly after, Sun *et al*. prepared $CQD_S$ with improved photoluminescence. Later on, CaO. *et al* has explored. Furthermore, in 2009, Yang *et al*, synthesized and consequently employed the surface passivated $CQD_S$ in *In-vivo* mice model imaging. Recently materials with fluorescent properties have gained the attention which can be used as powerful diagnostic tools as well as elements of controlled drug delivery and release systems. Some of them can also act as theragnostatic agents or as cell–labelling agents **[4, 5]**. Carbon-based $QD_S$ which can be applied in medicine and pharmacy due to their good biocompatibility as well as water dispersity. Carbon quantum dots with sizes of 2-10nm have become a promising photoluminescent (PL) nanomaterials in a variety of applications, especially in sensing and bioimaging, due to their high photoluminescence, hydrophilicity, quantum yield and low photo-bleaching **[6]**. Compared with traditional organic fluorescent dyes and inorganic quantum dots, $CD_S$ showed some unique properties, including good biocompatibility, water dispersability, photostability, eco-friendly, low cost, tunable emission and easy modification. Recently, various $CD_S$ have been reported using natural products as a carbon sources such as lemon juice, tomato

juice, carrot juice, watermelon peel, orange peel, strawberry juice, Curcuma longa, onion etc. **[7, 8]**. As the size of carbon dots decreases, the emission color shifts to the blue region. In other words, small carbon dots emits yellow, green or red light depending on their size **[9]**.

Common techniques have been used to prepare $CD_S$ such as electrochemical synthesis, chemical oxidation, laser ablation, ultrasonic methods, hydrothermal/ solvothermal and microwave-assisted pyrolysis. However, most of these techniques may involve complex reactions, time-consuming processes, post-treatment procedures and expensive carbon source and $CD_S$ made from standard chemical synthesis is complicated and expensive, requiring hazardous chemicals and multiple synthetic steps. Among all the available protocols, microwave-assisted methods are efficient, time-saving eco-friendly and narrow size distributing through the homogenous heating **[10, 11]**. This microwave mediated synthesis indications many preferable methods such as rapid reaction rate, controllable conditions, low cytotoxicity, non-hazardous, cheaper in handling, low cost and provide a facile and feasible route of preparing carbon dots. Within a few minutes, highly photoluminescent $CQD_S$ with good water solubility and biocompatibility were prepared. However, the stability of $QD_S$ is a challenging issue, which alters their ability in cancer cell diagnosis and treatment. Therefore, the cellular uptake of $QD_S$ rely on size, shape and surface functionalization **[12, 13]**.

The obtained nanomaterials were characterized UV-Vis spectroscopy, spectro-fluorimetry, Fourier transform infrared spectroscopy (FT-IR), transmission electron microscopy (TEM). Chromatographic methods, chemiluminescence, capillary electrophoresis and dipstick colorimetric methods are also used mainly for tetracycline analysis. However, most of the reported $CD_S$ emitted intense blue-green luminescence under excitation of UV light **[14-16]**. The other advantages of $CD_S$ are their high quantum yield and non-blinking fluorescent features. To solve the binding issue for these materials, many attempts have been made to control the PL fluctuations. Therefore, the non-blinking feature $CD_S$ is important for the applications in the chemical analysis and bioanalysis as the binding may result in signal loses while performing real-time tracking in living cells **[17]**.

## SYNTHETIC APPROACH

### Chemical ablation:

Strong oxidizing acids carbonize small organic molecules to produce carbonaceous materials, which can be further breakdown into small sheets by controlled oxidation. A simple route to prepare luminescent $CQD_S$

in an aqueous solution by dehydrating carbohydrate with concentrated $H_2SO_4$, followed by treatment with nitric acid to break carbonaceous material into individual $CQD_S$ and passivating with amine terminated compounds (4,7,10-trioxa-1,13-tridecanediamine) which is essential for the photoluminescence (PL). Photoluminescent $CQD_S$ were prepared in one-pot using polyethylenimine (PEI), cationic branched polyelectrolyte, as a carbon source and passivating agent via $HNO_3$. Photoluminescence of CQD is a pH sensitive.

