

# Biomedical applications of single-particle based material: quantum dots

## Abstract

Quantum dots are artificial “droplets” of charge that might include a single electron or a group of thousands. Their normal sizes range from nanometres to a few microns, and employing cutting-edge nanofabrication technology, it is possible to precisely regulate their size, shape, and interactions. These special qualities have drawn a lot of interest in the biomedical community recently because they make it possible for real-time tissue imaging (bioimaging), diagnostics, single molecule probes, and medication administration, among many other applications. Due to their high brightness, photo bleach resistance, multiplexing ability, and high surface-to-volume ratio, quantum dots are ideal candidates for intracellular tracking, diagnostics, *in vivo* imaging, and therapeutic delivery. The optical properties of quantum dots can be tuned by size and composition. In the current paper, we will review properties, preparation, characteristics as well as biomedical applications. In addition, some issues along with future aspects. Furthermore, several commercially accessible alternatives are technically contrasted with QDs. Finally, we suggest technical factors that must be considered to enhance the clinical outcome of QDs.

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## Introduction

In recent years, a novel class of fluorescent particles known as semiconductor quantum dots has emerged as a strong contender for single-molecule and single-particle (SPT) monitoring in live cells and animals. Quantum dots (QDs), often known as “artificial atoms,” have distinct energy levels and may accurately alter their band gap by modifying their structure. QDs are described as particles with physical dimensions smaller than the exciton Bohr radius and are group II to VI or group III to V element-based semiconductor crystals of nanometre-scale. QDs have distinctive luminescence characteristics and electronic characteristics include narrow emission spectra, wide and continuous absorption spectra, and great light stability.<sup>1</sup>

Depending on the material’s band gap, they absorb white light and emit a specified hue a few nanoseconds later. QDs are among the first nanotechnologies to be applied to biological sciences, and it is anticipated that they will eventually be used in several commercial consumer and medical goods. Because the secondary antibody conjugates consist of a core of cadmium selenide with a diameter of around 10 to 50 atoms and a total of about 100 to 100,000 atoms, CdSe/ZnS quantum dots, for instance, are now the most popular commercial product.<sup>2</sup>

The QD area generally has a diameter of 2 to 10 nm. QDs have a semiconductor core that is encased in a shell (like ZnS) to enhance optical characteristics and a cap to increase solubility in aqueous buffers. QDs have tiny structures, which causes several physical characteristics, such optical and electron transport properties, to be very different from those of bulk materials.<sup>3</sup>

A wide range of biomedical applications, including the molecular-level analysis of intracellular functions, high-resolution cellular imaging, long-term *in vivo* cell trafficking monitoring, tumour targeting, and diagnostics, have the potential to be made possible by the emergence of QDs as new generation materials.<sup>4</sup> Small voltages cause electron flow in QDs, which may be manipulated by making exact measurements of spin and other characteristics. They are regarded as a blessing for researchers in the biomedical sciences, notably in the fields of targeted treatment, medication

delivery, and diagnostics. QDs have a greater density of states than other geometric formations since they have a zero-dimensional geometry.<sup>5</sup> To comprehend the basic limitations associated with the manufacture of QDs, we first discuss the most recent characteristics, manufacturing techniques, and characterisation of QDs. Reverse micelles, which naturally create water-soluble QDs, have been used in early research to address aqueous-phase synthesis; however, these techniques often produce material of inferior quality than techniques employing organic coordination solvents.<sup>6</sup> Then, we go through some of the biomedical uses for QDs, their place in the healthcare industry, present difficulties, and prospects.

