

Review Article



# Biosynthesis of Quantum Dots and Their Therapeutic Applications in the Diagnosis and Treatment of Cancer and SARS-CoV-2

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## Abstract

Quantum dots (QDs) are semiconductor materials that range from 2 nm to 10 nm. These nanomaterials (NMs) are smaller and have more unique properties compared to conventional nanoparticles (NPs). One of the unique properties of QDs is their special optoelectronic properties, making it possible to apply these NMs in bioimaging. Different size and shape QDs, which are used in various fields such as bioimaging, biosensing, cancer therapy, and drug delivery, have so far been produced by chemical methods. However, chemical synthesis provides expensive routes and causes *serious environmental* and health issues. Therefore, various biological systems such as bacteria, fungi, yeasts, algae, and plants are considered as potent eco-friendly green nanofactories for the biosynthesis of QDs, which are *both economic and environmentally safe*. The review aims to provide a descriptive overview of the *various microbial agents for the synthesis of QDs* and their biomedical applications for the diagnosis and treatment of cancer and SARS-CoV-2.

## Introduction

Quantum dots (QDs) are semiconductor nanomaterials (NMs) with the size range 2-10 nm, which due to their tiny size, have different unique optoelectronic properties compared to their bulk.<sup>1</sup> The green synthesis of nanoparticles (NPs) has been introduced as an alternative method to chemical synthesis as it is safe, nontoxic, and highly applicable for biomedical applications.<sup>2-5</sup> Bio-based synthesis of QD is a type of bottom-up synthesis. Due to the proven applications of NMs, especially QDs in the field of biomedicine, and the need for developing cheaper and less polluting techniques, the biosynthesis of NP techniques, especially QDs, is developing gradually.<sup>2,6</sup> NPs produced by biosynthesis are more stable and have a more controlled shape.<sup>7</sup> The effects of the surface to volume ratio and quantum size on nanoscale cause them to exhibit new optical, electronic, magnetic, and structural properties and thus can be used in various fields of technology, especially in biomedicine.<sup>8</sup> In this regard, finding new biological sources such as plants, fungi, and microbial strains with a higher ability to produce biocompatible NPs with various sizes and shapes is one of the important steps developing the application of NMs in biomedicine.<sup>9-12</sup> Due to their special optical properties such as high brightness, photobleaching resistance, and highly good surface-to-volume ratio, QDs can be used in a variety of in-vitro and

in-vivo bioimaging, the feature of which can be applied to enhance imaging techniques, especially in the diagnosis of the early stage of cancerous tumors.<sup>13</sup> Further, because of the above-mentioned properties, various QDs have been introduced for treating microbial infections and cancer by assisting drug delivery mechanisms.<sup>14-17</sup> As the main physical feature, QDs are extraordinary NMs owing to their tiny size generating physically confined electron cloud as the quantum confinement resulting in unique optical (emitting higher energy light in blue color) or electronic properties.<sup>18</sup>

For semiconducting QDs, this property is resulted from the transition of an electron from the valence band to the conduction band, which the excited electrons can drop back into the valence band and release their energy as photoluminescence. In this way, optical applications of QDs are caused by their high extinction coefficient and optical nonlinearities suitable for all-optical systems.<sup>19</sup> In the case of therapeutic applications, these NMs have shown anticancer property as well as antibacterial activity against various strains of Gram-negative and Gram-positive bacteria in a dose-dependent manner.<sup>20</sup> However, the major disadvantages for biomedical application of QDs are potential toxicity in physiological conditions, poor aqueous stability and solubility, prone to photo-bleaching, complexity in controlling bio-distribution property for *in*

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*vivo* multiplex imaging.<sup>13</sup>

Coronavirus disease 2019 (COVID-19), an infectious disease, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been identified firstly in Wuhan, China in December 2019. Several antiviral drugs such as remdesivir/favipiravir (inactivator of RNA-dependent RNA polymerase) and lopinavir/ritonavir (the protease inhibitor) have been employed to hinder SARS-CoV-2.<sup>21</sup> However, the major side effects of these drugs including liver dysfunction, chest tightness, dark-colored urine, flushing, headache, hives, itching, light-colored stools, nausea, vomiting, and thrombocytopenia have led to finding more effective micro and nano formulations.<sup>22,23</sup> Antimicrobial activities of QDs have been reported by various studies.<sup>15,24</sup> According to recent studies,<sup>25-27</sup> NMs specifically QDs can be employed to diagnose and treat COVID-19. Nonetheless, the possibility of QD toxicity to cells in the human body is one of the main limitations in the development of their use, especially in the field of biomedicine.<sup>28</sup>

Given the above-mentioned explanations, this study aimed to investigate and introduce QD biosynthesizing organisms for the development of green chemistry mechanisms in nanobiotechnology. There are top-down and bottom-up approaches as two main ways for synthesis of various NMs (Figure 1A).<sup>29,30</sup> Top-down approach is majorly based on the physical methods such as X-ray lithography, molecular beam epitaxy, milling, and ion implantation, which high energy is needed to reduce size of bulk materials up to the nano scale (1-100 nm). In the case of bottom-up approach, in the colloidal solution, QDs are synthesized by self-assembly mechanism followed by chemical reduction.<sup>11,31</sup> In fact, one of the negative points in many studies in the biomedical field is the use of chemical techniques for the development of QDs. As mentioned earlier, these chemical techniques are destructive to the environment. Nevertheless, no QD-based techniques and drugs have been observed in biomedical applications due to the toxicity and biocompatibility of the QDs synthesized with these chemical methods, as well as the high cost of synthesizing these QDs.<sup>32</sup> In contrast, biosynthesis techniques can be considered as biocompatible and cost effective approach to prepare QDs.

