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A REVIEW ON : APPLICATION OF NANOPARTICLES IN CANCER

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Abstract:
Nanotechnology has emerged as a promising field in cancer therapy due to the unique properties exhibited by nanoparticles. These tiny particles, typically ranging from 1 to 100 nanometers in size, offer numerous advantages in the diagnosis, imaging, and treatment of cancer. This review summarizes the diverse applications of nanoparticles in cancer management.

One of the key applications of nanoparticles in oncology is drug delivery. Nanoparticles can be engineered to encapsulate chemotherapeutic agents, shielding them from premature degradation and enhancing their accumulation at the tumor site through passive targeting via the enhanced permeability and retention effect. Additionally, surface functionalization of nanoparticles enables active targeting, facilitating specific interaction with cancer cells while minimizing off-target effects.

In addition to drug delivery, nanoparticles play a crucial role in cancer imaging. Contrast agents based on nanoparticles offer superior imaging capabilities, enabling early detection, accurate diagnosis, and monitoring of therapeutic responses. Functionalization with targeting ligands further improves the specificity and sensitivity of imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), and fluorescence imaging.

Furthermore, nanoparticles are being explored for their potential in cancer theranostics, combining therapy and diagnostics in a single platform. Theranostic nanoparticles can deliver therapeutic payloads while simultaneously providing real-time feedback on treatment efficacy, allowing for personalized and adaptive treatment strategies.

Moreover, nanoparticles have shown promise in overcoming multidrug resistance, a significant challenge in cancer treatment. By modulating drug efflux mechanisms and bypassing resistance pathways, nanoparticle-based formulations have the potential to re-sensitize resistant cancer cells to chemotherapy.

Key Elements: Nanoparticles & its characters, Cancer, Cancer therapy, Current cancer treatment,Case studies and success stories**.**

I. Introduction to Nanoparticles

Definition and Characteristics: Nanoparticles are particles that range in size from 1 to 100 nanometers in diameter. To put that into perspective, a nanometer is one-billionth of a meter, making nanoparticles incredibly small. At this scale, they exhibit unique physical, chemical, and biological properties that differ from bulk materials of the same composition. These properties arise due to the increased surface area-to-volume ratio, quantum effects, and surface energy effects that dominate at the nanoscale.

The field of nanotechnology has unlocked the potential of nanoparticles across diverse domains, from healthcare to electronics, catalysis to environmental science. Their versatility arises from their tunable properties, allowing scientists to engineer nanoparticles with specific functionalities tailored to various applications.[1]

In medicine, nanoparticles have emerged as promising tools for targeted drug delivery, enabling precise administration of therapeutic agents to diseased tissues while minimizing side effects. Additionally, they play a crucial role in medical imaging, offering enhanced contrast and resolution for diagnostics.[12]

In electronics, nanoparticles contribute to the development of miniaturized devices with improved performance and efficiency. Quantum dots, for example, exhibit size-dependent optical properties, paving the way for vibrant displays and advanced sensors. [12]

Moreover, nanoparticles find applications in environmental remediation, where their high surface area facilitates efficient pollutant capture and degradation. In energy, they hold potential for enhancing solar cells, batteries, and fuel cells, driving forward the quest for sustainable energy solutions.[2]

Brief overview of there Unique Properties:

a) **Large Surface Area:** Nanoparticles have an exceptionally high surface area compared to their volume, which enhances their reactivity and makes them suitable for various applications such as catalysis and drug delivery.[4]
b) **Quantum Effects:** Quantum phenomena become more pronounced at the nanoscale, leading to unique optical, electronic, and magnetic properties. For instance, quantum dots are semiconductor nanoparticles that exhibit size-dependent fluorescence, making them valuable for imaging and sensing applications.[4]
c) **Surface Energy Effects:** At nanoscale dimensions, surface atoms or molecules comprise a significant proportion of the material, resulting in increased surface energy. This can influence the stability, reactivity, and interactions of nanoparticles with their environment.[4]
d) **Tunable Properties:** Nanoparticle properties can be tailored by controlling their size, shape, composition, and surface chemistry. This tunability allows researchers to design nanoparticles with specific functionalities for targeted applications in fields such as medicine, electronics, and energy.[4]
e) **Versatile Applications:** Due to their unique properties, nanoparticles find applications in diverse fields including medicine (drug delivery, imaging), electronics (nanoelectronics, sensors), catalysis, environmental remediation, and energy (solar cells, fuel cells).

