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CARBON DOTS HOPE FOR CANCER DIAGNOSIS

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Abstract:
Early and easy diagnosis of cancer is important to reduce cancer-related deaths. There are various methods designed to diagnose cancer. Carbon Dots (CDs) have received worldwide attention from the starting of this century and now, they have blossomed in all branches of applied science because of their excellent, physical and chemical properties through the combination of biocompatibilities. Where carbon dots (CD) are most effective in cancer screening. Various nanomaterial is available to detect cancer. Among those nanomaterial CDs have different properties. Some properties of CDs are like low cost of Synthesis or composition, high brightness, cell permeability, high affinity, specificity to target, photostability, good intracellular solubility, high surface area, non-toxicity, good permeability. Carbon Dots (C-dots) are a new category of carbon nanomaterial with a size less than 10 nm. Carbon dots have various applications such as biosensing, screening, imaging, antibacterial, drug delivery and more. The results indicate that the carbon dots produced diffuse in size (average 1.78 nm) and are amorphous and graphitic in nature. Brief details about the carbon dots are provided in this review.

Keywords: *Cancer, diagnosis, carbon dots, In vivo imaging, nanomaterial, Drug delivery.*

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1.INTRODUCTION:

Cancer is a large family of disease that involves abnormal growth of cells that have the ability to attack or spread to other parts of the body. They form a low set of neoplasm. The group of cells that is neoplasm or tumour grow uncontrollably, and form a mass or dough, but can be distributed diffusely. In the last few years cancer has been one of the leading causes of death. Thus, cancer detection is the only way to reduce cancer-related deaths worldwide. The number of cancer diagnostics has been developed in last few years. Cancer development is a multidisciplinary process whereby normal cells progress slowly to malignancy [1]. There are several ways to diagnose cancer. With advances in technologies that better understand cancer, there is an increase in diagnostic tools that can help diagnose cancer. Cancer staging used numbers I, II, III, IV and 0 to describe the increase in cancer.

Early detection of cancer greatly increases the chances of successful treatment. There are two key components to early detection of cancer: education to promote early diagnosis and identifying Symptoms of cancer and taking necessary action lead to early diagnosis. Increasing awareness of possible symptoms of cancer, among doctors, nurses and other health care providers and among the general public, can have a major impact on the disease. Some of the earliest symptoms of cancer include lumps, sores that fail to heal, abnormal bleeding, constant indigestion, and chronic nausea. Early diagnosis is most effective in breast, cervical, oral, lymph, colon and rectal and skin cancer. Early stage cancers, when they are not too large and they are not spread, are more likely to be treated successfully. If the cancer spreads then the most effective treatment becomes unsuccessful.

Carbon Dots stand out as the most valuable gifts in nanotechnology because of their mechanical properties and magical properties [2]. The most common CDs are carbon nanoparticles, most of which have a minimum thickness of less than 10nm. These are obtained from organic compounds and are stable in the most important water media depending on the point of view. Surface engineering plays a major role in CDs in various applications such as explosive detection, chemical sensing, food safety, chemical sensing, drug delivery, energy conversion, and Photocatalysis. Photophysical and chemical properties of CDs vary greatly by varying their composition and size and by incorporating heteroatoms such as oxygen, nitrogen, phosphorus, sulphur, and boron [3,4]. In addition, photostability, high quantum yield, biocompatibility, low toxicity, water solubility, good mobility, and natural density of CDs gain additional advantages over other well-recognized quantum dots (QDs) and graphene quantum dots (GQDs), iron oxides (ZnO, TiO2), and organic QDs (ZnO-PbS, CdSe, CuInS / ZnS, and CuInS / ZnS). In fact, noncarbon QDs are not good in their application category compared to CDs, due to their severe and environmental health problems [5]. CDs can be prepared by both natural and synthetic biological methods widely used in this concern with microwave irradiation, hydrothermal treatment, ultrasonic irradiation, laser ablation, electrochemical, arc discharge, and pyrolysis [6].

2. History of cancer

During the Renaissance in beginning in the 15th century, scientists developed an understanding of the human body.in 1761, Giovanni Morgangi of Pandu was the first to do something that has become standard practice today he made the connection of patients' illness with autopsies. This is the starting for scientific oncology, a cancer study.

Some early theories for cancer

2.1 Humoral theory: Some people believed that the body has 4 humors (body fluids): blood, phlegm, yellow bile and black bile. When humours were equal, a person was healthy. The belief was that too much or too little of any humors could cause disease. Excessive amounts of black bile in different parts of the body were thought to cause cancer. This concept of cancer was transmitted by the Romans and adopted by Galen's influential medical teaching, which remained an undeniable standard in the Middle Ages for over 1,300 years. At this time, physical examinations, including autopsies, were prohibited for religious reasons, namely the progress of medical knowledge.

2.2 Lymph Theory: Infectious Disease some ideas that replaced the myth of cancer were the formation of cancer by another body fluid, lymph. Life was believed to consist of continuous and proper movement of body fluids through solid components. Of all the fluids, the most important was blood and muscle. Stahl and Hoffman say that cancer was formed by inflammation and damage to lymph, varying in population, acidity and alkalinity. Lymph vision has received immediate support. John Hunter, a Scottish surgeon from the 1700s, acknowledged that tumor that grow from lymph often get rid of blood pressure.

2.3 Blastema theory: In 1838, German pathologist Johannes Muller pointed out that cancer was made from cells not from lymph, but he also believed that cancer cells did not come from normal cells. Muller suggested that cancer cells originate from tests (Blastema) between normal tissues. His student, Rudolph Virchow (1821-1902), a famous German pathologist, determined that all cells, including cancer cells, were derived from other cells.

2.4 Chronic irritation theory: Virchow suggested that chronic discrimination is the real cause of cancer, but he mistakenly believed that cancer "spreading like a liquid." In the 1860's, German surgeon Karl Thiersch pointed out that cancerous people associate with the spread of malignant cells and not with unknown fluid.

2.5 Trauma theory: In addition to advances in understanding cancer, from the late 1800s until the 1920s, some thought they were paralyzed by cancer. This belief was maintained despite the failure of the injury to cause cancer in the experimental animals.

3. Types of cancer:

Cancer is determined by its origin and the type of cells in which it is made, even if it spreads to other parts of the body. For example, cancer that starts in the lungs and spreads to the liver is called lung cancer. There are also several clinical terms used for certain types of cancer: Carcinoma is a cancer that begins in the skin or tumors that include other organs. Sarcoma is a cancer of affected tissues such as bones, tumors, cartilage and blood vessels. Leukaemia is a cancer of the bone marrow, which forms blood cells. Lymphoma and myeloma are cancerous cells of the body.

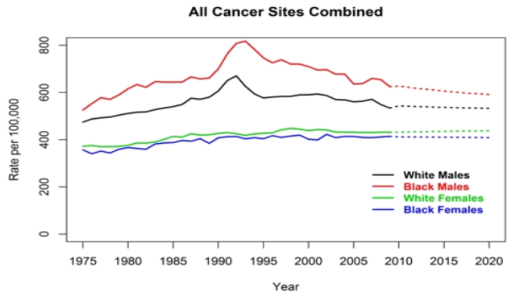

Figure 1 graph of cancer incidence rate in various races

4. Aetiology of cancer

Most cancers, some 90-95% of cases, are due to some environmental factors. The remaining 5-10% is due to inherited genes. Environmental incorporates lifestyle, economic and behavioural factors, not just pollution. Common environmental factors are like tobacco (25- 30%), diet and obesity (30-35%), infection and radiation, stress, physical inactivity pollute the environment. Most cancers have many possible causes. Cancer is caused by accumulated genetic damage. Such changes may be due to an accident. or exposure to cancer causing substance. The causes of cancer are called carcinogens. A carcinogen can be a chemical substance, such as certain smoking molecules. The cause of cancer can be by environmental agents, viruses or genetic factors.

