REVIEW PAPER

Quantum dot-based sensors and nanotheranostics for early detection and targeted therapy for colorectal cancer

***Dilpreet Singh*[1*], *Raj Kamal*[2]**

[1] *School of Pharmaceutical Sciences, CT University, Ferozepur Rd, Sidhwan Khurd, Punjab, India*
[2]*School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab, India*

ABSTRACT

Introduction: Colorectal cancer (CRC) remains one of the most prevalent and fatal cancers worldwide, highlighting the urgent need for the development of advanced diagnostic and therapeutic strategies.
Objective(s): Quantum dots (QDs), semiconductor nanomaterials with distinctive optical properties, have emerged as promising tools in the fight against colorectal cancer (CRC).
Materials and Methods: The ability of QDs to emit tunable fluorescence, combined with their small size and potential for surface functionalization, enables high sensitivity and specificity in early detection and targeted treatment. In the context of CRC, QDs can be used to identify biomarkers such as carcinoembryonic antigen (CEA) and folate receptors, facilitating non-invasive imaging with high resolution.
Results: Furthermore, QDs can be functionalized for targeted therapy, enhancing the selective delivery of chemotherapeutic agents to tumor sites, reducing systemic toxicity, and allowing real-time monitoring of treatment efficacy. Despite these advantages, the clinical application of QDs in CRC is limited by challenges, including toxicity, biocompatibility, long-term stability, and efficient targeting. This review examines the current state of quantum dot-based technologies in CRC diagnostics and therapy, emphasizing their potential as nanotheranostic platforms. We also address the key barriers to clinical translation and propose future research directions to improve quantum dots' safety, efficiency, and clinical utility in CRC management.
Conclusion: Ultimately, quantum dots offer significant potential to revolutionize the diagnosis and treatment of colorectal cancer, paving the way for more personalized and effective patient care.

Keywords: *Colorectal Neoplasms, Quantum Dots, Nanoparticles, Nanotheranostics, Targeted Therapy, Early Detection*

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INTRODUCTION

Colorectal cancer (CRC) remains one of the leading causes of cancer-related morbidity and mortality worldwide, placing an increasing burden on healthcare systems due to its high incidence and late-stage diagnosis [1]. Early detection of CRC is crucial for improving survival rates, as prognosis is heavily dependent on the stage at which the cancer is diagnosed [1, 2]. Unfortunately, current diagnostic methods, such as colonoscopy, computed tomography (CT) colonography, and fecal occult blood tests (FOBT), have significant limitations, including invasiveness, discomfort, and limited sensitivity, particularly in early-stage cancer or small lesions [2]. These shortcomings underscore the urgent need for novel, more effective diagnostic approaches that offer non-invasive, highly sensitive, and accurate detection of CRC at its earliest stages [2, 3].

Nanotechnology, particularly quantum dots (QDs), has emerged as a promising solution to address colorectal cancer (CRC) diagnostic challenges. Quantum dots are semiconductor nanocrystals with unique optical properties, including size-tunable fluorescence, high quantum yield, and narrow emission spectra [4]. These properties make QDs highly suitable for biomedical applications, especially in molecular imaging, where their fluorescence enables the detection of cancer biomarkers with high sensitivity and specificity [5]. Unlike traditional dyes, QDs can

**Corresponding author(s) Email: dilpreet.daman@gmail.com*
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generate multiplexed signals, allowing for the simultaneous detection of multiple biomarkers, which is essential for enhancing the accuracy of cancer diagnostics [6].

In addition to their diagnostic role, quantum dots (QDs) are increasingly being explored for their potential in targeted therapy, particularly colorectal cancer (CRC). Due to their small size and the ability to be functionalized with targeting ligands, such as antibodies or peptides, QDs can selectively deliver therapeutic agents to tumor sites, minimizing the side effects associated with conventional therapies [7]. Furthermore, QDs facilitate real-time monitoring of therapeutic progress through their optical properties, offering a non-invasive method to track treatment efficacy. The concept of "nanotheranostics," which integrates diagnostic and therapeutic functions into a single platform, holds significant promise for revolutionizing CRC treatment, enabling more personalized and effective patient care [7, 8]. Despite the exciting potential of QDs in CRC detection and therapy, several challenges remain. Issues such as toxicity, biocompatibility, long-term stability, and efficient targeting must be addressed before widespread clinical implementation can be realized [9]. Additionally, the regulatory and ethical considerations surrounding the use of nanoparticles in humans remain a critical concern, requiring careful attention.

This review aims to comprehensively explore the role of quantum dots in the early detection and targeted therapy of colorectal cancer (CRC). We will examine the fundamental properties of quantum dots, their applications in CRC diagnostics, and their potential in targeted treatment strategies [10]. Additionally, we will discuss the current challenges and future perspectives for the clinical translation of QD-based technologies in CRC management [10]. Through this discussion, we aim to highlight the transformative potential of quantum dots in colorectal cancer care, paving the way for more accurate, efficient, and personalized approaches to CRC diagnosis and treatment.