1. Understanding Cancer

Cancer: Cancer is a complex group of diseases characterized by the uncontrolled growth and spread of abnormal cells. Normally, cells grow, divide, and die in a controlled manner, but cancer disrupts this process. Instead of dying, cancerous cells continue to divide and form new abnormal cells, which can invade other tissues and organs, leading to the formation of tumors.

There are over 100 different types of cancer, each with its own specific characteristics and behaviors. Cancer can occur almost anywhere in the body and can affect people of all ages, though the risk increases with age.[10]

Some common risk factors for cancer include genetic predisposition, exposure to carcinogens such as tobacco smoke or ultraviolet radiation, unhealthy lifestyle choices like poor diet and lack of exercise, certain infections, and environmental factors.

Treatment for cancer varies depending on the type, stage, and location of the cancer, but it often includes a combination of surgery, chemotherapy, radiation therapy, immunotherapy, hormone therapy, or targeted therapy. Early detection and advances in treatment have improved outcomes for many cancer patients, but cancer remains a significant health challenge worldwide. [10]

Explanation of Cancer and its Mechanisms:

Cancer is a complex group of diseases characterized by the uncontrolled growth and spread of abnormal cells. Normal cells in the body grow, divide, and die in a regulated manner, maintaining tissue homeostasis. However, cancerous cells evade these regulatory mechanisms, leading to the formation of tumors and disruption of normal bodily functions. [10]

The development of cancer typically involves multiple steps, including:

a) **Initiation:** Genetic mutations or alterations in cellular DNA occur, often due to exposure to carcinogens such as tobacco smoke, ultraviolet radiation, or certain chemicals. These mutations can activate oncogenes (genes promoting cell growth) or inactivate tumor suppressor genes (genes inhibiting cell growth), initiating the transformation of normal cells into cancerous cells.
b) **Promotion:** Proliferation of initiated cells is promoted by various factors, including chronic inflammation, hormonal imbalances, and immune system dysfunction. This stage involves the expansion of the mutated cell population and the formation of pre-malignant lesions.
c) **Progression:** Additional genetic and epigenetic changes accumulate in the progressing tumor cells, leading to increased aggressiveness, invasion of surrounding tissues, and metastasis (spread) to distant organs. Tumor cells may also develop resistance to apoptosis (programmed cell death), enabling their survival and proliferation despite adverse conditions.

The heterogeneity of cancer, both within tumors and among different cancer types, presents significant challenges for diagnosis and treatment. Additionally, the tumor microenvironment, comprising various cell types, extracellular matrix components, and signaling molecules, plays a crucial role in cancer progression and therapy resistance.

Challenges in Current Cancer Treatments:

Despite significant advancements in cancer research and treatment, several challenges persist:[8]

i. **Treatment Toxicity:** Conventional cancer therapies such as chemotherapy and radiation therapy can cause severe side effects due to their non-specific targeting of rapidly dividing cells, leading to damage to healthy tissues and organs.
ii. **Resistance:** Cancer cells can develop resistance to chemotherapy, targeted therapy, and immunotherapy through various mechanisms, including genetic mutations, activation of alternative signaling pathways, and evasion of immune surveillance. This resistance often leads to treatment failure and disease recurrence.
iii. **Metastasis:** Metastatic spread of cancer cells to distant sites remains a major hurdle in cancer treatment. Metastatic tumors are often more challenging to treat and are associated with poorer prognoses.
iv. **Late Diagnosis:** Many cancers are diagnosed at advanced stages when treatment options are limited, highlighting the need for improved early detection methods and screening programs.