Roughly divide cancer risk factors into the following groups:

1. Biological or intrinsic factors, such as age, inherited genes and skin type
2. Natural exposure, for example, to radon and UV radiation, as well as good materials
3. Occupational hazards, including chemicals such as chemicals, radioactive materials and asbestos
4. Life-related factors.

Life related factors include

Tobacco
Alcohol
UV radiation in sunlight
Some food-related factors, such as nitrites and poly aromatic hydrocarbons generated by barbecuing food)
Lifestyles can prevent cancer

Environment and work-related factors:

Asbestos fibres
Tar and pitch
Polynuclear hydrocarbons (e.g. benzopyrene)
Some metal compounds
Some plastic chemicals (e.g. Vinyl chloride)

Bacteria and viruses:

Helicobacter pylori (H. pylori, which causes gastritis)
HBV, HCV (hepatitis viruses that cause hepatitis)
HPV (human papilloma virus, papilloma virus, which causes changes eg. Cervical cells)
EBV (Epstein-Barr virus, the herpes virus that causes inflammation of the throat lymphoid)

Radiation:

Ionising radiation (e.g. X-ray radiation, soil radon)
Non-ionised radiation (the sun's ultraviolet radiation)
Some drugs may increase the risk of cancer:
Certain antineoplastic agents
Certain hormones
Medicines that cause immune deficiency
In 5 -10 per cent of breast cancer genetic predisposition plays an important role in the emergence of the disease.

Lifestyle is an important factor in the development of many types of cancer. Behaviour and choice can affect our risk of cancer. But with reference to individual councils it is impossible to say exactly what causes cancer. A healthy lifestyle can prevent cancer. Everyone should exercise regularly and eat a variety. People need to eat more plant and fibre products, with only a little red meat and saturated fats, things to avoid smoking, drinking and exposure to the sun. You can take better care of yourself by having regular clinical trials and participating in scheduled cancer screenings.

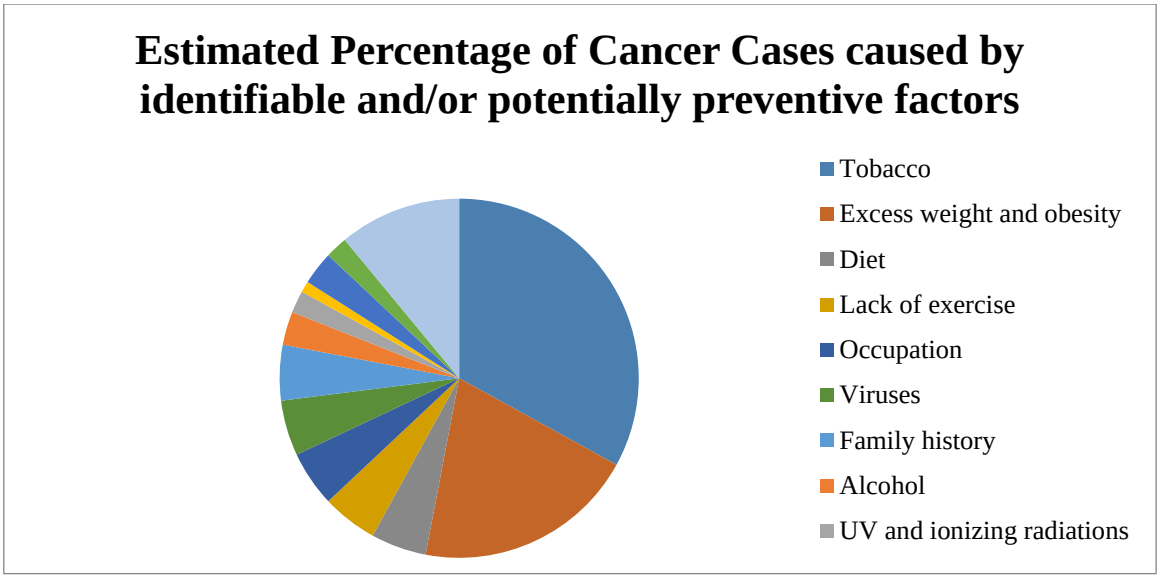

Figure 2: Etiology of cancer

5. Important of diagnosis in cancer:

If doctor detect the cancer at early stage then it provides best chance to find cure or treatment. For a few cancers, research shows screening tests are helpful to save lives by diagnosis of cancer. For some cancers only recommended for people with increased risk. The actual diagnosis aims to reduce the number of patients diagnosed late. Early detection of cancer includes three steps. Barriers exist during each of these three steps, and interventions are needed to address care delays.

Step 1: Information and access to care

To improve awareness and access to care, an integrated approach should be developed that incorporates the capabilities and involvement of integrated, person-centred services at all levels of care. This includes improving health literacy and reducing cancer discrimination.

Step 2: Clinical examination, diagnosis and staging

Developing a diagnostic capacity and optimizing transmission methods can overcome common barriers to diagnosis over time. Health care providers at all levels of care should be equipped with the ability to recognize cancer symptoms and run or use diagnostic tests. Pathology is very important in diagnosing cancer; the patient usually should not start cancer treatment unless there is a definitive diagnosis of cancer. Ultimately, it is transferred to an appropriate facility capable of providing advanced cancer care.

Step 3: Find a cure

Financial, environmental, social and social barriers must be addressed and addressed in the context of the country to improve access to timely cancer treatment. In 2015, less than 30% of low-income countries reported that medical resources were generally available, compared with more than 90% of high-income countries. To ensure quality access, timely cancer treatment is essential for improving cancer outcomes.

6. Diagnostic tools for cancer

There are several methods of diagnosing cancer. With the advances in technologies that better understand cancer, there is an increase in diagnostic tools that can help to detect cancer. Once suspected, the diagnosis is usually done by medical practitioners and oncopathologists and radiology radiologists. Some types of cancer, especially lymphomas, can be difficult to isolate, even by a specialist [10].

There are several methods of diagnosing cancer.

Physical test: Doctors may look for abnormalities such as changes in skin colour or enlargement of any organ.

Laboratory test: Urine or blood test.

Imaging test: MRI, bone scan, ultrasound test

Biopsy: (with needle)

6.1 Biopsy: This is a test in which a small sample of tissue is taken from a suspected cancer with the help of a sharp needle (desirable needle - FNA), or a long core biopsy or by surgical resection. The tissue is then examined under a microscope in the presence of cancer cells. Depending on the location of the tumor, some biopsies can be performed on the external surface only with local anaesthesia.

6.2. Endoscopy: A flexible plastic tube with a small camera is finally inserted into the veins and organs, allowing the doctor to look at the suspicious area. There are many types of scales, each designed to look at specific areas of the body. For example, a colonoscopy is used to detect

growth inside the colon, and then a laparoscope is used to examine the abdominal cavity.

6.3. Diagnostic Imaging: There are several ways of diagnosis cancer. These include X-rays, CT scans, and MRI scans of various parts of the body. X-rays are common imaging techniques and can be specified using Barious enema. This is used for a detection of stomach and small intestine tumor growth and cancer. Mammogram is an X ray of breasts that is used to wrap and / or find lumps of grain and grow. CAT scan (computerized axial tomography) uses radiographic lines to create detailed images on a computer. It's much clearer than the standard X ray. Magnetic Resonance Imaging (MRI) uses powerful magnetic fields to create detailed computerized images of soft tissues, large blood vessels and large organs. Both scanning and MRI can also be used with thin dye to obtain a clear and precise image of the cancer. Ultrasound uses high frequency sound waves to determine whether a suspicious cone is solid or wet. These sound waves are transmitted to the body and converted into a computer image. Bone scan is specifically used to detect and detect new cancerous areas of the bone. Usually a Positron imaging test is used (PET scan). The Gallium test is another drug test in which a special camera takes photos of body tissues after a special tracer is implanted. Cancer sites are illuminated under a scanner [11].

