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RESEARCH ARTICLE

QUANTUM DOTS: THE DUAL MODALITY IN CANCER THERANOSTICS

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Abstract

Nanotechnology has emerged as a groundbreaking approach offering new therapies and hope for treating malignant diseases. The remarkable and tunable optical capabilities of semiconductor-based nanoparticles, known as quantum dots (QDs), depending on size and composition, have enabled a multitude of applications in the biological areas. They are perfect for drug delivery, biomolecular tracking, in vitro and in vivo imaging, photodynamic therapy, and the diagnosis and treatment of different cancers due to their great photostability and resistance to photobleaching. Tagged with biopolymers, proteins, and antibodies, QDs accumulate at target sites, fluorescing upon irradiation for imaging or inducing apoptosis in tumor cells for therapy. Notably, carbon quantum dots exhibit low cytotoxicity, positioning QDs as a promising technique for diverse disease management[1].

Introduction:-

Quantum dots (QDs) are nanoscale semiconductor crystals first described by Ekimov and Onushenko in 1981 and applied to biological imaging in 1998. These particles, composed of 100-100,000 atoms and measuring 2-10 nanometers, emit light ranging from UV to IR based on their size and composition. This unique property, known as "quantum confinement," along with a significant Stokes shift, enhances their sensitivity and reduces optical overlap. QDs find applications in solar cells, LED technology, imaging, drug delivery, and cancer therapy. Despite their potential, clinical adoption remains limited. This article reviews recent QD preparation and characterization methods, biomedical applications, ongoing clinical trials, and compares QDs to commercial alternatives, highlighting essential considerations for improving their clinical viability.

Preparation Of Quantum Dots

The preparation of QDs involves assembling molecular precursors into nanocrystals through various physical and chemical approaches, focusing on uniformity, reproducibility, and scalability.

1. Colloidal Synthesis: This widely used method involves injecting precursor metals into a high-temperature solvent, followed by nucleation and crystal growth. While this method yields QDs with high monodispersity and quantum yield, the use of organic solvents poses toxicity risks and necessitates post-synthesis modifications for aqueous solubility[1].

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2. Plasma Synthesis: This gas-phase method allows precise control over the size, shape, surface, and composition of QDs, making it ideal for tailored applications. However, plasma-synthesized QDs typically require surface modifications for dispersion in solvents [2].
3. Biotemplate-Based Synthesis: Utilizing biomacromolecules as templates offers precise control over QD characteristics, enhancing stability and solubility. However, the mild reaction conditions required can impact optical properties[3].
4. Electrochemical Synthesis: This eco-friendly method combines QDs with nanoparticle-loaded graphene, offering high yield, low biotoxicity, and broad application potential. However, it requires significant pre-treatment and purification steps, limiting mass production[4].