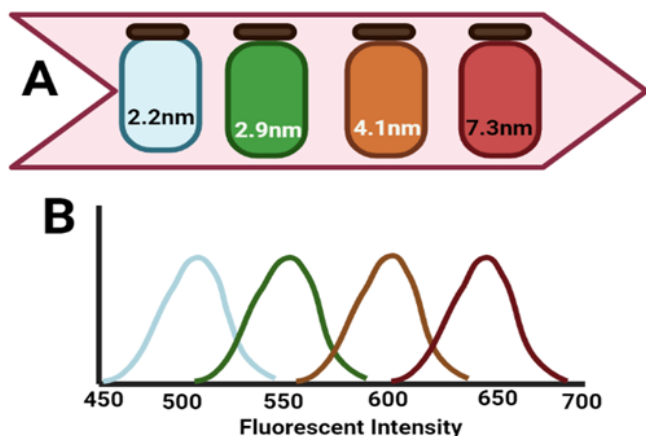
## Properties, preparations and characterization of QDs

### Properties of QDs

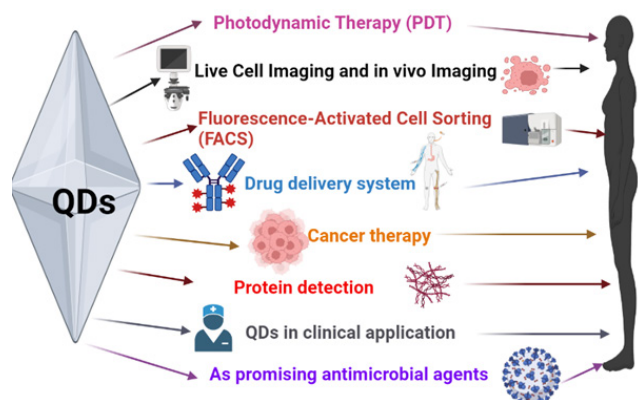
The small semiconductor particles known as quantum dots. They include atoms of various sorts including cadmium, selenium, copper, and/or zinc. A quantum dot is always a container that contains either one or more electrons or one or more holes (lack of electrons). Depending on their size and form, they have different optoelectronic characteristics. Longer wavelengths and hues like orange or red are emitted by larger QDs, 5–6 nm in diameter. Shorter wavelengths are emitted by smaller QDs (2–3 nm), producing hues like blue and green.<sup>7</sup> The precise makeup of the QDs will, however, affect the specific hues. Single electron transistors, solar cells, LEDs, lasers, single photon sources, second harmonic generation, quantum computing, cell biology research, microscopy, and medical imaging are a few potential uses for quantum dots. Some QDs can be suspended in solutions due to their tiny size, which enables their usage in spin coating and inkjet printing. The Langmuir-Blodet thin films have employed them. These processing approaches lead to less expensive and time-consuming semiconductor production processes.<sup>8</sup>

Fluorescence is arguably the most researched and admired characteristic of quantum dots. Quantum dots are a special type of nanomaterial because they emit photons with a particular wavelength when stimulated by an external electrical or light source.<sup>9</sup> Additionally, for a certain size and structure, the precise size of the nanocrystals

determines the wavelength of the light that is emitted. The inverse link between nanocrystal size and energy band gap—i.e., the idea that as nanocrystal size lowers, energy band gap widens and the accompanying excitation/emission wavelength shortens—is the most well-documented and understood feature. The quantum size effect is what is meant by this.<sup>10</sup> In Figure 1A, the fluorescent color emitted by the QDs upon ultraviolet exposure can be tuned simply by varying the size of the particle. In Figure 2B, tuning the particle size.



**Figure 1** The quantum size ability causes CdSe QDs, which are distributed in chloroform, to have their optical characteristics tweaked. (A) Fluorescence picture of monodisperse QDs with sizes ranging from 2.2 to 7.3 nm following UV light. The same four QD samples' fluorescence spectra are shown in (B). Low variation in particle size is indicated by the observation of compact and symmetric emission bands.<sup>7</sup> Created by BioRender.com.



**Figure 2** Some of biomedical applications of QDs. Created by BioRender.com.

### Preparation of QDs

The production of semiconductor nanoparticles is accomplished using two key techniques. Molecular beam epitaxy (MBE) and electron beam lithography are two processing methods used in the first method, which is a top-down synthesis approach. By using a bottom-up strategy, the second is accomplished by the precursor material self-assembling and reacting in solution to produce colloidal QDs. These top-down synthetic techniques are not covered in depth here since we only describe the bottom-up technique because colloidal quantum dots already have the optical characteristics necessary to bioimaging.<sup>11</sup>

These may be broken down into four fundamental strategies: biotemplated synthesis, colloidal synthesis, electrochemical assembly, and biogenic synthesis.