6.4. Mammography: It is an X ray picture of breast .It can be used to check or breast cancer in women.

6.5. Blood test: Some tumors release substances called tumor markers, which can be detected in the blood. A blood test for prostate cancer, for example, determines the amount of prostate specific antigen (PSA). High PSA levels can indicate cancer. However, blood tests by themselves can be inconclusive, and other methods should be used to confirm the diagnosis.

6.6. Pap test: Pap test (Pap smear) is a routine test where a sample of cells from a woman's Cervix is examined under the microscope. This helps identify changes in the cells that could indicate cervical cancer or other conditions.

7. History of carbon dots:

CDs were accidentally discovered in 2004 during the purification of single carbon nanotubes (SWCNTs) by Xu et al [12]. Two years later, in 2006, Sun et al. it was first developed and stabilized photoluminescent carbon nanoparticles of various sizes and called them "carbon quantum dots" (CQDs)[13]. Within a year, water-soluble CDs containing poly-propionylethimnine-co ethylenimine were reported by Sun et al. The prepared CDs showed two photon- induced luminescence spectra and were used to detect human MCF-7 breast cancer cells [14].

Carbon dots have different chemical properties that have been successfully prepared by the application of compaction, swelling / surface modification, and purification. Physicochemical CD structures are conceptually incorporated to improve the performance of many systems, including transmission diodes, bio imaging, and tumor therapy.

Carbon dots are emerging nanomaterial materials, defined by signal sizes <10 nm. CDs form a carbon base that works with various surface groups. These materials showcase a wide range of bodybuilding materials making them an ideal platform for several important biological, biological and energy applications. however, elucidating the molecular origins and important regulatory factors in which biological diversity remains a prominent challenge. Some structures are acquired by primarily by the context of CD, while other structures are derived primarily from overlapping functional groups.

Carbon dots (CDs) are a mass of nanoparticles, defined by quasi-spherical morphology with a size of <10 nm. The CDs were first separated from the arc-discharge in 2004, and quickly attracted much attention due to their photo luminescent properties. In 2006, the use of passivation was started to improve the photoluminescence of CDs by altering the surface chemistry. In 2010, crystalline CDs were successfully separated, showing size-dependent photoluminescence. In 2013, amorphous CDs (polymer dots) began to be refined, expanding the portfolio of transparent CDs from graphite to include cross-linked-polymeric materials. Today, CDs with a well-defined chemical structure and morphology are still being developed. Recent examples include: (i) chiral CDs from chiral beginners; (ii) 2D crystalline C3N of various sizes; and (iii) CD-shaped nanoparticles such as thin-walled nanoparticles that exhibit low bandwidth photoluminescence.

8. Milestones in carbon dot (CD) development.

(A) Fluorescent CDs were first obtained via traditional gel electrophoresis of crude single walled carbon nanotube (CNT) suspensions in 1% agarose gel. The electrophoretic profile was measured under UV light reproduced with permission. (B) Illustrative schematic of poly (ethylene glycol)-passivated CDs. Reprinted with permission. (C) Crystalline CDs: high-resolution transmission electron microscopy image (HRTEM, left) and size-dependent fluorescence images of aqueous solutions under UV-light excitation

(right); scale bar = 2 nm reprinted with permission 3, 49. (D) HRTEM image of polymer dots; scale bar = 20 nm reprinted with permission. (E) Circular dichroism spectrum of chiral CDs reprinted with permission. (F) The chemical structure of the C3N CDs Reprinted with permission. (G) Aberration-corrected high-angle annular dark-field scanning transmission electron microscopy images of triangular CDs; scale bar = 2 nm.

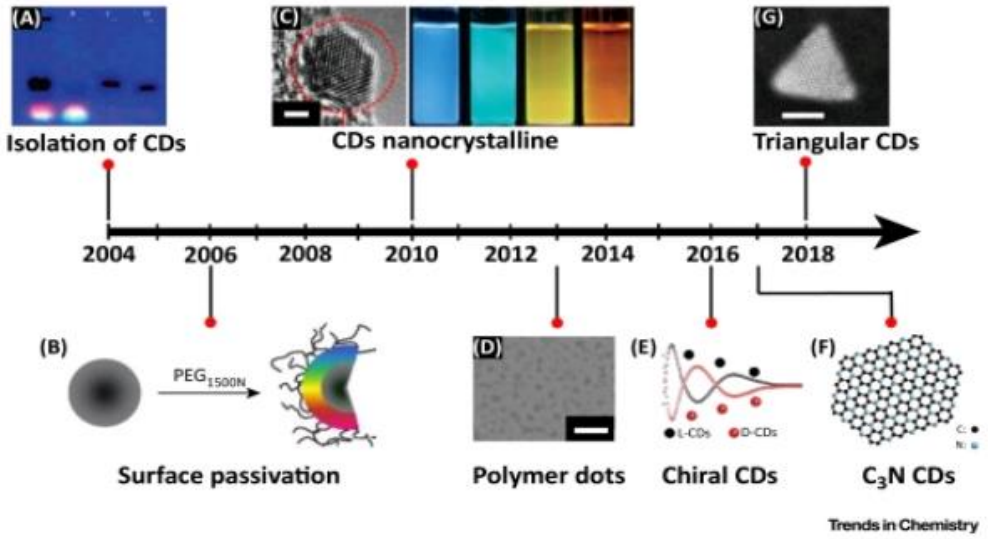

Figure.3. several major milestones in carbon dot (CD) development.

9. Synthesis of carbon dots:

Carbon quantum dots (CQDs) are a novel class of zero-dimensional nanomaterial in the carbon family [15-16]. Since carbon is widely available as a basic element in all living things, carbon nanomaterial they have the right to have low or no biological toxicity, and to work effectively [17]. These nanoparticles are also environmentally friendly, exhibit high chemical and photographic properties, and can easily form bio conjugates [18-19]. It is noteworthy that the CQD preparation method has many advantages including the need for a simple apparatus, gentle response conditions, low cost and its large computational power. These positive features make CQDs a promising nanoparticle for biomedical and clinical applications [20-25]. To date, various approaches to CQD have been proposed. In accordance with their sequence, these methods can be divided into main top down and bottom up methods [26]. In a high-throughput process, CQDs are generated from a carbon source or are exposed to carbon nanoparticles in such a way as laser ablation [27-28], electrochemical oxidation [29] and arc discharge [30] and in these ways, the difficulty about complete dissolution of the carbon artery from. The first carbon source in carbon nanoparticles can be limited. In Bottom up method, techniques such as heating , burning or microwave are used to determine the cause of carbon, which is used for it produce CQDs by chemical oxidation[30], pyrolysis[31], microwave-the catalytic mechanism[32], or vector synthesis[33], is hydrothermal[34-37] . The chemical method of oxidation is effective; it is possible mass production, because it does not require any unusual tools sources. Candle grey as [38] and phenolic resins [39] are among the many carbon sources used for preparation. In the last few years, a number of facile synthetic methodologies have been developed for making CDs with varied functionalities and Photophysical properties.