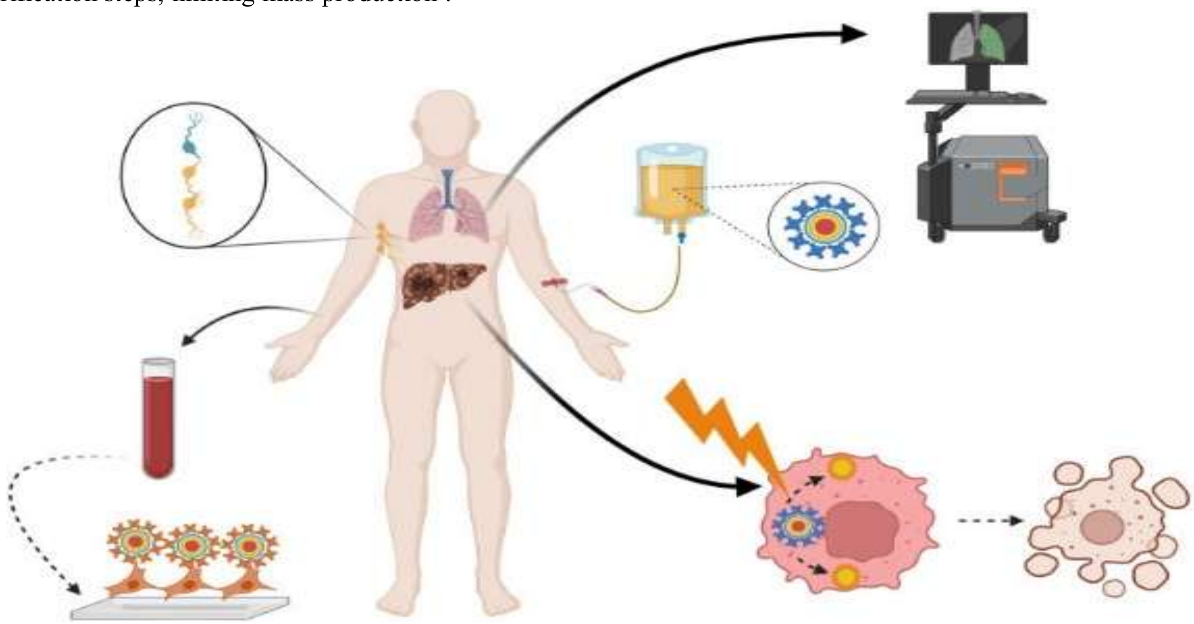

Figure 1:- Theranostic Uses of Quantum Dots: Cell Imaging, Fluorescence imaging, Lymph node metastasisdiagnosis, Photo dynamic therapy.

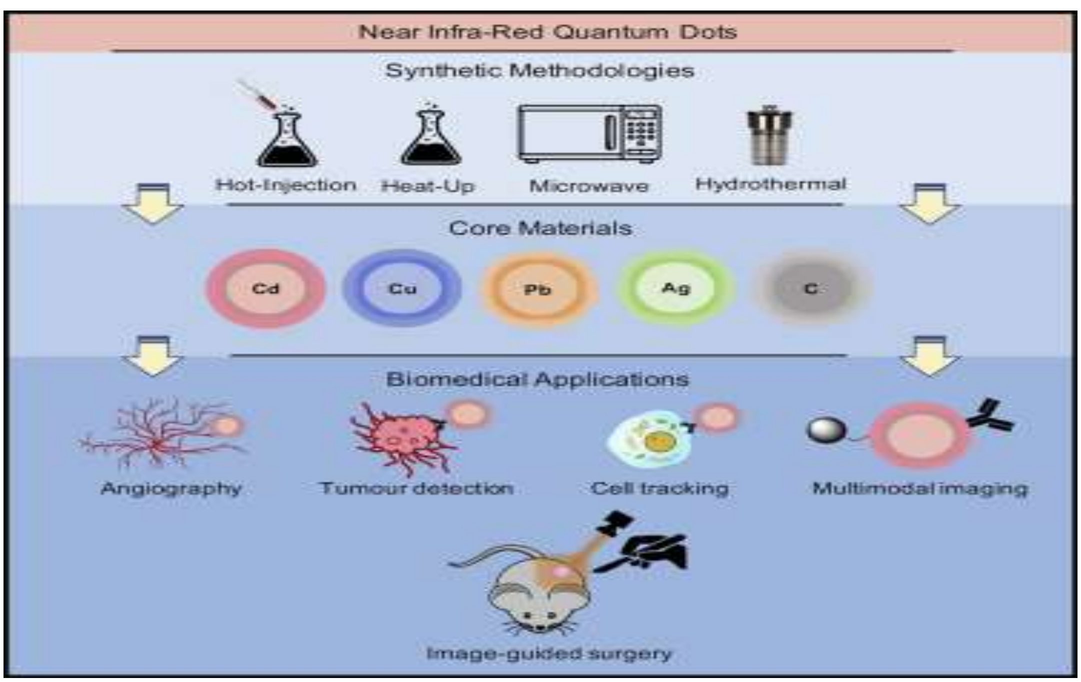

Figure 2:- Graphical abstract representing the methods of preparation, core materials used in its synthesis And their biomedical applications.