Fundamentals of quantum dots

Quantum dots (QDs) are nanoscale semiconductor materials that exhibit unique optical and electronic properties, including size-dependent fluorescence, high quantum yield, and tunability across the electromagnetic spectrum by adjusting their size and composition [11]. These properties result from quantum confinement effects, where the motion of charge carriers is restricted in all three spatial dimensions, creating discrete energy levels. Quantum dot-based imaging offers several advantages over traditional diagnostic methods [11, 12], such as enhanced sensitivity and real-time monitoring, while addressing some of the limitations of colonoscopy and CT colonography, including invasiveness and radiation exposure (Table 1). A detailed depiction of the core-shell structure of quantum dots, including surface functionalization with targeting ligands (e.g., antibodies, peptides) for specific cancer cell recognition and drug delivery, is shown in Figure 1.

Quantum dots (QDs) are typically composed of elements from groups II-VI (e.g., CdSe, CdTe), III-V (e.g., InP), and IV-VI (e.g., PbS) of the periodic table. Their surface properties are engineered to enhance stability and prevent aggregation [13]. Various quantum dot materials, such as CdSe, CdTe, InP, and PbS, exhibit distinct optical properties and varying levels of toxicity, with carbon-based QDs emerging as a promising alternative due to their biocompatibility and tunable fluorescence for colorectal cancer (CRC) applications (Table 2).

Table 1. Comparison of Quantum Dots and Traditional Diagnostic Methods in Colorectal Cancer Detection

Diagnostic Method	Sensitivity	Specificity	Invasiveness	REF
Quantum Dot-Based Imaging	90-95%	85-90%	Non-invasive	[16]
Colonoscopy	85-90%	95%	Invasive (requires sedation)	[17]
CT Colonography (Virtual Colonoscopy)	80-90%	90-95%	Non-invasive (with radiation)	[17]
Fecal Occult Blood Test (FOBT)	60-75%	90-95%	Non-invasive	[18]
CT Scan (Abdominal)	70-80%	85-90%	Non-invasive (with radiation)	[19]
MRI (Magnetic Resonance Imaging)	80-85%	85-90%	Non-invasive	[19]

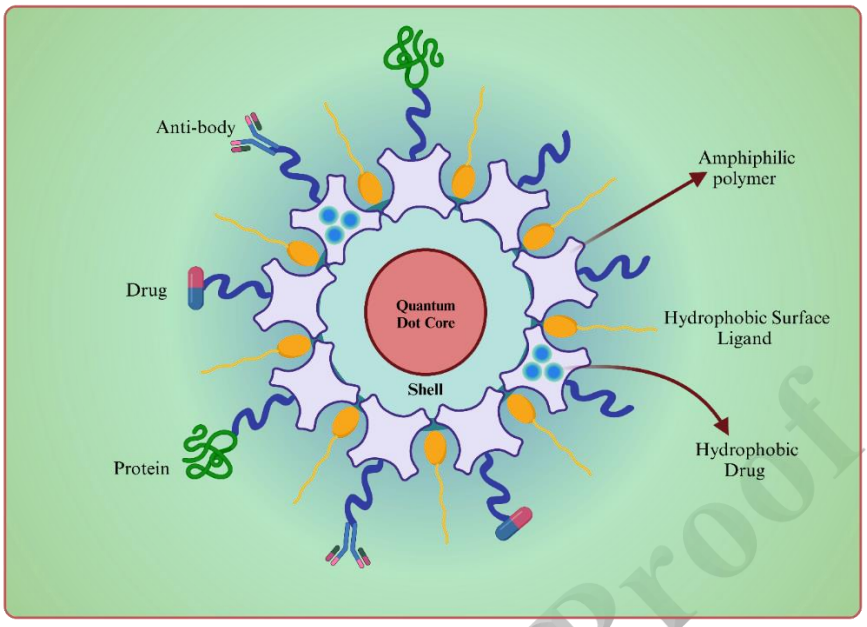

Fig. 1. Schematic Representation of Quantum Dot (QD) Structure and Functionalization

Table 2. Properties of Different Quantum Dot Materials for Colorectal Cancer Applications

Quantum Dot Material	Composition	Optical Properties	Toxicity Concerns	Synthesis Method	Applications in CRC
CdSe	Cadmium selenide	Tunable fluorescence, high quantum yield	High toxicity (Cd2+)	Colloidal synthesis, chemical vapor deposition	Imaging, drug delivery
CdTe	Cadmium telluride	Strong fluorescence, high stability	High toxicity (Cd2+, Te2-)	Colloidal synthesis	Imaging, targeting CRC cells
InP	Indium phosphide	Narrow emission spectrum, low toxicity	Lower toxicity than Cd-based QDs	Colloidal synthesis	Imaging, potential theranostics
PbS	Lead sulfide	Infrared emission, stable in biological systems	Toxicity from lead (Pb)	Colloidal synthesis, laser ablation	In vivo imaging, drug delivery
Carbon-Based QDs	Carbon nanostructures	Broad emission spectrum, high biocompatibility	Non-toxic	Chemical vapor deposition, laser ablation	Imaging, sensing, drug delivery