Synthetic pathway for CDs are mainly divided into two categories

1. Bottom Up
2. Top down

Bottom up method

1. Microwave
2. Hydrothermal
3. Solvothermal
4. Pyrolysis

Top down method

1. Arc discharge
2. Laser ablation
3. Electrochemical
4. Chemical ablation

CDs using the arc disposal method became an accidental event. This method was first reported by Xu et al. during the synthesis of SWCNTs. Electrification of all two graphite electrodes results in the formation of a carbon clip or CD. Bottini et al. the reported CDs are based on pristines and SWCNTs in the form of an arc-shaped arc with a bright violet-blue and blue region, respectively [40]. Recently, Boron- and nitrogen-doped QDs have been synCDs in the form of arc-induced accidental events they used B2H6 to obtain doping boron and NH3 with nitrogen [41].

9.1.2. Laser ablation method:

The laser ablation method has been widely used for making CDs of various sizes. In In the laser ablation pathway, the exposed organic macromolecules are exposed under laser beams used in CW or in a drop-down mode and activated carbon particles are found in large parts of the cells. Synthesis of CDs laser ablation process was first reported by Sun et al. in 2006 from graphite powder [42]. They arranged the CDs on the laser excerpts from the Nd: YAG source (1064 nm, 10 Hz) in the Argon condition at 900 ° C and 75 kPa. Thongpool et al. compact CDs were emitted in a quantitative graphite in the presence of ethanol using the Nd: YAG laser of wavelength1064 nm. The compact CDs showed a large absorption mirror of up to 325nm[43]. Recently, 3 3mm-thick photoluminescent CDs were prepared by means of laser irradiation from carbon-containing polyethylene glycol 200 particles. CDs so prepared are applied in bioimaging for cancer epithelial human cells [44]. Synthesis of carbon dots by laser ablation

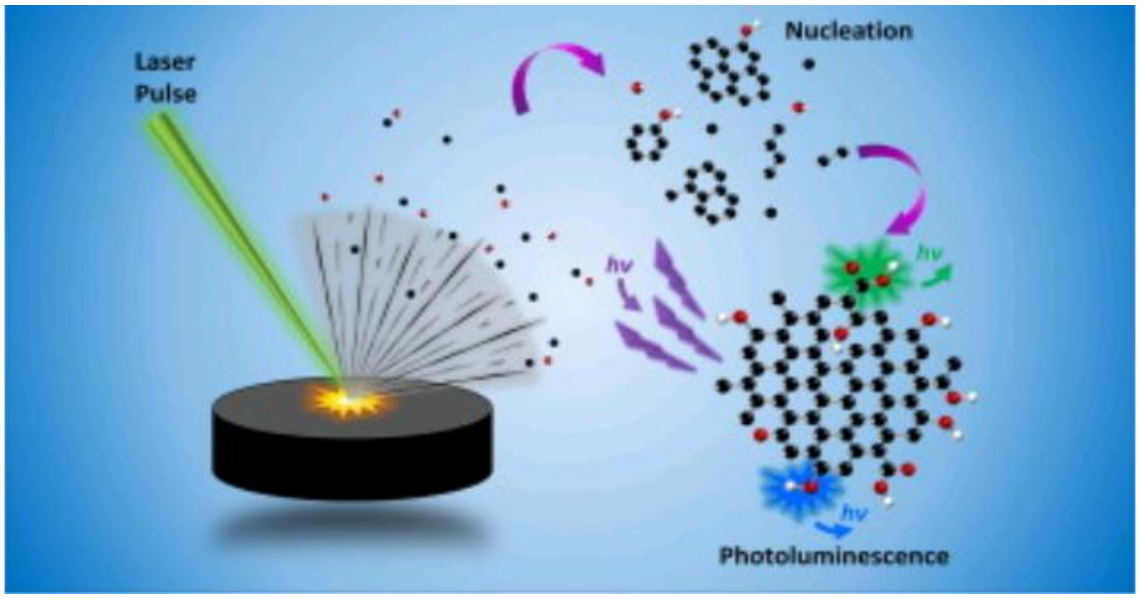

Figure. 4: Synthesis of carbon dots by laser ablation

9.1.3. Electrochemical method:

The electrochemical method is used to synthesize ultrapure CDs from large objects such as carbon nanotube, graphite, and carbon fibre in an electrolytic process when large molecules are used as electrodes in the presence of suitable electrolytes. Zhou et al. for the first time CDs were reported from carbon nanotubes in the presence of tetrabutylammonium perchlorate as an electrolyte [45]. Zheng et al. CDs of soluble pure synthesized water soluble pure were applied in an electrochemical manner using graphite as an electrode in the presence of phosphate buffer at neutral pH. The prepared CDs have been successfully used as a potential biosensor [46]. Li et al. prepared crystalline CDs by electrochemical method from graphite. The prepared CDs as shown in size are dependent on the up-conversion photoluminescence (PL) properties and used in Photocatalysis [47]. Recently, a CD with a polyaniline hybrid was performed in an electrochemical manner with high QY and purity. The CD-polyaniline compound designed to be reported shows high potential and has been used in energy-related devices [48].