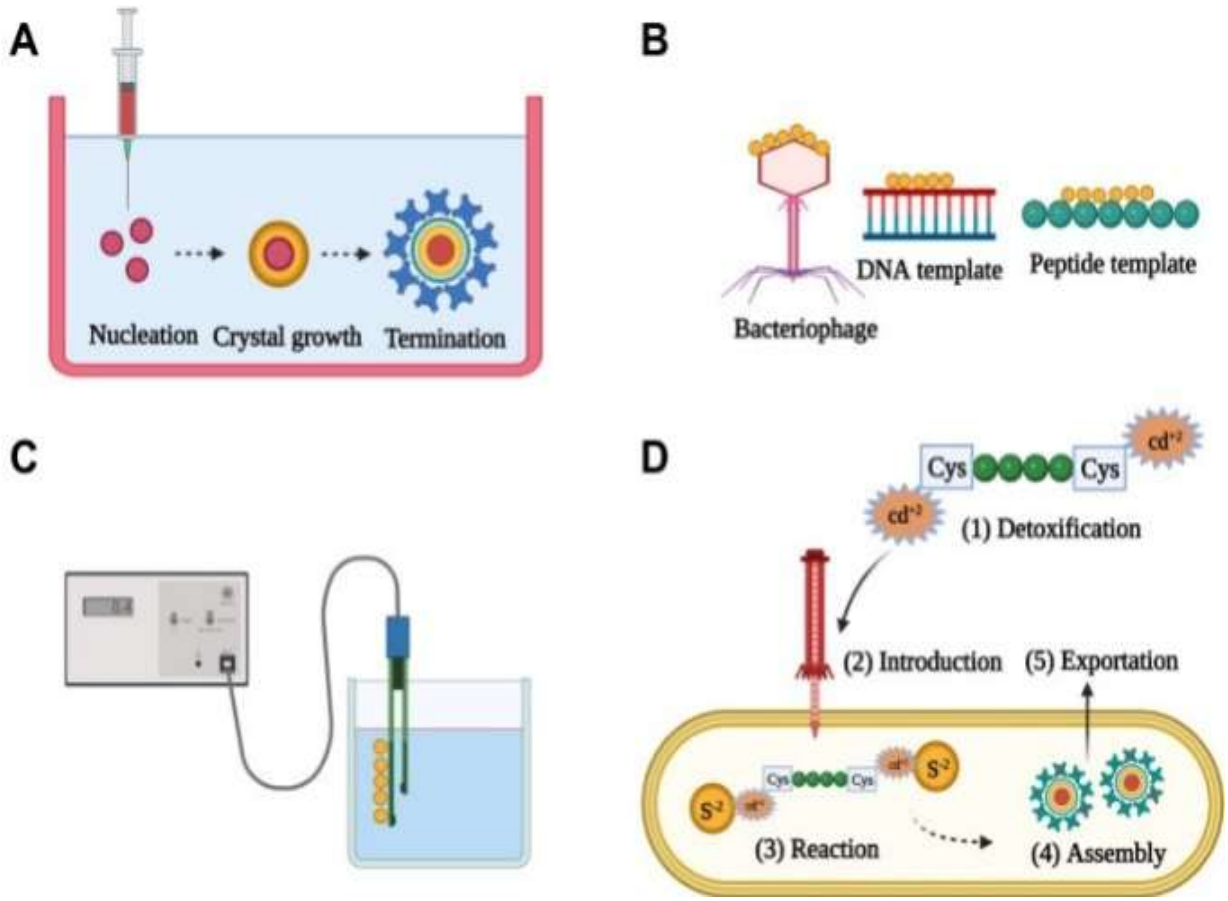

Figure 3:- Methods used for preparation QDs.

A: Colloidal Synthesis: To facilitate QDs conversion into molecular state precursors are injected into organic or aqueous system under high temperature.

B: Bio-template based synthesis: Biological entities like bacteriophages, genetically-engineered viruses are used as precursors inti QDs.

C: Electro-chemical assembly: QDs acts as a precursor ions at the electrolyte metal interface.

D: Bio-genic synthesis: Detoxified heavy metal ions are introduced into microorganism via binding to cysteine-terminated peptides, where they react with endogenous co-precursors and assemble into QDs, which are later exported out of the microorganism**.**

Properties Of Quantum Dots

QDs are tiny metal particles that emit light when exposed to UV light, with emission color determined by size. These properties, including small size, tunable emission, high brightness, and photostability, make them advantageous for imaging and therapeutic applications[5].

Optical Properties:

QDs absorb light, elevating electrons and creating excitons that release energy as light (fluorescence). The confinement energy, determined by QD size, allows tuning of absorption and emission properties, enhancing detection sensitivity and reducing optical overlap[6].

