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Photoresponsive polymer–quantum dot nanocomposites for targeted therapy

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ABSTRACT

This perspective explores the promising role of photoresponsive polymer–quantum dot nanocomposites in targeted therapy. These materials are notable for their ability to allow controlled drug release while simultaneously providing real-time imaging capabilities. The focus is on developing biocompatible and multifunctional platforms that address existing issues such as toxicity and stability. Such innovations could result in more personalized, image-guided cancer treatments that offer greater precision and safety.

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1. Introduction

Targeted therapy has emerged as a revolutionary strategy in modern medicine, particularly in the treatment of cancer and chronic diseases. This approach emphasizes targeted drug delivery to diseased tissues, aiming to improve therapeutic efficacy while minimizing adverse effects on healthy cells [1-3]. In recent years, various techniques and nanotechnologies have been explored to achieve this goal. Among them, photoresponsive nanomaterials have garnered significant interest due to their unique capacity to respond to light stimuli with high spatiotemporal precision [4]. Light has been accepted as a popular method for controlling drug delivery systems. Its tunable parameters such as power density, irradiation duration, and localization of exposure make it an efficient and suitable option for targeted therapies.[5] This level of precision also enables dynamic modulation of engineered cell culture systems, which are designed to replicate the complexity and diversity of human tissues. Accordingly, light-mediated control can facilitate on-demand drug release and enhance the design of adaptive and physiologically relevant cell culture environments [6]. Photosensitive polymers have attracted considerable attention due to their ability to exhibit dynamic and reversible behavior upon exposure to light [7-11]. These polymers typically contain photosensitive moieties such as azobenzene [7, 8], spiropyran [10, 12], and diarylethene [13, 14], which undergo reversible photoreactions. Such reactions allow for precise spatiotemporal control over polymer properties. Synergistic bidirectional light-responsive communications between

photosensitive polymers and functional nanofillers provide nanocomposites with reversible and precisely controllable optical-electrical characteristics. Nanofillers modulate both their own physicochemical properties as well as photochemical reactions, enabling advanced and non-invasive control of material behavior across multiple scales [15].

Nanoscale photosensitive polymer nanocomposites are of particular interest due to their nanoscale dimensions, which allows for deep tissue penetration. Combining this technology with photoactivated mechanisms provides the conditions for precise drug delivery and effective control of the treatment process [16]. These systems typically utilize photoluminescent nanoparticles and reversible photochemical processes, such as photoisomerization, to activate drug delivery in a controlled and on-demand manner. The reversibility of this technology allows for repeated and programmable treatment cycles in response to light, which is a significant advantage compared to irreversible photorefractive techniques [15].

Photoluminescent nanoparticles are divided into different categories, including semiconductor quantum dots (QDs), carbon dots, and other types [17, 18]. QDs have attracted much attention due to their size- and shape-dependent optoelectronic properties [19] and exhibit unique properties. Known for their outstanding photostability, tunability of emission wavelengths, distinct quantum phenomena, and nanoscale dimensions, these dots are usually embedded in bulk materials or attached to surfaces for practical applications [20, 21]. When incorporated into photosensitive polymers, QDs create versatile nanocomposites that

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can combine diagnostic imaging and therapeutic functions. These properties make them a very promising candidate for precise, light-controlled therapies [22]. QDs are capable of emitting light over a wide spectrum, and the emission colors are directly affected by their particle size due to the quantum confinement effect. This size-dependent luminescence has made the application of QDs significantly valuable in bioimaging and monitoring drug delivery processes [17]. QDs are categorized by their composition into single-element materials such as silicon and germanium, or compound semiconductors such as CdSe, CdTe, PbS, PbSe, as well as carbon-based materials [17]. In this context, we focus on the exciting intersection of photoresponsive polymer and quantum dot nanocomposites for targeted therapy, exploring their potential to develop precision treatment strategies. This perspective article discusses the current state of the field and identify key challenges and opportunities for advancing these systems toward clinical applications. Our focus is on the biocompatibility, and emerging multifunctional designs that integrate imaging, sensing, and therapy in a single platform. We discuss about the biodistribution and toxicity of QDs, and explain recent advances to improve long-term stability in biological buffers, increase quantum yield following bioconjugation, and improve clearance from the body.