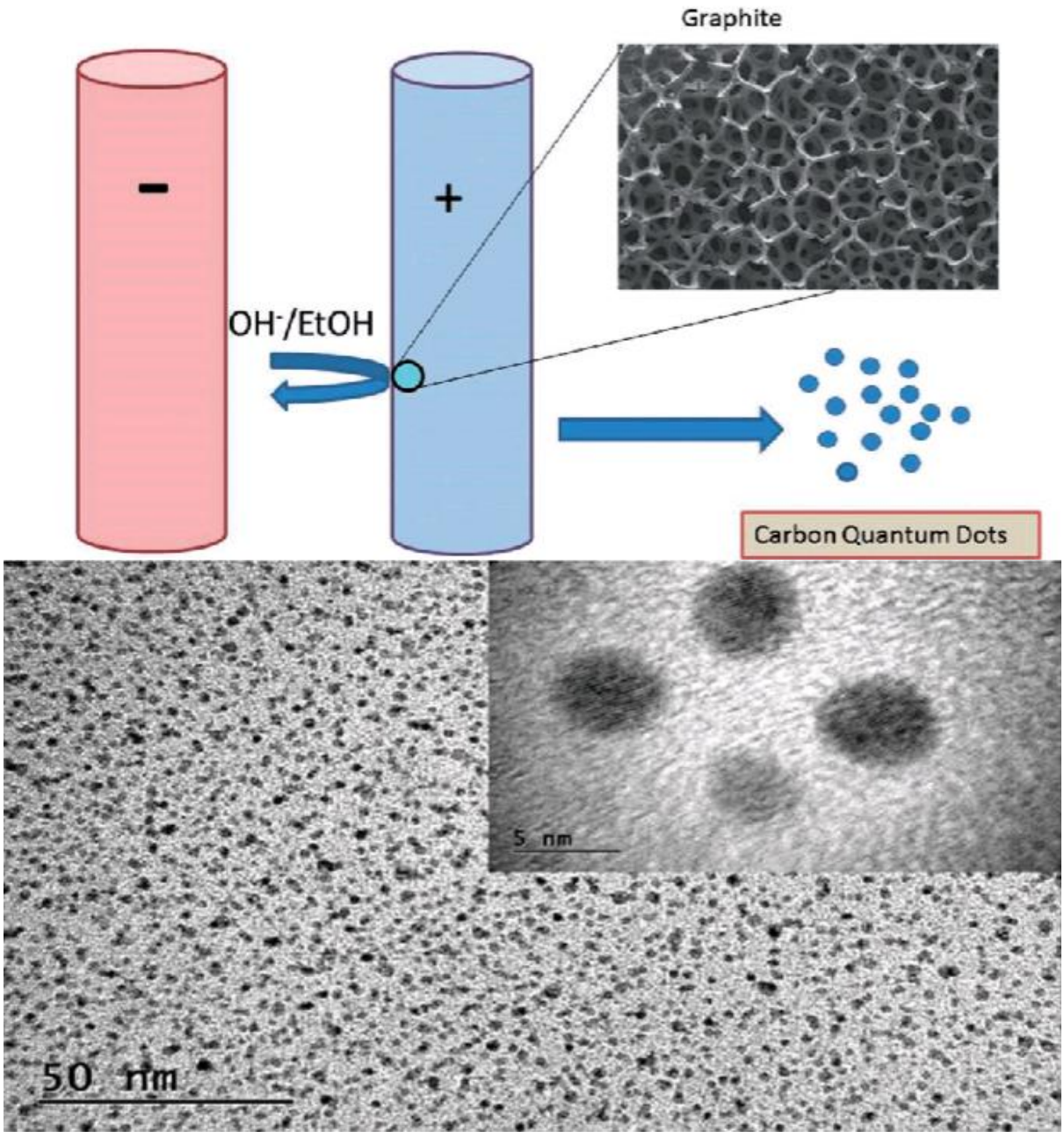

Figure 5 Processing diagram for electrochemical fabrication of CQDs

9.1.4. Chemical ablation:

This process works with acids that remove from the carbonized organic molecule, where careful control of oxidation can lead to small CQDs. In this way, a variety of accessible items can be used as a precursor. However, the critical conditions required and the large processes may not be as bad as this. Peng and TravasSejdic reported a high-resolution process to produce luminescent CQDs using carbohydrates as precursors. First, they produce carbonaceous substances through water-soluble carbohydrates using concentrated sulphuric acid. Subsequently, the carbonaceous material was treated with nitric acid and subjected to microscopic CQD. Finally, as a step to pass, a number of amino-terminated surface passivation reagents including ethylenediamine, oleylamine, bis (3-aminopropyl) are dissolved in poly (ethylene glycol) (PEG1500N) and 4, 7, 10-trioxa-1, 13-tridecanediamine (TTDDA) is being investigated. Nontoxic environment and many CQD exit skills make good choices in biomedical research.

9.2. BOTTOM UP METHOD:

9.2.1. Microwave method:

Microwave- (Mw-) has been used in novel formulations that have received considerable attention in the scientific community due to its time-saving, energy-efficient, and eco-friendly environment and in this method the natural

carbonization of small molecules emitted by microwave heating within a very short time. In 2009, Zhu et al. first reported CDs with the help of Mw pathway from carbohydrates with excellent photographic properties in a very short reaction time [49]. Liu et al. Synthetic synthesized CDs were derived from glycerol and 4, 7, 10-trioxo-1, 13 tridecylenediamine as a surface-crossing agent for the Mw translocation pathway. They reported comparatively high quantum yield (QY) of 12% due to the addition of amino groups (NH2) on the surface of CDs [50]. Feng et al. CDs aggregated with QY ~ 46% by Mw irradiation from silkworm chrysalis [51]. CDs were made as they were used in the synthesis of living organisms due to their low toxicity and Photoluminescent environment. More recently, Liu et al. The CDs were obtained with a photoluminescent CD in the form of Mw heat from citric acid, L-cysteine, and dextrin with a high QY of 22%. Synthesized CDs are said to be photographed and used to detect Cu2 + in drinking water[52]. Recently, Sun et al. The synthesized N-ethyl carbazole CDs were activated by a microwave method that showed excellent photoinduced redox properties [53].

9.2.2. Hydrothermal method:

The Hydrothermal method is probably the most promising approach in recent years for the manufacture of CDs because of their non-toxic, environmentally friendly, low cost, and easy-to-operate method. In this method, the pre-organic solution is sealed in a hydrothermal synthetic reactor where the reaction occurs at high temperature and pressure. In 2010, Zhang et al. first report a hydrothermal pot in a single pot to form a CD from ascorbic acid in the presence of ethanol as a solvent. The QY and particle size of their synthesized CDs were 6.79% and ~ 2 nm, respectively [54]. Pang et al. cod-and-sulphur-based nitrogen incorporation into CDs (NS-CDs) is reported from methionine in a hydrothermal manner [55]. NS-CDs, as found in their arrangement, indicate the selective availability of heavy metal ions in water. More recently, Shen et al. reported photoluminescent CDs from sweet potatoes as a natural source of carbon in the form of hydrothermal with high QY. Compact CDs were used for $Fe3^{+}$ detection [56]. In another report, Zhang et al. more prepared CDs were modified with polyethyleneimine from hyaluronic acid with a higher QY 26%. CDs were synthesized using those photoluminescent CDs in tum or targeting and gene delivery [57].