Functionalization of QDs is essential to improve their biocompatibility and enable targeting of specific cells or tissues. Surface coatings, such as polyethylene glycol (PEG), and conjugation with targeting ligands like antibodies, peptides, or aptamers make QDs ideal candidates for biomedical applications [14], particularly in molecular imaging and therapy. In vivo, QDs can be tracked using fluorescence microscopy, confocal microscopy, or other imaging modalities, providing high-resolution detection of disease markers, such as those associated with CRC [14, 15]. Quantum dots are primarily synthesized through colloidal synthesis and chemical vapor deposition (CVD). Colloidal synthesis involves the nucleation and growth of QDs in a solution containing precursor compounds, surfactants, and stabilizing agents, allowing for precise size control [14]. This method is widely used due to its scalability and tunable optical properties. Alternatively, CVD and molecular beam epitaxy (MBE) facilitate QD growth on substrates under controlled conditions, often employed in electronic and optoelectronic applications. Post-synthesis surface modification, such as ligand exchange or passivation, further enhances QD stability and functionality for biomedical and diagnostic applications [15]. A combination of optical properties, ease of functionalization, and tunability makes QDs a significant tool for cancer diagnosis and targeted therapy, especially in the early detection of CRC, where precise identification of tumor markers and tracking their progression are crucial for effective management.

Quantum dot-based sensors in early detection of colorectal cancer

Quantum dot-based sensors have emerged as a promising tool for the early detection of colorectal cancer (CRC), utilizing the unique optical properties of quantum dots (QDs) to enhance sensitivity and

specificity in detecting cancer biomarkers [20]. The size-tunable fluorescence emission of QDs enables multiplexed imaging, where different QDs can be functionalized with antibodies or ligands specific to various CRC-related biomarkers [21], such as carcinoembryonic antigen (CEA), Kirsten rat sarcoma viral oncogene homolog (KRAS) mutations, or microsatellite instability. The detailed mechanism of quantum dots in the early detection of colon cancer is illustrated in Figure 2. Quantum dots can be functionalized with various targeting ligands, including anti-CEA antibodies, folate, and peptides like RGD, facilitating selective targeting of colorectal cancer biomarkers and enhancing their effectiveness in imaging and therapy (Table 3). These bio-functionalized QDs can selectively bind to their target biomarkers on cancer cells or body fluids, such as blood or stool, enabling early detection even in asymptomatic stages [21]. The bar chart illustrates the detection accuracy of different quantum dot (QD) types—CdSe, CdTe, InP, PbS, and carbon QDs—when targeting key colorectal cancer biomarkers, including CEA, epidermal growth factor receptor (EGFR), folate receptor, KRAS mutation, and mucin-1 (MUC1) [21, 22] (Figure 3).