### Biosynthesis of QDs

To date, the biosynthesis of QDs has been reported in a variety of organisms.<sup>33</sup> Among the various NP biosynthesis techniques, extracellular biosynthesis is more cost-effective than intracellular biosynthesis due to the lack of special treatments to purify the produced NPs.<sup>2</sup> Preparation of NMs is the first step in nanobiotechnology.<sup>29,34,35</sup> Biosynthetic organisms, when exposed to metal ions, accumulate them in or on their cell wall, which eventually leads to the production of NPs.<sup>36</sup> It should be considered that the main goal is to obtain biocompatible QDs without disadvantages of

expensive methods of laser irradiation, spray pyrolysis, electrolysis, and radiolysis or using toxic materials such as N,N-dimethylformamide, cetyl trimethylammonium bromide, and sodium dodecyl sulphate.<sup>37</sup> There are three stages in the formation of NPs in living systems, including biodegradation, biomineralization, and enzymatic reactions. Biodegradation is the first organism response to toxic ions.<sup>12,38,39</sup> Furthermore, biomineralization leads to the stabilization of NPs on the solid phase, and finally, enzymatic reactions lead to the growth of QDs.<sup>33</sup> The main steps of each QD biosynthesis process are presented in the following sections.

### Biological synthesis of QDs under different strategies

According to previous research, different strategies such as wet biomass (growing cultures/ resting cultures), culture supernatant, cell-free extract, and dry biomass are used in the biosynthesis process of different metal/metalloid NPs and QDs as intracellular or extracellular pathways (Figure 1A-B).<sup>40-42</sup>

### Evaluation of the effect of different parameters on QD synthesis

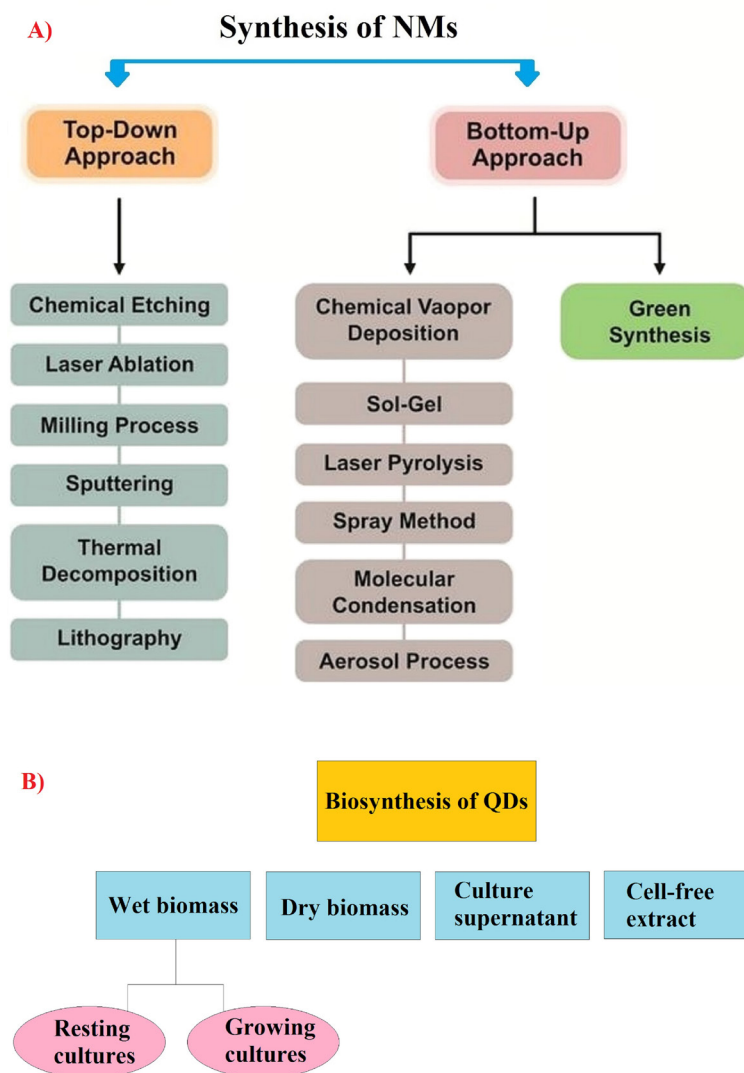
The effects of various parameters such as precursor concentration, temperature, pH, stirring time, reaction time, and inoculum amount can be evaluated on the yield, morphology, and size of the NPs. More precisely, the amount of produced QDs is majorly affected by the changing these parameters, thus this stage is highly important in the overall process of biosynthesis, the details of which are depicted in Figure 2.<sup>33,45-47</sup>