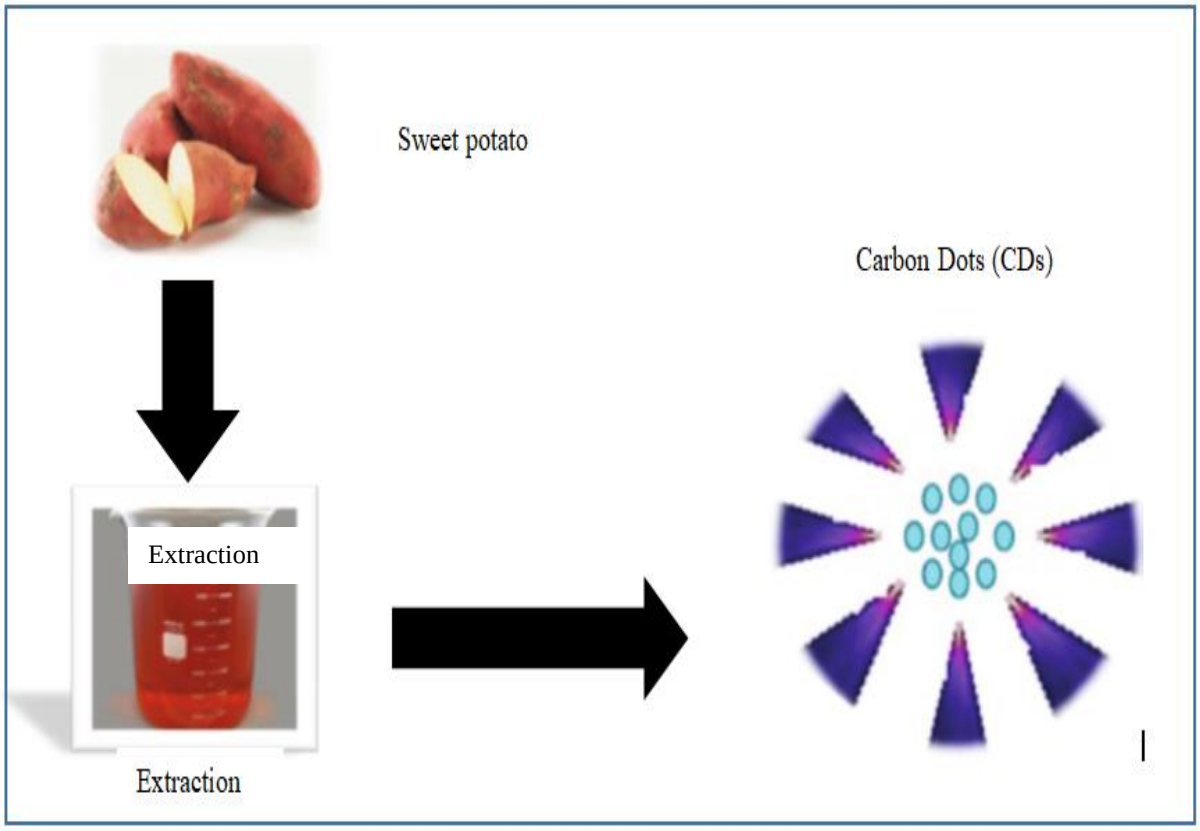

Figure 6: steps in hydrothermal process

9.2.3. Pyrolysis method:
Pyrolysis is a facile method to synthesize CDs from organic molecules that react with simple chemical reactions performed at very high temperatures in the presence of strong acid or alkali. Martindale et al. Compact CDs of average diameter ~ 6nm by pyrolysis of citric acid at 180 ° C to obtain the generation of hydrogen energy [58]. Guo et al. composite CDs from hair (keratin) in the form of a single pyrolysis step at 200 ° C for 24 hours of reaction time. They have successfully acquired CDs and used their CDs for Hg2 + detection with high sensitivity and selectivity [59]. Recently, Rong et al. stained nitrogen-doped CDs (N-CDs) consisting mainly of guanidinium chloride and citric acid by the pyrolysis method and fluorescence staining observed in the presence of Fe3 +[60]. N-CDs obtained by their invention are widely used in the detection of iron ion and in air structures.

10. Characteristics of carbon dots
Carbon dots have many features because of them which they consider to be an excellent cancer diagnostic tool. It has properties such as cytotoxicity, absorption, Photoluminescence, optical properties etc.

10.1. Absorbance:
CQDs often have transparent deposits in the UV-visible region[60]. Most CQDs, no matter how they are integrated, have an input band around 260-32 nm. In some cases, the n-ptransition of the C¼O bond or the p-p modification of the C¼C may cause the shoulders to be implicated in absorption spectra. It is found that the CQD emission by various molecules results in a shift of absorbance of longer wavelength.

10.2. Photoluminescence:
One of the most fascinating is the Photoluminescent (PL) CD material that can be influenced by the surface regions, the oxidation degree, and the frequency of the heteroatoms. The continuation of the colourful compositions (ranging from deep ultraviolet to near infrared) with high quantum yields (QYs) of CDs allows them to expand their system in a variety of sensing and sensing fields [64]. Although the mechanism of CDs PL is still unclear, it was suggested that luminescence originated from carbon emissions, emissive traps, quantum confinement, aromatic structures, oxygen-containing groups, free zigzag sites and edge damage. The average PL emission spectra of CDs in most studies are found in the green region. In the ultraviolet or shortwavelength optical region, autofluorescence from living organisms and severe Photo damage caused by ultraviolet irritation limit their further use in bio-imaging. Low yields of CDs in the red region affected their effectiveness in in vivo imaging applications. Therefore, the realization of highly efficient red CDs is crucial for its wide application in the field of bio-imaging. Karakoçak et al. has developed a microwave-assist pyrolysis method for the synthesis of deep red CDs (lex / em ¼ 540 nm / 600 nm) PL. The efficacy of red-emissive CDs has been investigated by the function of cell balancing, reactive oxygen species (ROS) generation, and the degree of apoptosis in three different cell lines (epithelial retinal, epithelial lens, and hamster egg cells ovary). Wavelength-dependent behaviour of CDs is one of the attractive features of PL of CDs that relies on a high-frequency distribution of the wavelength. This behaviour may be due to the size distribution of the dots (quantum effects) and surface chemistry, different types of radioactive traps (solvation effect), or the machine that can be prepared yet. The PL-dependent behaviour of CDs may apply to multicolour imaging systems. The wavelength and QY of the detected CDs are affected by various reaction factors, such as the synthesis, composition / rate, reagent's, reaction time, temperature and separation methods. Due to unstable surface damage leading to reduced radiation frequency, PL QY of green CDs is usually very low. It has recently been reported that surface transfer and / or dehydration, such as nitrogen, phosphorus, boron and sulphur can be improved through PL QY CDs. The results of the study indicate that the most popular doping is nitrogen doping [62] on the other hand, the purification of the prepared CDs using high resolution anion exchange high-performance liquid chromatography [63].

10.3. Electrochemical Properties:
Carbon nanomaterials are ideal for electrode surface modification because of their electrochemical activity. CDs can be used separately from the interface and, therefore, can provide an electronic transmission path over the electrode. The electrochemical (electron transfer) characteristics of CDs depend on the interaction between the carbon core, the functional groups, and the formed heteroatoms. The presence of hydrophilic edges and hydrophobic planes on the CDs enhances the absorption of the analyst on the surface of the electrode and receives an enhanced response towards the exemplary analyst. Therefore, CDs have proven that would be a good choice of electrode operation due to the increase in electrode area [65]. However, CD is a type of semiconductor material with low electronic performance. Much effort has been given to improve their catalytic properties through the use of doping heteroatoms[66], as well as the synthesis of CDs with fine metal nanoparticles[67] and graphene aerogel to produce novel noanocomposites with improved electrochemical properties.

10.4. Electrochemical Luminescence:
Electrochemical luminescence (ECL) signal originates from the excited region of the ECL luminophore produced at the electrode back to the lower regions during the electrochemical reaction. CDs, such as the promising new ECL luminophore, can work in promising genomic areas that produce new generation of ECLs and eco-friendly common ECL labeling agents for immunoassays of cancer. The ECL features of the CDs were made available for the first time in Chi and colleagues[68]. Coreactants have an important role in the generation of CDs ECL signal. Because of this, $S2O8^{2-}$ [64e74], $S2O4^{2-}$, H2O2[69], L-cysteine, and triethanolamine (TEA) are used as effective CD-elements in ECL reactions leading to significantly increased cathodic ECL output of CDs. Most studies focused on the use of $S2O8^{2-}$. The cathodic ECL pathway for CDs using S2O8 2- enter the following steps: functional groups containing more oxygen than CDs can facilitate the generation of electro-CDs.— radicals, then SO4.- radicals produced by the electrochemical reduction of $S2O8^{2-}$ formation of excitatory CDs (CDs) of the ECL.

10.5. Cytotoxicity
CDs are well recognized for their biocompatible and relatively nontoxic nature, which is a condition required for bio application. The cytotoxicity of CDs has been extensively investigated in vitro and in vivo[70]. Cytotoxicity of red, green, blue CDs was evaluated using standard MTT assay in MCF-7 cells. Addition of three CDs in concentrations ranging from 10 to 50 mg mL-1 to MCF-7 cells did not weaken cell viability significantly, confirming that CDs had low cytotoxicity and could be used in the combination of bioimaging and others. Biomedical systems at high speeds [71]. Ser et al. investigated the cytotoxicity of zwitter ionic CDs in two oral cancers namely FaDu and Cal- 27. The high availability of CDs has been confirmed by cell viability studies and isolated dispersion since no change in granularity was observed even at maximal growth of 1600 mg ml-1. Karakoçak et al. the last three independent methods were used including energy, generation of reactive oxygen species, and percentage of apoptotic cells to assess the level of CD toxicity in the cell culture. Parvin's group used the MTT assay to test the cytotoxicity of P and N co-doped CQDs (PNCQDs) through the mouse leukemic monocyte macrophage cell line RAW264.7. PN-CQDs were apparently pain-free in cells until they reached a maximum concentration of 1 mg mL-1. Also, they studied the efficacy of PN-CQDs in vivo imaging using mice with venomous tumors as animal models. The position of PN-CQDs in the abdomen helps to accurately characterize the area of the tumor and significantly increase the use of peripheral CDs. The results of cell viability tests showed that CDs had low cytotoxicity at the concentration required for bioimaging applications.