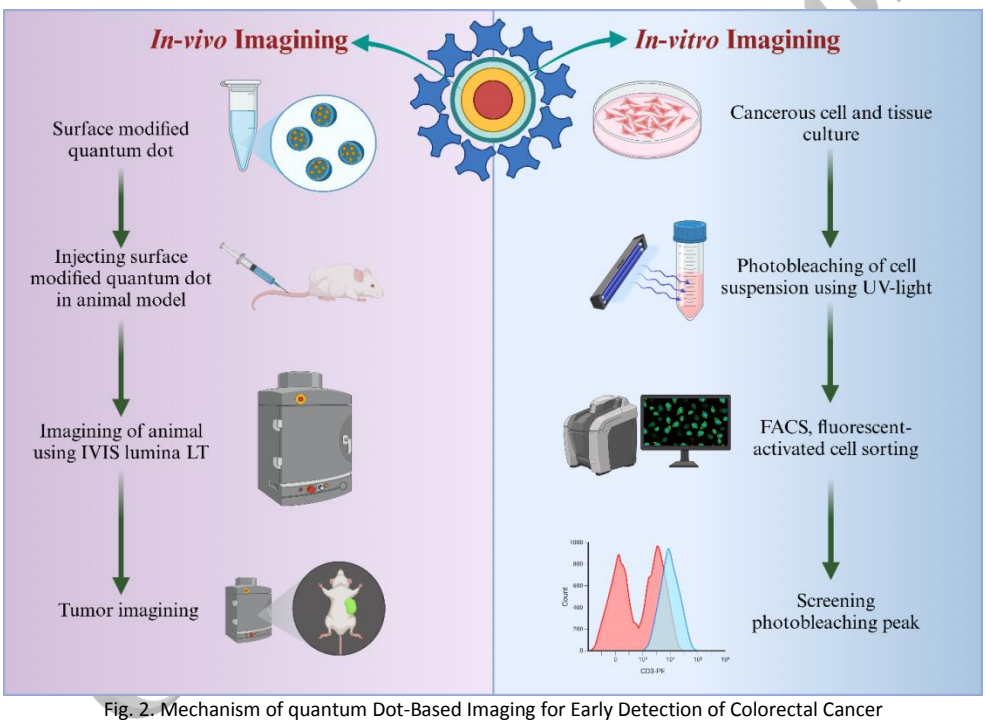

Fig. 2. Mechanism of quantum Dot-Based Imaging for Early Detection of Colorectal Cancer

Table 3. List of Targeting Ligands Used for Quantum Dot Functionalization in Colorectal Cancer

Targeting Ligand	Type	Target Biomarker	Functionalization Method
Anti-CEA Antibody	Monoclonal antibody	Carcinoembryonic Antigen (CEA)	Conjugation via thiol groups
Folate	Small molecule (vitamin)	Folate receptor overexpressed in CRC cells	Covalent bonding via amine groups
Anti-EGFR Antibody	Monoclonal antibody	Epidermal Growth Factor Receptor (EGFR)	Bioconjugation using EDC/NHS
Peptide (RGD)	Peptide	Integrin αvβ3 (expressed in tumors)	Peptide conjugation to QDs
Anti-MUC1 Antibody	Monoclonal antibody	Mucin 1 (MUC1)	Conjugation via carboxyl groups
Aptamers	Nucleic acid-based ligand	CRC-related biomarkers (e.g., KRAS mutations)	Covalent linkage through thiol groups

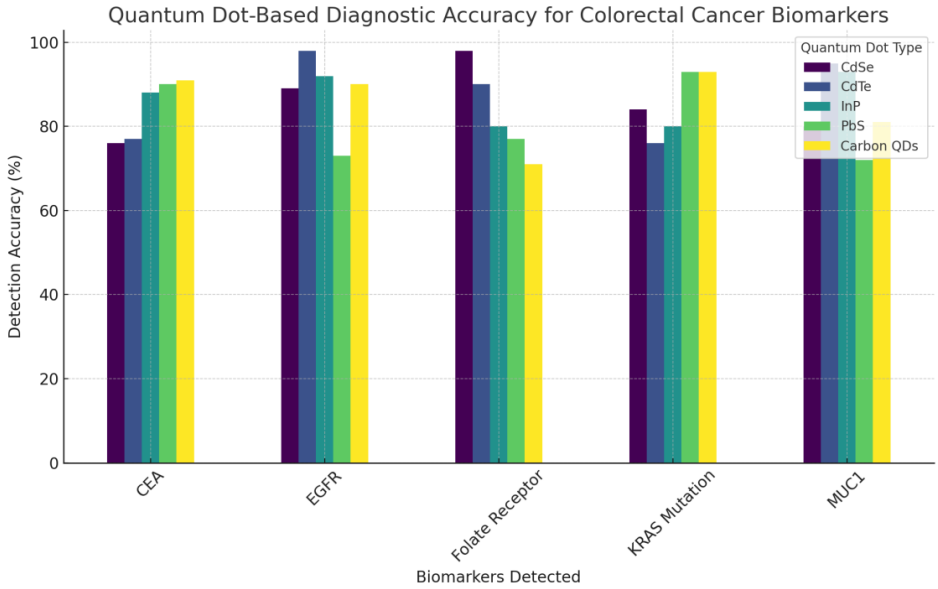

Fig. 3. Quantum Dot-Based Diagnostic Accuracy for Colorectal Cancer Biomarkers

The detection efficiency is represented as a percentage, highlighting variations in quantum dot (QD) performance across different biomarkers. Recent advancements in QD-based biosensors leverage surface plasmon resonance, fluorescence resonance energy transfer (FRET), and Förster resonance energy transfer (FRET) to achieve higher sensitivity in detecting minute quantities of biomarkers [22, 23]. Additionally, incorporating QDs into imaging modalities such as fluorescence tomography and magnetic resonance imaging (MRI) has enabled deeper tissue penetration, making them suitable for non-invasive in vivo detection of colorectal tumors [24]. QDs have also demonstrated the potential to enhance the accuracy of traditional diagnostic methods, such as colonoscopy and endoscopy, by providing real-time molecular imaging of lesions with sub-cellular resolution [24, 25]. Despite these advances, challenges remain in optimizing targeting efficiency and minimizing non-specific binding, affecting detection sensitivity. Furthermore, addressing the potential toxicity of quantum dots, particularly those containing heavy metals such as cadmium, continues to be an active area of research [26]. Nevertheless, integrating quantum dots into CRC detection represents a significant step toward more precise, early, and non-invasive diagnostic methods, offering a promising alternative to current screening techniques.

