Carbon Dots (CDs) - A versatile Biosensor

(Mini review)

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Introduction

Biosensors are devices that can engulf receptor-transducers to envision analytical values of any preferred target analyte, which highly depends on the type of bioreceptor [1–3].Response time, sensitivity, and specificity are the crucial parameters which any Biosensor should possess [4–7]. The scientific challenge every biosensor needs to fulfil is accuracy, precision, and early diagnosis of emerging diseases [8, 9] in the field of medicine. Biosensors also have wide applications in the fields of food security, environmental monitoring, and biosafety [2]. The risen need for biosensors in recent decades has lead researchers towards developing new sensors using nanomaterials which are economical to the end user, possess high sensitivity and selectivity along with other biosensor parameters [10–12].

Carbon Dots (CDs) function as potential probe with wide scope in the field of sensors. The chemically inert, biologically compatible, and less cytotoxic nature of CDs and also a definite signal-response for molecular recognition make [13, 14] it superior amongst other nano materials. But it comes with a challenge i.e to function as a sensor they need to be tailored with suitable functional groups which exhibit affinity with targeting biomolecule [13]. On studying the journey of CDs since its discovery from carbon nanotubes in 2004 named as carbon nanoparticle and later on in 2006 renamed as CDs till date its observed that, today various methods are used to synthesise CDs with various functional properties, applications, exhibit brilliant fluorescent properties which are efficient, economical and rapidly synthesizable in large scale using environmental-friendly methods like calcination, ultrasonication, electrochemical oxidation, microwave-assisted methods [15–17]. etc which can aptly perform as a biosensor, fulfilling the mentioned requisites along with high photostability and being a novel sensing probe [17, 18]. The important aspect of carbon quantum dots is its simple fabrication methods differing it from the same carbon-nano family like nanotubes, graphene dots or quantum dots [19, 20].

CDs with carboxyl, amine, and hydroxyl functional groups on its surface has the ability towards detection of metal ion through bonding and chelating leading to complexation using various mechanisms, making an account as a potential biosensors [17, 20-22]. In this mini review, methods of synthesis of various types of CDs, various mechanism used for sensing biomolecules, application of the various CDs towards biosensing few biomolecules which are important for human health are discussed and their detection limits are explained considering the research works reported from 2017 till 2023.

Synthesis

Many convenient precursors, such as natural sources that are renewable, economical, non-toxic, organic solvents, small molecules (Ex: Ethylenediamine) that are quick, highly efficient providing good quantum yield, etc are used to synthesize CDs,. Similarly, on the contrary bigger molecules or materials which can break into pieces are also used to synthesize them. Since the serendipitous discovery of this zero-dimensional carbon dots by Xu et al in

2004, two key techniques are used to generate CDs. either bottom-up or top-down methods [23, 24].

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i. Top-down methods

"Top down" method involves the decomposition/break-down of large pieces to raw carbon material such as carbon soot, carbon fibre, activated carbon and carbon black. Synthetic technique include predominantly laser ablation, arc release, exfoliation and treatment with oxidizing acids. The disadvantage in this technique is the extreme conditions applied to these reactions. Devices that absorb high energy are typically needed with high pressure, high temperatures which leads to higher costs[22]

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ii. Bottom-up methods

“Bottom up” method involves the synthesis of CDs from carbon containing molecules through a “decomposition-polymerisation-carbonization” process. The carbon containing molecules could be small organic molecules such as citric acid, polyols and amino acids, synthetic polymers, natural products as well as biomass. Preparation methods mainly include pyrolysis-solvothermal, hydrothermal carbonization and microwave/ultrasonication[22].

iii. Green Route Synthesis

Green chemistry reflects on the relationship between organisms, chemistry, and the environment. As a consequence, the primary purpose of green chemistry is to develop products and procedures that minimize the use and production of hazardous substances. The theme of green chemistry is to optimize the integration of the starting material into the finished product and to create a strategy by adding smaller fundamental building blocks (at the molecular level) to synthesize a desired product rather than breaking down a larger material to eliminate any products that are undesirable. There are also several green routes for the synthesis of carbon dots[22]. For bioimaging and biosensing purposes, Sahu et al synthesized an extremely luminescent carbon dot from orange juice with a high quantum yield, low toxicity, and a high photostability of 26% [25]. The nitrogen-doped intensely fluorescent carbon dot of 3nm size reported by Li Wang et al[26] were synthesized by hydrothermal heating of milk .The synthesised carbon dots are highly recommended for brain glioma cancer cell imaging . Bibekananda et al [27] synthesized Green luminescent water-soluble oxygeneous carbon dots of 3nM size by simply heating banana juice for 4 hours at 150 C. A Quantum yield of 8.95 with 360 nM wavelength on excitation is been reported. X. Yang et al[28] synthesized novel carbon dots from honey for sensing and imaging applications. Their synthesis was based on a green technique with a quantum yield of almost 19.8% . A one-step green approach for the synthesis of carbon nanodots from bamboo leaves was followed by Y Liu et al[29] for the detection of copper (II). The synthesized CQDs with an average size of 3.6 nM and a quantum yield of 7.1 % allows sensitive detection of Cu^{2+} with a detection limit of 115 nM and a linear range of 0.333 to 66.6μM . Y. Feng et al[30] reported a simple method for carbon dot synthesis from

rose flower for the detection of tetracycline with a detection limit of 3 x 10^{-9} mol/l and a linear spectrum range of 1.0 × 10^{-8} - 1.0 × 10^{-4} mol/l. V N Mehta et al[31] synthesized carbon dots from apple juice via a one-step hydrothermal approach for mycobacterium and fungal cell imaging. Under UV light, the CDs displayed a bright blue emission. The findings revealed that the prepared CDs had no toxic impact on the cells demonstrating the strong biocompatibility nature of the CDs . For the green synthesis of biocompatible carbon dots, Mewada et al[32] in the absence of any additional oxidizing agent and at a working temperature condition of 90°C reported the synthesis of luminescent water soluble Cdots using Indian water plant Trapa bispinosa peel extract which exhibit a prominent green fluorescence. Cdots synthesized by this method were found to be remarkably biocompatible. Zhou et al.[33] synthesized carbon dots from the peel of watermelonl. The blue CDs obtained had a particle size of about 2 nm . D Gu et al[34] synthesized nitrogen doped carbon dots from lotus root for the identification of Hg (II) ions. The one pot microwave treatment of the lotus root provided a simple, green, and quick method of synthesis of carbon dots without using any other surface passive agents. A detection limit of 18.7 nm and a linear spectrum from 0.1 to 60.0 μM is reported. A green synthesis technique was reported by W Liu et al for identification of Fe^{3+} and cell imaging using CDs synthesised from rose-heart radish as a carbon source. The prepared CDs demonstrate outstanding benefits of a high quantum yield of 13.6 percent, low toxicity, excellent biocompatibility and chemical stability. The N-CDs in presence of Fe^{3+} also produce a good fluorescence response [35]. Similarly CDs are also synthesised from biowaste like waste tea leaves [36].

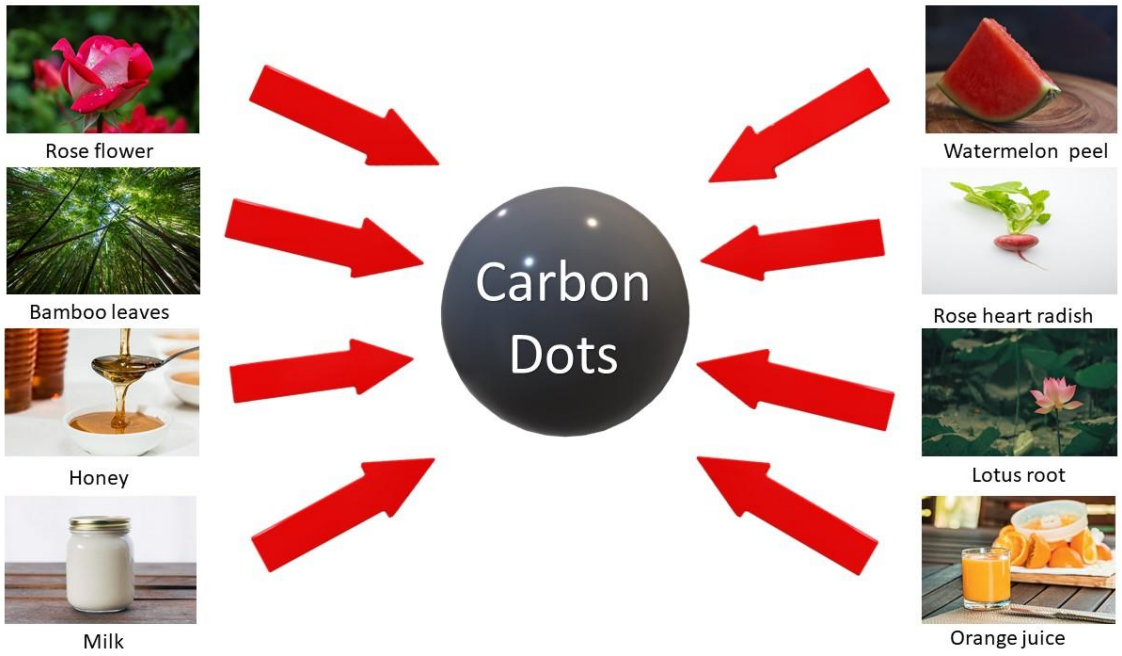

Fig.1 Various green route sources for carbon dot synthesis. All images used are royalty-free images obtained from pexels.com

Mechanism

Liu et al explains that due to their intrinsic fluorescent properties, high sensitivity, rapid response, low cost, and convenient preparation methods CDs have been widely used as fluorescent probes to identify different analytes in the atmosphere or biological systems. They

also say that CDs are very reactive and responsive to the environment, such as temperature, ionic strength and solvent etc. The abundant surface functional groups are responsible towards the change in their optical properties, such as fluorescence enhancement/activation (turn-on) and quenching (turn-off) mechanisms[37]. The fluorescence origin of the CDs is an unceasingly debated topic as the same CDs reported by various researchers exhibits variations in size and properties [36,38].

