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Original Article

Effects of Fluorescent Quantum Dots on COVID-19 Detection: A Survey on Present Findings, Challenges, and Future Viewpoints

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ABSTRACT

Acute coronavirus syndrome (SARS-CoV-2) leads to the COVID-19 epidemic. In accordance with the WHO, the epidemic remains a serious danger to the general health because of its global spread and higher transmission rates. A scope of measures is needed to slow the spread of the epidemic and save lives, including the continuous assessment and cautious adjustment of general health reactions to the medical treatment. In such a manner, the expansion of antiviral nanostructures by improved surface designing may be valuable in combating this new virus. Quantum dots are multifaceted agents with the potency to fight or prevent the activity of the Coronavirus. For qualitative diagnosis, a simple and inexpensive bioassay method based on Fluorescence-based QDs nanoparticles can be used to detect SARS-CoV-2 antibodies. Optimization of quantum dots with effective functional molecules against SARS-CoV-2 could extend the nanostructures to the antiviral treatment and eradicate future epidemics, slowing down and possibly ending the spread of viral infections. QDs can be used to promote individual clinical therapy in the future based on each patient's molecular protocols individually. This study addresses how quantum dots (QDs) are useful in diagnosing SARS-CoV-2 infection and future pandemics.

Keywords: SARS-CoV-2, COVID-19 Epidemic, Nanotechnology, Antiviral Nanomaterials, Quantum dots (QDs).

1. Introduction

COVID-19 is a viral infection such as extremely pathogenic viral pneumonia that has now turned into a significant epidemic. Based on available data, infected people are reported to experience mild to severe acute respiratory infections [1]. The host exposes the animal to humans and causes mild respiratory illness to serious illness, respiratory failure, and even death in these severe conditions [2]. COVID-19 is stable for up to 24 hours on the surface, stainless steel, and plastic for two to three days, and aerosols such as rain, wet mud, air pollution, and smoke for up to three hours. The incubation time is among 2-14 days, as yet, numerous recommendations have been made to limit disposal, like personal hygiene, and social distance [3]. To overcome the SARS-CoV-2 epidemic worries, practical strategies are needed, which contain continuous assessment and fine-tuning of general health reactions [4]. It has been suggested that nanomaterials based on quantum sciences can have vast antiviral activity and can be used in preventive, diagnostic, and therapeutic applications [5]. Today, the biological system forms a strong connection with the field of nanoscience and combines both nanobiotechnology and nanomedicine phenomena for the diagnosis, prevention, and treatment of diseases. The properties of nanostructures such as size, surface area, and surface loads are known as the attractive tools for viral treatment [6]. QDs have proven their suitability as imaging probes that are more sensitive to diagnosis and prognosis, and as controlled drug-releasing carriers that focus on the virus infection. In addition, quantification in accordance with quantum sciences of nanoparticles and nanotechnology provides visions and ways to deal with future epidemics [7]. The unique properties of quantum dots link them to a high-fluorescence probe to detect and continue the use of fluorescence molecular imaging [8]. Figure 1 displays some of the actions performed by QDs on viruses [9,10].