### Characterization techniques

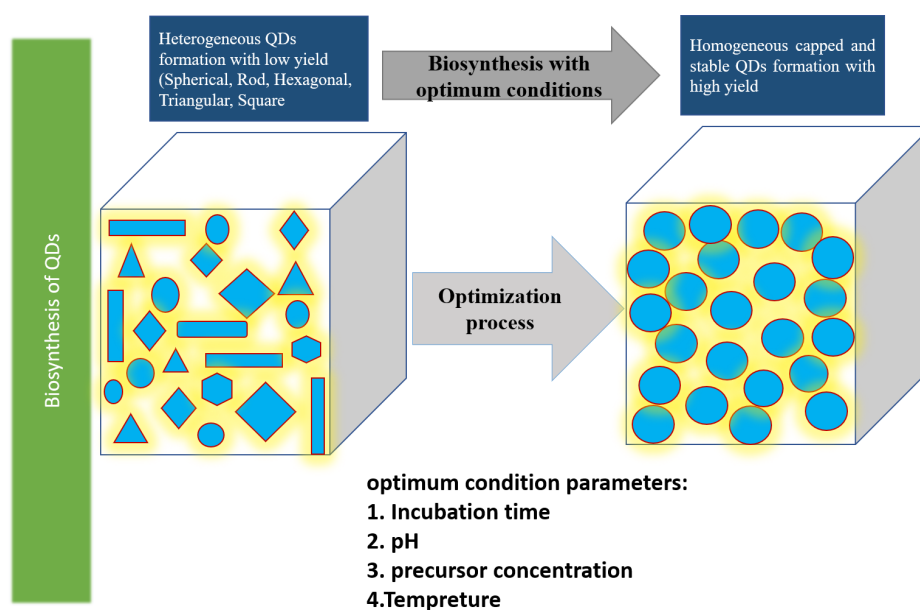
QDs have been characterized using different techniques, including UV-Vis spectroscopy, Fourier transform infrared spectroscopy, X-ray photoelectron spectroscopy, X-ray absorption spectroscopy, N<sub>2</sub> adsorption-desorption, high-resolution transmission electron microscopy, scanning electron microscopy, energy dispersive X-ray analysis, dynamic light scattering, and X-ray diffraction.<sup>28,49-51</sup>

### QD biotoxicity tests

Low toxicity includes requirements for the use of metal QDs in biomedical applications. The produced QDs must have the least amount of toxicity to vital factors in living cells. One of the advantages of QD biosynthesis is its safety due to the presence of capping proteins on the produced QD for reducing its toxicity. MTT assay and inhibition zone are the two most common tests at this stage. The bioassay of biological systems and the toxicity of produced QDs in-vitro are measured in MTT assay. In this technique, 3-(4,5-dimethylthiazol-2-yl)-5-(3-methyladenine) tetrazolium bromide is used in 96 wells. Cell and sample uptake are then divided by control sample uptake and multiplied by 100 to determine cell viability. In the inhibition zone, model organisms such as *Escherichia coli* are applied, followed by employing the



**Figure 1.** Two approaches for synthesis of NMs (A) and various strategies for biosynthesis of quantum dots (B). (Note: QD: Quantum dot). Copyright under the conditions of the Creative Commons Attribution (CC BY) license<sup>43,44</sup>



**Figure 2.** The effect of different parameters on the biosynthesis of QDs for detecting optimum conditions such as optimum pH, precursor concentration, temperature, and incubation time. Note: QD: Quantum dot<sup>48</sup>

radius of the non-growth zone after a certain period of incubation to determine the toxicity of QDs.<sup>28,52</sup> Table 1 summarizes a collection of different species used for the synthesis of QDs.

### Diagnosis and treatment of cancer

QDs, as semiconductor NMs, are most commonly used in the diagnosis, imaging, labeling, and treatment of various diseases. Highly applied QDs include CdS, CdTe, CdSe, PbSe, PbS, SnTe, PbTe, InP, and InAs, but Cd-based QDs have the most applications due to their unique physicochemical

properties.<sup>76</sup> The unique photoluminescence properties of QDs have led to their application in in-vitro and in-vivo imaging, and they can also play an important role in drug delivery processes used for cancer treatment. Due to the toxicity of ordinary QDs, carbon dots have been considered for radiotherapy applications.<sup>77</sup> According to some findings, carbon dots can damage bacteria, yeasts, and other organisms by generating oxygen radicals, but it is not yet clear whether these substances can damage human cells.<sup>1</sup> This antibacterial mechanism is critical issue to hindering pathogenic bacteria specifically antibiotic-