Mechanisms used for Sensing Biomolecules

CDs due to their unique photoluminescence property makes them standalone as a versatile recognition system/ Biosensor using various mechanisms [36] . The optical signals observed when CDs are used as biosensor are like presence/ absence/ variation in PL intensity, change in colour of PL or change in wavelength [36]. Theoretically, the mechanisms mainly include Static quenching, Dynamic quenching, photo-induced electron transfer (PET), fluorescence resonance energy transfer (FRET), and the inner filter effect (IFE).

Static Quenching

The interaction of CDs and quencher results in the formation of a non-fluorescent ground-state complex, leading to static quenching. When the complex absorbs light, it returns to its ground state quickly without emitting a photon. For static quenching (a) $\tau_0/\tau = 1$ (b) the ground-state complex will cause a shift in the absorption spectra of CDs' (c) the stability of the ground-state complex might deteriorate as the temperature rises and reduce the effect of static quenching [36,39].

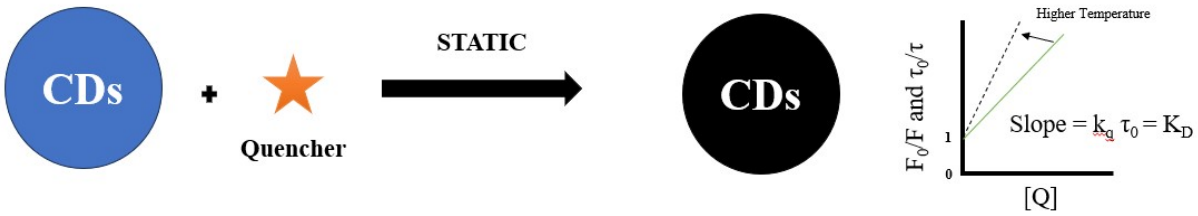

Fig 2. Schematic illustration on formation of non-fluorescent CDs due to static quenching

Dynamic Quenching

The excited state of CDs returns to the ground state due to a collision between the quencher and CDs with the mechanism of energy transfer or the mechanism of charge transfer, which is known as dynamic quenching. (Fig 3)

When compared to static quenching, there are a few differences. (a) In the absence and presence of quencher, the lifetime of CDs would differ. (b) The excited states of the CDs were solely impacted by dynamic quenching, therefore no changes in the absorption spectra of the CDs were detected. (c) The effect of dynamic quenching can be amplified as temperature rises[36,39]

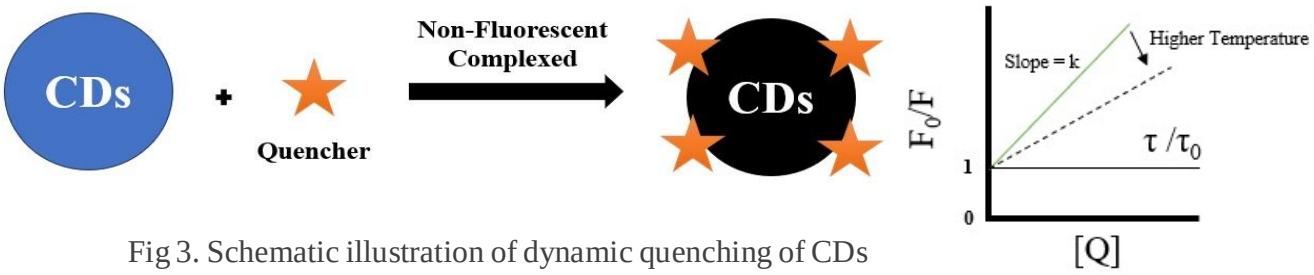

Fig 3. Schematic illustration of dynamic quenching of CDs

Photo-induced Electron Transfer

The electron transfer happens between the CDs (electron donor or electron receptor) and the quencher (electron receptor or electron donor), resulting in the formation of the cation and anion radicals respectively. Between the electron donor and the electron receptor a complex is created, that may return to the ground state without emitting a photon. There ae two types of process in PET (Fig 4 and Fig 5), Reductive PET and Oxidative PET. CDs, as electron receptors, received electrons from the electron source in reductive PET. Oxidative PET was the absolute opposite of reductive PET. The energy gap between the lowest unoccupied molecular orbitals (LUMO) of quencher and the highest occupied molecular orbitals (HOMO) CDs is the driving factor for reductive electron transfer. The energy difference between the LUMO of the CDs and the LUMO of the quencher is the driving factor for oxidative electron transfer [36,39].

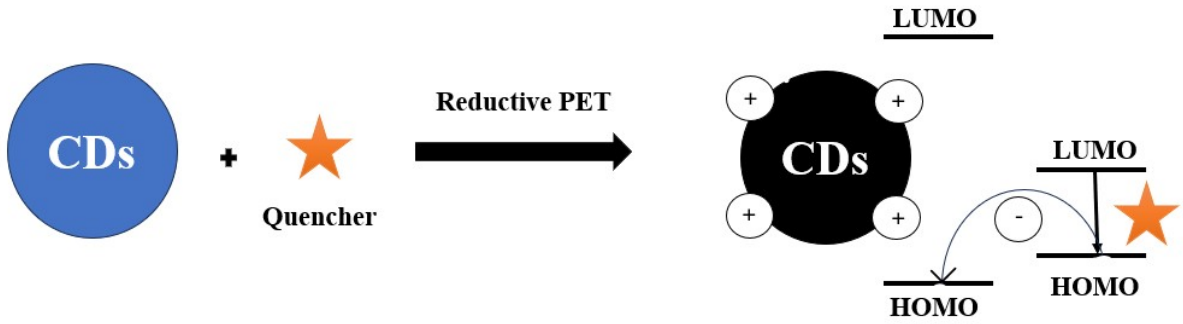

Fig 4. Schematic illustration of reductive PET (CDs accepts electron from the electron sources)

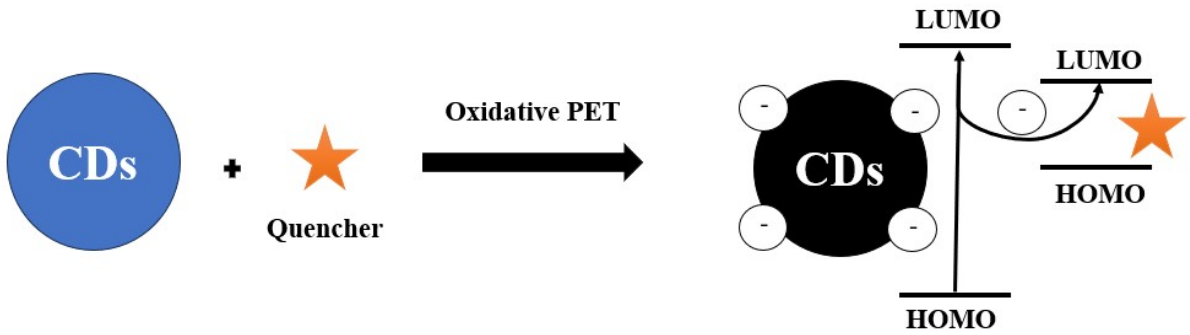

Fig 5. Schematic illustration of oxidative PET (CDs donate electrons to the electron source)

FRET

With classical physics, we can explain FRET an electrodynamic phenomenon. When the emission spectra of CDs coincide with the absorption spectrum of the quencher, FRET occurs between CDs in the excited state and quencher in the ground state (Fig 6). Due to long-range dipole–dipole interactions between CDs and quencher, FRET occurs without the appearance of a photon. The distance between the CDs and the quencher is between 10 Å and 100 Å. Hence, (a) CDs' fluorescence spectra and the quencher's absorbance spectra intersect (b) CDs' fluorescence lifespan will be reduced and (c) The CDs quencher distance will be in the range of 10 Å –100 Å, indicating that the CDs-quenching mechanism was FRET [36,39].

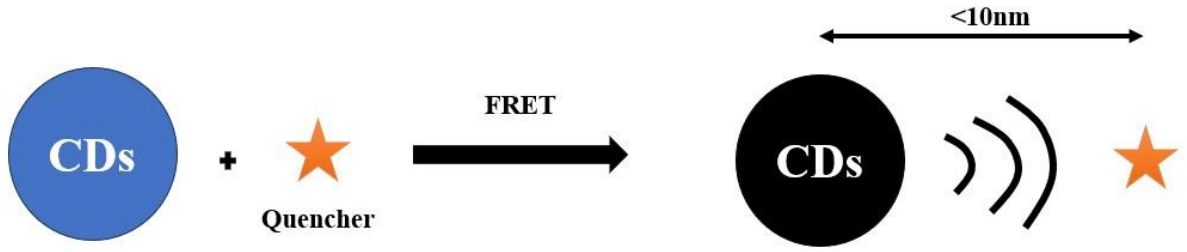

Fig 6. Schematic illustration on emission spectra of CDs coinciding with the absorption spectrum of the quencher (FRET)

IFE

The absorption spectrum of the quencher in the detection system on collision with the excitation or emission spectra of CDs, results in IFE (Fig 7). IFE is frequently referred to as apparent quenching, although it is caused by an attenuation of the excitation beam or absorption of emitted radiation caused by an excess concentration of CDs or the quencher in solution, rather than by a quenching process. Although this effect causes a drop in intensity (but not decay time), it should not be referred to as "quenching." Instead, a second absorber merely filters out a particle's emission. This can also happen if the distance between the emitter and the re-absorber is more than 10 nm. Because IFE does not belong to either the static or dynamic quenching processes, the absorption peaks of the CDs do not shift, indicating that no new material is forming. As a result, CD fluorescence lifespan will remain unchanged[36,39].