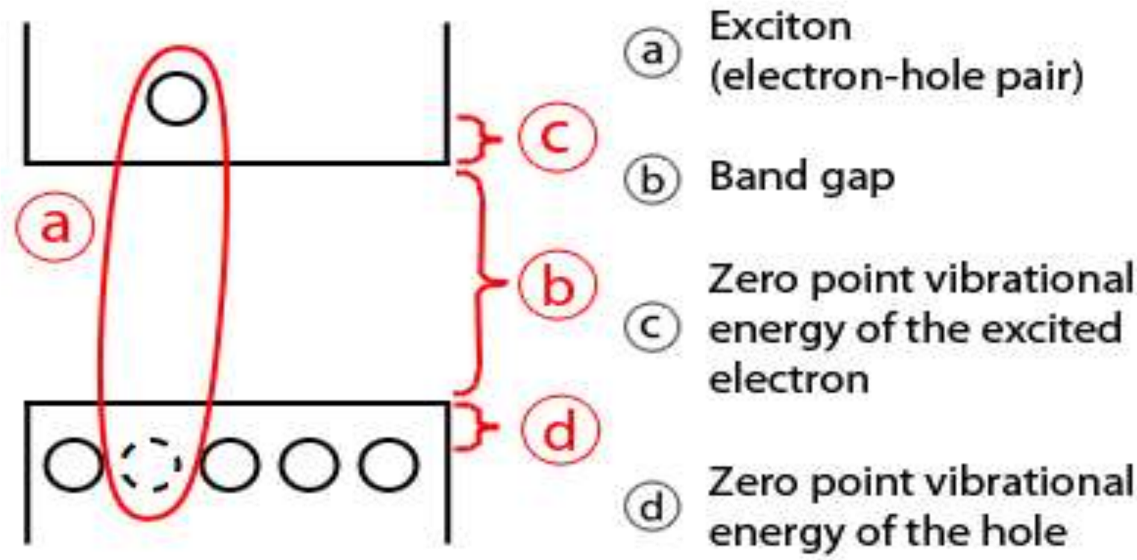

Figure 4:- Depiction of photo excitability of the electron causing photo sensitivity.

Advantages Of Quantum Dots

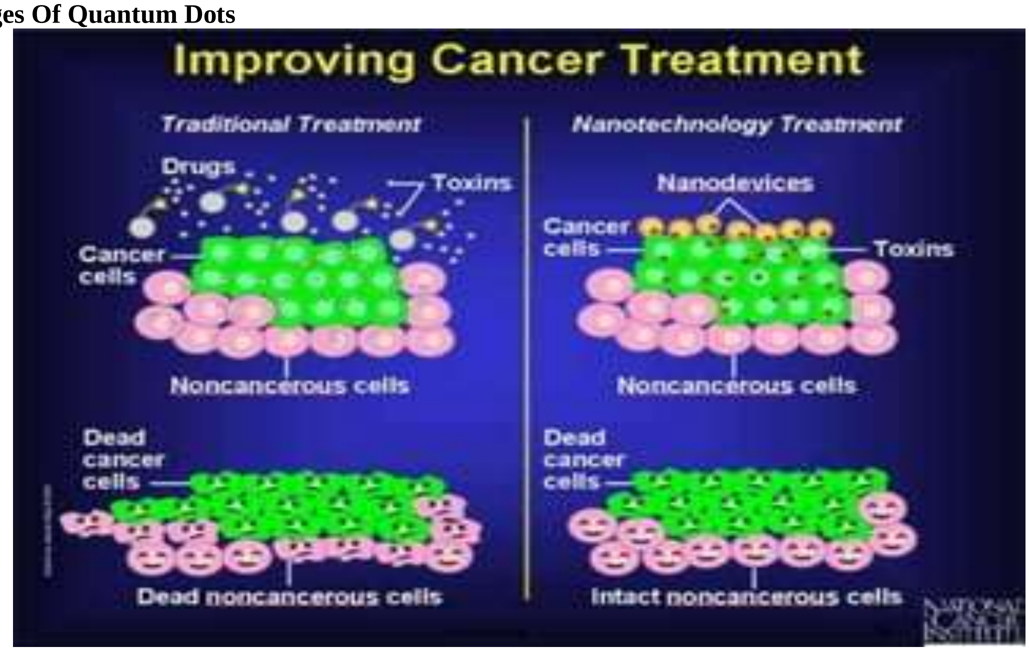

Figure 5:- Improved advantage due to reduced side effects as the nano drugs bind only to the cancerous cells and Does not effect the healthy noncancerous cells.

1. Photostability: QDs maintain consistent excitation levels under prolonged light exposure[7].
2. Signal-to-Noise Ratio: Efficient excitation sources enhance the signal-to-noise ratio[8].
3. Emission Precision: Symmetrical emissions enable multiplexing assessments[9].
4. Fluorescence Lifetimes: Longer lifetimes make QDs suitable for photogrammetric applications[10].
5. Single Excitation Source: QDs can be excited using common light sources, facilitating imaging customization[11].
6. High Sensitivity: Broad excitation spectra allow compatibility with existing sources and emission frequency customization[12].

Disadvantages Of Quantum Dots

1. Toxicity: QDs can generate reactive oxygen species (ROS), induce apoptosis, cause mitochondrial damage, and exhibit renal retention[13].