Molecular targeting using quantum dots in colorectal cancer therapy

Quantum dots (QDs) have emerged as highly effective tools for molecular targeting in colorectal cancer (CRC) therapy, leveraging their unique ability to conjugate with targeting moieties such as antibodies, peptides, or small molecules, which enhance their specificity for cancer cells [27]. These functionalized QDs can selectively deliver therapeutic agents directly to CRC cells, which minimizes off-target effects and improves the overall therapeutic index. QDs can serve as carriers for various therapeutic payloads, including chemotherapeutic drugs, small interfering RNA (siRNA) [28], or genetic material, enabling a targeted delivery approach that maximizes therapeutic efficacy while minimizing systemic toxicity [28, 29]. The surface modification of QDs with tumor-specific ligands, such as anti-CEA antibodies or folate [24, 25], facilitates their selective accumulation at the tumor site via receptor-mediated endocytosis, a critical step in molecular targeting [29].

In addition, the surface of quantum dots (QDs) can be further engineered to incorporate drugs released in response to environmental stimuli, such as pH or specific enzymes in the tumor microenvironment. This allows for the controlled release of therapeutic agents precisely where needed [30]. Moreover, QDs enable the tracking of therapeutic delivery and the monitoring of treatment progress in real-time using their fluorescence properties, providing clinicians with a non-invasive means to assess the treatment's effectiveness [30, 31]. The application of QDs in photodynamic therapy (PDT) has also been evaluated, where QDs, upon exposure to specific light wavelengths, generate reactive oxygen species that induce localized tumor cell death [28].

However, challenges remain in optimizing the size, surface coating, and stability of QDs to ensure efficient drug delivery while minimizing potential toxicity [32]. Additionally, the long-term biocompatibility and clearance of QDs in vivo remain significant concerns that require further investigation [33]. Despite these challenges, the potential of QDs for targeted delivery and therapy in CRC is immense, offering the possibility of more effective and less toxic treatment strategies [34].

Table 4 lists clinical and preclinical studies showing quantum dot-based sensors, particularly those functionalized with CEA or folate, provide high sensitivity and specificity for early detection and imaging of colorectal cancer, often outperforming traditional diagnostic methods. A schematic illustrating the targeted drug delivery process using QDs—from functionalized QDs binding to CRC cell surface receptors to the release of therapeutic agents within cancerous cells—is shown in Figure 4.

Table 4. Clinical Applications and Preclinical Studies of Quantum Dot-Based Sensors in Colorectal Cancer Detection

Study Type	Study Focus	Quantum Dot Material	Target Biomarker	Key Findings	Ref
Preclinical	Early detection of CRC in animal models	CdSe/ZnS QDs	Carcinoembryonic Antigen (CEA)	QDs successfully detected early-stage tumors in mice models, providing real-time tumor localization	[35]
Clinical Trial	Imaging of CRC biomarkers in patients	InP QDs	Folate receptor α, CEA	QDs demonstrated enhanced imaging compared to traditional methods like colonoscopy	[36]
Preclinical	Detection of CRC-related gene mutations	CdTe QDs	KRAS mutation biomarkers	QDs used for multiplexed detection of mutations, improving diagnostic precision in CRC	[37]
Preclinical	Fluorescence-guided CRC surgery	PbS QDs	MUC1 antigen, EGFR	Real-time fluorescence imaging assisted in the precise surgical removal of CRC tumors	[38]
Clinical Trial	Evaluation of QD-based endoscopic imaging	Carbon QDs	CRC-specific biomarkers	Carbon-based QDs offered a non-invasive, effective imaging tool for early CRC detection during colonoscopy	[39]
Preclinical	Tumor-targeted drug delivery in CRC	CdSe/ZnS QDs	CEA, EGFR	Quantum dots enabled targeted delivery of chemotherapeutics, reducing systemic toxicity and enhancing therapeutic efficacy	[40]