An innovative method for creating different crystals of medicinal relevance, including QDs, is biotemplate-based synthesis. For assembling precursor molecules into viral QDs, biosurfaces such as DNA, RNA, peptides, or bacteriophages are employed. The use of such biotemplates has improved stability and solubility while also enabling fine control over the size, shape, and optical characteristics of the manufactured QDs. An illustration of such a synthesis using a peptide-based template to create CdSe@ZnS core-shell QDs.<sup>12,13</sup> Due to the synergistic interactions between nearby QDs built on the peptide template, the as-prepared QDs displayed a noticeable red-shift in their emission spectra. On the other hand, the use of biotemplates necessitates operation in circumstances of light reaction, which can impact the optical characteristics of the produced QDs.<sup>14</sup>

The process that is most well-known and established is colloidal synthesis. The idea is to heat up the precursor and then inject it into a solvent to make it into a molecular state. For the nucleation stage, which results in the development of the nanocrystals, the molecules that were injected group together. The final process that flips the physico-chemical characteristics of the QDs is the crucial one. Crystallization halts after the required particle size is attained, and QDs are then removed from the solvent. Although the solvents utilised in this synthesis are organic in nature, the stability and toxicity hazards posed by residual solvents are increased using organic solvents in this procedure.<sup>15</sup> The creation of QDs with large polydispersity, high quantum yield, and narrow peak emission via organometallic synthesis serves as another example of this technique and makes them great candidates for clinical imaging.<sup>16</sup> Furthermore, the QDs made using this method are typically covered in hydrophobic ligands, necessitating post-synthesis modifications to the QDs to make them water soluble. These modifications can include exchanging the hydrophobic ligands for hydrophilic ones, coating the QDs with polymers like amphiphilic block copolymers, or adding silica-based shells.<sup>17</sup>

Another method for creating QDs is electrochemical synthesis, which use electrochemical forces to propel the assembly of precursors into the QDs. The applied voltage, redox duration, and concentration of the reference electrode may all be used to control the size of the QDs that are created. The generated QDs were utilised as moisture in the soil sensors and had an outer thickness of 3-5 nm.<sup>18</sup>

An innovative biotechnological method for producing QDs on a large scale is called biologic synthesis. Through conjugation to cysteine-terminated peptides, toxic cadmium ions that are damaging to living things are first detoxified. Following their introduction into the bacterium, the detoxified ions combine with endogenous sulphide ions to form CdS-QDs, which are then exported and extracted from the organism.<sup>19</sup>

### Characterization

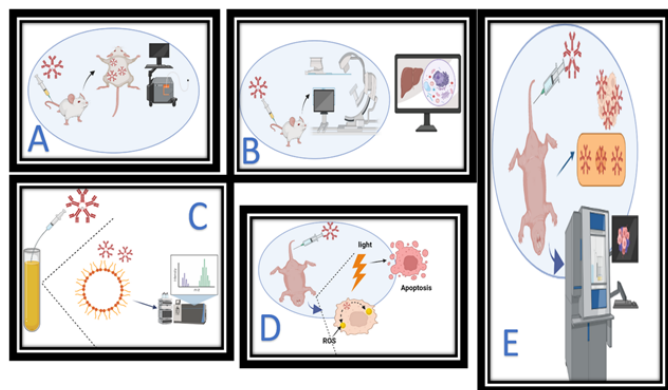
Transmission electron microscopy (STEM), scanning X-ray diffraction, and X-ray fluorescence scanning X-ray diffraction were used to investigate the dimensions, characteristics, and make-up of the QD-doped materials.<sup>20</sup> By utilising UV-Vis and photoluminescence spectroscopy, the QDs are visually identified. Typically, traditional methods like dynamic light scattering, transmission electron microscopy (TEM), and scanning electron microscopy (SEM) are used to calculate the size of QDs (DLS).<sup>21</sup> Using photoluminescence excitation, photoluminescence, and Raman scattering spectroscopy, we have measured the size and structure of optically active QDs. To track the size of epitaxially formed QDs, techniques including TEM, atomic force microscopy (AFM), scanning tunnelling microscopy,