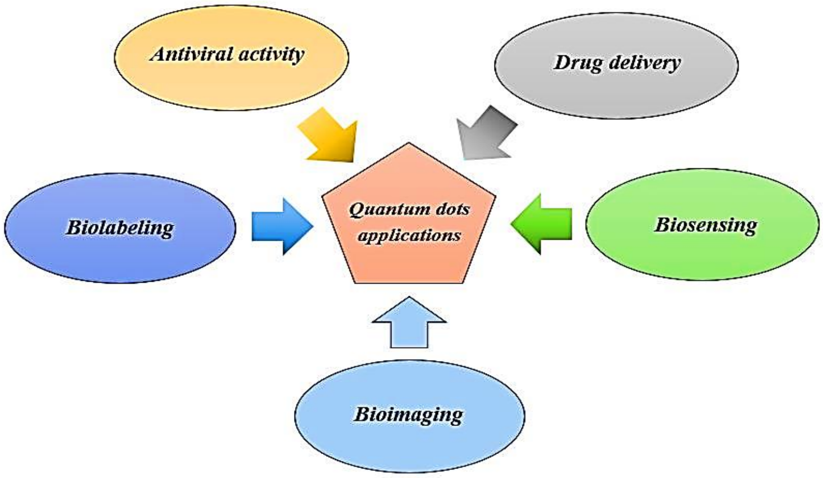

Figure 1. Different applications of quantum dots

2. Nanotechnology and Quantum dots (QDs)

QDs are semiconductor nanocrystals with an intermediate size of 1-10 nm and are generally utilized in cellular labeling, image detection and tracking with specific size-reliant optical attributes [11]. The electron energy levels are measured at discrete QDs, like an atom or a molecule, not like a regular semiconductor in which electrons are scattered in energy bands [12]. These small nanoparticles have high quantum efficiency, constant composition, high image stability, and fluorescent emission properties that can be adjusted according to size (Figure 2). The QDs importance is their antiviral attributes, along with their biocompatibility carrier for experimental methods and other research. The principal character of QDs in labeling and transporting agents in antiviral treatment methods [13].

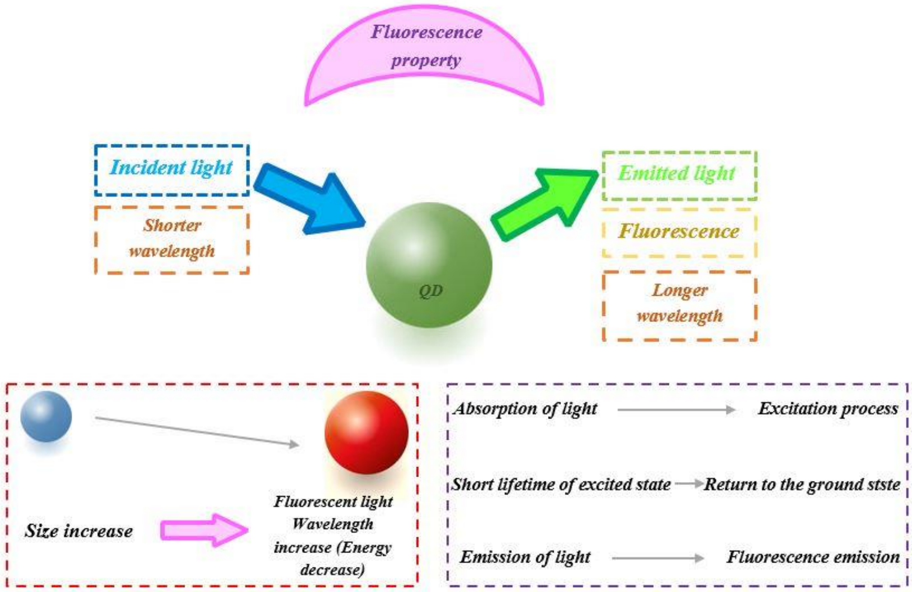

Figure 3. Fluorescence mechanism of Fluorescent QDs

3. Biology and Virology of COVID-19

Coronavirus is classified in the (+) ssRNA group (+) RNA strands (e.g., coronavirus, toga virus, and Picornavirus) that can be accessed straight by the host ribosome to form proteins and through a simple reproductive pathway (polystyrene mRNA via Viruses). Coronaviruses are associated with human and vertebrate sicknesses [14]. This is because of the specific structure of the virus giving the superficial bumps on the viral cover a crown-like appearance (Figure 3) [15].

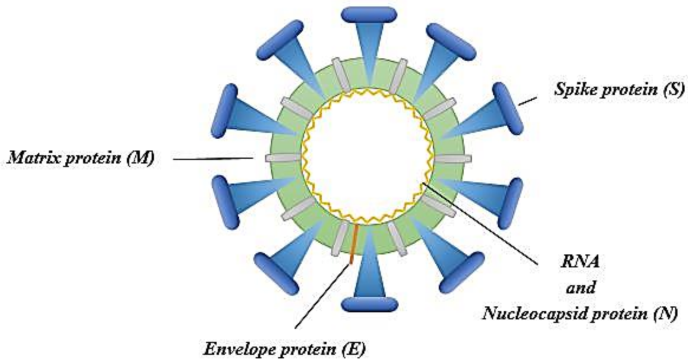

Figure 4. General structure of Coronaviruse-2

4. Quantum dots fight COVID-19

The character of nanomaterials can likewise be expanded to viral illnesses for example, HIV, Ebola virus, and COVID-19 (Figure 4) [16,17]. Nanoparticles have a high surface-to-volume ratio that permits them to bind to multiple ligands on host cells, making them resistant to viral binding by polyvalent interaction. Quantum dots combine with high-fluorescence probes that are important for the detection and imaging of long-term fluorescence of different cell processes [18]. In this way, quantum dots have been recognized as novel probe for subatomic imaging [19]. Currently, QDs are utilized in different applications, for example, bioimaging, bioassay, and bio-labeling. In view of these outstanding properties, QDs can be measured a significant factor in the fight against viral infections.