3. Nanoparticles in Cancer Therapy

Nanoparticles have emerged as powerful tools in the field of cancer therapy, offering innovative approaches to improve treatment efficacy while minimizing side effects. Here's how nanoparticles are revolutionizing cancer therapy:[10]

1. **Targeted Drug Delivery:** Nanoparticles can be engineered to deliver therapeutic agents, such as chemotherapy drugs or molecular targeted therapies, directly to cancer cells while sparing healthy tissues. This targeted drug delivery is achieved through various mechanisms, including:

- Surface functionalization: Nanoparticles can be coated with ligands or antibodies that specifically recognize and bind to receptors overexpressed on cancer cells, facilitating their internalization and drug release within tumor tissues.
- Passive targeting: Nanoparticles can exploit the enhanced permeability and retention (EPR) effect, which allows them to accumulate preferentially in tumor tissues due to the leaky vasculature and impaired lymphatic drainage characteristic of solid tumors.
- pH or stimulus-responsive drug release: Nanoparticles can be designed to release their payload in response to specific stimuli present in the tumor microenvironment, such as acidic pH, enzymes, or temperature changes, enhancing drug delivery efficiency while reducing systemic toxicity.[10]

2. **Enhanced Permeability and Retention (EPR) Effect:** The EPR effect is a phenomenon where nanoparticles preferentially accumulate in tumor tissues due to their unique characteristics, including leaky vasculature and impaired lymphatic drainage. By leveraging the EPR effect, nanoparticles can passively target and accumulate within tumors, enhancing the delivery of therapeutic agents while minimizing exposure to healthy tissues. This selective accumulation enables higher drug concentrations at the tumor site, improving treatment efficacy and reducing systemic side effects associated with conventional chemotherapy. [10]

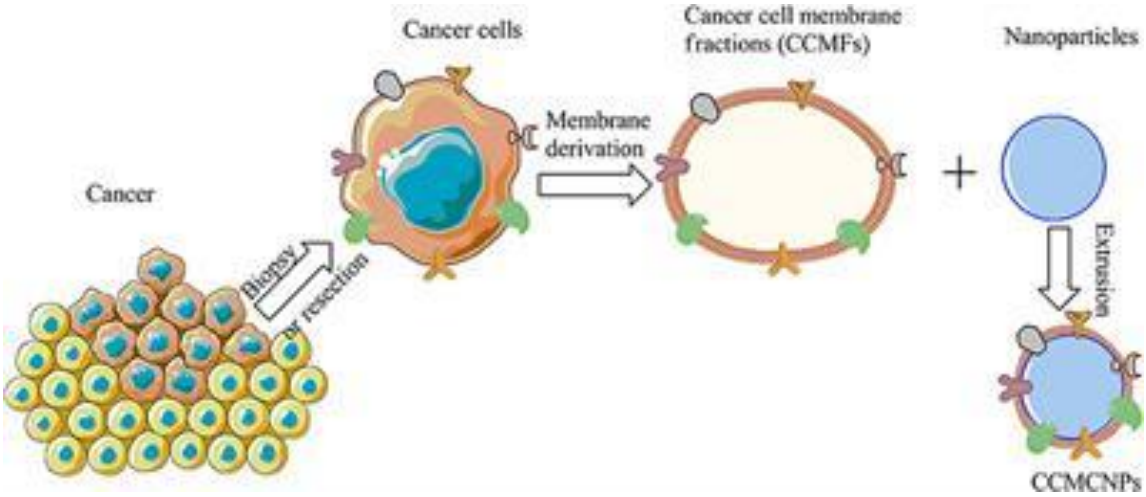

Fig-01

3. **Overcoming Multidrug Resistance:** Multidrug resistance (MDR) is a major obstacle in cancer treatment, where cancer cells develop resistance to multiple chemotherapy drugs through various mechanisms, including drug efflux pumps, altered drug metabolism, and anti-apoptotic pathways. Nanoparticles offer several strategies to overcome MDR and enhance the sensitivity of cancer cells to chemotherapy, including:

- Co-delivery of multiple drugs: Nanoparticles can encapsulate multiple chemotherapy drugs or combination therapies within a single carrier, allowing for synergistic effects and overcoming resistance mechanisms.
- Inhibition of drug efflux pumps: Nanoparticles can be engineered to inhibit drug efflux pumps overexpressed on cancer cells, preventing the extrusion of chemotherapy drugs and enhancing intracellular drug accumulation.
- Targeting drug-resistant pathways: Nanoparticles can deliver therapeutic agents targeting specific signaling pathways involved in drug resistance, such as anti-apoptotic proteins or DNA repair mechanisms, to sensitize cancer cells to chemotherapy. [10]

4. **Types of Nanoparticles**

Nanoparticles come in various forms, each offering unique properties and applications. Here are three major types of nanoparticles and their roles in drug delivery and imaging:[4]

i. **Liposomes:** Liposomes are spherical vesicles composed of lipid bilayers, typically ranging from tens to hundreds of nanometers in diameter. They are widely used as carriers for drug delivery due to their biocompatibility, versatility, and ability to encapsulate both hydrophobic and hydrophilic drugs. Liposomes can be functionalized with targeting ligands or antibodies to achieve specific delivery to cancer cells or diseased tissues, minimizing systemic toxicity. Moreover, liposomes can be engineered to release their payload in response to stimuli such as pH, temperature, or enzymatic activity, enabling controlled drug release at the target site. Besides drug delivery, liposomes also find applications in imaging and diagnostics, serving as contrast agents for various imaging modalities such as MRI, CT, and ultrasound.[4]

ii. **Polymeric Nanoparticles:** Polymeric nanoparticles are nanoparticles composed of synthetic or natural polymers, typically ranging from 10 to 200 nanometers in size. They are versatile carriers for drug delivery and imaging agents due to their tunable properties, biocompatibility, and ability to encapsulate a wide range of therapeutics. Polymeric nanoparticles can be engineered to control drug release kinetics, enhance drug stability, and target specific tissues or cells. Additionally, they can be functionalized with imaging probes or contrast agents for molecular imaging and visualization of biological processes. Polymeric nanoparticles offer advantages such as sustained drug release, prolonged

circulation time, and protection of drugs from degradation, making them promising candidates for various therapeutic applications, including cancer therapy, infectious diseases, and inflammatory disorders.[6]

iii. **Metallic Nanoparticles:** Metallic nanoparticles consist of metallic elements such as gold, silver, iron, or platinum, typically ranging from 1 to 100 nanometers in size. They exhibit unique optical, electronic, and magnetic properties that make them valuable for therapeutic and diagnostic applications. Metallic nanoparticles are used in cancer therapy as photothermal agents, where they convert light energy into heat to selectively ablate cancer cells while sparing healthy tissues. Additionally, metallic nanoparticles can serve as radiosensitizers, enhancing the effectiveness of radiation therapy by increasing the local dose of radiation to tumor tissues. In diagnostics, metallic nanoparticles are employed as contrast agents for various imaging modalities, including CT, MRI, and photoacoustic imaging. Their high surface area-to-volume ratio allows for functionalization with targeting ligands or imaging probes, enabling specific molecular imaging and early detection of diseases.

5. Targeted Drug Delivery with Nanoparticles

Targeted drug delivery using nanoparticles is a promising approach in medicine, offering more precise treatment with reduced side effects. Here's a breakdown of the two main strategies:[4]

a) Passive Targeting:

- Passive targeting relies on the unique characteristics of tumors or diseased tissues. Many tumors have leaky blood vessels with larger gaps between cells, allowing nanoparticles to accumulate more readily in these areas through a phenomenon known as the Enhanced Permeability and Retention (EPR) effect.
- Nanoparticles designed for passive targeting are often engineered to have sizes ranging from 10 to 200 nanometers, which enables them to escape from circulation and accumulate in the tumor tissue while avoiding clearance by the immune system. [4]

b) Active Targeting:

- Active targeting involves the surface modification of nanoparticles with specific ligands that can recognize and bind to receptors overexpressed on the surface of target cells, such as cancer cells.
- Ligand-mediated targeting enhances the specificity of drug delivery to the desired site, improving efficacy and reducing off-target effects.