and magnetic tunnelling studies have also been reported.<sup>22</sup>

Other characterization methods include spectroscopy, scattering, electrochemistry, electrophoresis, Raman spectroscopy, mass spectrometry, small angle neutron scattering, nuclear magnetic resonance, infrared and, UV-visible light, X-ray diffraction, scanning electron microscopy, atomic force microscopy, rheology, and physical properties (differential scanning calorimetry, dielectric spectroscopy).<sup>23</sup>

### Biomedical applications of QDs

QDs with acceptable optical and transport characteristics for usage in biological devices. Surface plasmon resonance may be seen in the luminescence spectrum of QDs generated in a locally increased electromagnetic field, which is excellent for optical multiplexing and encoding applications. Cellular imaging, tissue labelling, and biomolecular tracking within cells. QD tracking, QD biodistribution, vascular imaging, and tumour imaging. QDs pertaining to neuroscience Fluorescence microscopy is used to view and complete molecular processes utilising QDs. They are employed, for instance, in the tiny synaptic cleft, for the interactions between nerves and ganglions.<sup>24</sup> From Figures 2 & 3 we can observe some of biomedical treatments and their names.



**Figure 3** A few QD uses in biomedicine. (A) Imaging within cells. To see intracellular structures using fluorescence microscopy or confocal laser scanning microscopy, QDs are coated with targeting moieties (CLSM). In vivo imaging is (B). Using in vivo imaging equipment, QDs customised with tissue-specific targeting moieties may be utilised to see specific organs after injection (IVIS). (C) Cell sorting using fluorescence activation (FACS). During flow cytometry, QDs coated with cell-specific ligands can be utilised as fluorescent probes for cell sorting. QDs have a greater capacity for polychromatic cell sorting than traditional organic dyes because of their many benefits. Photodynamic treatment (D) (PDT). After exposure, QDs can function as photosensitizers or energy suppliers to other photosensitizers to produce reactive oxygen species (ROS) in situ, which causes apoptotic cell death when used as a cancer therapy. (E) Drug delivery systems that can be tracked. Thanks to their ultra-fine particle sizes, QDs may be employed as drug carriers to numerous tissues with high extravasation and tissue penetration capabilities. Since QDs have quantum qualities, it is simple to monitor their accumulation within target tissues. Created by BioRender.com.

### Photodynamic therapy (PDT)

A photosensitizer, often a pigment of the porphyrin type, is preferentially accumulated in the target tissue during PDT, which is then treated with visible light. QDs can function as both photosensitizers and energizers for other photosensitizers in this range. In comparison to organic photosensitizers, QDs have several benefits, such as strong light absorption, strong emission, high photostability, water solubility, tunable optical characteristics, and

high tissue accumulation.<sup>25</sup> Additionally, QDs' structure and shape may be changed to maximize near-infrared (NIR) emission, showing strong tissue penetration appropriate for the treatment of deep-seated malignancies. This photosensitizer can absorb light of the right wavelength when combined with QDs, then use the energy to excite oxygen to its singlet form, which causes cancer cells to die.<sup>26</sup> E.g., CdSe QD with silicon phthalocyanine photosensitizer, for instance (PC4). Additionally, according to recent research, carbon QDs may be useful in the PDT of COVID-19 because to their dual mechanism of ROS production and activation of the interferon type I response.<sup>27</sup>