**Table 1.** Potential biological sources used for the biosynthesis of different QDs

Type of QDs	Size and shape	Organism	Extracellular/Intracellular	Reference	Year
CdSe	Spherical QDs with an average size of 11 nm	<i>Fusarium Oxysporum</i>	Extracellular	53	2007
CdTe	The size range of 2-3.6 nm with spherical shape	Yeast cells	Extracellular	54	2010
CdS	Spherical QDs by an average size of 6 nm	<i>Saccharomyces cerevisiae</i>	Extracellular	55	2012
CdTe	15–20 nm, spherical	<i>Fusarium oxysporum</i>	Extracellular	51	2013
CdS	A mean grain size of 2.56 nm with spherical shape	<i>Phanerochaete chrysosporium</i>	Extracellular	56	2014
CdS	A spherical shape and 4-5 nm in size	<i>Pleurotus ostreatus</i>	Extracellular	57	2015
CdSe	15 to 20 nm and spherical	<i>Saccharomyces cerevisiae</i>	Extracellular	58	2015
ZnS	4 nm and spherical	<i>Clostridiaceae</i> sp.	Extracellular	40	2016
CdS	6.11 nm and circular	<i>Fusarium oxysporum</i> f. sp. <i>lycopersici</i>	Extracellular	59	2017
ZnS	20–40 nm with a large agglomerated structure	SRB	Extracellular	60	2017
Ag	<10nm and spherical	<i>Eichhornia crassipes</i>	Extracellular	61	2017
CdS	10 nm and spherical	<i>E. coli</i>	Extracellular	47	2017
CdS	<20 nm and spherical	<i>Acidithiobacillus thiooxidans</i>	Extracellular	62	2018
CdS	Spherical shape with the size of 2.31, 2.59, and 2.59 nm for green, orange and yellow fluorescent QDs, respectively	<i>Pseudomonas fragi</i>	Extracellular	63	2019
CdSe	2 to 4 nm with cubic shape	<i>Providencia vermicola</i>	Extracellular	46	2019
ZnS	An average particle size of 6.5 nm with circular shape	SRB	Extracellular	64	2019
CdSe	An average size of 3.1 nm with spherical shape	<i>E. coli</i>	Extracellular	65	2019
CdS	Spherical morphology with a size of 2–7 nm	<i>Rhaphanus sativus</i> (hairy roots)	Extracellular	66	2020
CdS	A mean size of 6.7 nm with spherical shape	<i>Pseudomonas chlororaphis</i>	Extracellular	45	2020
CdSe	A narrow size distribution of 3.2 nm and spherical QDs	<i>Rhodotorula mucilaginosa</i>	Extracellular	67	2020
Ag <sub>2</sub> Se	Spherical QDs with an uniform size of 3.9 nm by	<i>Saccharomyces cerevisiae</i>	Extracellular	49	2021
ZnCdS	An average particle size of 6.12 nm in monodisperse spheres	SRB	Extracellular	68	2021
CdS	An average size of 6 nm with circular shape	<i>E. coli</i>	Intracellular	69	2011
CdTe	Spherical QDs with a mean diameter of 2.33 nm	<i>Lumbricus rubellus</i> (earth worm)	Intracellular	70	2013
CdS	Spherical shape by a diameter predominantly from 5 to 7 nm	Plant hairy root ( <i>Linaria maroccana</i> )	Intracellular	71	2014
Ag <sub>2</sub> S	Spherical QDs and an average diameter of 5.21 nm	Wheat endosperm cells	Intracellular	72	2016
HgTe	Non-spherical shape with up to 20 nm in diameter	<i>Allium fistulosum</i>	Intracellular	73	2016
SnO <sub>2</sub>	A mean particle size of 7 nm and spherical morphology	<i>Clitoria ternatea</i> (plant)	Intracellular	50	2020
PbS	A particle size in the range 3.47–11.45 nm and spherical shape	<i>Pseudomonas aeruginosa</i>	Intracellular	74	2020
CdS	Sphere-shaped QDs with the size in the range 4.63-17.54 nm	<i>Pseudomonas aeruginosa</i>	Intracellular	75	2021

Note. CdS: Cadmium sulfide; ZnS: Zinc sulfide; Ag<sub>2</sub>Se: Silver selenide; SnO<sub>2</sub>: Tin(IV) oxide; CdTe: Cadmium telluride; CdSe: Cadmium Selenide; ZnCdS: Zinc cadmium sulfide; PbSe: Lead selenide; Ag<sub>2</sub>S: Silver sulfide; PbS: Lead sulfide; Ag: Silver; HgTe: Mercury telluride; SRB: Sulfate-reducing bacteria; *E. coli*: *Escherichia coli*; QD: Quantum dot.