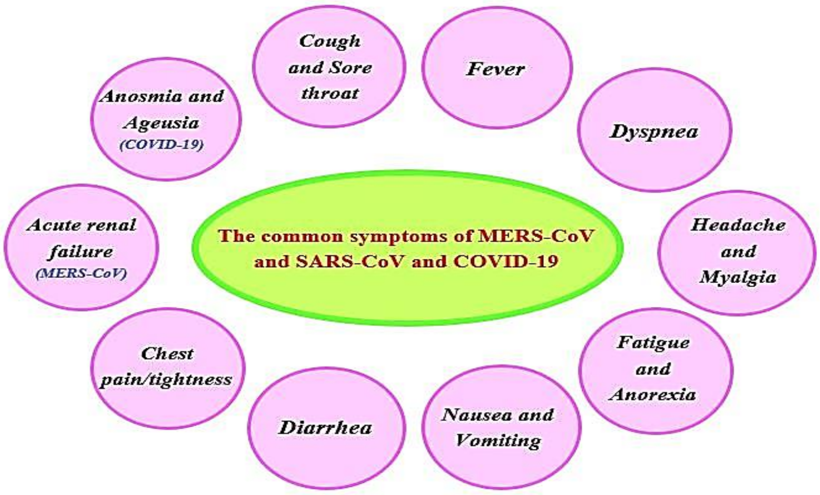

Figure 4. Common symptoms of Beta coronaviruses.

5. Mechanism of action of QDs

Concentration, forms, size, structure of ions on the surface of nanomaterials, and equilibrium space of NPs and QDs affect the intensity of antiviral activity. The main reason for using QDs can be attributed to their traceability under a particular frequency [20]. In addition, quantum dots can be adjusted to the ideal shape and size (1-10 nm) which successfully targets/penetrates SARS-CoV-2 with a size range of 60-140 nm. The cationic surface charge of QDs interacts via the SARS-CoV-2 genome, causing the production and accumulation of ROS (reactive oxygen species), which prevents the regulation of the next negative RNA strand. Likewise, QDs activate interferon gene production and prevent virus replication. Cationic charge on the QDs surface makes the virus to accumulate through electrostatic interactions and reduce viral infection (Figure 5) [21].

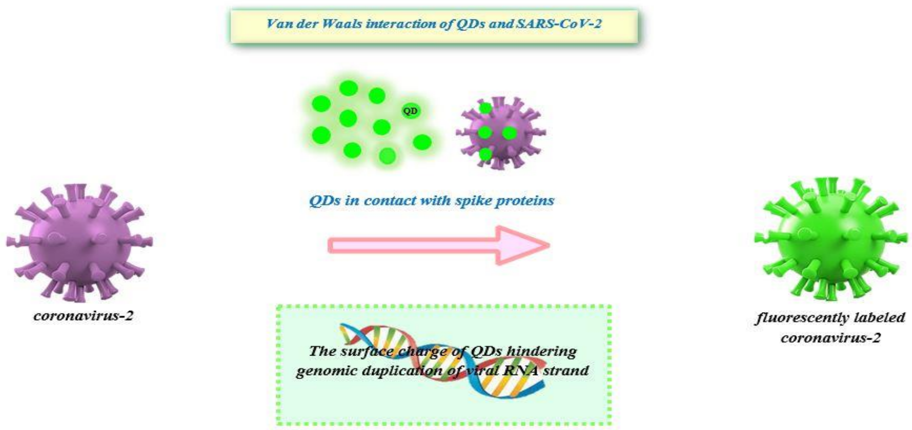

Figure 1. Schematic diagram of interaction of QDs and SARS-CoV-2

Unique catalytic and photonic properties of QDs along with their molecular interactions, are the principles of virus detection detected using different techniques [22].