### Live cell imaging and in vivo imaging

QDs are employed in medicine and may have uses in the expression of the nervous system because to their distinctive optical features. In cultures of primary spinal cord neurons, lateral diffusion of the glycine receptor is followed by antibody-functionalized QDs. In cultured neurons, biocompatible, water-soluble QD micelles exhibit uptake and intracellular dispersion. The detection and cellular labelling of DNA defects (produced by different DNA defects), other biomolecular, and proteins are done via QDs-ligand interactions.<sup>28</sup> Unlike other typical fluorescent probes with continuous fluorescence emission, the distinctive blinking property of QDs facilitates the identification of a single QD event, with the subsequent ability to visualize specific subcellular components such as proteins. Following the administration of QDs that have been functionalized with specific ligands to increase their affinity for organs or tissues of interest, QDs are also used for *in vivo* imaging of various organs and tissues.<sup>29</sup>

### Fluorescence-activated cell sorting (FACS)

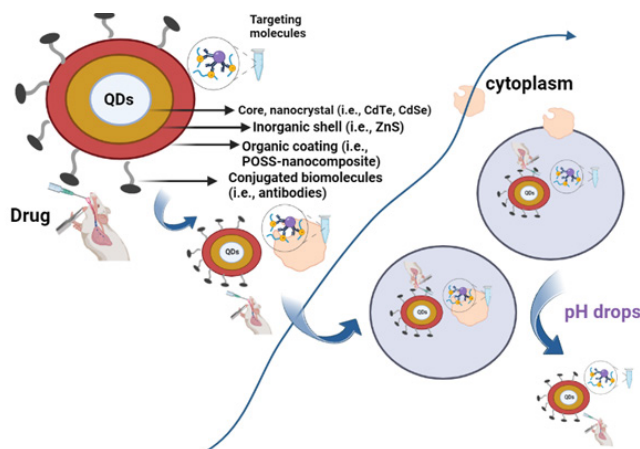
FACS is a widely utilised method for many biological purposes, such as determining how well drug delivery systems are absorbed by cells, separating various cell populations, describing specific disease models, and identifying immune cells and cell markers. Maps are provided. Since QDs are brighter than most organic dyes, detection precision is improved.<sup>30</sup> Filho and others CdTe QDs were employed as fluorescent probes for the FACS technique to detect the blood groups using monoclonal antibodies against the A and B antigens on the surface of red blood cells (RBCs).<sup>31</sup> The bioconjugate demonstrated great efficacy and exhibited stability for more than six months. Furthermore, when acted with specific targeting ligands to identify target markers, QDs have the potential to replace antibodies that are widely used to stain cell surface markers due to their superior stability and affordable cost. is used from. Unlike antibodies, QDs are readily absorbed into cells, allowing intracellular markers to be stained. This eliminates the need for permeabilization buffers, which negatively affect cell viability and fluorophore potential and adds complexity to FACS assays.<sup>32</sup>

### Drug delivery system

Due to its focus on the delivery mechanism and ability to distinguish between sick and healthy cells through metal affinity-driven self-assembly between synthetic polypeptides and semiconductor core QDs, QDs have relatively few side effects. As drug delivery methods, QDs offer several appealing qualities, including as their simplicity of production, versatility in drug conjugation, comparable physicochemical characteristics, and intriguing optical properties that make them traceable drug carriers which, upon administration, may be conveniently tracked.<sup>33</sup> Principle of traceable medication delivery to tumours utilising QDs. To achieve the significant tumor accumulation required for cancer therapy, PEGylation is commonly used to prolong the circulation time after intravenous administration.



The fabricated QDs exhibited high stability and biosafety as well as blue photoluminescence and pH-responsive drug release under physiological condition.<sup>34</sup> Figure 4 shows how drug delivery is done with the help of QDs.