2. Target Specificity: QDs may enter various cells without specific ligands, leading to off-target effects[14].
3. Environmental Biocompatibility: Non-biodegradable QDs can impact the food chain and are consumed by animals[15].
4. Clinical Trials: Research on QDs is nascent, with limited efficacy in vivo compared to in vitro and few active clinical trials[16].

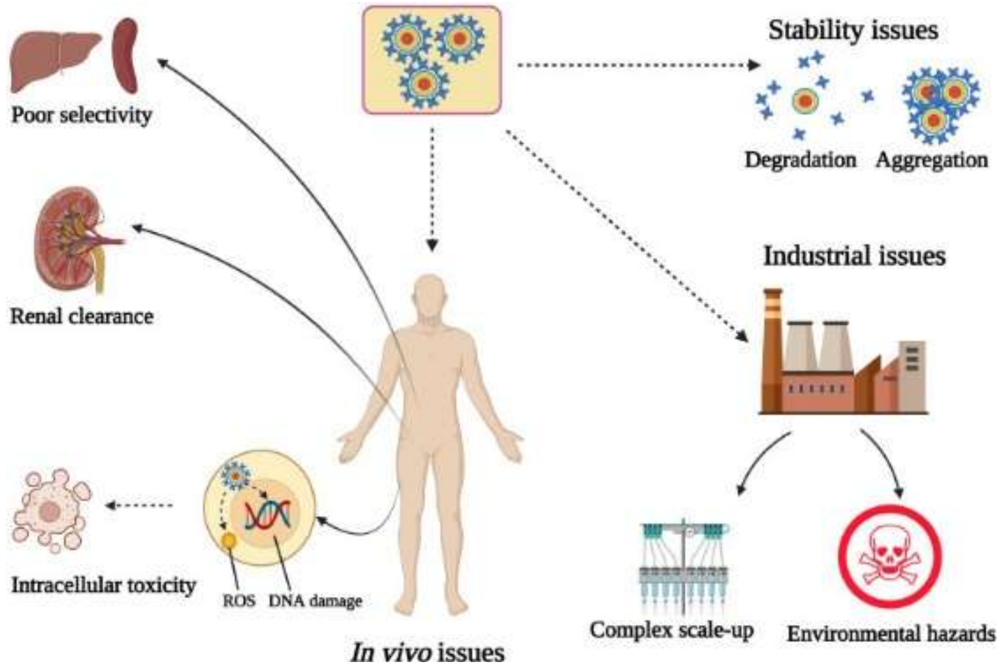

Figure 6:- Disadvantages of Quantum Dots.

Functional Quantum Dots: Fabrication
QDs can be paired with particles that aid in distinguishing targets and surface modifications can reduce non-specific binding, minimize aggregation, and enhance imaging clarity. Key challenges include toxicity, fluorescent properties, surface chemistry alteration, and specific objectives[17].