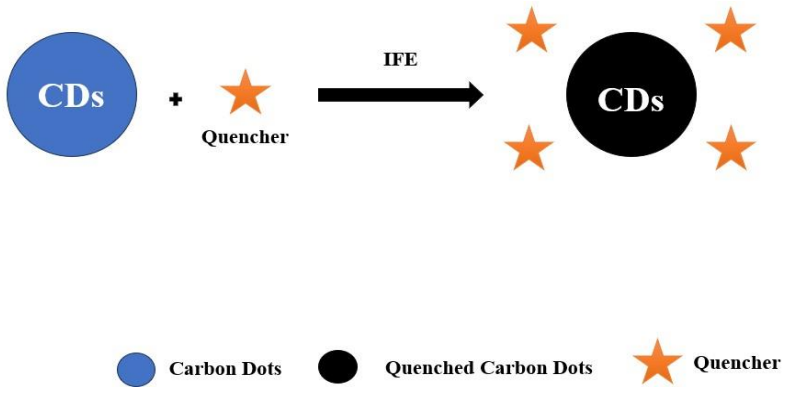

Fig 7. Schematic illustration of IFE of CDs

Significant characteristics of Carbon dots as a biomolecule sensor

CDs have a high two-photon excitation cross-section, which makes them superior candidates in bio-oriented application. What makes CDs function as a potential candidate in the field of biosensor? Based on the carbon precursor, synthesis conditions and heteroatom doping , CDs can be tuned from the visible to NIR range .Therefore, CDs are extremely suitable nanoprobes for (optical) biosensor development The pictorial representation given below explains how Cdots function as a biomolecule sensor.

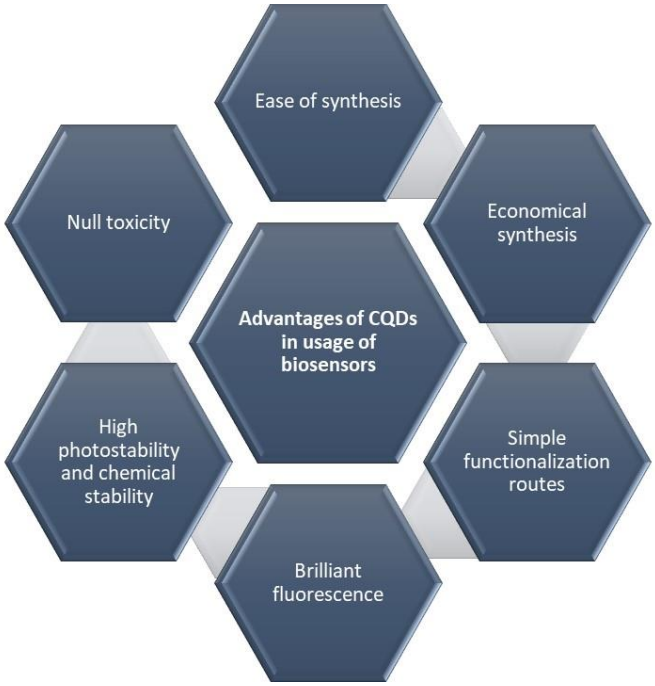

Fig 8. Pictorial representation of advantages of CDs in the field of biosensors

CDs a versatile probe to biomolecule

i. Detection of Ascorbic acid

Anjali Devi et al [40] reports Ascorbic acid (AA) as an essential micronutrient, antioxidant, and enzyme cofactor. As a neuromodulator, accurate selective detection of AA in biological fluids is highly desirable in fields like cell biology, medical diagnostics and therapeutic screening [41]. A turn on fluorescence assay for detection of ascorbic acid using Nitrogen doped Carbon dots (NCDs) and Fe^{3+} using microwave assisted method[42] .Citric acid and Urea are used as carbon and nitrogen sources, that fluorescence of NCDs quenched (turn off) in presence of Fe^{3+} and recovered (turn on) in the presence of AA (Fig 9). NCDs have the potential to be used as fluorescent turn on sensor for AA [43]. Turn off sensors are always preferred due to their high selectivity and reasonable detection nature [40, 44]. NCD/Fe^{3+} detects AA with a detection limit of 96 µM.

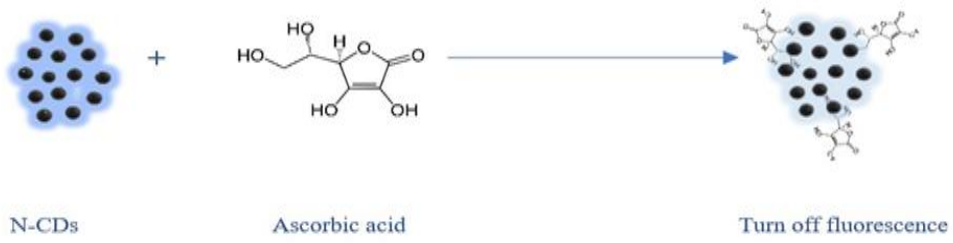

Fig 9. Pictorial representation of Ascorbic acid sensing using N-CDs

A carbon-dots-based sensor for dynamical and reversible detection of ClO− and AA was successfully developed by Wei eta [45] . As the content fluctuation of ROS and antioxidant OCl/ClO− and AA could interrupt intracellular homeostasis leading to diseases such as cancer, neurodegenerative disease, cardiovascular disease, and diabetes mellitus, which pose a threat to human life a fluorescent dual-mode carbon dots (RD-CDs) were synthesized by a one-pot hydrothermal method to detect ClO− and AA simultaneously. The RD-CDs can respond n the range of 5−200 μM and 1−30 μM. The nanosensor possessed high selectivity toward ClO− in the range of 0.1−100 μM with a detection limit of 83 nM, and can be selectively recovered by AA. probe for dynamic detection of ClO− and AA in living cells, which can be monitored by a fluorescence microscope. In the colorimetric manner, ClO− and AA can be detected by UV−vis in the range of 5−200 μM and 1−30 .Carbon quantum dots (CQDs) were synthesized[46] by microwave irradiation and electropolymerized on glassy carbon electrode (GCE) to construct an electrochemical sensor for the selective detection of ascorbic acid (AA). Electrochemical behaviours of the prepared sensor were investigated by cyclic voltammetry (CV), differential pulse voltammetry (DPV), and electrochemical impedance spectroscopy (EIS). The electrochemical sensor is reported to successfully sense AA in presence of DA and UA with separate oxidation peaks for AA, DA, and UA. Two wide linear responses are reported in ranges of 0.01-3 mM and 4-12 mM with a lower detection limit of 10 μM to AA. An "on-off-on" fluorescent sensor using sulfur and nitrogen co-doped carbon dots (S, N-CDs) was reported for the identification of Cr (VI) and ascorbic acid (AA) [47] which showed a good selectivity and anti-interfere ability to more than 30 interfering substances. The fluorescence recognition was conducted in liquid and solid media under optimal conditions based on the internal filtration effect (IFE). In liquid medium, the linear dynamic range of Cr (VI) was 0.03–50 μM and the limit of detection (LOD) was 21.14 nM. The linear detection range and the LOD of AA were 1–1000 μM and 0.28 μM. For solid-phase detection S, N-CDs were embedded into polyvinyl alcohol (PVA) to obtain a visual fluorescent film sensor, which was irradiated by 365 nm ultraviolet light, for easily and accurately detecting Cr (VI) and AA on-site. The ranges of linearity were 0.1–50 μM and 10–500 μM, respectively, and the LODs were 92.48 nM and 6.99 μM, respectively. Fluorescent nitrogen doped carbon dots (N-CDs) were synthesized by microwave digestion method using glucosamine and ethylenediamine [48].The synthesized N-CDs were used to explore its sensing ability against 4-nitrophenol (4-NP), Cr(VI), and Ascorbic acid. The 4-NP, Cr (VI) and ascorbic acid showed a detection limits of 0.05, 0.08 and 0.15 μM respectively. The quench in fluorescence of N-CDs against 4-NP and Cr(VI) is reported due to the inner filter effect (IFE), whereas in case of AA, sensing is reported due to the weakening of IFE, resulting in restoration of fluorescence for a 0.25 to

175 µM concentration range of AA in presence of N-CDs/Cr(VI) fluorescent probe. The probe was also used to detect AA in urine sample

ii. Detection of Arginine

Arginine plays a vital role in cell division, trauma recovery. Administration of arginine improves the immune system, digestive functions and functions against carcinogenesis. Zhang et al [49], developed a Magnesium ion doped Carbon dots (Mg-CDs) as a rapid detection probe for Arginine, with Adenosine triphosphate (ATP) as a switch (Fig 10), which also enhances the fluorescence due to electrostatic interaction exhibiting covalent stability between arginine and ATP. Citric acid and Urea were used as source for carbon and nitrogen and Magnesium acetate is used as doping agent.A detection limit of 0.15 µmol/l is reported. They concluded that the use of Mg-CDs as a fluorescence probe had good precision, stability, and no matrix interference, making it as a powerful tool in clinical trials for the quantitative detection of Arginine. Wang et al [50] has reported an easy synthesis of dual emission fluorescence carbon quantum dots using o-phenylenediamine and 2-hydroxy-3-methoxybenzaldehyde as precursors, which can detect arginine using ratiometric fluorescence method. They found that Arginine recovery ranged from 95.8%-108.9%, specifying that Arginine in water samples can accurately be measured with higher recovery. The CDs exhibited excellent photostability, good stability in presence of higher concentrations of NaCl and strong anti-inference ability, with a linear detection range of 27 to 107 µm [50].