2. Photo-responsive polymers: Fundamentals and functions

Photo-responsive polymers are a class of smart materials that undergo reversible or irreversible changes in their

physicochemical properties upon exposure to specific wavelengths of light [23].

These changes can include photoisomerization, photocleavage, photodimerization, or photothermal conversion, depending on the chemical structure of the photoactive moieties incorporated into the polymer backbone or side chains [24].

The most common photoresponsive mechanisms are shown in Table 1. The tunability of photoresponsive polymers lies in their chemical composition and the type of light they respond to. Also shown in Fig. 1 are different photosensitive groups added to methacrylate polymers to permanently degrade the block copolymer micelles upon irradiation with light [25]. NIR-responsive systems are particularly attractive for biomedical applications due to deeper tissue penetration and reduced phototoxicity compared to UV or visible light. Moreover, these polymers can be tailored to respond to specific thresholds of light intensity or duration, enabling precise spatiotemporal control over therapeutic action [26].

3. Biomedical applications

In the context of targeted therapy, photoresponsive polymers offer on-demand activation, allowing clinicians to externally trigger therapeutic effects with minimal invasiveness. They have been successfully employed in Controlled drug release [33], Shape-transformable nanoparticles, Self-immolative systems, Dual-mode therapeutic platforms, often in synergy with other stimuli such as pH, redox potential, or enzymes.

Table 1

The most common photo-responsive mechanisms.

Photoresponsive Mechanism	Components	Notes	Refs.
Photoisomerization	Azobenzene, Spiropyran	Light induces a reversible conformational switch (e.g., trans-cis isomerization) that can alter hydrophobicity, polarity, or steric configuration of the polymer, enabling drug release or shape change.	[25, 27, 28]
Photocleavage	O-nitrobenzyl derivatives	UV or visible light triggers bond cleavage in specific linkers, facilitating cargo release or disassembly of the nanoparticle or polymer system.	[29]
Photodimerization	Cinnamic acid derivatives, Anthracene, Coumarin	Light induces bonding between two chromophores, forming dimers or crosslinks that can be reversible under different wavelengths, controlling the assembly/disassembly process.	[30-32]

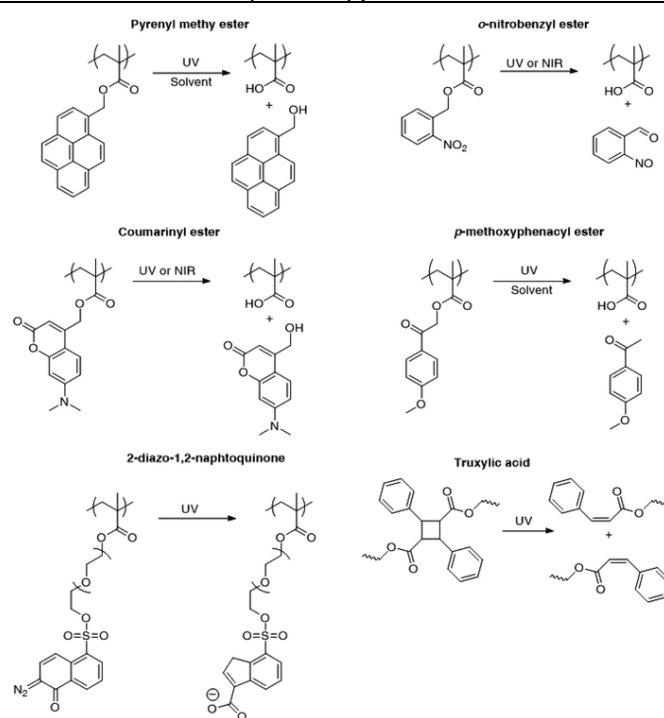


Fig. 1. Various photosensitizing moieties have been employed for the irreversible photoinduced destruction of aqueous micelles [25].

On the other hand, the unique properties of QDs have attracted much attention in the biomedical field to enable real-time bioimaging, diagnostics, drug delivery, and single molecule probes, among many other areas. Their high brightness, resistance to photobleaching, multiplexing capacity, and high surface-to-volume ratio make them excellent candidates for intracellular tracking, diagnostics, in vivo imaging, and therapeutic delivery [19, 34].