**Electrochemical Carbonization:**

Electrochemical soaking is a best method to prepare $CQD_S$ using various carbon materials as precursors. Synthesis of $CQD_S$ via the electrochemically carbonizing the low molecular weight alcohols. Two platinum sheets were used as working and auxiliary electrodes and calomel electrode mounted on a freely adjustable Luggin capillary was used as the reference electrode. The alcohols were converted into $CQD_S$ with after electrochemical carbonization using basic conditions. The graphitization degrees and size of the $CQD_S$ increase with the increasing applied potential. The yield of these $CQD_S$ can be upto 15.9% and showing low toxicity to human cancer cells.

**Laser ablation:**

$CQD_S$ were produced via laser ablation of a carbon target in the presence of water vapour with argon as carrier gas at 900°C and 75kPa followed by treatment with $HNO_3$ for 12h and passivating the surface by attaching simple organic species such as $PEG_{1500N}$ (amine-terminated polyethylene glycol) and poly (propionylethyleneimine-co-ethyleneimine) (PPEI-EI), acid treated $CQD_S$ gave bright luminescence emission. Fluorescent $CQD_S$ are prepared by laser irradiation of a suspension of carbon materials in an organic solvent. By using organic solvents, the surface states of the $CQD_S$ could be modified to achieve better light emission. Laser ablation method is used to synthesize $CQD_S$ using nano-carbon material as starting material and solvents such as acetone, ethanol or water, and then sonicated solution is subjected to laser irradiation followed by centrifugation to obtain the supernatant liquid containing the $CQD_S$.

**Microwave irradiation:**

This method is a rapid and cheap to synthesize $CQD_S$. Using sucrose as the carbon source and diethylene glycol (DEG) as the reaction media green luminescent $CQD_S$ were produced within a minute under MI. DEG-stabilized $CQD_S$ are well dispersed in water with transparent appearance. Microwave mediated pyrolysis of citric acid with various amine molecules to synthesize highly luminescent $CQD_S$.

The primary amine molecules play a dual role as N-doping precursors and surface passivating agents for the $CQD_S$, with enhanced the PL performance, highly biocompatible. The quantum yield values greatly with an increase in N- content.

**Hydrothermal /solvothermal treatment:**

Hydrothermal carbonization (HTC) or solvothermal carbonization is a cheap, environmentally friendly, non-toxic route to synthesize carbon based materials from precursors. An organic precursor solution is packed and processed in a hydrothermal reactor at high temperature. $CQD_S$ were synthesized via HTC from many precursors such as glucose, citric acid, chitosan, banana juice and protein. Highly photoluminescent $CQD_S$ with a quantum yield 26% which is prepared from orange juice in one step by HTC followed centrifugation. These $CQD_S$ with sizes of 1.5-4.5 nm were applied bioimaging due to their photostability and low toxicity. One-step synthesis of amino-functionalized fluorescent $CQD_S$ by HTC of chitosan at 180°C for 12hours. Solvothermal carbonization followed by extraction with an organic solvent is a popular approach to prepare $CQD_S$. Carbon yielding compounds were subjected to heat treatment in high boiling point organic solvents, followed by extraction and concentration. Two kinds of $CQD_S$, such as hydrophilic and hydrophobic are synthesized with the diameter less than 10nm from the carbonization of carbohydrates. Hydrophobic $CQD_S$ are synthesized by mixing with different amounts of carbohydrates, octadecylamine and octadecene then heated up to 70-300°C for 10-30min. the hydrophilic ones are prepared by heating an aqueous solution of carbohydrates within broad range of pH **[18, 19]**.

**Table 1: Synthesis Of Carbon Quantum Dots By Different Techniques**

| Method | Source | Product | Reference |
|---|---|---|---|
| Electrochemical Method | Tea leaves | Carbon Quantum Dots | 01 |
| Hydrothermal Method | Ginger juice | Carbon Dots | 06 |
| Hydrothermal Method | Prunuscerasifera fruits | Fluorescent Carbon Dots | 07 |
| Microwave Irradiation Technique | Gelatin, PEG | Fluorescent Carbon Dots | 11 |
| Microwave Irradiation Technique | Succinic acid | Fluorescent Carbon Dots | 13 |
| Microwave Irradiation Technique | Glycerine, PDA | Carbon Dots | 14 |
| Electrochemical Method | Lemon juice | Fluorescent Carbon Dots | 15 |
| Microwave Irradiation Technique | Citric acid | Fluorescent Carbon Dots | 17 |
| Hydrothermal Method | Carrot juice | Fluorescent Carbon Dots | 20 |
| Hydrothermal Method | Cucumber and pineapple peels | Carbon Dots | 21 |
| Electrochemical Method | Bamboo leaves | Carbon Quantum Dots | 25 |
| Hydrothermal Method | Spices | Fluorescent Carbon Dots | 26 |
| Hydrothermal Method | Cabbage juice | Carbon Dots | 27 |
| Hydrothermal Method | Fruit juice | Carbon Dots | 28 |
| Hydrothermal Method | Malic acid, EDA | Fluorescent Carbon Dots | 29 |