Ligands commonly used for active targeting include antibodies, peptides, aptamers, and small molecules. These ligands can selectively bind to receptors or antigens on the target cells, facilitating internalization of the nanoparticles into the cells through receptor-mediated endocytosis. [4]

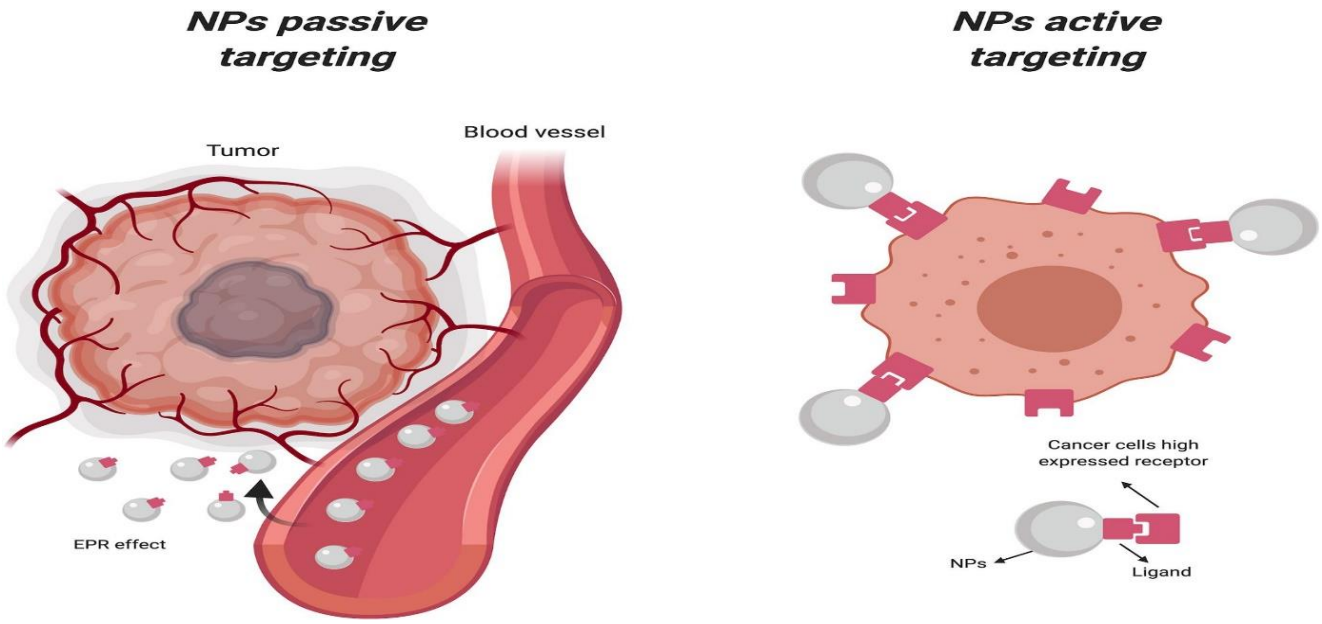

Fig no. 2. **Targeted Drug Delivery with Nanoparticles**

6. Applications in Imaging

Nanoparticles offer versatile solutions for enhancing imaging modalities and combining therapy with diagnostics, ushering in a new era of precision medicine. Here's how nanoparticles are transforming medical imaging:[15]

- **Contrast Agents:** Nanoparticles serve as powerful contrast agents across various imaging modalities, including Magnetic Resonance Imaging (MRI), Computed Tomography (CT), and Positron Emission Tomography (PET). By enhancing the contrast between tissues or highlighting specific molecular targets, nanoparticles improve the sensitivity, resolution, and accuracy of diagnostic imaging. Key examples include: [15]