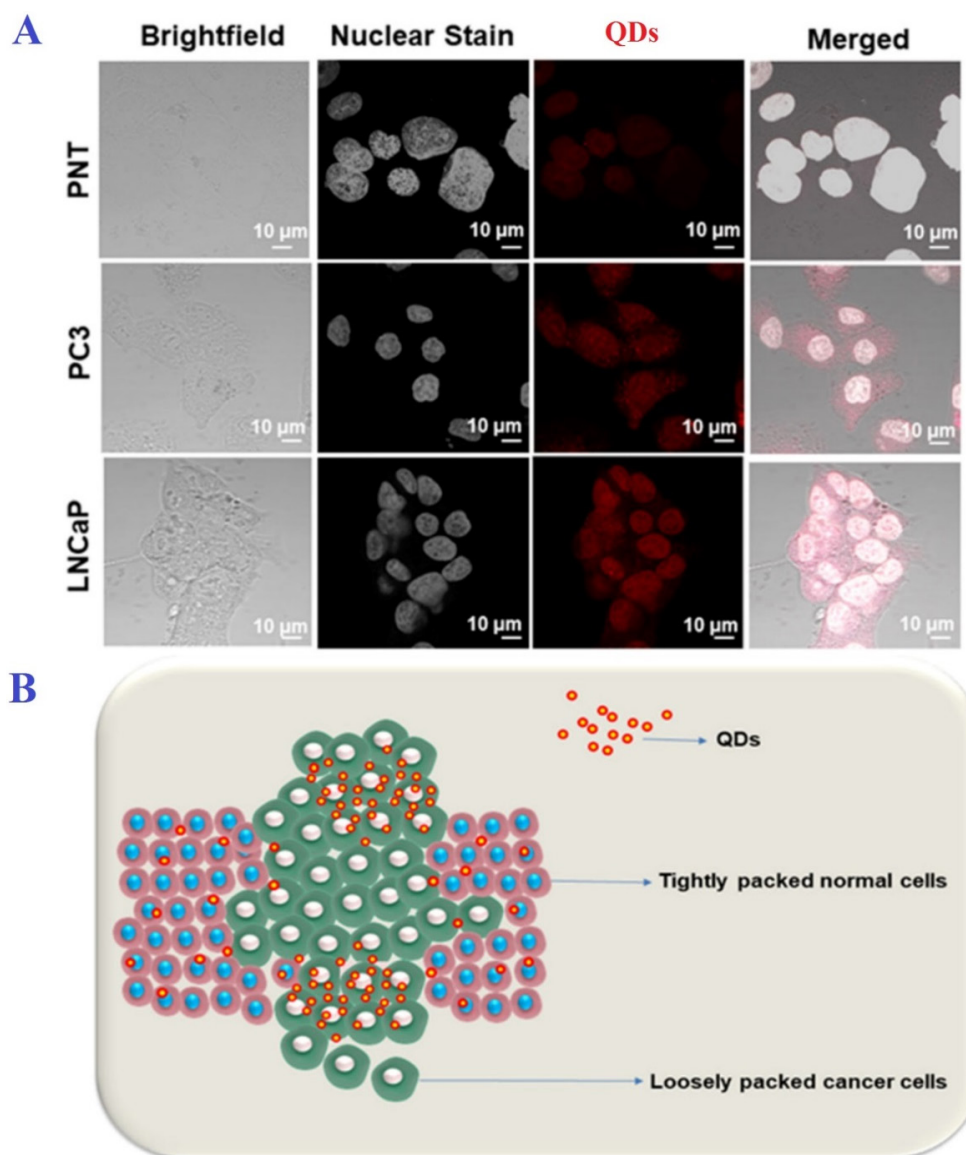
resistance ones.<sup>78,79</sup> However, the use of QDs in bioimaging is limited due to their low specificity and inability to detect early-stage cancer tumors.<sup>80</sup> Produced QDs by biological sources make these QDs biocompatible in bioimaging and anti-cancer drug applications. In fact, different metals may normally be non-toxic in the body but become toxic when their structure is at the quantum level. Therefore, determining the biotoxicity of the applied QDs is highly important in preclinical studies in this field.<sup>81</sup>

### Bioimaging of cancer cells

Detection of cancer in the early stages can reduce its risks by 30-50%. Therefore, due to their extraordinary fluorescent properties, QDs can be used in bioimaging to identify cancer cells, even in extremely small tumors.<sup>82</sup> Conventional imaging techniques such as MRI and photoluminescence are unable to accurately detect cancerous tumors, especially in small cases due to their low

resolution, and have a significant error rate. Accordingly, QDs have been proposed to increase the resolution of these imaging techniques.<sup>83</sup> In other words, bioimaging by QDs is based on the identification of the specific biomarkers of cancer cells and is divided into in-vitro and in-vivo categories. In in-vitro bioimaging, numerous studies have been considered to develop the use of QDs to image the cancer cells of melanoma, ovary, breast, pancreatic, glioblastoma, ovarian epidermoid, lung, hepatocellular, and adenocarcinoma.<sup>1,84</sup> For example, in a study by Ncapayi et al., prostate cancer cells with high specificity, compared to normal prostate cells, were imaged by AgInSe/ZnS QDs (Figure 3).<sup>85</sup> In in-vivo bioimaging, the biomarkers of cancerous tumors by binding to QDs are involved in in-vivo imaging techniques.<sup>1</sup> In these techniques, fluorescent QDs are injected into mice, and their fluorescent activity is identified by detectors.<sup>86</sup>

The stability of the applied QD during the imaging



**Figure 3.** A) *In vitro* bioimaging of prostate cancer cells (PC3), normal prostate cells (PNT), and human adenocarcinoma cells (LNCaP); B) Possible pathway for the uptake of QDs in normal and cancer cells. Note. QD: Quantum dot. As shown, AgInSe/ZnS QDs could distinguish cancer cells from non-cancerous cells. Copyright under the conditions of the Creative Commons Attribution (CC BY) license<sup>85</sup>

process is one of the important points in bioimaging. Studies demonstrate that the biological samples are exposed to QDs after a while, and their illumination represents a significant reduction. Thus, Kim et al. used a CdSeZnS/ZnS QD alloy alongside multi-layered QDs. Finally, the QD-Cd alloy produced extremely sharper images. This sharpness was more evident in both in-vivo and in-vitro bioimaging.<sup>87</sup> In addition, Ag-In-S/ZnS (AIS/ZnS) QDs with fluorescent emission in red color were used to *In vivo* fast imaging of the rat lymphatic tumor.<sup>88</sup>