**Figure 4** QDs as drug delivery systems. Created by BioRender.com.

Examples are Cd/Se QDs containing vapreotide, which can be used to treat blood malignancies,<sup>35</sup> and PEGylated MoS<sub>2</sub> QDs can be used for traceable delivery of doxorubicin to cancer cells.<sup>36</sup>

Dynamin, a membrane protein, then facilitates the release of these vesicles from the cell membrane into the cytoplasm where endosomes are formed. QDs are released into the cytosol and are available to function and release their cargo if they can exit the endosomes. Otherwise, they are broken down by lysosomal degradation. In caveolae-mediated endocytosis, binding of functional particles to their receptors facilitates their internalization into target cells via caveolae, the invasion of cholesterol-rich flask-shaped membranes that detach from the cell membrane, create caveosomes. To optimise the effectiveness of medication delivery to the target cells, caveosomes are hypothesised to be fewer damaging vesicles than endosomes. In the process of macropinocytosis, certain ligands can cause cell membrane ruffles to develop, engulfing the particle and leaking it into the cytosol as macropinosomes.<sup>37</sup>

## Quantum dots for the detection and treatment of cancer

Imaging is a crucial diagnostic tool for selecting the best cancer treatment. For cancer screening and staging, several imaging methods are being employed, including X-rays, computed tomography, ultrasound, radionuclide imaging, and MRI. evaluating the success of cancer treatment and keeping track of recurrence (reviewed in) However, there are two significant drawbacks to existing imaging techniques. First, they lack the sensitivity to identify tiny numbers of malignant cells at original or metastatic locations. Is Second, cancer cell surface markers were not intended to be detected by the imaging techniques.<sup>38</sup> These cell surface indicators can frequently serve as cancer therapeutic targets and aid in the detection and categorization of malignancy. These restrictions call for the development of novel imaging techniques that are extremely sensitive and bispecific quantum dot (QD) imaging probes, even if they are still in the early phases of research, in order to satisfy the demands of *in vivo* imaging. visualising a cancer patient.<sup>39</sup>

One of the most promising items in the arsenal of nanomedicine is bioconjugation quantum dots. Numerous medical uses for these

nanocrystal fluorophores are possible, including photodynamic treatment, targeted drug administration, nano diagnostics, and imaging. Bioconjugation quantum dots' distinctive optical characteristics, including as broadband excitation, size-tunable narrow emission spectra, and strong photostability, are responsible for the wide range of possible applications.<sup>40</sup>

When stimulated by light, drug delivery quantum dot nanocrystals fluoresce and release vivid colours that may be used to recognise and monitor many biological characteristics and processes. They have several benefits over traditional fluorophores, including the ability to be tweaked reliably based on their size, shape, and inherent solid-state characteristics. Due to its adaptability, it has uses in a variety of sectors, including cancer research, drug development, and cell biology.<sup>41</sup> Millions of individuals lose their lives to cancer every year, particularly lung cancer. Even though there is currently no cure for cancer, tumour therapeutic options including surgery and quantum dots are new fluorescent probes for molecular and cellular imaging that are extremely small, nanometre-sized light-emitting particles. Quantum dot cancer therapy provides special optical and electronic qualities in cellular imaging such as wavelength-tunable emission, improved signal brightness, resistance to photobleaching, etc. in contrast to organic dyes and fluorescent proteins. It took QD. -based probes with warheads aimed at the tumor to attain such remarkable optical characteristics.<sup>42</sup>

## Protein detection

Today, several methods for protein detection have been developed. General technique illustration: First, the target protein is selectively recognized and bound to by a monoclonal biotinylated antibody. The biotin-labeled antibody is then bound by a QD-avidin. A QD-Biotin then binds to a QD-Avidin. A QD-avidin finally binds to a QD-biotin. These actions are repeated until numerous QDs have been sequentially enriched on an antibody, increasing the fluorescence intensity.<sup>43</sup>

The imaging of intracellular target proteins in living cells, on the other hand, is crucial for comprehending intracellular processes and clarifying a variety of biological phenomena. Due to their long-term photostability and adjustable narrow emission spectra with wide excitation, QDs have been widely used for a variety of cellular imaging applications. Surface-decorated QDs can be created and tuned for precise intracellular targeting in living cells using PEGylation and cell-penetrating peptide (CPP).<sup>44</sup>