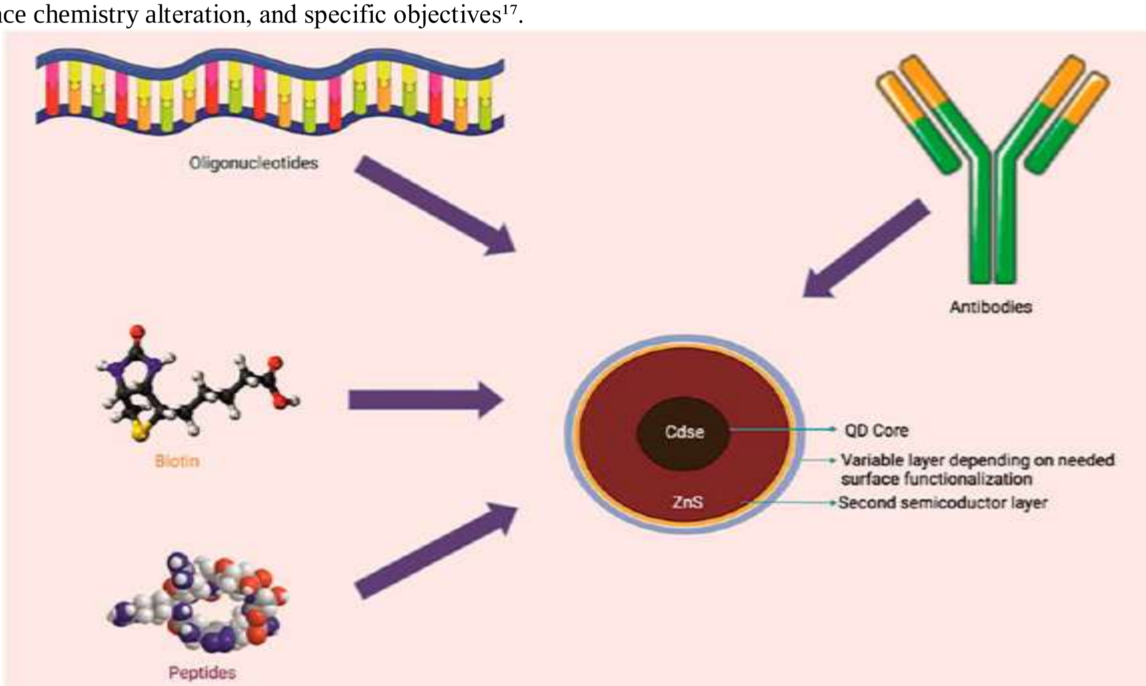

Figure 7:- Schematic representation of simple quantum dot assembly.

Applications Of Quantum Dots

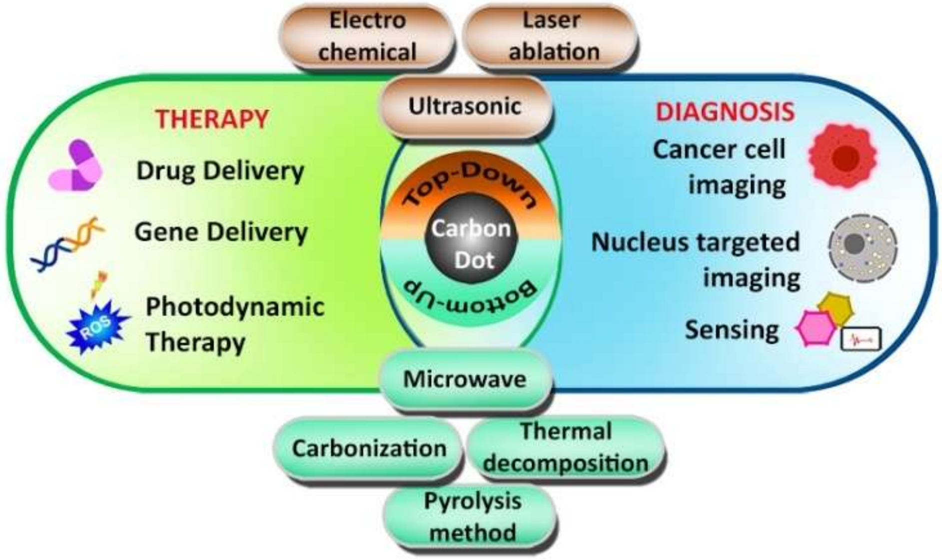

Figure 8:- Various applications of Quantum dots in bioimaging and diagnosis.

1. Biomedical Imaging Applications: QDs' photostability, surface chemistry, and significant Stokes shift make them ideal for repeated imaging, cell tracking, and image-guided surgery. They enable multiplex imaging and comprehensive tissue visualization[18].