### Cancer drug targeting

Chemotherapy is one of the main methods of killing cancer cells because cancer cells have a higher growth rate compared to normal cells. However, chemotherapy targets cells with a high growth rate, some normal cells (Skin, hair follicles, and the cells of the gastrointestinal tract) also have high growth rates and are affected by this treatment. Nanocarriers can target cancer cells efficiently by passive and active targeting as two main targeting methods.<sup>89</sup> Passive targeting is based on the property of the enhanced permeability effect, which occurs due to the permeability of the arteries in the tumor-containing area and causes anti-cancer drugs to spread more in the tumor-containing areas.<sup>90</sup> In active targeting, the specific and altered surface of cancer cells and their ability to bind to anti-cancer drugs are specifically applied in this technique (Figure 4).<sup>91</sup> Nanocarriers increase the half-life of the drug in the body, increase the solubility of anti-tumor substances, and can play a highly significant role in enhancing the performance of anti-cancer drugs.<sup>92,93</sup> The structure of QD-based carriers includes a core, a shell, and a capping structure on them. Graphene QDs, cadmium QDs, and carbon QDs are typically used as the major carriers of anticancer drugs. The discussion of the difference in the function of cancerous tumors from one person to another is one of the main challenges in the development of the anti-cancer quantum drug carrier, and

this personalization is extensively important in therapeutic discussions, as well as the unknown factors in different cancers. This is the next challenge that must be solved in the future. Highly sensitive DNA nanostructures with a hybrid structure can be extremely important candidates in the field of drug delivery.<sup>94</sup> Some studies have combined QDs applied in biomedical fields, including carbon and Cd-based QDs, with magnetic NPs to use both specific optical and magnetic properties in combination in drug delivery processes in order to enhance the performance of nanocarriers. It is noteworthy that the biotoxicity of these manufactured nanocarriers is one of the main limitations in this field.<sup>95</sup> The mentioned nanocarriers cannot be employed for metastatic tumors. Another discussion is the development of more cost-effective nanocarriers in this field that may enable the development of effective and cost-effective anti-cancer nanocarriers in the future.<sup>96</sup> QDs can bind to antibodies, peptides, small molecules, and the like and deliver substances with medicinal properties to their target cells with high specificity. Various anti-cancer drugs such as doxorubicin (ZnO QDs), cisplatin (graphene QDs), and paclitaxel (ZnSe:Mn/ZnS QDs) have been linked to different QDs, and research is ongoing to find the best QDs to connect the identified common anticancer drugs.<sup>97</sup> As shown in Figure 4, QDs nanocarriers can be used for passive and active targeting in cancer therapy.<sup>94</sup>

### Application of QDs in detecting and treatment of COVID-19

The virus-sensitive properties particularly electrochemical and biochemical features for the production of next-generation viral biosensors have been utilized for detecting various pathogens.<sup>98,99</sup> In this technique, the specific antibody of each virus is placed on the probe in contact with a QD, and the virus-related antigen can be detected by various detectors such as spectroscopy and the like if it is attached to the antibody on the fluorescent prop.<sup>25,100</sup>

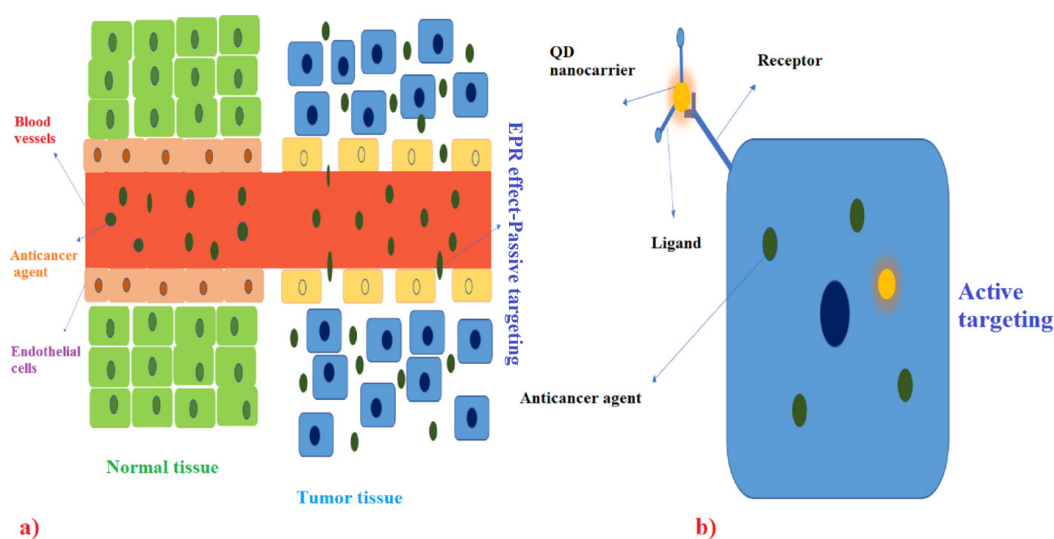


Figure 4. Passive and active targeting in cancer therapy by QDs nanocarriers. Note: QD: quantum dot<sup>94</sup>