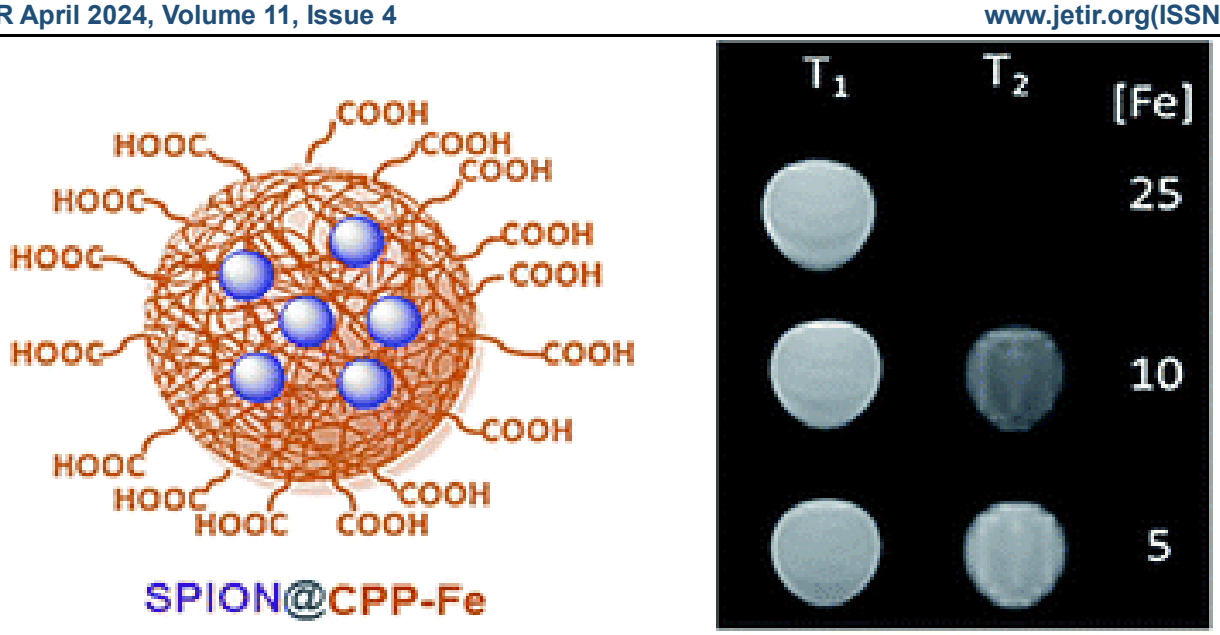

Fig-03

- **MRI Contrast Agents:** Superparamagnetic iron oxide nanoparticles (SPIONs) and gadolinium-based nanoparticles are used as MRI contrast agents, providing high contrast for visualizing anatomical structures and detecting pathological changes such as tumors, inflammation, or vascular abnormalities. [15]
- **CT Contrast Agents:** Gold nanoparticles and iodine-based nanoparticles are utilized as CT contrast agents, enabling precise delineation of tissues and vascular structures in high-resolution imaging. Their high X-ray attenuation properties enhance the contrast between tissues, facilitating the detection and characterization of tumors, vascular diseases, and other abnormalities. [15]
- **PET Contrast Agents:** Nanoparticles labeled with positron-emitting radionuclides, such as ^18F or ^64Cu, serve as PET contrast agents for molecular imaging of metabolic processes, receptor expression, and disease biomarkers. These nanoparticles enable non-invasive visualization and quantification of biological processes at the molecular level, aiding in early disease detection, treatment monitoring, and personalized medicine. [15]
- **Theranostic Nanoparticles:** Theranostic nanoparticles represent a paradigm shift in healthcare by integrating therapy and diagnostics into a single platform. These multifunctional nanoparticles enable simultaneous imaging and targeted therapy, allowing clinicians to monitor treatment response in real-time and tailor therapeutic interventions based on individual patient characteristics. Theranostic nanoparticles offer several advantages, including: [15]
- **Personalized Medicine:** By combining imaging and therapeutic functionalities, theranostic nanoparticles enable personalized treatment strategies based on the specific molecular signatures and characteristics of each patient's disease.
- **Real-time Monitoring:** Theranostic nanoparticles provide real-time feedback on treatment efficacy, allowing clinicians to adjust therapy dosages or modalities as needed to optimize patient outcomes.
- **Targeted Therapy:** By delivering therapeutic agents directly to diseased tissues or cells, theranostic nanoparticles minimize off-target effects and enhance therapeutic efficacy while reducing systemic toxicity.
- **Multimodal Imaging:** Theranostic nanoparticles can be engineered to incorporate multiple imaging modalities (e.g., MRI, CT, fluorescence), providing complementary information for accurate diagnosis, localization of tumors, and assessment of treatment response.