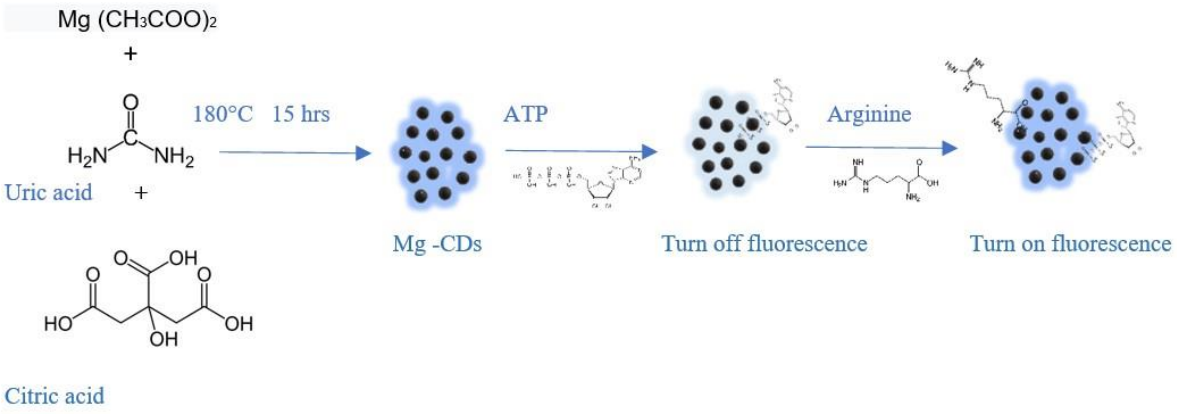

Fig 10. Pictorial representation of Arginine sensing using Mg-CDs

A ratiometric fluorescent hybrid nanoprobe CDs-1 for arginine (Arg),[49] exhibiting high sensitivity (the limit of detection, LOD, being 6.5×10^{-8} mol/L) and excellent selectivity and anti-interference ability due to fluorescence resonance energy transfer (FRET) and electrostatic attraction between positively-charged hemicyanine molecules and negatively-charged carbon dots (CDs). Arg can be quantitatively detected in the concentration range from 6.0×10^{-5} mol/L to 2.7×10^{-4} mol/L. Synthesis of Nitrogen-doped carbon dots (*N*-CDs) were reported[51] using a simple one-pot hydrothermal carbonization method for the detection of cinnamaldehyde (CAL) and L-Arginine/L-Lysine (L-Arg/L-Lys). CDs are reported to be highly

efficient fluorescent probe with significant sensitivity and selectivity toward cinnamaldehyde and L-Arg/L-Lys over other analytes with a lower detection limit of 58 nM and 16 nM/18 nM, respectively. The fluorescence of *N*-CDs quenched through an electron transfer process. The strong electrostatic interaction between L-Arg/L-Lys and *N*-CDs resulted in efficient fluorescence recovery. AuNPs/ CQDs[52] synthesised for the detection of arginine composites were characterized and their quenching mechanism was analysed. The amount of AuNPs/ CQDs, the pH and the reaction time were optimal during which the fluorescence system was used to detect the content of arginine, showing a good linear relationship (R^2=0.993) between fluorescence intensity and concentration of arginine in the range of 0. 1-10. 0 µmol/ l, and the detection limit was 5. 8 nmol/ l. The content of arginine in grape juice was determined with recoveries of 105. 4%-110. 8%, which indicated that the proposed FRET mechanism had the potential for practical detection of arginine in fruit juice.

iii. Detection of Melamine

Melamine contamination in milk products can cause reproductive and urinary system damage, urinary calculi, acute renal failure, bladder cancer, and infant death. As a consequence, both US and China have set a melamine content limit for infant formula powder of one part per million (ppm) [53,54]. Dai et al [55] reported an amino-functionalized carbon dots (C-dots) doped with gold nanoparticles (AuNPs), CDs as energy donors, while AuNPs as energy acceptors. The novel "turn-on" fluorescence sensor for melamine is based on melamine-induced decrease of the FRET efficiency between gold nanoparticles (AuNPs) and the C-dots. With addition of CDs into AuNPs solution, the CDs move close to the surface of AuNPs, resulting in the fluorescence quenching. Melamine contains amino groups, which can compete with the CDs leading to the restoration of the fluorescence. Incubation time, AuNPs concentration, and media pH, all of which reported to have an effect on the system's performance. A detection limit of 36 nM is reported. The turn on fluorescence assay is applied to detect melamine level in raw milk and milk powder. Good recoveries ranging from 90.475% to 111.35% prove the reliability of the sensor .In 2019, Hu et al [56] used a smartphone for the visual detection of melamine in milk based on Au@Carbon quantum dot nanocomposites. The fluorescence standard array and smartphone were used to visually detect the average concentration of melamine adulterated in milk samples based on fluorescence light. For detection of melamine in the range of 1 µM to 10 µM, a calibration curve and fluorescence standard array were created. The quantification and detection limits were 12 nM and 36 nM, respectively. The fluorescence standard array in milk can be used to detect melamine rapidly, reliably, and visually, often outside of the lab and without the use of specialised instruments. It is ideal for detecting melamine concentration in milk and determining milk safety.

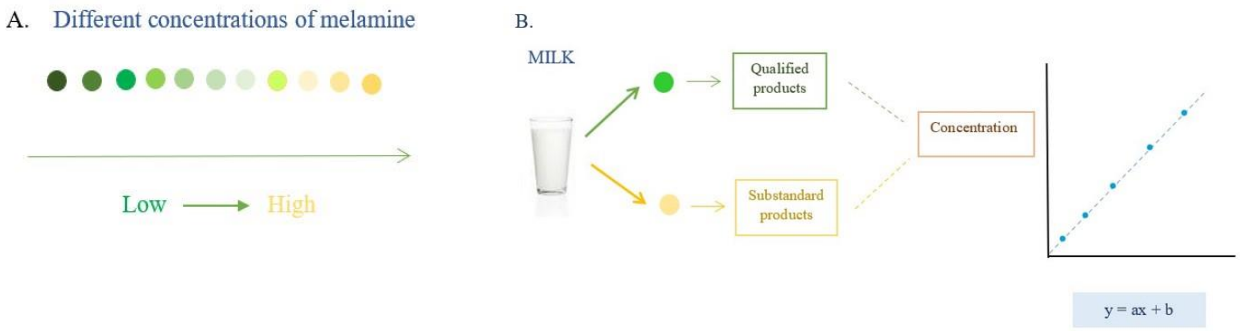

Fig 11. A. Au@CQD based fluorescence method for detecting melamine B. Detection of milk adulterated by melamine

iv. Detection of Cholesterol

Cholesterol is a fatty component found in food that is formed by the liver. Steroid hormones, vitamin D, and bile are all produced as a result of it. But maintaining a particular concentration of cholesterol in our body is a key balance for a healthy lifestyle. A simple, highly sensitive, selective, rapid, and cost-effective cholesterol biosensor was developed by Trang Thi Bui and Soo-Young Park [57] using a fluorescence method by CD-Haemoglobin complex. The basic mechanism of cholesterol sensing is that when CD interacts with cholesterol, its fluorescence is enhanced, while disturbed – interactions (π-π) between CD and Hb, quenches CD fluorescence. The CD/Hb combination allowed for selective cholesterol detection throughout a linear range of 0 to 800 µM, with a detection limit of 56 µM in blood plasma. (Carbon dot–haemoglobin complex-based biosensor for cholesterol detection).

Fig 12. Pictorial representation of Cholesterol biosensor detection by the formation of CD-Haemoglobin complex

A highly rapid and non-enzymatic method[58] for detection of cholesterol using yellow g-C_3N_4 obtained by direct pyrolysis of melamine where fluorescence intensity of the system intermittently decreased with the increase of cholesterol concentration, and it decreased to a stable value as the cholesterol concentration gradually increased to 3000 mmol/l The fluorescence of CNQDs could be quenched more than 90% within 30 seconds by cholesterol through the formation of hydrogen bonds between $–NH_2$, –NH on the surface of CNQDs and cholesterol containing –OH. Cholesterol detection limit as low as 10.93 µmol $L^{-1}$is been reported and it is found to be advantageous of being a very rapid process and avoiding the use of enzymes. A new kind of well selective and highly sensitive ratiometric fluorescent probe for cholesterol and uric acid determination in human blood serum was developed [59] on the basis of the inner filter effect (IFE). Nitrogen, cobalt co-doped carbon dots (N,Co-CDs) with 2,3-diaminophenazine (DAP) was synthesised. Fluorescent magnetic N,Co-CDs possessing blue emission and magnetic property were obtained through a facile one-pot hydrothermal strategy by using citric acid, diethylenetriamine, and cobalt (II) chloride hexahydrate as precursors. IFE process between N,Co-CDs and DAP, N,Co-CDs were the ratiometric fluorescent probes for the indirect detection of cholesterol and uric acid.. The established IFE-based fluorescent

probes exhibited relatively lower detection limits of 3.6 nM for cholesterol and 3.4 nM for uric acid.

v. Detection of Uric acid

Uric acid (UA) is a vital biological substance and the primary end product of purine metabolism in the human body. The level of UA in a healthy person's blood sample should be in the range of 0.15–0.42 mM. Gout, high blood pressure, kidney illness, leukaemia, pneumonia, cardiovascular illnesses, high cholesterol, and multiple sclerosis are disorders that can be caused by excess of UA concentration. Wang et al [60], synthesized S, N co-doped Carbon dots with blue fluorescence that quenched when hydroxyl radicals were generated on Fenton reaction between H_2O_2 and Fe^{2+} which is facilitated by enzymatic reaction occurring in Uric acid. The fluorescent intensity of the C-dots oxidized by hydroxyl radical could be recovered when sodium borohydride (NaBH4) was added into the solution of the C-dots oxidized with hydroxyl radical, indicating that the fluorescence nature of the C-dots was related to the groups on the surface of C-dots This built in nanosensor has good selectivity, rapid response which enable it to be used to determine UA in real samples with a linear range of range of 0.08–10 µM and detection limit upto 0.07 µM.