## QDs in clinical application

With the help of QDs, cancer in cancer cells can be identified. It is utilized for clinical therapy, disease stage prognosis, and diagnosis. Comparable fluorescent tubes are 20 times slower and 100 times less stable than QDs. When it comes to getting siRNA, a tool for silencing genes, into cells, QDs are vastly superior than current delivery techniques.<sup>45</sup>

They may be altered using various molecules and linkers to enhance their functionality for certain applications, which is a major characteristic. QDs have been employed to specifically label important molecules, proteins, and cells.<sup>46</sup> About sentinel lymph node (SLN) mapping, which entails locating the first lymph node that drains a tumor, diagnostic tools (such as imaging), therapeutic uses (such as medication administration and cancer treatment), live cell labelling, and long-term tracking, QDs hold a lot of promise.<sup>47,48</sup> Without QDs, it would not have been possible to undertake non-invasive surgery in the manners that multicolor *in vivo* imaging has enabled.<sup>49</sup>

## As promising antimicrobial agents

There have been reports of considerable antibacterial activity in several metal oxides, including TiO<sub>2</sub>, MgO, and ZnO. These compounds are safer and more heat-resistant than traditional organic antimicrobials. It has been demonstrated that ZnO-QDs are effective against *Escherichia coli* and *Bacillus subtilis*.<sup>50</sup>

A variety of clinical trials are being carried out in response to the epidemic of the new coronavirus, known as SARS-CoV-2, which occurred in January 2020, with the goal of totally controlling or curing the illness. Coronavirus disease 2019 (COVID-19) detection tools or vaccinations, however, are still elusive. To battle this unique virus, surface engineering may prove useful in the production of antiviral nanomaterials with improved specificity. Quantum dots (QDs) are adaptable substances with the capacity to combat or hinder the COVID-19 virus's activities.<sup>51</sup>

## QDs in the healthcare market: the associated challenges

### QDs in the Healthcare Market

According to the company's projection, NANOCOTM would hold a significant share of the USD 1 billion QD healthcare industry by 2022. One of NANOCO's QDs-based marketing products for use in medical biosensing applications is HEATWAVETM. This device can non-invasively measure a variety of biomolecules of interest in human blood, such as hemoglobin (at 575 nm), bilirubin (at 455 nm), and glucose, throughout a broad range of electromagnetic spectrum (400-1650 nm) (at 1650 nm can be used in series). Another commercially available tool, VIVODOTS®, use QDs to interactively map tumour tissue and prevent the needless removal of healthy tissue. In 2021, the market for QDs was estimated to be worth USD 4 billion, and in the following five years, it is expected to reach USD 8.6 billion. There is growing interest in the biological uses of QDs, even though this industry is dominated by display devices and LED applications. Quantum Dots (QD) Market is expected to reach US\$ 5.76 Bn. by 2026, at a CAGR of 29.9% during the forecast period.<sup>52</sup>

## Challenges hampering the clinical translation of QDs

Despite the advantages, there are still some significant restrictions on the general application of QDs as bioimaging instruments. QDs behave like nano colloids when compared to typical organic fluorophores. This makes their long-term usage in biocompatibility more challenging.

### Pharmaceutical issues

QDs are ultrafine colloidal particles having a large surface and a metallic character, making them susceptible to aggregation, degradation, hygroscopicity, or redox chemical changes from a pharmacological perspective.<sup>53</sup> Any small modification to the physico-chemical characteristics of QDs can have a significant impact on their optical characteristics. Regardless of particle size or native surface ligands, the suggested technique successfully shields QDs from oxygen and enhances their quantum characteristics. In a different method, the INP/ZnSeS core/shell QDs and the CdSe/CdC core/shell QDs are shielded from heat and oxidation by being covered in a crosslinked biopolymer shell (methyl methacrylate-b-glycidyl methacrylate). was preserved.) block copolymer ligands (P(MMA-b-GMA)-SH. The inner cross-linked shell offered defence against oxidation, whereas the outer transparent PMMA shell did not alter

the optical characteristics of the QDs.<sup>54</sup> When forming QDs by the very productive and popular method of organometallic synthesis, there is an additional issue of poor water solubility. The previously described suggested remedies include covering with hydrophilic shells, replacing hydrophobic surface ligands with hydrophilic thiol-containing compounds, and using water-based synthesis.<sup>55</sup>