## CHARACTERIZATION

**NMR spectroscopy:**

Nuclear Magnetic Resonance is used for determining the content and purity of a sample as well as its molecular structure. It is also used for determining the size of $CQD_S$ **[6]**.

**SEM Studies:**

Scanning electron microscopy analysis is used to study the particle size and morphology of $CQD_S$ **[10]**.

**Optical properties:**

To explore the optical properties of $CQD_S$, UV-Vis and Photoluminescence spectral studies are carried out. Fluorescence emission of $CQD_S$ was measured at different pH values by adjusting the solution pH with 0.1N HCl and 0.1N NaOH solution **[18, 19]**.

**UV-Visible spectroscopy:**

UV-Visible spectroscopy is one of the important characterization techniques to study the optical properties. The obtained $CQD_S$ were characterized by UV-Vis Spectrophotometer. The absorption bands and excitation wavelength are attributed and the obtained $CQD_S$ under UV light shows fluorescence. This was carried over a wavelength range of 200nm to 800nm.

**FT-IR spectroscopy:**

FT-IR is used to produce an infrared absorption or emission spectrum of a solid, liquid or gas. An FT-IR Spectrophotometer simultaneously collects high spectral-resolution data over a wide spectral range. The sample to be dried on a glass plate at 150°C and then collected in powdered form and KBr was used as the condition of analysis. The FT-IR spectrum of $CQD_S$ which was used for identification of functional groups and characteristics chemical bonds present.

**TEM and HR-TEM studies:**

Transmission electron microscopy and high-resolution transmission electron microscopy is used for the study of nanomaterials with structural features of atleast one dimension in the range of 1-100nm.

**XRD Analysis:**

X-Ray diffraction is a primary tool for probing structure of nanoparticles. It is used for the study of nanomaterials with structural features of atleast one dimension in the range of 1-100nm.

**XPS Analysis:**

X-ray photoelectron spectroscopic measurement is used to determine the elemental composition of $CQD_S$ **[20]**.

**HPLC analysis:**

It is used for quantitative analysis of $CQD_S$ solution. It is used to separate, identify and quantify each component in a mixture **[21]**.

**Biological properties:**

Biocompatibility of the functionalized $CQD_S$ is a critical issue for further applications in live cells, tissues and animals. During last few years, systemic

cytotoxicity evaluations were carried out on both raw $CQD_S$ and passivated $CQD_S$. $CQD_S$ produced by arc discharge of graphite rods and refluxed for 12h with concentrated $HNO_3$ for cytotoxic assay. The bare $CQD_S$ and luminescent $CQD_S$ synthesized by electrochemical treatment of graphite were evaluated for cytotoxic assay, in which cell viability is not affected by carbon dots. The cytotoxicity of the $CQD_S$ passivated with functional groups such as PEG, PPEI-EI, PEI, BPEI (branched polyethylenimine) and PPA(poly(acrylic acid) were evaluated for cytotoxic assay. PEGylated $CQD_S$, $CQD_S$ functionalized with $PEG_{1500N}$, PPEI-EI-passivated $CQD_S$ were shown nontoxic to the cells. A PEI free sample was nontoxic to HT-29 cells at high concentrations in MTT assay. PEI functionalized $CQD_S$ were more toxic than PPEI-EI functionalized $CQD_S$. Both PAA free samples and PAA functionalized $CQD_S$ were toxic to the cells with an equivalent concentrations and at exposure time of 24h. Overall, PEG and PPEI-EI are suitable for $CQD_S$ functionalization even at high concentrations these molecules were shown low toxicity which are used *In vivo* imaging and biosensing.