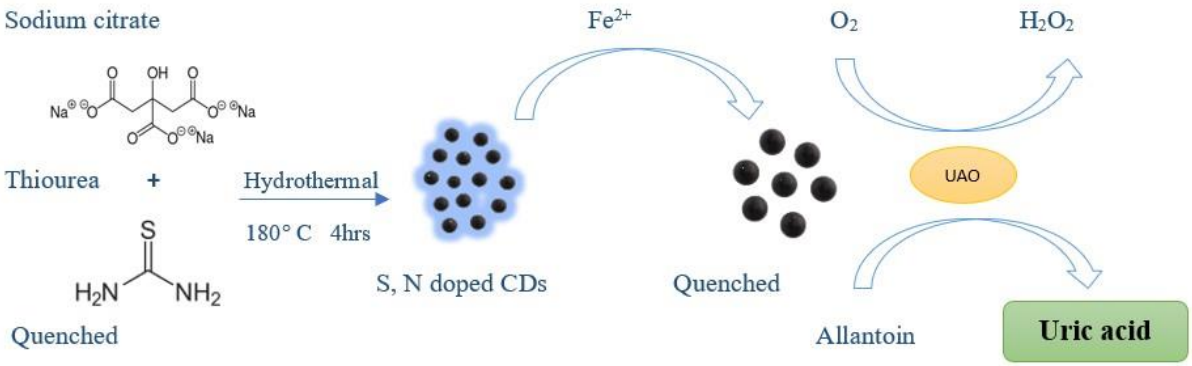

Fig 13. Pictorial representation of detection of Uric acid using S, N co-doped CDs

Mathew et al, in a novel method reports a method to convert Cr (VI) to Cr (III)/ Cr (0) using Uric acid as a reducing agent in presence of N-CDs. N-CDs function as a turn-off sensor due to Inner filter effect, which has been eliminated by FRET mechanism which is induced when UA is added to the sample.A detection limit of UA upto 2.5 nM concentrations is reported [61]. Green fluorescent Nitrogen doped Carbon Dots (N-CDs) was synthesized by solvent free pyrolysis technique . Using the synthesized N-CDs, for first time we report the synthesis of Blue fluorescent Nitrogen doped silver and copper carbon dot nano composite using a Simple, Solvent free Green method. The N-CDs function as reducing agent to reduce Ag+ and Cu2+ ions to Ag0 and Cu0 which leads to the formation of composite. The synthesized N-CDs and nano composites were applied as Uric Acid(UA) sensor. With addition of Uric acid there was a quench in fluorescence which is immediately visible by our naked eye The quench in fluorescence is due to the synergistic effect between the fluorescence Inner Filter Effect (IFE)

and the static quenching effect, with a Lower detection limit (LDL) of 4µM thus functioning as a highly rapid UA biosensor[62]

vi. Detection of Dopamine

Dopamine (DA) is a catecholamine and a neurotransmitter that plays a key part in the functions of renal, cardiovascular, and central nervous systems. Deficiency in DA is primarily responsible for neurological disorders like Parkinson's disease, schizophrenia, epilepsy, and attention deficit hyperactivity disorder[63]. Louleb et al [63] proposed a method to synthesize N-CDs in order to detect DA in human fluids at nanomolar concentrations rapidly and with high sensitivity. The function of the biosensor was studied with DFT calculations which revealed that the bonding between the $-NH_3^+$ moiety of DA and the corresponding N-CD surface ligand forms hydrogen bonds. It is reported that the linear range is 0 and 652 nM and the detection limit is 4 nM.

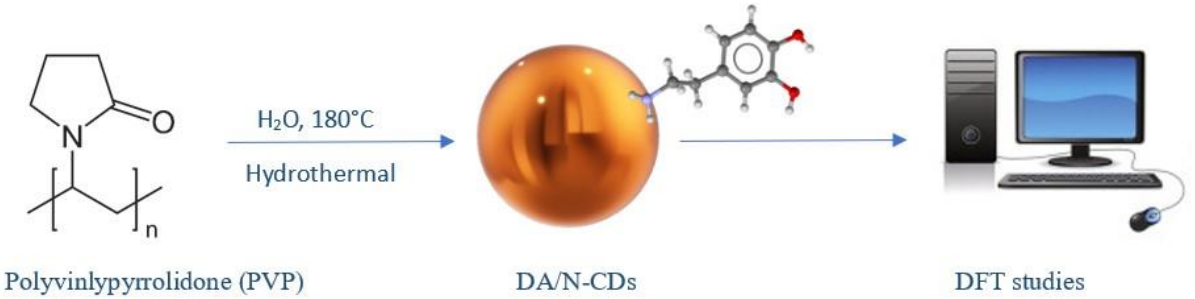

Fig 14. Schematic illustration of detection of dopamine and DFT studies using N-CDs

The use of CQDs in the preparation of SPR sensor chips for DA detection was not been reported before this. Thus in this work[64] is the first study on the detection of DA utilizing a CQD thin film-based SPR sensor where the active layer improves the SPR sensor sensitivity to DA is reported. The direct detection of DA with high sensitivity was studied. In addition, the structural analysis of the sensor film in the absence and presence of DA was studied. The findings revealed that DA binding to CQD thin film strongly affected its morphology. Following that, the experimental SPR curves were mathematically processed in order to investigate the variation of the refractive index of the sensing medium as well as to analyze the optical properties of DA and CQD thin film. Increase in DA concentrations increased the change in η-value of the sensor film. This in turn increased the change in the resonance angle and indicated the high possibility of the proposed sensor to detect extremely low levels of DA depending on the variation that occurred in the refractive index of the sensing layer. The observed reduction in surface roughness using AFM also demonstrated that DA was bound to the sensor layer. This sensor exhibited an excellent sensitivity response of 0.138°/pM in a linear range from 0.001 to 100 pM and a high binding affinity of 6.234 TM^{-1}. An electrochemical sensor [65] using carbon quantum dots CQDs and copper oxide (CuO) nanocomposite for detection of dopamine is the first report on electrochemical DA detection with an electrode composed of mainly CQDs-CuO nanocomposite as the

chemical modifier where the CuO NPs prepared via chemical precipitation technique and incorporated into a composite with CQDs, prepared from the carbonization of pencil graphite, the (CQDs/CuO) modified on glassy carbon electrode (GCE) detected DA at 0.3 V, detection limit of this sensor via square wave voltammetry (SWV) was 25.40 µM over a wide linear range of 1–180 µM. This sensor confirmed its suitability for detection of DA in pharmaceutical samples. A novel dual-emission ratiometric fluorescence sensing system based on a hybrid CDs and 7-amino-4-methylcoumarin (AMC) to quickly monitor DA reported by Jia An et.al [66], CDs linked via amide bonds where the CDs and AMC emit dual-emissions with peaks located at 455 and 505 nm respectively under a single excitation wavelength of 300 nm, the fluorescence of the CDs and AMC in the nanohybrid system can be quenched by DA, therefore the concentration of DA could be quantitatively detected by monitoring the ratiometric ratio change in fluorescent intensity. More importantly, the CDs-AMC-based dual-emission sensing system demonstrated a remarkable linear relationship in the range of 0–33.6 µM with a lower detection limit of 5.67 nM. A boronic acid-functionalized fluorescent sensor [67]was developed by adapting the conveniently accessible biomass such as coffee waste for the detection of neurotransmitters like DA. carbon dots (CDs) were synthesized using coffee waste via a simple hydrothermal treatment (C-CDs). The fluorescent sensor was designed using phenylboronic acid namely 3-aminophenylboronic acid (APBA)-modification to the C-CDs through 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide/N-hydroxy-succinimide (EDC/NHS) to obtain B-CDs. Both C-CDs and B-CDs shows photoluminescence (PL) emission maxima around 452 and 469 nm under the excitation maxima of 335 and 371 nm, respectively. The PL response showed distinct excitation-dependent and independent emission behaviour when shifting the excitation wavelengths from 300–500 nm to 300–390 nm, respectively. The C-CDs and B-CDs displayed light and strong-blue colored emissions under ultraviolet (UV)-light. The B-CDs have shown a quench in fluorescence for DA concentrations ranging from 0 to 30 µM with a lower detection limit of 4.25 nM. The study was also carried out in real samples like human serum, which exhibited good recovery values of 95.9–101.35 %

Detection of Tryptophan

Tryptophan (Trp) is an essential amino acid for appropriate new-born growth and adult nitrogen balance. In the human body, Trp can be metabolised to important neurotransmitters like serotonin, melatonin, and nicotinamide. Trp can induce confusion, nausea, and a loss of appetite, as well as produce a toxic waste substance in the brain that causes psychotic symptoms, when digested improperly. Wenshuai Li et al [68] proposed a novel method to detect Trp with rapid and highly effective way. They synthesised Pyridine functionalized carbon dots by typical one pot hydrothermal method, the mechanism works with Py-CDs' surface pyridine ring served as an active site, forming a non-fluorescence composite with Trp. It just consumes a quarter of a minute and performs highly sensitive and selective towards Trp with a linear range of 0.02–20 µM and limit of detection at 5.7 nM.