When photoresponsive polymer combined with QDs, these nanocomposites provide both a responsive matrix for drug delivery and optical feedback for real-time monitoring, enhancing the functionality of the overall nanocomposite system [35].

Recent advances in medical imaging and therapy have paved the way for better brain tumor treatments. For example, Karthik et al. [36] combined nanotechnology, imaging, and AI to potentially change brain tumor therapy with greater effectiveness and safety. The hybrid architecture allowed real-time data analysis, offering detailed insights into tumor features. The AI-driven framework achieved high accuracy, with tumor segmentation metrics like IoU of 0.89 and Dice of 0.95, and processes images in just 65 ms. Moreover,

Soltani et al. [37] studied graphene quantum dot-hyaluronic acid-quinoline nanocomposites (GQD-HA-Qu NCs) and their effects on multiple cancer cell lines. The NCs, about 225 nm in size, showed uniform spherical shapes. They induced significant, dose-dependent cell death, especially in MCF-7 and A2780 cells, and increased apoptosis via the p53 pathway. The results displayed their potential as selective anticancer agents with strong antioxidant properties, meriting further research for clinical use.

In another study, Nazri et al. [38] developed a fiber optic SPR sensor using polymer-coated carbon QDs (NCQD) for detecting chlorophyll. The sensor, coated with silver and NCQD-PVA, showed high sensitivity in the 0.01–2.0 ppm range, with a detection limit of 1.90 nm ppm⁻¹ and 0.78 ppm. It effectively distinguished chlorophyll without interference from other ions, confirmed by density functional theory.

The device demonstrated strong potential for real-time environmental monitoring, closely matching standard methods. Furthermore, Nakajima et al. [39] demonstrated real-time, high-speed charge sensing in a Si/Si_{0.70}Ge_{0.3} double quantum dot using a feedback-controlled sensor. The digital controller compensates for disturbances, enabling fast, accurate charge measurements and stable charge diagrams. This rapid tuning allows for real-time quantum dot adjustments and sub microsecond spin readout, essential for quantum information processing.

4. Benefits

Biomedical optical imaging is rapidly developing because of its desirable features of rapid frame rates, high sensitivity, low cost, portability and lack of radiation. QDs are attractive as imaging agents owing to their high brightness, and photo- and bio-stability [40].

Table 2

Key advantages of photoresponsive polymer–QD nanocomposites for targeted therapy.

Advantages	Notes	Refs.
Spatiotemporal drug control	Light-responsive polymers enable precise, localized drug release triggered by specific wavelengths (e.g., UV/visible light), minimizing off-target effects	[42, 43]
Real-time tracking	QDs' exceptional fluorescence allows simultaneous drug delivery monitoring and tumor imaging	[17, 40, 44]
Enhanced targeting	QDs functionalized with ligands (e.g., folate) improve tumor-specific accumulation via passive (EPR effect) and active targeting	[17, 45]
Multi-stimuli responsiveness	Independent control of drug release and imaging using different light wavelengths enables complex therapeutic protocols	[37, 42]
Blood-brain barrier penetration	Certain QDs (e.g., carbon/graphene variants) facilitate brain tumor drug delivery	[17, 44]

QDs possess many advantageous features, including bright fluorescence and precise targeting, making them highly promising for noninvasive in vivo imaging and image-guided surgery.

QDs present a versatile tool to enable more accurate diagnostic tools and fluoroimmunoassays, multiplexed imaging, dual imaging and therapeutic platforms, real-time *in vivo* and cellular process imaging, and tracking of single cells and biological molecules [19].

Future development efforts focus on synthesizing high-quality near-infrared QDs, identifying effective targeting molecules, understanding pharmacokinetics, and advancing imaging technology.

Combining QDs with other components like photoresponsive polymer to develop multifunctional systems for detection, imaging, and therapy holds exciting potential [41]. Photoresponsive polymer–QD nanocomposites merge the precision of light-controlled drug release with the multifunctionality of QDs, creating advanced platforms for targeted therapy.

Ultimately, designing innovative, biocompatible hybrid nanocomposites incorporating biofunctionalized QDs could pave the way for safer and more effective clinical applications. Key advantages are shown in Table 2.