**PHARMACEUTICAL APPLICATIONS**

**Biomedical/Drug delivery system:**

It is a combine medical therapy and bioimaging diagnostics for visualizing the drug distribution and monitoring their effects. A theranostic agents (CD-Oxa) was synthesized by the conjugation of an anticancer agent (oxidized oxaliplatin, Oxa (IV)-COOH) on the surface of $CQD_S$ having amino groups. CD-anticancer drugs exhibit the optical properties of the CDs and therapeutic effects of anticancer drugs. The *In-vitro* results have shown that CD-anticancer drugs possess good biocompatibility, bioimaging and anticancer properties. The *In-vivo* results demonstrate that it was able to follow the distribution of drug by monitoring the fluorescence signal of CD-anticancer drugs, which helps to customize the dose and injection time of the medicine. $CQD_S$ functionalized gold nanorods were used for the delivery of doxorubicin in a multi-functional fashion including photo thermal therapy, drug delivery and bioimaging using same platform. In Hixson-Crowell model, haloperidol (HaLO) (an anti-psychotic drug)-grafted $CQD_S$ with cyste-amine hydrochloride (CysHCl) (linker) exhibits controlled release under physiological conditions for more than 40h. The ciprofloxacin, a broad spectrum antibiotic attached to $CQD_S$ with bright green fluorescence can provide an effective new nanocarrier for controlled drug release with high antimicrobial activity under physiological conditions and bioimaging **[18, 22]**.

**OTHER APPLICATIONS**

**Biosensors:**

$CQD_S$ have been used as biosensor carrier for their flexibility in surface modification, high water solubility nontoxicity, excitation-dependent multicolour emission, good cell permeability, excellent biocompatibility and high photo stability. The $CQD_S$ based biosensors can be used for visual monitoring glucose, potassium, iron, phosphate, cellular copper, pH and nucleic acid. $CQD_S$ can be used as an efficient fluorescent sensing platform for detecting nucleic acid with selectivity single mismatch. A boronate based $H_2O_2$ recognition element, boronate protected fluorescein was covalently linked to the $CQD_S$. It can be used for tracking the exogenous $H_2O_2$ in the cells of L929 and also can be visualize the $H_2O_2$ produced RAW 264.7 macrophage cells **[23]**.

**Bioimaging:**

As fluorescent nanomaterials have good biocompatibility and low biotoxicity, $CQD_S$ shows greater potency for fluorescent bioimaging and multimodal bioimaging of cells and tissues. It is an attractive multi-imaging technology for one agent for understanding the state of illness. The nanostructured multimodal imaging probes are the combinations of magnetic resonance imaging (MRI) and optical imaging modalities. Simultaneously physiological and anatomical information can be obtained by high resolution MRI whereas rapid screening can be produced by optical imaging. The iron oxide-doped $CQD_S$ (IO-$CQD_S$) were prepared using thermal decomposition of organic precursors in presence of small iron oxide nanoparticles for multimodality bioimaging. The IO-$CQD_S$ can be taken by RAW 264.7 cells and fluorescent property was detected in cell cytoplasm. In *In-vivo* imaging, IO-$CQD_S$ were administered through IV injection in rats. Fluorescent signals of IO-$CQD_S$ were observed in spleen samples and MRI results shows enhanced signals brain blood vessels **[24]**.

**FUTURE SCOPE**

The carbon dots have the high surface passivation effects. The new method of synthesis of carbon dots is to improve mechanistic elucidation. It also gives the fluorescence imaging of the cells and tissues. Fluorescent carbon dots have optoelectronic and biomedical properties. Carbon dots have the photostability, versatility, low cytotoxicity and a good biocompatibility. The carbon dots have multicolour luminescence in the entire visible part and the surface passivating agent is not added. $CQD_S$ has impressive studies, selectivity and sensitivity and it has biological, organic molecules and a targeted gases. $CQD_S$ have surface chemistry, size and wavelength dependent luminescence emission and it is different and it is different from semiconductor of

quantum dots. $CQD_S$ used in the sensors, bioimaging and energy related devices. The covalent dots exhibited excitation pH dependent luminescent behavior, concentration and the wavelength. $CQD_S$ has the good bioimaging agents and the fluorescent ink due to their well dispersability, long emission life time and stable emission and then good compatibility with cells.