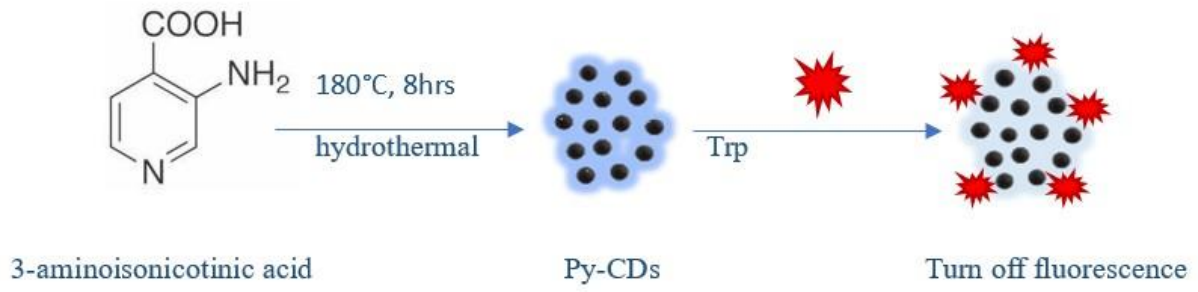

Fig 15. Pictorial representation of biosensing of Tryptophan using Py-CDs

Fluorescent nitrogen and fluorine doped carbon dots (CDs) were prepared by a hydrothermal method [69]. A using levofloxacin (LVFX) and cucurbit [6] uril (Q [6]) as the nitrogen and carbon sources. The synthesized *N*,*N*′-DLH containing Q [6]-CDs emitted intense blue fluorescence with high photostability and exhibited stability at high ionic strength. the obtained Q [6]-CDs, an efficient sensing method for L-tryptophan (L-Trp) and capecitabine (CAP) has been developed based on macrocyclic host–guest chemistry. Under applicable conditions, the detection limits for L-Trp and CAP were calculated to be 5.13×10^{-8} M and 1.48×10^{-8} M. A novel nanocomposite was fabricated using overoxidized polypyrrole film doped with nano-carbon dots (nano-CDs) on the pencil graphite electrode (PGE) surface for sensitive evaluation of Trp in human serum [70]. Using square wave voltammetry (SWV), the overoxidized polypyrrole/carbon dots/pencil graphite electrode (Ov-Ox PPy/CDs/PGE) achieved excellent electrochemical catalytic activity for evaluating Trp. The modifed electrode, known as Ov-Ox PPy/CDs/PGE, demonstrated superior electrochemical catalytic activity compared to bare PGE, CDs/PGE, PPy/PGE, and PPy/CDs/PGE for evaluation of Trp. The method's excellent sensitivity was confirmed by the low limits of detection (LOD=0.003 μmol L−1) and limit of quantitation (LOQ=0.009 μmol L−1). The biosensor that was developed can measure tryptophan (Trp) levels in the serum of both healthy individuals and female breast cancer patients with high accuracy and sensitivity.

vii. Detection of Cysteine

Cysteine is an essential amino acid that plays an important role in protein synthesis, detoxification, and metabolism. Novel magnesium and nitrogen co-doped carbon quantum dots (Mg-N-CQDs) were developed [71] as a fluorescent switch for sensitive and selective sensing of Hg (II) and cysteine (Cys). The fluorescence of the Mg-N-CQDs aqueous solution containing Hg (II) could be recovered gradually in the presence of Cys, due to the stronger binding affinity of Hg (II) toward Cys than toward Mg-N-CQDs. Liao et al. [73] developed a low-cost method for synthesising multifunctional S, N-CQDs with a high fluorescence quantum yield of 63.82 percent, which can be used as a signal-on sensor for cysteine in aqueous medium. They have a linear range of 10-120 μm as well as a detection limit of 0.35 μm. Furthermore, the extent of cysteine research with carbon dots have been emerged enough to be getting derived from Cys itself [72]. Apart from Ag+, various inorganic metal ions such as Cu2+ and Hg2+, as well as organic compounds such as fluazinam and lucigenin, have been used in such mechanism. [71-78].

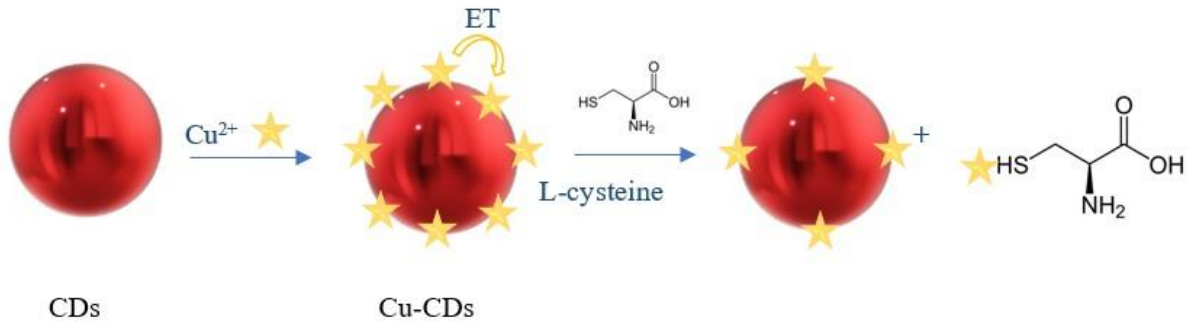

Fig 16. Schematic illustration of Cu^{2+} and L-cysteine detection using CDs

viii. Detection of Bilirubin

Toxic levels of Bilirubin (BR) cause neurotoxicity in neonates, resulting in neurodevelopmental problems such as cognitive impairment, athetosis, and, in rare cases, intellectual impairments, and even death or lasting neurologic sequelae (kernicterus). The only approach to avoid this dangerous condition is to diagnose and treat hyperbilirubinemia as soon as possible. Anjana et al[79], synthesized sulfur and nitrogen doped carbon dots (S,N-CDs) were prepared from citric acid (CA) and L-Cysteine. CA functions as a carbon source. L-Cysteine, a proteinogenic amino acid act as nitrogen and sulfur source. The molecular origin of fluorescence in the citric acid based CDs is due to the presence of derivatives of citrazinic acid. Citric acid contains three carboxyl functionalities, which undergo intramolecular condensation and cyclisation with β-amino thiols like cysteine to form derivatives of citrazinic acid The fluorescent intensity of S,N-CDs can be significantly quenched by Fe(III) ions where the Fe(III) absorbs and reacts with phenolic -OH, −COOH and –NH2 groups present on the surface of S,N-CDs leading to chelation or co-ordination, complexations facilitate non-radiative electron hole recombination leading to fluorescence quenching and can be effectively restored by the addition of BR due to its tetrapyrrole ring structure which has an affinity towards Fe(III) which emits a brilliant blue fluorescence emission. The detection limit of Fe(III) is 23.08 μMand for bilirubin is 0.12 nM proving when BR comes into contact with S,N-CDs/Fe(III), an electron transfer reaction may take place between the lone pair of nitrogen atoms present in the pyrrole ring of BR and Fe(III) enabling a complex formation between them. Turn on fluorescence analysis were performed in BR spiked human serum, urine samples and paper based test stripes were also designed for direct detection of BR.

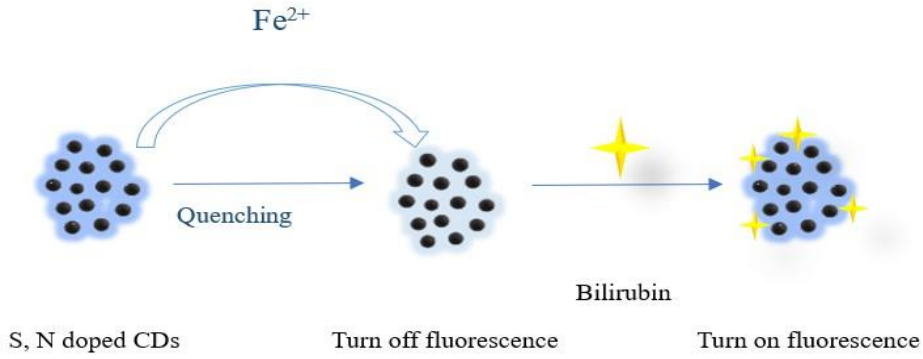

Fig 17. Schematic representation of detection of bilirubin using S, N doped CDs

Sasikumar et al [80] reported CDs for the highly sensitive and selective detection of bilirubin in human urine. The CDs showed the fluorescent emission, which peaked at the wavelength of 511 nm under the excitation wavelength of 435 nm. The CDs' emission intensity reduced with increasing the bilirubin concentration, which was ascribed to the strong inner filter effect (IFE). The excellent spectral match between the bilirubin absorbance and the CDs excitation allowed the fluorescence sensor to be markedly specific only to the presence of bilirubin, permitting the identification of bilirubin even in the presence of other potentially interfering elements. The fluorescence sensor displayed a good linear response to the bilirubin concentration in the wide range of 3.5–45.5 μM with a limit of detection (LOD) of 34 nM. Carbon dots synthesised from resorcinol and sucrose (rsCDs) hydrothermally with green emission and the intense emission of rsCDs is quenched upon the addition of Cu^{2+}, in the presence of bilirubin (BR)[81], the emission intensity is enhanced due to the competitive binding of Cu^{2+} with bilirubin releasing rsCDs to the sensing medium with a turn-on fluorescence towards BR with a detection limit of 85 nM in the presence of other comparable biomolecules, the sensor is selective and ultrasensitive to bilirubin. A cellulose paper-based sensor strip Yellow emissive carbon dots (Y-CDs, λ_{ex} 430 nm, λ_{em} 550 nm) synthesized utilizing a one-pot solvothermal approach with *o*-phenylenediamine (oPDA) as a precursor is reported for the naked-eye detection of BR in blood serum [82]. The fluorescence of Y-CDs was quenched with the addition of bilirubin due to the inner filter effect mechanism where the fluorescence intensity of Y-CDs decreases as bilirubin concentration increases and can be completely quenched with approximately 90 μM bilirubin. The Y-CD probe exhibited selectivity for bilirubin in presence of other interferents. More crucially, a smartphone can capture the visible color intensity change of the Y-CD probe under a 365 nm UV lamp and later with the aid of computer software, RGB (red/green/blue) analysis was performed for the quantification of colors. This provides computer vision-based detection and sensitive bilirubin assay with a linear range of 4.0–225 μM and a limit of detection of 1.37 μM. Furthermore, the proposed fluorescent probe was applied in real samples (newborn serum, serum and urine of adults with hyperbilirubinemia) with satisfactory recoveries (96–102%).