6. Current Investigations

QDs have revolutionized the labeling processes of molecules in research environments. Their new optical and physical characteristics have appealed much interest in their development for biological usages that require long-term, multi-objective, and ultra-sensitive imaging. Recently, they have been widely used to diagnose COVID-19. The exclusive properties of QDs, for instance, their optical characteristics, make them a superior candidate for use as a fluorescent tag. Furthermore, their propagation wavelengths can be simply and accurately adjusted by resizing them. Because of its excellent properties, QDs at the moment are the dominant imaging probes for measurement [23]. In one of the latest research projects, in 2022, Hatamluyi *et al.* fabricated a promising biosensor for the detection of COVID-19 RNA in applications of medical science. They designed a new ssDNA/FGNs/BNQDs/SPCE platform by boron nitride QDs/flower-like gold nanoscale structures to amplify the electrical signal [24]. In another study, Zheng *et al.* for the first time, produced the fluorescent sensor including QD-peptides, for detecting COVID-19-positive serum that compared with the traditional methods illustrated more sensitivity with a detection limit of 100 pm [25]. In another experimental analysis in 2022, Zhang *et al.* fabricated a special sensor for assaying SARS-CoV-2. They combined fluorescent QD microspheres (QDMS) with Cas13a-based nucleic acid test strip and developed immunochromatography technique based on QDMs and CRISPR/Cas13a that their diagnosis method can be proposed for epidemiologic surveys [26]. In addition to the above-mentioned in 2022, Zhao *et al.* used a COVID-19 protein sensor using special QD modified quantum electrodes on a gold electrode, detecting the particular binding reaction between the antigen and the antibody. This sensor provides the benefits of speed, accuracy, convenience, low cost, and is also suitable for home use [27]. Bardajee *et al.* designed a fluorescence nanoprobe for target complementary DNA or Covid-19 RNA diagnosis using FRET method. In this technique, conjugated QDs to DNA or RNA used in different utilization including nanosensors [28]. Moreover, in another novel successful research, Pramanik *et al.* demonstrated that HNP1 and LL-37 peptide-conjugated graphene quantum dots can to hinder the incoming of COVID-19 Delta variant into host cells. Their research team showed that fluorescent GQDs functional groups have the capability for the inactivation of virus and the elimination of spike proteins [29]. In another creative study in 2022, a fluorescent LFIA with signal amplification capability was developed by Jia *et al.*, using hydrophobic quantum dots. In this approach, the produced compact QDs assemblies as fluorescent label formed an improved SQS-LFIA sensitive platform based on the dual-antigen sandwich structure for COVID-19 total antibody detection [30]. Also, Lee *et al.* successfully synthesized the QDs of graphene fluorescent and Ag @ Au nanoparticles. They proposed a novel type of antibody fluorescence immunoassay by combining QDs and Ag @ Au nanoparticles. In their research, GQDs were applied as fluorescent probes. Furthermore, this probe has been effectively practical to synthetic serum samples, which confirms the performance of the suggested probe for the detection of 2019-nCoV mAb in mixed samples. This antibody detection procedure offers another option for 2019-nCoV diagnosis [31]. In 2021, Zhou *et al.* produced polymer matrices by embedding multiple quantum dots labeled Signal Amplification in Lateral Current Immunoassay (LFIA), using quantum dot nanobeads (QBs). QB-LFIA can enable the rapid detection in 15 minutes for all SARS-CoV-2 antibodies compared with LFIA [32]. In another study, Xu *et al.* successfully detected SARS-CoV-2 nucleocapsid proteins with a new LFI method. Their work was based on red emission-enhanced carbon dot. In this experiment, CD-based silica nanoscale spheres with improved red emission property were used as the LFI signal [33]. Wang *et al.* fabricated an immunoassay biochip based on the graphene oxide QDs. Their produced microfluidic platform was capable of simultaneous diagnosis of several SARS-CoV-2 antibodies and antigens [34]. In another experimental study in the same year, Wang *et al.* published the unique fluorescence LFA method for simultaneously diagnosis of anti-SARS-CoV-2 IgM and IgG in human samples. Produced biosensor was based on quantum dot-s protein conjugates used in rapid and sensitive detections [35].

Table 1. A summary of the research conducted on the use of quantum dots in the detection of the new strain of the coronavirus