10.6. Photo stability
Considering the efficiency of CDs as fluorescent probes for cell imaging, it is interesting that they investigate their potential for Photostability targeting various cancerous and normal cells. Photostability means the elasticity of the emission of labelled cells remains stable over long-term secretions. Mehta et al. it has been reported that the PL size of CDs in HeLa cells remains stable under continuous UV light (l ¼ 365 nm) for 60 minutes. Zhang et al. evaluated the production of P, N-CDs by exposure under UV light (at 365 nm). After 60 min incubation, the FL strength of P, N-CDs did not decrease the obvious and a small amount of corrosion was detected (12%). The strength of FL for P, N-CDs has not been reduced to a pH of 3e9, which has proven that CDs can be used in the imaging of intestinal cells. The stability of the CDs at high NaCl concentrations, suggested that they could be used under physiological salt conditions for effective use. Zhao et al. synthesized green-type Nano platforms based on CDs covalently bonded to F-substituted Nano-hydroxyapatite (NFAp) and have shown excellent promise in flexible bio application due to their attractive properties and no cytotoxicity. Photostability comparisons between CD- COOH @ PEA-NFAp decreased slightly, saving more than 90% of the initial amount even after 180 minutes of irradiation [72]. As recent research has shown that CDs are high-quality photostability and low-quality photo bleaching, they have been used as specific cell labelling for word processing and application [73].

11. Drawbacks of carbon problems:
C-dots show instability, with those created using organic material that stay stable for a few weeks. Therefore, it is difficult to control the properties of the C-dots term. The techniques used to produce C-dots, such as carbonization and pyrolysis, lead to complex molecular structures that can be difficult to interpret using quantitative techniques, such as Nuclear magnetic resonance (NMR) and IR spectroscopy. The various carbon sources, structures, and surface waves used in the manufacture of C-dots also affect their chemical, electrical and physical properties [74].

12. Carbon Dots in Diagnosis (imaging):
Imaging is needed for disease identification in vivo and targeted drug delivery. For in vitro diagnostic and in vivo imaging, fluorescent NPs are the basic units for determining the performance of NPs as imaging agents. Cytotoxicity of NPs plays an

important role in diagnostic imaging. However, environmental constraints arising from the use of semiconducting Q-dots, such as CdSe and other limitations, limit their use of imaging. In contrast, C-dots are still emerging as diagnostic criteria for biomarkers due to high bioavailability, low cytotoxicity, Nano size, excellent Photostability, and multicolor emission. Zhai et al. A photoluminescent C-dots was performed to label L929 cells at lex 405, 488, and 543 nm. EDA-C-dots emitted green fluorescence blue and green respectively. Cellular sites showing fluorescence emission showed the presence of C-dots. C-dots were mainly reported around the cell nucleus and in the cytoplasm and cell membrane [75]. Wu et al. performed in vivo photoacoustic (PA) imaging of the sentinel lymph node (SLN) using C-dots. The processes of thinking about ideas have provided a notable force optical input signals in the near-infrared (NIR) region after 2 min. The rapid regeneration of the SLN occurs due to the small size of the control and rapid lymphatic movement, overcoming the complications associated with the use of dye. In another study, Kasibabu et al. C-dots are synthesized from Punicagrantum fruits as bacterial cell and fungal cell imaging. These C-dots showed no cytotoxic effects and prevented the growth of Bacillus subtilis. Therefore, C-dots can also be useful in imaging animal and plant cells [76]. Ge et al. were designed for C-dots by hydrothermal treatment of polythiophene phenyl propionic acid (PPA) imaging of propionic acid, leading to widespread exposure in the NIR region. In addition, under intense NIR irradiation, C-dots showed high Photo thermal fluctuations. Photo thermal Laser Scavenging of xenografted tumor in mice was detected at 671 nm. In one experiment, C-dots showed fluorescence imaging in zebra fish embryos. More than 80% and 55% embryo or larval operations were reported with C-dots in the 1.25 and 2.5 mg ml1 collections, respectively. This showed several high concentrations and low toxicity of C-dots. Jiang et al. three isomers were selected for phenylenediamines, namely, o-, m-, and p-phenylenediamines, to form C-dots for Solvothermal facile treatment. Incorporation of the three C-dots with MCF-7 cells for 4 h followed by a further laser at 405 nm resulted in the cells showing different colored emission [77]. Wang et al. and performed systematic in vitro and in vivo bioimaging studies using high-performance photoluminescent C-dot assays. Fluorescence signals were observed at 535 nm and 695- 770 nm following subsequent injections of 0.5 and 5 mg C-dots, respectively, into athymic BALB / C-nu mice. The better penetration ability of C-dots compared to visible light showed their potential for use in vivo imaging. Li et al. N of phosphonomethylaminodiacetic acid and NDA-labelled EDA, N, p-C-dots. At emission at 418 nm, N, P-C-dots show bright fluorescence in blue. Differential scattering of N, P-C-dots with an average diameter of 3.3 nm, 17.5% QY, good stability, and low toxicity demonstrated their successful use as a fluorescent nanomaterial probe for cellular imaging. Recently, Parvin and Mandal created P, N-C-dots using hydrothermal treatment of a mixture of phosphoric acid (PA), EDA and citric acid. C-dots found use in PA imaging and fluorescent imaging of living tissues due to energy-dependent emission, indifference to pH changes, C-dot concentration, green fluorescence at 430 nm at 30% QY, and with fluorescence red at 500 nm and 78% QY, with improved spatial resolution and deep tissue imaging.