### In vivo issues

Through interactions with DNA or oxidative damage to biological components, QDs are linked to intracellular toxicity. The danger rises with the usage of heavy metals like lead and cadmium, which build up in the bones without being significantly excreted from the body. Additionally, QDs' ultrafine particle size accelerates their early removal from the body through renal clearance. It has been suggested that PEGylation of QDs is a generic method for altering their biodistribution and lengthening their lifetime in circulation.<sup>56</sup> In comparison to cations, QDs with neutral or negatively charged surfaces are less susceptible to glomerular filtration. It is also possible to alter the size and stiffness of QDs to alter the rate of glomerular filtration. Alternatively, several surface alterations have been created to enable the elimination of metal QDs, which accumulate hazardous waste in the body.<sup>57</sup>

### Industrial issues

QDs encounter several industrial obstacles when going from mass production at the laboratory size to industrial scale. First, the mass manufacture of QDs is an extremely intricate and multi-step procedure due to the numerous surface alterations needed to alter their performance.<sup>58</sup> Second, it is challenging to keep the physico-chemical characteristics of large-scale QDs uniform. Third, residues of contaminants in components or solvents, which on a small scale have no noticeable effects, grow, and have a significant negative impact on the quality and effectiveness of the QDs created.<sup>59</sup> Fourth, the large-scale manufacture of QDs involves environmental risks brought on by poisonous organic solvents or harmful heavy metals like Cd and Pb.<sup>60</sup> To lessen the environmental risks associated with heavy metals and to demonstrate equivalent optical performance, cadmium-free QDs such as silicon, graphene, and carbon QDs were introduced. Other environmentally friendly techniques have been created, including ones that utilise reused parts, dry heating, or microwave-based synthesis.<sup>61</sup>

### Future perspectives

To increase the clinical transferability of QDs, there are few important considerations that should be considered. To reduce environmental risks, increase scalability, and avoid unneeded post-synthetic changes that eventually raise system complexity and production costs, it is first necessary to employ green, green, and aqueous solvent-based or bioengineered synthesis processes. will lessen Second, to increase stability and scalability, functionalized coatings with intelligent materials such pH-responsive polymers and tissue-affinity self-locating biomaterials should take the place of the current ligand-based alterations.<sup>62</sup> Third, to lessen the biosafety risks brought on by the build-up of heavy metals in the body, the idea of heavy metal-free QDs should be embraced. Fourth, to ensure that administered QDs remain in the body long enough to achieve their intended application, a balance between the body retention and clearance capacity of QDs must be reached through modification of particle size, charge, and surface area attributes. may be used while holding. Withdrawal from the body to reduce the chance of ingesting poison. Fifth, to compete with traditional alternatives that have widespread commercial availability and have well-established methods, it is crucial to build adequate experimental techniques for

a variety of QD applications. To bring this incredible technology to the clinic for the benefit of patients and the industry, QD research and development must continue.<sup>63</sup>

## Conclusion

Quantum dots (QDs) are a versatile tool for fluorine immunoassay, multiplex imaging, dual imaging, and therapeutic platforms that enable real-time and cellular process imaging *in vivo* and the tracking of individual cells and biological components. They also represent a more accurate diagnostic tool. The design and development of QDs has advanced dramatically over the past ten years as a result of the sharp rise in interest in inorganic particles. The most promising publications to far have only dealt with *in vitro* and *ex vivo* applications, even though QDs as biological probes have shown promise in a variety of domains. Along with a focus on their professional standing, the significance of QDs in biological sciences is also given in terms of their properties. These QD-based techniques should result in considerable improvements in enabling pre-treatment analysis and predicting therapeutic success in particular individuals - a key goal for the achievement of personalised medicine - with further validation of the technology.

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## Conflicts of interest

All authors declare that there is no conflicts of interest.

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