The production of strong and detectable light with an extremely small amount of QDs is the main advantage of using QDs in the preparation of virus detector props over fluorescent proteins, representing the extensively high sensitivity of QDs in detecting viruses.<sup>101</sup> The COVID-19 pandemic has killed approximately 6 million people by March 2022 around the world.<sup>102</sup> The development of new and highly sensitive and cost-effective techniques in the field of SARS-CoV-2 virus detection is one of the main steps, along with extensive and comprehensive vaccination in the field of pandemic control. In the use of the QD props for SARS-CoV-2 detection, props are based on the detection of antibodies, antigens, and RNA/DNA (Table 2). In this regard, Li et al. developed a kit based on the lateral flow assay technique that detects antibodies to the virus with high specificity.<sup>103</sup> One of the key benefits of using QDs is the lack of a need for initial pretreatment for

the real-time polymerase chain reaction, minimizing the risk of aerosols and thus laboratory personnel (Figure 5).<sup>104</sup>

### COVID-19 treatment

SARS-CoV-2 binds to angiotensin-converting enzyme 2 (ACE2) receptors through its receptor-binding domain (RBD) portion. In a bioinformatics study by Ramezani et al, connectivity between carbon QDs binding energy levels (-699.3 kJ/mole) have been extremely lower than favipiravir as effective nonspecific antiviral drugs (-487.2 kJ/mole), indicating the potential of carbon QD as an antiviral that can be prescribed at a lower dose and with fewer side effects for treating COVID-19 patients. The main function of these QDs is to cover the RBD to prevent the virus from attaching to the ACE2 receptor (Figure 6).<sup>26</sup> Additionally, QDs can act as a delivery system for COVID-19 vaccines and drugs to reduce the side effects of various COVID-19 drugs with high accuracy by taking lower doses of drugs. According to some studies, QDs can also be useful in the development of inhibitory drugs.<sup>110</sup>

### Conclusion

This review article attempted to explain the general principles of QD biosynthesis and biomedical applications as an effective, environmentally-friendly, biocompatible, and cost-effective technique. To develop this green technique, we must continue to seek new organisms in nature. There must be potentially undiscovered biosynthetic strains in nature that have not been tested yet. The application of QDs has been proven in the diagnosis and treatment of different illnesses. This review focused on investigating the use of QDs for diagnosing and treating two important and deadly diseases of the present age, namely, COVID-19 and cancer.

### Authors' Contribution

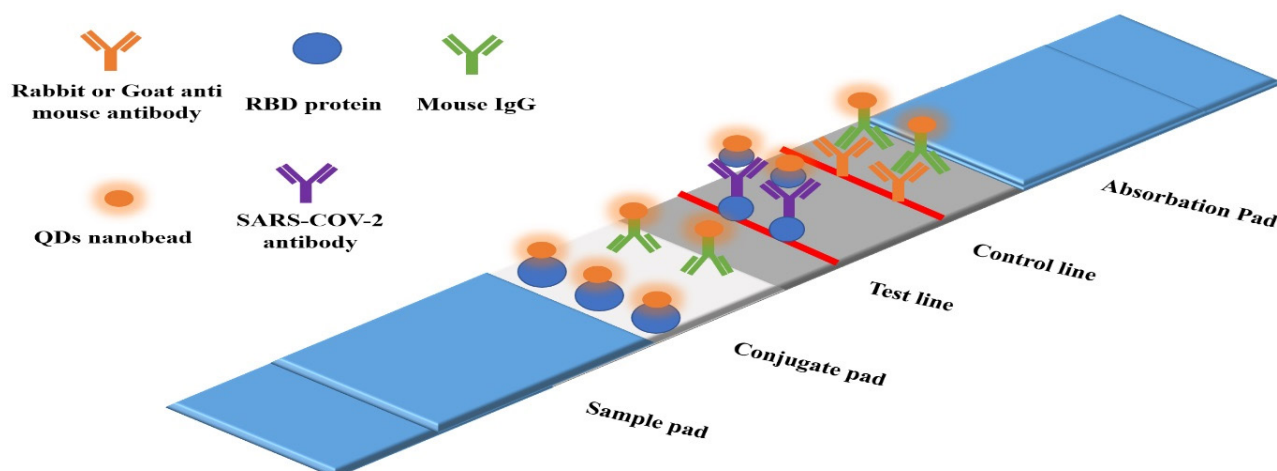
**Conceptualization:** Morahem Ashengroph, Mehran Alavi.