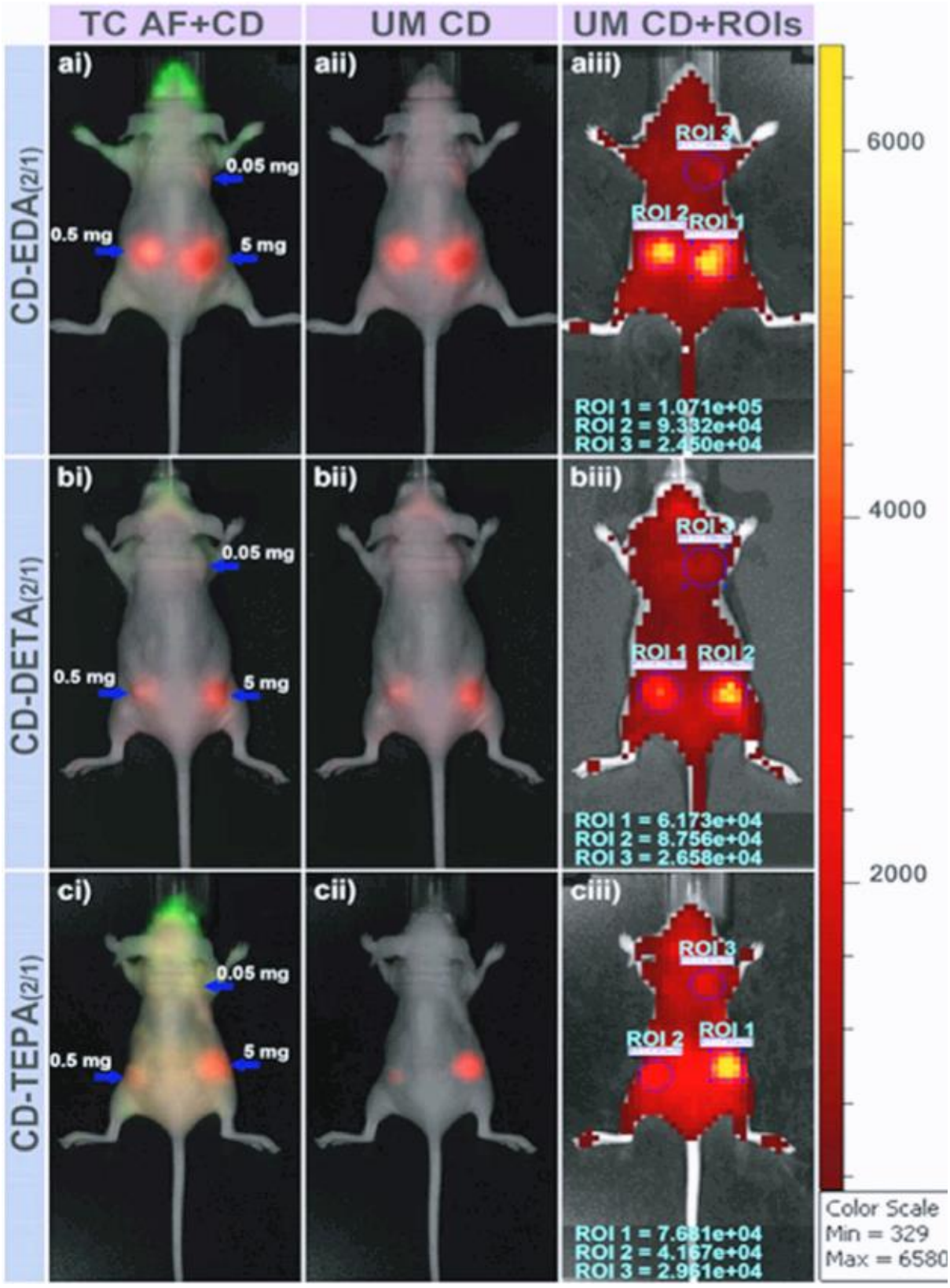

Figure 7 description: In vivo fluorescence imaging of nude mice injected subcutaneously with carbon quantum dot (CQD) 1,2-ethylenediamine (EDA) (2/1), CQD-diethylenetriamine (DETA) (2/1), and CQD tetraethylenepentamine (TEPA) (2/1) at three injection sites (blue arrow) with increased doses (ai, bi, ci). The true color (TC) fluorescent composite images of CQD fluorescence and autofluorescence (AF) from mice (aii, bii, cii), unmixed (UM) images of CQD fluorescence (aiii, biii, ciii). Fluorescent intensities measured in region of interest measured in region of interest (ROI).

13. Advantages of carbon dots:

Their unique and inexpensive nature of rendering techniques offers C-dots stars in the carbon nanomaterial family. Judging by their high affinity groups, C-dots have a tendency to bind inorganic and organic molecules. In addition, C-dots are made up of a variety of techniques useful for emotional healing, chemical sensing and diagnostic thinking. Given that the basic building blocks of C-dots are carbon, they are also low-risk and their nano size enables cellular penetration in vivo. Although carbon shows poor performance in water, C-dots show water solubility and photoluminescence. C-dots can be transmitted through a variety of channels, including the nasal, oral, parental, and pulmonary arteries. C-dots formed from prehistoric plants, such as plants and shrubs, can serve as drugs for various diseases. For example, C-made dots from ginger and tea inhibit HeLa, HepG2, MCF-7, and MDAMB- 231 cells [74].

14. Comparative study:

There are several methods for diagnosis of cancer. There are many advance techniques for the diagnosis like mammography, histopathology, biopsy, imaging test, physical test, endoscopy, etc. But there are some drawbacks of this diagnosis test. Many times, doctor conduct biopsy test for the diagnosis of cancer according to biopsy test If (1) the fluid is green, tan. Or brown then the cells are non-cancerous cell. (2) The fluid is bloody or clear then the cyst may be cancerous or not (3) If lump is present then cancer is diagnosed.

But there are some drawbacks of the biopsy test that is it removes very small sample of tissue or cells. If it is benign then it is ideal procedure. However, if it is cloudy or solid then it is not an ideal.

Mammography is conduct mainly for diagnosis of breast cancer in women. Mammograph is an X- ray picture of the breast. But in this test sometimes doctors find something that look like abnormal but isn't cancer. It is not accurate for diagnosis of cancer.

Histopathology is another test for diagnosis but is time consuming. And in this test it is difficult to identify specific types of cells. The method is subject to human error during the preparation of slides and analysis. It is less specific.

While carbon dots are very convenient for the diagnosis of cancer they have high brightness with low cost of synthesis or fabrication, they are cell permeable, they are non-toxic, they have good biocompatibility, they have high affinity and specificity to target, they have high surface area.

14. Other uses of carbon dots:

14.1. Drug delivery:

C-dots are an excellent tool for drug delivery due to their compact size, simple fabrication and purification methods, stable drug release, chemical performance, low cytotoxicity and other properties. C-dots overcome the small problem of attention and general drug tracking. Fluorescent C-dots are used as drug delivery sites due to their modified functional groups, low cytotoxicity, and high drug loading capacity [74].

14.2. Gene delivery:

Gene therapy, a promising option for the treatment of many diseases, requires a safe and effective carrier for fluorescent and biocompatible loading. The characteristics of the C-dot spots make it effective for emerging carriers of gene delivery. Liu and co-workers used PEI (bPEI25K) Cdots for transporters as transfer agents. The results showed bright fluorescence and good water solubility with low cytotoxicity and efficient in vitro DNA transfer. Kim et al. performed the transmission of in vitro DNA and monitored the cellular trafficking of the plasmid. The authors compared the use of PEI-functionalized C-dots (PEI-Cdots), PEI-functionalized gold colloids (PEI-AU), and plasmid DNA (pDNA) delivery type the first interaction of PEI-Cdots with -PEI-A showed weak fluorescence at the time of transmission. In high-frequency attacks, pDNA and high fluorescence are reported for the isolation of PEI-C dots from PeI-AU, thus facilitating gene delivery and monitoring of cellular trafficking [74].

14.3. Photo catalyst:

Pure or compound CDs can both absorb light at wide wavelength and are used for different photo catalytic activities. Generation H2 gasoline emissions using CD-based photo catalysts have been an excellent research topic in recent years. The sun et al. recently reported the photodecomposition of CO2 using CDs doped with Au as a Photo catalyst. Liu et al. reported a low and natural amount of CD-C3N4 composite material that successfully produced H2 by separating water. BiVO4- and CD compounds are also employed as Photo catalyst for environmental degradation and water separation. PEG1500 CDs is a work is capable of converting the most active components of greenhouse gas, CO2, into formic or acetic acid.

15. CONCLUSION:

There are various diagnostic tools for diagnosis of cancer, but they have many drawbacks, Cancer is very dangerous and very crucial disease for the worldwide. Before spreading of this chronic condition, we should have to detect it for the successful treatment of the cancer. So there are various methods like physical, chemical, radiation,

imaging etc, so one of them is carbon dots. Fluorescent carbon dots are a tool in which carbon dots can use as markers/diagnosis tool to detect tumor. This tools that is carbon dots are chemically inert on that basis CDS are safe mechanical tool to detect carcinoma. The main principle of this diagnostic tool is depending on the early diagnosis of cancer and highlightment of tumor by using radiation, so that's why we cannot called as a fully assured method but it is a safe diagnostic tool for cancer, possibly uses for the detection of breast cancer, oral cancer, etc. It gives up to 89-90% assured in testing. The main reason of this review is to introduce the application of CDs in diagnosis of cancer. By using CDs we can diagnose cancer in very convenient way.

DECLEARATION OF COMPETING INTREST

The authors report no conflict of interest in this work

List of Abbreviations:

Abbreviations	Full forms
CD	Carbon Dots
QY	Quantum Yield
ECL	Electrochemical Luminescence
PL	Photochemical Luminescence
QD	Quantum dots
GQD	Graphene Quantum Dots

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