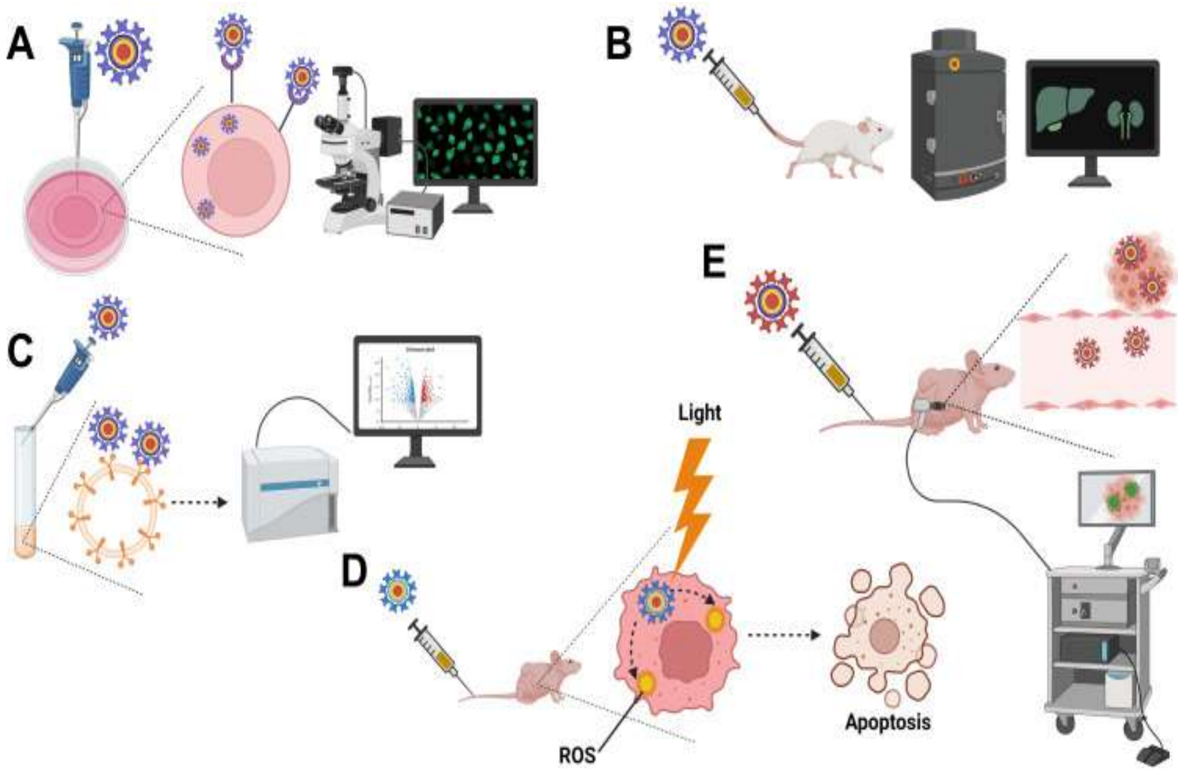

Figure 9:- Pictorial representation of applications of Quantum Dots

(A) Cellular imaging. Quantum dots which are functionalized by binding with specific targeting molecules are utilized as fluorescent markers that help in visualizing cells internally through fluorescence microscopy or confocal laser scanning microscopy (CLSM).

(B) Live imaging. Quantum dots which are modified with tissue-specific targeting molecules can be employed to visualize specific organs using in vivo imaging systems (IVIS) after administration.
(C) Flow cytometry. Quantum dots that are decorated with ligands specific to certain cells are used as fluorescent probes for cell sorting during fluorescence-activated cell sorting (FACS). Additionally Quantum dots offer superior capabilities in polychromatic cell sorting compared to traditional organic dyes.
(D) Photodynamic therapy (PDT). Quantum dots, on being exposed to light, function as photosensitizers or transfer energy to other photosensitizers which produce reactive oxygen species (ROS) in the targeted area, inducing apoptotic cell death during cancer therapy.
(E) Tractable drug delivery systems. Quantum dots can act as carriers for drugs, delivering them to various tissues with excellent extravasation and tissue penetration abilities due to their extremely small particle sizes.

2. Live Cell Imaging and In Vivo Imaging: QDs' high quantum yield, brightness, and stability against photobleaching make them excellent fluorescent probes for visualizing intracellular components and organs[19].
3. Photodynamic Therapy (PDT): QDs serve as photosensitizers or energy donors, inducing ROS production and apoptosis in targeted tumor cells. Their properties can be optimized for effective treatment of deep-seated tumors[20].

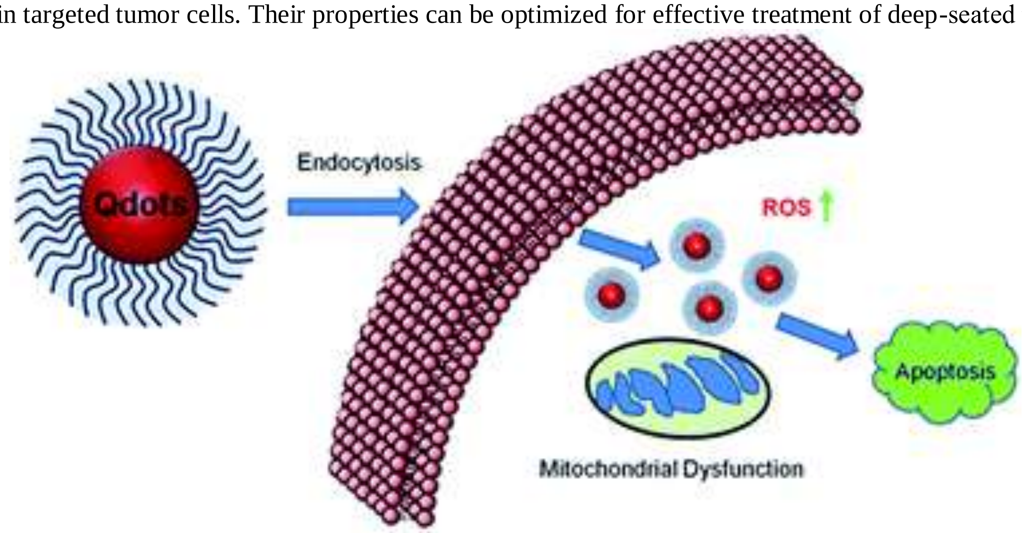

Figure 10:- Pictorial representation of Photo dynamic therapy.