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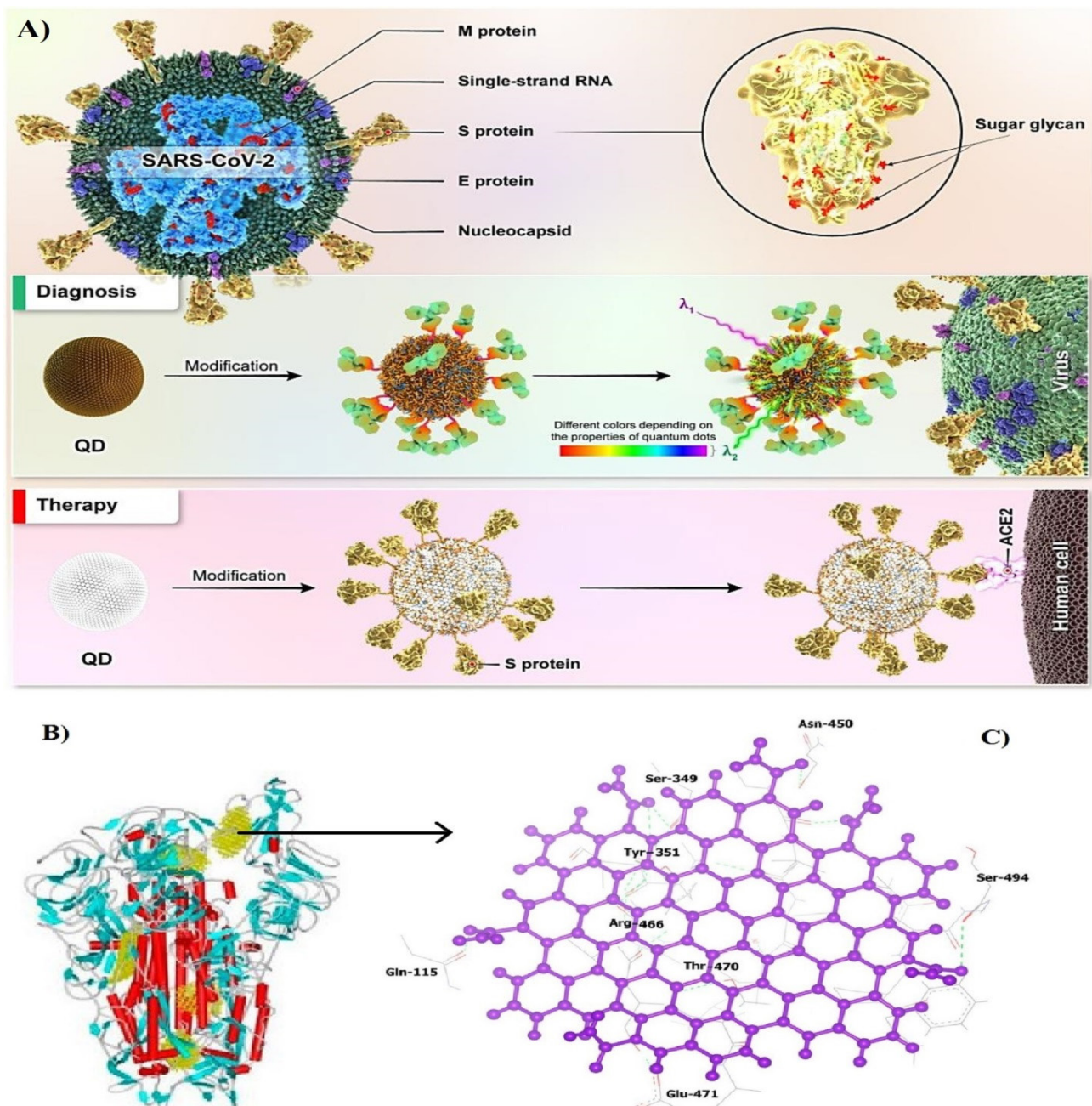
**Table 2.** Different QDs reported for SARS-CoV-2 detection

Type of QDs	Description	Reference
Polystyrene-based QDs	Lateral flow assay for identifying the SARS-CoV-2 virus by antibody detection	103
Magnetic graphene GQDs	Detection of SARS-CoV-2 by ultra-low field NMR relaxometry with low price (1.25 USD)	104
PbS Colloidal QDs	Electronic labeling strategy of protein has advantages over the standard ELISA technique	106
Niobium carbide MXene QDs	Use for identifying the N-gene of SARS-CoV-2	107
SQS QDs	Representation of 100% sensitivity in modified QDs compared to RT-PCR technique	108
CdTe QDs	Detection of RNA or DNA from SARS-CoV-2 using FRET experiment	109

Note. SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; QD: Quantum dots; RT-PCR: Real-time polymerase chain reaction; NMR: Nuclear magnetic resonance; ELISA: Enzyme-linked immunosorbent assay; FRET: Fluorescence resonance energy transfer.



**Figure 5.** Overview of SARS-CoV-2 detection kit based on QDs nanobeads. Note. SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; RBD: Receptor binding domain; QDs: Quantum dots; IgG: Immunoglobulin G<sup>103,105</sup>



**Figure 6.** A) The inactivation and analysis of SARS-CoV-2 by QDs. B) Molecular docking of NH<sub>2</sub>-OH-CQD molecules within SARS-CoV-2 S protein, C) overview of the connection of NH<sub>2</sub>-OH carbon QDs to RBD. Note. NH<sub>2</sub>-OH: Hydroxylamine; QD: Quantum dots; RBD: Receptor binding domain<sup>26,105</sup>

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**Competing Interests**

Authors declare no conflict of interests.

**Ethical Approval**

Not applicable.

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