ix. Detection of Aspartate transaminase

The liver enzyme aspartate transaminase is mostly present in hepatocellular tissues. The apparent increase in mortality owing to liver diseases such as liver cirrhosis highlighted the urgent need for quick and precise disease detection. One of the most important indicators for the diagnosis and study of liver disorders is liver enzymes. Thus, Krishna et al [83] developed blue fluorescent N-CDs to detect the enzyme Aspartate transaminase by monitoring its biomarker Oxaloacetate either, directly or indirectly. The abnormally high quantity of AST in the blood causes a rise in oxaloacetate levels. For the direct detection of AST, fluorescent carbon dots are employed as a probe. With an increase in AST concentration, the fluorescence intensity of NCDs was quenched. The probe was able to detect oxaloacetate concentrations up to 100 µM using the indirect approach.

x. Detection of Glucose

Chemiluminescence (CL) assays have recieved a lot of attention as a flexible analytical technique because of its rapidity, high sensitivity, and wide variety of applications. A natural enzyme, such as horseradish peroxidase, is used in a conventional CL immunoassay approach. Natural enzymes, on the other hand, are frequently restricted due to significant flaws. CDs, have a unique electron transfer, a large specific surface area, broad light-absorbing capacities, function as artificial enzymes when functionalized with metal nanoparticles and MOFs. Copper doped CDs as a catalyst for detection of Glucose reported by Duan etal [84]S through the H_2O_2 mediated oxidation reaction was done in serum samples and allows them to detect analyte because of its peroxidase like behaviour of Cu-CDs even under wide pH ranges and temperatures. Thus, Cu-CDs as new CL sensing catalyst is able to sensitive detection of Glucose with a limit of detection of 0.32 µM.

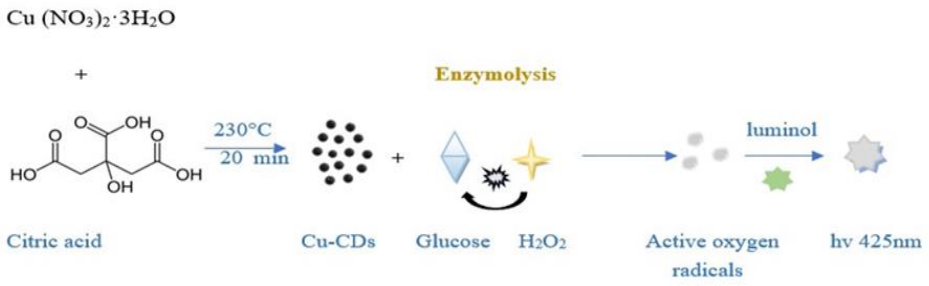

Fig 18. Pictorial representation of chemiluminescence detection of glucose using Cu-CDs

A fluorescent and colorimetric sensor, for both hydrogen peroxide (H_2O_2) and glucose [85] based on the metal oxide – carbon-dot hybrid structure reported by Hung Hur et. al functions with the catalytic oxidation of glucose-by-glucose oxidase (GOx) to H_2O_2 where a metal oxide hybrid with nitrogen-doped carbon dots (MFNCDs) with intrinsic peroxidase-like activity was synthesized and used as a catalyst to oxidize 3,3′,5,5′-tetramethylbenzidine (TMB) to blue-emitting oxidized TMB (oxTMB) in presence of hydrogen peroxide (H_2O_2). The fluorescence of MFNCDs/TMB at 405 nm quenched in the presence of H_2O_2 through the inner filter effect (IFE) and electron transfer within MFNCDs, oxTMB, and glucose system. The detection limit for H_2O_2 and glucose based on the fluorescent method are as low as 97 nM and 0.85 mM. A

Non-enzymatic amperometric sensor[86] for the detection of glucose using nanocomposites (CuO-CDs), were CuO-CDs modified on the surface of a screen-printed carbon electrode (SPCE) increase the sensitivity and selectivity of glucose detection. The SPCE modified with CuO-CDs possess desirable electrocatalytic properties for glucose oxidation in alkaline solutions. Moreover a linear range of 0.5 to 2 and 2 to 5 mM for glucose detection with high sensitivity of 110 and 63.3 μA $mM^{-1}cm^{-2}$, good selectivity and stability, potentially serve as an effective alternative method of glucose detection. A facile one-pot hydrothermal route was employed to synthesize a series of fluorescent CDs using 20 natural amino acids as the starting materials [87], where the CDs synthesized using phenylalanine possess the intrinsic peroxidase-like activity that effectively catalyze 3, 3', 5, 5'- tetramethylbenzidine (TMB) in the presence of H_2O_2 to produce a blue solution proving a catalytic sensing system for H_2O_2 with the Limit of detections (LODs) for H_2O_2 and glucose reported to be 6.5 and 0.84 μM, respectively.

Detection of Vitamin B_{12}

Vitamins are chemical molecules that are required for proper human function. Vitamin B12 (VB12) is a cobalt tetra azamacrocyclic complex that aids in the production of red blood cells and the upkeep of nerve cells. Anemia, metabolic problems, and psychosis are among symptoms of VB12 insufficiency, which is permanent. Excessive V B12 absorption might potentially have unintended consequences. As a result, the identification of VB12 has gotten a lot of interest in recent decades. Jilong Wang et al [88] introduced a novel FRET-based optical sensor of CDs to detect VB12. Thermally reduced Carbon dots (t-CDs) was synthesised from Citric acid for CDs then they reduced thermally using TGA to obtain t-CDs. T- CDs is able to detect VB12 in aqueous solutions containing concentrations ranging from 1 to 12 g ml^{-1}, with a limit of detection (LOD) as low as 0.1 g ml^{-1}. Meng et al [89] developed orange fluorescent multifunctional carbon dots (O-CDs)for label-free vitamin B12 detection using safranine T and ethanol as precursors. The O-CDs with excitation-independent properties was synthesized in a one-step hydrothermal method where VB12 used as a quencher to quench the fluorescence of O-CDs due to internal filtering effect with a detection limit is 0.62 μM.

xi. Detection of Chlorpromazine

An antipsychotic drug called chlorpromazine is generally used to treat psychotic conditions such as schizophrenia, bipolar disorder, and acute psychosis. It belongs to a special class of neuroleptic drugs termed first-generation antipsychotics. It belongs to the family of phenothiazines and works as a dopamine receptor inhibitor in the brain. Carbon dots synthesized from kiwi peel by Zhiwei Lu et al. [90] modified Au/N-GOQDs/NiS_2/BC/MIP/GCE composites by electrochemical polymerization. Since chlorpromazine is an electrochemically active drug, it uses a single electron mechanism that is based on the electrochemical oxidation of nitrogen atoms. The sensing system that was carried out during the experiment proved to have a good selectivity for chlorpromazine. Chlorpromazine's electrochemical oxidation is discovered by Au/N-GOGD's /NIS2/BC/ MIP/ GCE electrode. It was decided to calculate the electrochemical behaviour using the electron transfer process that is occurring in CPZ. So, the electrochemical oxidation process of CPZ is

determined by the CDs modified nanocomposite's good catalytic behaviour ability. For comparison, DPV was performed under optimized parameters for simultaneous determination of DA (2–40.0 µM) and CPZ (0.2–2.0 µM) by Au/N-GOQDs/NiS2/BC/NIP/GCE.