**CONCLUSION**

In this review, we are able to gain the vast knowledge about the carbon dots and its applications. The fluorescence carbon dots show the efficient therapy and destroy or inhibit the growth of tumor cells. The different synthetic methods and approaches are discussed. Comparing the synthetic methods, the hypothermal and microwave irradiation techniques are widely used. The carbon dots can penetrate the cancer cells and effectively delivers the drug. These carbon dots do not affects the normal cells, tissues or organs. It only affects the tumors cells and inhibits or destroys the growth of cancer cells. These $CQD_S$ have the unique properties like photostability, low cost, environmental friendliness, and good biocompatibility. The $CQD_S$ are characterized by using spectral methods, chromatographic techniques and also using particle size characteristics. UV-Vis spectroscopy, FT-IR spectroscopy, XRD, XPS, HPLC, TEM, SEM, NMR spectroscopy are the tools used. The optical properties such as photoluminescence, fluorescence properties are described. The carbon dots have the vast applications in drug delivery and also used as the diagnostic tools like bioimaging, biosensing and optronics. In drug delivery, drug directly reaches the target and produces effect on the specific target. In the purpose of diagnosing, it images the cancer cells or tumors forming cells and further on treatment the cancer cells are eradicated.

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**CONFLICTS OF INTEREST**

Authors declare no conflicts of interest.

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**REFERENCES**

**[1]** Shivaji K, Balasubramaniyan MG, Devadoss A, Asokan V, De Castro CS, Davies ML, *et al,* Utilization of waste tea leaves as bio-surfactant in CDs quantum dots synthesis and their cytotoxicity effect in breast cancer cells, Appl Surf Sci., 2019, 487, 159-70.

**[2]** Rady I, Bloch MB, Chamcheu R-CN, Banang Mbeumi S, Anwar

MR, Mohammed H *et al*, Anticancer properties of graviola (*Annona Muricata*): A comphrehensive mechanistic review, Oxid Med Cell Longev., 2018, 2018, 1-39.

**[3]** Nisa FZ, Astuti M, Murdiati A, Haryana SM, Anti-proliferation and apoptosis induction of aqueous leaf extract of *Carica papaya* L. on human breast cancer cells MCF-7, Pak J Biol Sci., 2016, 20, 36-41.

**[4]** Kandaswamy GL, Recent advancements indoped/co-doped quantum dots for multi-potential application, Journal of Carbon Research C., 2019, 5(24), 1-42.

**[5]** Janus L, Pialkowski M, Radwan-Praglowska J, Bojdal D, Matysek D, Chitosan-based carbon quantum dots for biomedical application: Synthesis and characterization, Nanomaterials., 2019, 9(274),1 -13.

**[6]** Li CL, Ou CM, Huang CC, Wu WC, Chan YP, Lin TE *et al*, Carbon dots prepared from ginger exhibiting efficient inhibition of human hepatocellular carcinoma cells, J Mater Chem B., 2014, 2(28), 4564-71.

**[7]** Ma H, Sun C, Xue G, Wu G, Zhang X, Han X *et al,* Facile synthesis of fluorescent carbon dots from *Prunus cerasifera* fruits for fluorescent ink, Fe3+ ion detection and cell imaging, Spectrochim. Acta A., 2019, 213, 281-7.

**[8]** Shen G, Hu M, Qi J, Progress of luminescent carbon dots in biomedicine engineering, Nano Biomed Eng., 2016, 8(3), 190-202.

**[9]** Saliha D, Kara M, Synthesis and applications of carbon dots from food and natural products: A mini review, Journal of Apitherapy and Nature., 2018, 1(1), 33-7.

**[10]** Shivaji K, Mani S, Ponmurugan P, De Castro CS, Davies ML, Balasubramanian MG. *et al*, Green-synthesis-derived CDs quantum dots using tea leaf extract: Antimicrobial, bioimaging and therapeutic applications in lung cancer cells, ACS Appl Nano Mater., 2018, 1, 1683-93.

**[11]** Arsalani N, Nezhad-Mokhtari P, Esmaiel J, Microwave assisted and one–step synthesis of PEG passivated fluorescent carbon dots from gelatin as an efficient nanocarrier for methotrexate delivery, Artif Cells Nanomed and Biotechnol., 2019, 47(1), 540-7.