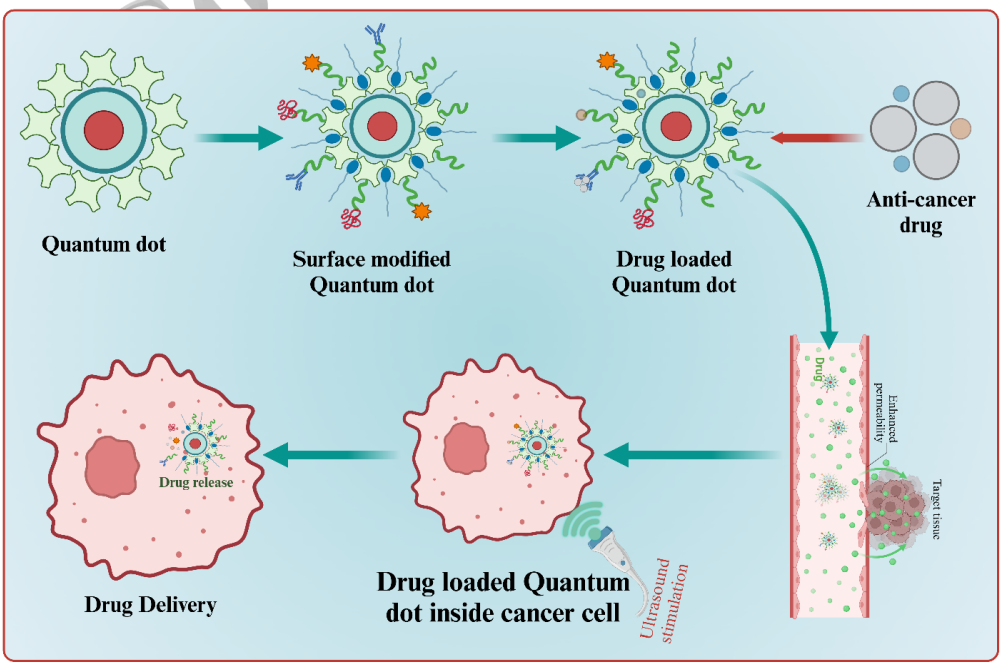

Fig. 4. Mechanism of Quantum Dot-Mediated Drug Delivery in Colorectal Cancer Therapy

Quantum dots in nanotheranostics for colorectal cancer

Nanotheranostics, which integrates diagnostic and therapeutic modalities into a single platform, represents a cutting-edge approach in colorectal cancer (CRC) treatment, with quantum dots (QDs) playing a central role in this emerging field [41]. QDs enable simultaneous tumor detection and therapy, leveraging their unique optical properties for real-time imaging while delivering therapeutic payloads directly to the cancer site [42, 43]. This dual functionality is particularly valuable in CRC, where early detection and localized treatment are crucial for improving patient outcomes [44]. QDs can be conjugated with targeting ligands, such as antibodies or peptides specific to CRC biomarkers (e.g., CEA or folate receptors), facilitating the selective targeting of malignant tissues [45].

Once bound to cancer cells, quantum dots (QDs) can be used in non-invasive imaging techniques such as fluorescence microscopy, positron emission tomography (PET), and fluorescence-guided surgery, providing detailed insights into the tumor's size, location, and molecular characteristics [46]. Simultaneously, QDs can be loaded with therapeutic agents—chemotherapeutic drugs, gene therapies, or RNA-based therapies—released in response to tumor-specific triggers, such as acidic pH or specific enzymes. This ensures the therapy is delivered precisely to the cancerous cells while sparing healthy tissue [47, 48]. Figure 5 illustrates the dual function of quantum dots in both the diagnosis (fluorescence imaging) and therapy (drug delivery and photodynamic therapy) of colorectal cancer (CRC) within a single system.

Additionally, the ability to modify quantum dots (QDs) with photosensitizers opens up the possibility for photodynamic therapy (PDT), where QDs, upon light activation, generate cytotoxic species that specifically target and kill cancer cells [48]. Figure 6 depicts a scatter plot comparing different quantum dot types based on their imaging sensitivity (%) and therapeutic effectiveness (%) in colorectal cancer applications as nanotheranostic agents [49, 50]. InP QDs demonstrate the highest therapeutic potential, while CdSe QDs excel in imaging. Figure 6 also highlights the trade-off between diagnostic efficiency and drug delivery capability among quantum dots [50]. The integration of QDs in nanotheranostics presents the advantage of personalized treatment, as the same nanocarrier can be tailored for both the detection and treatment of CRC based on the patient's specific tumor profile [50].

While early studies and clinical trials have shown promising results, challenges remain in optimizing the size, surface modification, and toxicity of quantum dots (QDs) to ensure their safe and effective use in clinical settings [51]. Additionally, the long-term clearance of QDs from the body, particularly those containing heavy metals like cadmium, requires further investigation. Nevertheless, the potential of QDs in nanotheranostics for colorectal cancer (CRC) holds immense promise, offering a powerful tool for accurate diagnosis and precision treatment, which could revolutionize the management of colorectal cancer in the future [51].