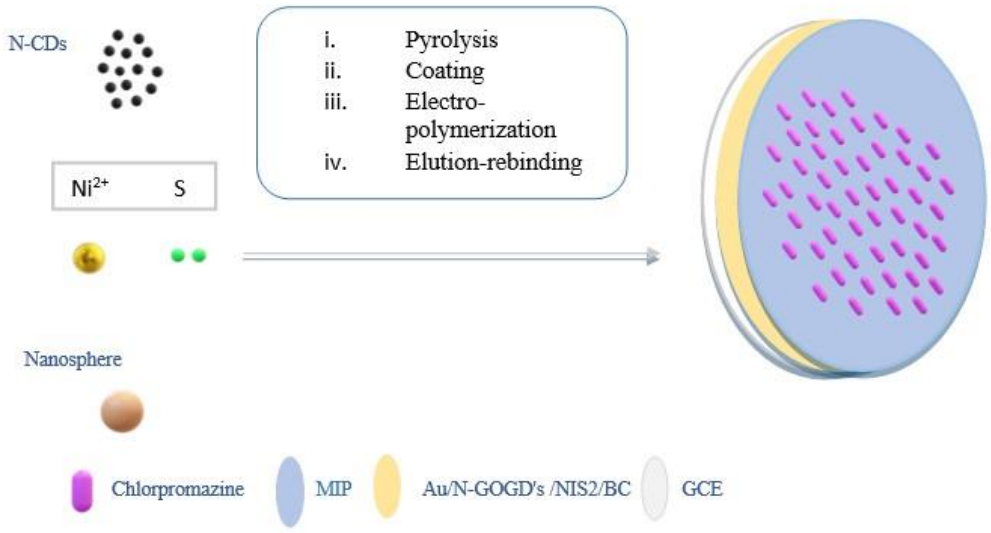

Fig 19. Pictorial representation of electrochemical detection of chlorpromazine

xii. Detection of metronidazole

Metronidazole belongs to the group of nitroimidazoles, which are often prescribed antibiotics. It is employed to treat parasite infections such as giardiasis, trichomoniasis, and amebiasis, as well as gastrointestinal infections. It is also used as a preventative after surgery to treat Crohn's disease. Studies have shown that it is also utilised to treat periodontal problems and prevent preterm deliveries. Haiyan Qi et al. [91] synthesized novel N-doped carbon dots from urea and citric acid. According to the investigations, pH and response time play a crucial role in selecting a more accurate quantitative analysis of N-CDs for metronidazole detection. The findings showed that under strong acidic conditions, N-CD fluorescence intensity falls within 5 s and remains constant and unchanged within 100 s. This demonstrated how quickly metronidazole have been detected in the analysis process.

Metronidazole enhances the fluorescence intensity of N-CDs, indicating the formation of a complex between the metronidazole and N-CDs. The paper's evidence showed that IFE is responsible for the quenching mechanism.

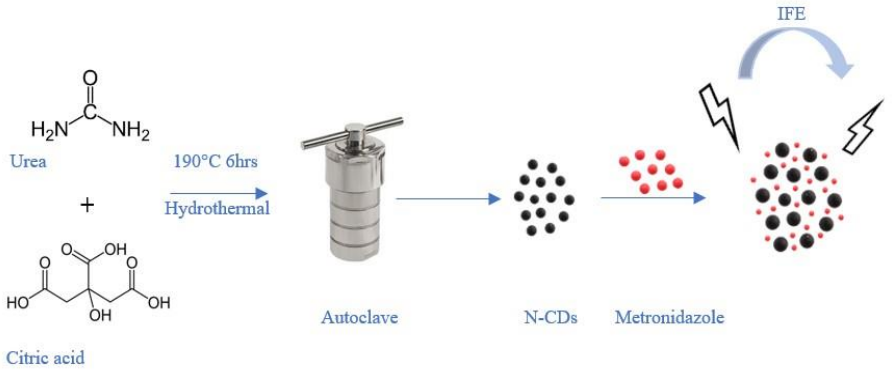

Fig 20. Schematic illustration of synthesis of N-CDs for the detection of metronidazole

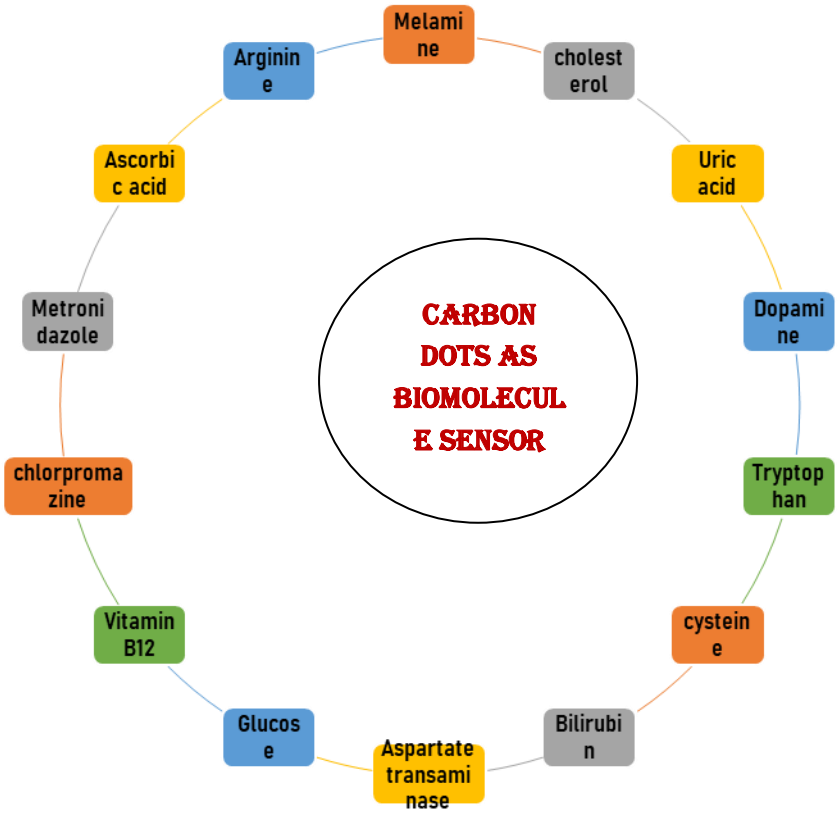

Fig 21. Systematic smart art of Cdots as a sensor for the various Biomolecules

Table 1 A comparative table showing the types of Carbon dots, synthesis, mechanism used in sensing the biomolecule and their detection limit.

Biomolecule	Type of Carbon Quantum Dots	Precursor	Method	Mechanism used for sensing Biomolecule	Detection Limit	Reference
Ascorbic acid	NCDs	Urea, Citric acid	Microwave assisted	TBA -	96 µm -	[44]
	RD-CDs	2,5-Diaminobenzenesulfonic acid, ethanol	hydrothermal	oxidation and reduction of surface functional groups of RD-CDs by ClO− and AA	83 nM	[45]
Arginine	Mg-CDs	Urea, Citric acid	Hydrothermal	Electrostatic interaction -	0.15 µmol/L	[49]
	CDS	o-phenylenediamine, 2-hydroxy-3-methoxybenzaldehyde	Hydrothermal	Ratiometric fluorescence	27 to 107 µM	[50]
Cholesterol	CD/Hb	Citric acid, EDA	Hydrothermal	hydrophobic interactions	56 µM	[57]
Uric Acid	S, N-CDs	Sodium citrate, thiourea	Hydrothermal	TBA	0.07 µM	[60]
Biomolecule	**Type of Carbon**	**Precursor**	**Method**	**Mechanism**	**Detection Limit**	**Reference**

	Quantum Dots					
	NCDs	Monoethanolamine, H_2O_2	Hydrothermal	FRET	2 nM	[61]
	Cu/NCDs & Ag/NCDs	Monoethanolamine, H2O2	Hydrothermal	IFE, static quencing	4μM	[62]
Dopamine	NCDs	Polyvinylpyrrolidone	Hydrothermal	electrostatic, hydrogen bonding	4 nM	[63]
Tryptophan	Pyridine functionalized carbon dots	Pyridine	hydrothermal method	static quenching process	5.7 nM	[68]
Cysteine	magnesium and nitrogen co-doped carbon quantum dots	citric acid, Mg $(OH)_2$, ethylenediamine (EDA)	hydrothermal method	fluorescent complex	9–15 μM	[71]
	SWNT–DNA-5 conjugates	Single-Walled Carbon-Nanotube	SONICATION	p–p stacking interactions between nucleotide bases and SWNT sidewalls	9.5 nm	[72]
	S, N-CQDs – Ag+	Citric acid, thiamine hydrochloride	Hydrothermal	- Cys exhibited stronger complexation capability towards Ag+ than S, N-CQDs	0.36 μM	[73]
Bilirubin	S, N-CDs	Citric acid, L-Cysteine	Microwave	Electron transfer	0.12 nM	[79]
Aspartate transaminase	N-CDs	Tris-Acetate-EDTA, Starch	Microwave	unclear	100 μM	[83]
Glucose	Cu-CDs	Citric acid, Cupric nitrate	Pyrolysis	Charge transfer	0.32 μM	[84]
	MFNCDs	CH_3COONa, ethylene glycol (EG). $MnCl_2$&$4H_2O$, $FeCl_3$&$6H_2O$	hydrothermal	Iinner filter effect (IFE) and electron transfer	0.85 mM	[86]
Vit B12	thermally reduced carbon dots.	carbonization of citric acid	thermal	FRET	0.1 mg ml1	[87]
	orange emission fluorescent multifunctional carbon dots (O-CDs)	safranine T and ethanol	hydrothermal process	internal filtration effect (IFE)	0.06 μM	[89]
Biomolecule	**Type of Carbon**	**Precursor**	**Method**	**Mechanism**	**Detection Limit**	**Reference**

	Quantum Dots					
chlorpromazine	nitrogen-doped graphene oxide quantum dots coated on NiS_2/biomass carbon	Kiwi peel	electrochemical polymerization	electron transfer process	0.25 nM	[90]
metronidazole	N-doped carbon dots	citric acid and urea	hydrothermal method	inner filter effect	0.25 µM	[91]

Conclusion

Carbon Dots are potential candidates towards Biomolecule sensing. This chapter, a mini review summarizes on the recent advances on the various types of CDs synthesised, technique used for the synthesis of CDs, mechanisms applied towards sensing of biomolecules, limit of detection and advantages of CDs as biosensor probe. Only a few biomolecule detection methodologies are explained as it is a mini review.

Author contribution: Writing— All the authors have equally contributed towards the original draft preparation and have read and agreed for the published version of the book chapter.

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