Detection method	Results	Refs.
Electrochemical detection (turn-off/turn-on approaches)	Production of a new platform for accurate analysis of coronavirus RNAs Successful testing on RNAs of 120 samples without nucleic acid amplification	[24]
Coupling of QDs with coronavirus peptides	Biological signal amplification using optical signal and highly sensitive detection of COVID-19 antibody Rapid increase in detection accuracy with a limit of 100 pm	[25]
Development of immunochromatography technique	Fabrication of a biosensor from quantum dots for nucleic acid detection using fluorescent signal Good stability of the fluorescent strip up to 3 months at room temperature and powerful in quantitative detection	[26]
Labelling of COVID-19 proteins	Modification of virus protein detection electrode The correlation coefficient of the quantitative analysis of antibodies is about 93.8% compared with the ELISA method; along with the ability to distinguish between patient and normal samples with an accuracy range of 90%.	[27]
Virus DNA detection using quantum dot and DNA conjugation	Decrease in fluorescence intensity with increasing DNA concentration The detection limit was 0.000823 μm	[28]
Preventing the entry of the Delta type of Covid-19 into the host cell by conjugation of graphene quantum dots with HNP1 and LL-37 peptides	Complete inhibition of the entry of the virus into the host cell Increasing the efficiency of quantum dots attached to the mentioned peptides	[29]
COVID-19 total antibody detection using a compact fluorescent label based on dual-antigen sandwich structure	Accurate matching of diagnosis results with CLIA and RT-PCR results with 100% sensitivity High sensitivity to low concentrations of COVID-19 serums	[30]
Antibody fluorescence immunoassay method with the combination of QD and Ag@Au nanoparticles	Design of a highly sensitive fluorescent probe with appropriate selectivity The detection limit in the concentration range of 0.1 pg mL^{-1}-10 ng mL^{-1} was about 50 fg mL^{-1}	[31]
Development of LFIA method using QBs	Better sensitivity than LFIA method and quick detection of virus total antibodies in 15 minutes	[32]
Integration of LFI method with carbon dot nanostructures	A practical method with good detection and stability	[33]
Development of an immunoassay method by integrating the features of a microfluidic chip and graphene quantum dots	Simultaneous detection of several antibodies and virus antigens Detection limit in the range of 0.3 pg/mL Ability to detect in less than 10 minutes with high efficiency	[34]

A new fluorescence LFA method based on quantum dot-s protein conjugates	Accurate detection of IgM/IgG with a ratio of 1:10^7 from 1 μL of serum within 15 minutes The practicality of the proposed method by performing tests on 114 samples of Covid-19 patients with a sensitivity of 97.37% and 202 samples of negative cases with a sensitivity of 95.54%.	[35]

7. Current Challenges and Future Viewpoints

The optimization of nanoparticles should be considered from various aspects, including toxicity and their usage against the treatment of COVID-19, biodegradable to ensure complete elimination from the human body of the safety challenges of nanomaterials. Therefore, more trustworthy *in vivo* studies are needed to superior understand the toxic-kinetic behavior of nanostructures in the body, in the long run [36]. Multidimensional behavior between nanomaterials and *in vivo* when nanoparticles enter the body, they can interact with biological molecules, mainly proteins, to form a protein crown determined by the physicochemical features of the nanostructures [37]. Under the influence of these factors, it can regulate interactions of protein-nanostructure and protein-protein, regulating protein uptake at nanoparticle surfaces [38]. Using various factors of intrinsic physicochemical features and environmental conditions for example size, color, dose of QDs, bioactivity of the coating, etc. the cytotoxicity level can be determined. Due to the QDs toxicity, their use in biomedical applications and *in vivo* studies is limited. Other disadvantages of QDs are that they have extremely deprived stability under environmental conditions, and novel procedures can improve its stability in solution, and their base life should also be investigated [39]. The optimization of quantum dots with effective functional molecules against COVID-19 could extend the area of nanostructures toward antiviral therapy and eradicate future epidemics, slowing down and possibly ending the spread of viral infections.

8. Conclusion

In this brief review, we tried to give researchers an overview of the role of quantum dots in detecting the new strain of the coronavirus. First, we gave a brief introduction of quantum dots and the new coronavirus, and then the performance of these nanostructures was demonstrated in the diagnostic processes of the new and dangerous type of coronavirus. In the following, with a quick look at the research conducted in the recent pandemic, we tried to give a new insight into the role of nanostructures of quantum dots in the diagnosis and coronavirus control. Using different properties of quantum dots, including their fluorescence property, we can achieve a novel application in labeling and tracking viruses and even with the help of these nanostructures, the virus reproduction can be prevented. In fact, it can be mentioned that nanotechnology research is one of the best weapons to act the SARS-CoV-2 virus because it can detect the virus due to the unique properties of nanoscale materials. However, there are important questions that still need to be answered, and one can hope for the future of QDs. Questions have been raised about their toxicity and metabolic excretion from the organs. Advances are being made in the modelling and engineering of QDs for biological and biocompatible functions. Prior to their administration in clinical settings, further research should be conducted to combat the inherent toxicity of QDs and their *in vivo* distribution and excretion.

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