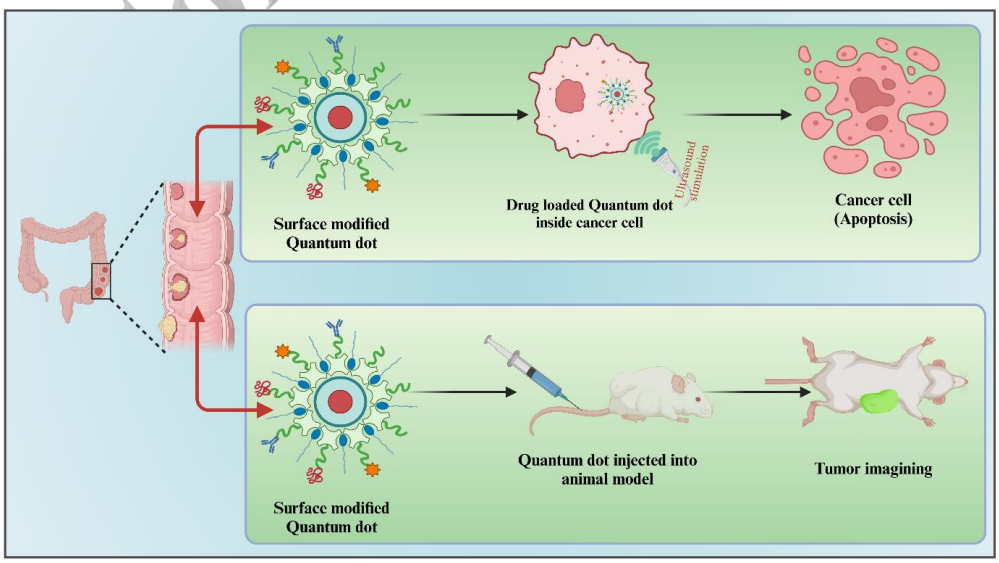

Fig. 5. Quantum Dot Conjugates in Nanotheranostic Applications for Colorectal Cancer

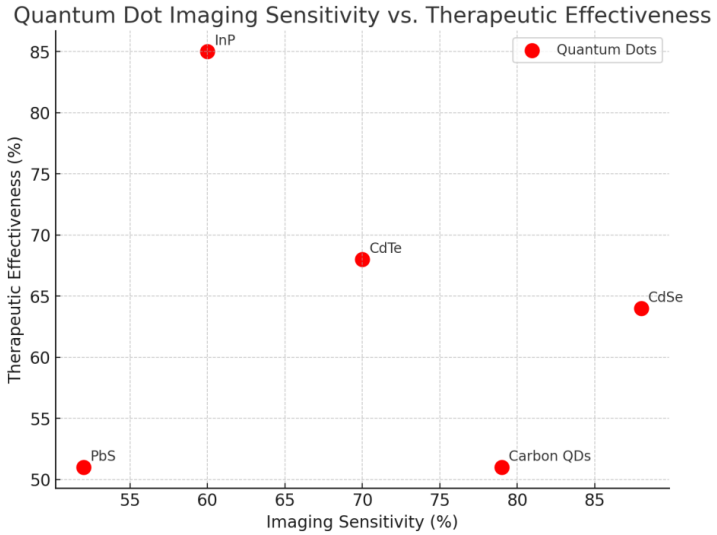

Fig. 6. scatter plot showing the relationship between Quantum Dot Imaging Sensitivity and Therapeutic Effectiveness

Toxicity and biocompatibility of quantum dots in colorectal cancer applications

The use of quantum dots (QDs) in colorectal cancer (CRC) applications raises critical concerns regarding their toxicity and biocompatibility, which should be thoroughly addressed to ensure their safe clinical use [52]. While QDs offer significant advantages in imaging and therapy, particularly for the early detection and targeted treatment of CRC, the potential for toxicity primarily arises from the heavy metals (such as cadmium, lead, and selenium) commonly used in their composition [52]. These metals can leach from the quantum dots, especially in the physiological environment, leading to cellular damage, oxidative stress, and inflammation [53], which can result in adverse effects on normal tissues and organs, such as liver or kidney damage, which are especially concerning in the context of systemic drug delivery [53].

Additionally, the small size and surface charge of quantum dots (QDs) enables them to accumulate in various organs, raising concerns about their long-term clearance from the body and the potential for chronic toxicity [54]. Significant efforts have been made to address these concerns and develop safer, more biocompatible QDs. Surface modifications with biocompatible polymers, such as polyethylene glycol (PEG) or inorganic materials like silica, have reduced toxicity by preventing QD aggregation, enhancing stability, and promoting renal clearance [55]. Moreover, QDs can be functionalized with ligands that enable selective targeting of colorectal cancer (CRC) cells, minimizing the exposure of healthy tissues to the potentially harmful effects of the QDs [56]. Researchers are also evaluating non-toxic alternatives, such as carbon-based or graphene quantum dots, which offer comparable optical properties without the associated risks of heavy metals. Furthermore, studies on the biodistribution and metabolic pathways of QDs in animal models have been essential for understanding their potential long-term effects [57]. While advances in QD design and functionalization have mitigated some of these concerns, further research is needed to ensure their safe use in clinical settings [58]. Regulatory bodies and ethical considerations also play a key role in establishing safety guidelines and standards for using QDs in biomedical applications. Ensuring the safe integration of quantum dots into CRC therapies and diagnostics will be essential for realizing their full potential in clinical practice.