**[12]** Milosavljevic V, Moulick A, Kopel P, Adam V, Kizek R, Microwave preparation of carbon quantum dots with different

surface modification, J. Metallomics Nanotechnol., 2014, 3, 16-22.

**[13]** Chae A, Choi Y, Jo S, Nuraeni, Peopraserk P, Park SY *et al,* Microwave assisted synthesis of fluorescent carbon quantum dots from an $Al_2B_3$ monomer set, RSC Adv., 2017, 7, 12663-9.

**[14]** Bai Y, Zhang B, Chen L, Lin Z, Zhang X, Ge D *et al*, Facile one-pot synthesis of polydopamine carbon dots for photothermal therapy, Nanoscale Res Lett., 2018, 13(287), 1-9.

**[15]** Ding H, Ji Y, Wei JS, Gao QY, Zhou ZY, Xiong HM, Facile synthesis of red-emitting carbon dots from pulp-free lemon juice for bioimaging, J Mater Chem B., 2017, 5(26), 5272-7.

**[16]** Saliha D, A simple and green extraction of carbon dots from sugar beat molasses: Biosensor applications technology, Sugar Ind., 2016, 141(9), 560-64.

**[17]** Bhaisare ML, Talib A, Khan MS, Pandy S, Wu HF, Synthesis of fluorescent carbon dots via microwave carbonization of citric acid in presence of tetraocetyl-ammoniumion and their application to cellular bioimaging, Microchim. Acta., 2015, 182, 2173-81.

**[18]** Wang Y, Hu A, Carbon quantum dots; synthesis, properties and applications, J Mater Chem C., 2014, 2, 6921- 39.

**[19]** Das R, Bandyopadhay R, Pramanik P, Carbon quantum dots from natural resource: A review, Mater Today Chem., 2018, 8, 96-109.

**[20]** Liu Y, Liu Y, Park M, Park SJ, Zhang Y, Akanda MR *et al,* Green synthesis of fluorescent carbon dots from carrot juice for in vitro cell imaging, Carbon Lett., 2017, 21, 61-67.

**[21]** Himaja AL, Karthik PS, Sreedhar B, Singh SP, Synthesis of carbon dots from kitchen waste: Conversion of waste to value added product, Journal of Fluoresc., 2014, 24(6), 1767-73.

**[22]** Mishra V, Patil A, Thakur S, Kesharwani P, Carbon dots: Emerging theranosticnano architectures, Drug Discov Today., 2018, 23(6), 1219-32.

**[23]** Zuo J, Jiang T, Zhao XZ, Xiong X, Xiao S, Zhu Z, Preparation and application of fluorescent carbon dots, J. Nanomater., 2015, 1-13.

**[24]** De Medeiros TV, Manioudakis J, Noun F, Macairan JR, Victoria F,

Naccache R, Microwave-assisted synthesis of carbon dots and their applications, Journal of Mater Chem C., 2019, 7, 7175-95.

**[25]** Fahmi MZ, Haris A, Permana AJ, Nor Wibomo DL, Purwanto B, Nikmah YL *et al,* Bamboo leaf-based carbon dots for efficient tumor imaging and therapy, RSC Adv., 2018, 8, 38376-83.

**[26]** Vasimalai N, Boas VV, Gallo J, Fatima Cerqueira MD, Miranda MM, Costa-Fernandez JM *et al,* Green synthesis of fluorescent carbon dots from spices for *in-vitro* imaging and tumor cell growth inhibition, BEILSTIEN J Nanotechnol., 2018, 9, 530-44.

**[27]** Alam AM, Park BY, Ghouri ZK, Park M, Kim HY, Synthesis of carbon quantum dots from cabbage with down and up-conversion photoluminescences properties: Excellent imaging agent for biomedical applications, RSC Green Chem., 2015, 17(7), 3791-97.

**[28]** Dias C, Vasimalai N, Sarria MP, Pinherio I, Boas VV, Peixoto J *et al*, Biocompatibility and bioimaging potential of fruit-based carbon dots, Nanomaterials., 2019, 9(2), 1-19.

**[29]** Li J, Ma S, Xiao X, Zhao D, The one-step preparation of green-emissioned carbon dots through hydrothermal route and its application, J Nanomater., 2019, 2019, 1-10.