4. Early Diagnosis of Cancer: QDs enhance fluorescence imaging, aiding in early tumor detection and improving diagnostic accuracy. They are used in various biomedicine applications, including cellular transport investigation, imaging, and bioassays[21].

5. Diagnostics and Imaging: QDs assist in identifying cancer markers, enhancing fluorescence labeling, and monitoring disease progression[22].
6. Drug Delivery and Therapeutics: QDs enhance therapeutic outcomes and enable tailored drug administration, especially in the treatment of cancer[23].

Mechanism Of Actions Of Quantum Dots
QDs' fluorescence and biosensing capabilities make them valuable in diagnosing and treating infections, including viral diseases like COVID-19. They are used in detecting organisms and biomolecules, providing a promising approach for clinical diagnostics[24].

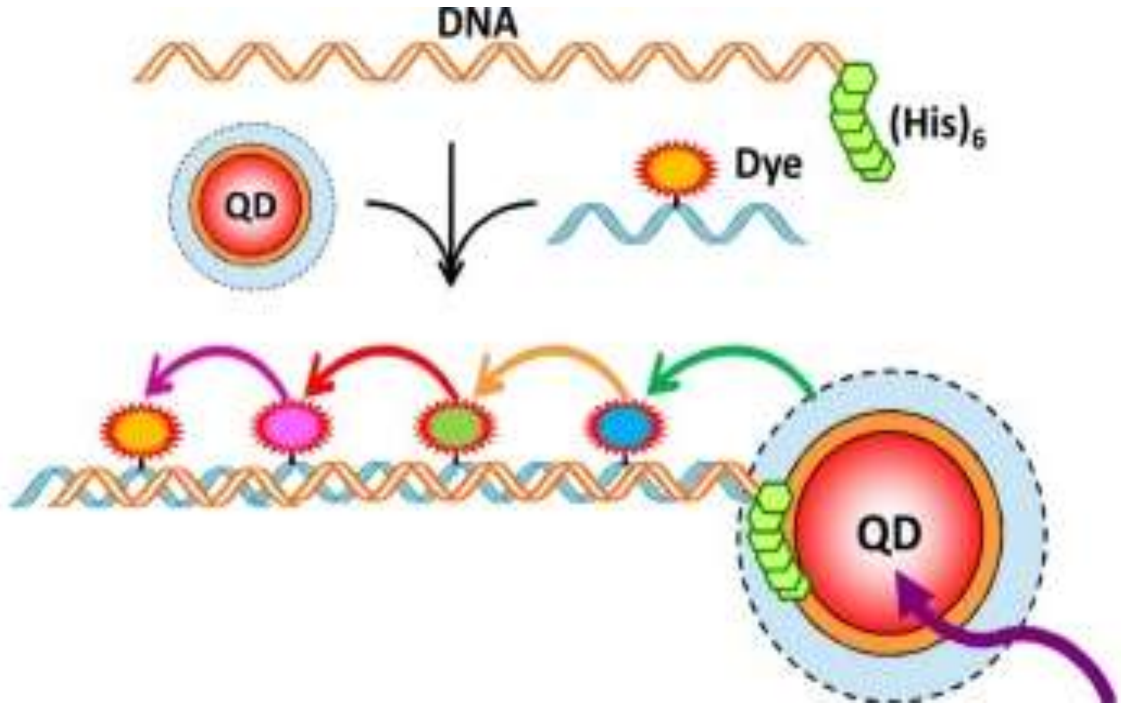

Figure 11:- Quantum Dots on being administered parenterally identify the target and bind to them and emit light depending on their size.

Conclusion:-

QDs offer significant potential in cancer diagnosis, treatment, and prevention. Despite challenges in toxicity and clinical adoption, ongoing research and development promise advancements in QD-based therapies. Further efforts are expected to enhance QD applications in nanomedicine, leading to improved cancer management[25].

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