Recent advances and future perspectives

Recent advances in quantum dot (QD) technology have significantly expanded their potential applications in colorectal cancer (CRC) detection and therapy, offering promising solutions to current clinical challenges [58]. The synthesis of QDs with improved biocompatibility and lower toxicity profiles is one of the most notable developments. Innovations in surface coating techniques, such as silica or lipid-based shells, have mitigated the harmful effects of traditional heavy-metal-containing QDs, enabling their safe use in vivo [59]. Furthermore, advancements in QD conjugation techniques have allowed for the incorporation of multiple functional groups on a single particle, facilitating the simultaneous targeting of various CRC biomarkers and enhancing detection sensitivity and therapeutic efficacy [60]. Additionally, integrating QDs with other

nanomaterials, such as gold nanoparticles or magnetic nanoparticles, has led to the creation of multifunctional nanocomposites that combine imaging, targeted therapy, and even gene editing into a single platform, providing a more holistic approach to CRC treatment [61].

The advent of quantum dot-based nanotheranostics represents another significant area of progress, where quantum dots (QDs) can simultaneously function in diagnostic imaging and as delivery vehicles for chemotherapeutic agents, RNA-based therapies, or photodynamic therapy [62]. These multifunctional systems offer unprecedented precision in targeting and treating colorectal cancer (CRC) while enabling real-time monitoring of therapeutic responses. Looking ahead, the future of QDs in CRC applications is likely to be driven by the incorporation of artificial intelligence (AI) and machine learning (ML) technologies, which could facilitate the development of more intelligent, adaptive systems capable of optimizing drug delivery and diagnosis based on real-time data [62]. Moreover, as personalized medicine advances, QDs may play a pivotal role in tailoring treatments to individual CRC patients by identifying unique molecular signatures and guiding the development of personalized therapeutic strategies [63].

Despite these exciting advancements, challenges such as improving the long-term stability, in vivo clearance, and standardization of quantum dot (QD)-based systems must be addressed before widespread clinical adoption [64]. In summary, the future of quantum dots in colorectal cancer (CRC) detection and treatment is promising, with ongoing innovations pushing the boundaries of precision medicine. Their integration into clinical practice could revolutionize diagnosing and treating CRC [65]. Figure 7 presents a stacked chart summarizing the cumulative contributions of quantum dots across various performance categories, highlighting their overall potential for CRC applications.

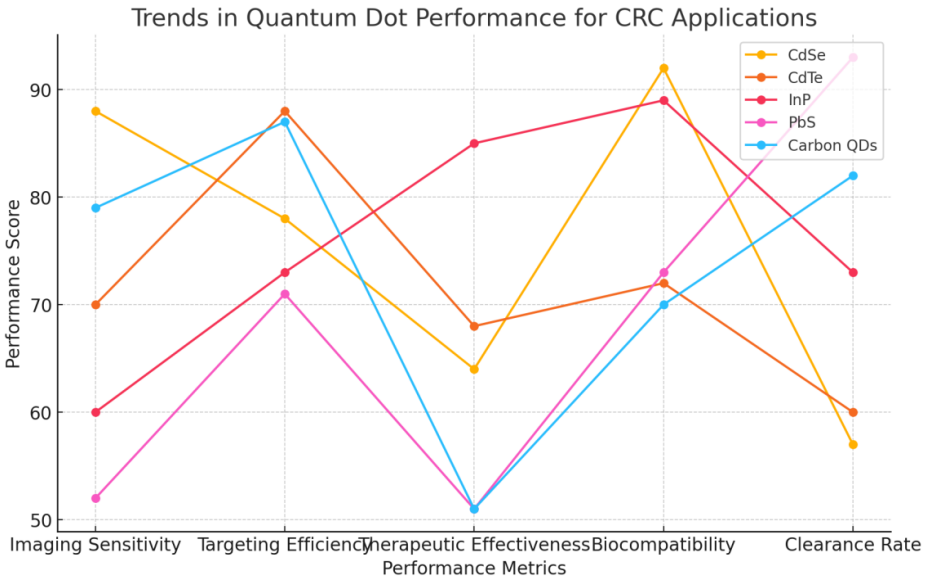

Fig. 7. Trends in quantum dots in CRC theranostics, as summarized in performance metrics

CONCLUSION

Quantum dots represent a transformative approach to colorectal cancer (CRC) diagnosis and treatment, integrating imaging and therapeutic functions within a single nanoplatform. Although challenges remain regarding toxicity and targeting efficiency, quantum dot (QD) synthesis and functionalization advances provide promising solutions. As research progresses, quantum dots may become essential tools in the early detection and precise treatment of CRC, ultimately leading to improved patient outcomes and enhanced personalized care.

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Na

CONFLICT OF INTEREST

The authors declare that there are no conflict of interest

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