5. Challenges and limitations

Using QDs in medical and theranostic applications presents significant challenges, primarily due to their water-insolubility, which hampers their proper use in bioimaging. To address this, researchers often encapsulate QDs within hydrophilic materials such as polymers or hydrogels, enhancing their water solubility and stability in biological environments [19].

A major obstacle limiting wider adoption of QDs is their potential toxicity. While some studies report no adverse effects at optimal concentrations over several months, the presence of heavy metals like cadmium, mercury, lead, and arsenic, intrinsically toxic, is a concern for human safety. Surface coatings, such as ZnS or polyethylene glycol (PEG), are commonly used to improve stability and reduce toxicity, but the risk of ion leaching remains uncertain.

Furthermore, issues like QD aggregation, non-specific binding to cell membranes and proteins, and the generation of reactive oxygen species pose additional safety concerns. In vivo, larger QDs are rapidly cleared by the immune system, complicating their use as imaging agents, and surface functionalization molecules might introduce further toxicity risks [41].

Despite these issues, a promising future involves creating hybrid nanostructured systems that conjugate polymers, biomolecules, and QDs into integrated composites. Such multifunctional nanoplateforms aim to overcome current limitations and address the safety, stability, and targeting challenges faced in biomedical applications [41]. Table 3 summarizes some limitations of these nanocomposites.

Table 3

Limitations of these nanocomposites

Challenges	Impact	Mitigation Strategies	Refs.
Toxicity	Heavy metals (Cd, Pb) in QDs cause oxidative stress, inflammation, and organ damage.	Biocompatible QDs (carbon, silicon); surface coatings (PEG, silica)	[17, 37, 45]
Stability	Degradation in biological environments compromises drug delivery efficiency	Encapsulation; surface modifications (e.g., ZnS shells)	[17, 37, 45, 46]
Targeting Specificity	Non-specific ligand binding reduces tumor selectivity.	Optimized conjugation (click chemistry, pH-sensitive linkages).	[17, 44, 45]
Long-term Effects	Unknown biodistribution and chronic toxicity risks.	Rigorous in vivo studies; renal-clearable QD designs.	[37, 45]
Optical Interference	Conjugation can alter QD photoluminescence, hindering imaging.	Advanced polymer-QD architectures preserving optical properties.	[17, 37, 42]

6. Conclusion

The incorporation of photoresponsive polymers with QDs offers a promising technique in nanomedicine, mainly for applications in targeted drug delivery and real-time monitoring. These systems impact the light-triggered properties of photoresponsive polymers together with the exceptional photostability, tunable emission spectra, and unique quantum features of QDs to produce multifunctional nanocomposites. Such improvements allow precise control over therapeutic release while providing optical response, consequently enhancing treatment specificity and monitoring capabilities. However, advancing this field requires interdisciplinary efforts focused on several important areas. Firstly, addressing biocompatibility concerns is dominant; efforts should focus on developing heavy-metal-free QDs, such as graphene quantum dots, and biodegradable photoresponsive polymers to decrease toxicity risks. Secondly, the design of multi-stimuli-responsive nanocomposites which are responsive to combined triggers like light and pH, could significantly improve tumor targeting and treatment efficiency. Furthermore, integrating theranostic functionalities i.e., combining photodynamic or photothermal therapy with drug delivery, can form synergistic therapeutic effects. The development of closed-loop smart nanosystems, which are capable of autonomously adjusting drug release in response to real-time tumor microenvironment cues, can be considered as an exciting cutting-edge approach.

Moreover, for successful clinical translation, efforts towards standardizing synthesis protocols, scaling up production processes, and establishing comprehensive long-term toxicity assessments are vital. Overall, the conjunction of photoresponsive polymers and QDs has the potential to modify oncology by offering extraordinary control over drug delivery and real-time diagnostics. Overcoming current challenges related to toxicity and stability through innovative material strategies will accelerate the clinical translation of these nanoplateforms, finally enabling personalized, image-guided cancer therapies.

Author contributions

Mahsa Borzouyan Dastjerdi: Investigation, Writing – original draft, Writing – review & editing; **Reza Khoda dadi:** Writing – original draft, Writing – review & editing, **Jalaladdin Hosseinzadeh:** Writing – review & editing.

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Conflict of interest

The authors declare no conflict of interest.

Data availability

No data is available.

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