Examples of theranostic nanoparticles include multifunctional liposomes, polymeric nanoparticles, and hybrid nanomaterials capable of carrying therapeutic payloads (e.g., chemotherapy drugs, siRNA, photothermal agents) while simultaneously providing imaging contrast for visualization and monitoring.

7. Challenges and Future Directions

Nanoparticle-based therapies hold tremendous promise for revolutionizing cancer treatment, but several challenges must be addressed to realize their full potential. Here are key challenges and future directions in nanoparticle research for cancer treatment: [10]

1. Toxicity Concerns: Despite their numerous benefits, nanoparticles may pose safety concerns due to potential toxicity issues. Understanding the interactions between nanoparticles and biological systems is essential for mitigating risks and ensuring patient safety. Key areas of focus include:

- **Biocompatibility:** Designing nanoparticles with biocompatible materials and surface coatings to minimize adverse effects on cells and tissues.
- **Biodistribution and Clearance:** Studying the pharmacokinetics of nanoparticles to optimize their biodistribution, accumulation in tumors, and clearance from the body to minimize off-target effects and long-term toxicity.
- **Immunogenicity:** Investigating the immune response to nanoparticles and developing strategies to mitigate immunogenic reactions, such as PEGylation or surface modifications to evade immune recognition.

2. Clinical Translation: Translating nanoparticle-based therapies from preclinical studies to clinical applications poses significant challenges and requires overcoming various hurdles. Key considerations for successful clinical translation include: [11]

- **Regulatory Approval:** Meeting regulatory requirements and safety standards for clinical trials, including rigorous preclinical testing, toxicity studies, and documentation of manufacturing processes.

- **Scalability:** Developing scalable manufacturing processes to produce nanoparticles reproducibly and cost-effectively for large-scale clinical applications.
- **Clinical Validation:** Conducting well-designed clinical trials to evaluate the safety, efficacy, and therapeutic benefits of nanoparticle-based therapies in human patients, including randomized controlled trials and long-term follow-up studies.

3. Future Prospects: Despite existing challenges, nanoparticle research for cancer treatment continues to evolve rapidly, with exciting opportunities for innovation and advancement. Key future prospects and emerging trends include: [11]

- **Precision Medicine:** Harnessing the unique properties of nanoparticles for personalized cancer therapy, including targeted drug delivery, imaging-guided treatment, and combination therapies tailored to individual patient profiles.
- **Multifunctional Nanoparticles:** Developing multifunctional nanoparticles with integrated diagnostic and therapeutic capabilities (theranostics) for real-time monitoring of treatment response and optimization of therapeutic outcomes.
- **Smart nanomaterials**:Designing "smart" nanoparticles capable of responding to specific stimuli in the tumor microenvironment (e.g.,
- pH, temperature, enzymes) to achieve controlled drug release, enhanced targeting, and synergistic therapeutic effects.
- **Nanotechnology Integration:** Integrating nanotechnology with other emerging technologies, such as artificial intelligence, microfluidics, and gene editing, to develop novel approaches for cancer diagnosis, treatment, and monitoring.

8. Case Studies and Success Stories

Nanoparticle-based cancer therapies have demonstrated remarkable potential in improving treatment outcomes and patient quality of life. Here are some notable examples of successful applications: [13]

1. **Abraxane (Albumin-bound paclitaxel nanoparticles):** Abraxane is a nanoparticle formulation of paclitaxel, a widely used chemotherapy drug for various solid tumors, including breast, lung, and pancreatic cancers. In Abraxane, paclitaxel is bound to albumin nanoparticles, which enhances its solubility and allows for targeted delivery to tumors. Clinical studies have shown that Abraxane offers improved efficacy and reduced toxicity compared to conventional paclitaxel formulations, leading to its approval for the treatment of metastatic breast cancer, non-small cell lung cancer, and advanced pancreatic cancer. [13]

Fig-4 Abraxane

2. **Doxil (Doxorubicin liposomes):** Doxil is a liposomal formulation of doxorubicin, a potent chemotherapy drug used in the treatment of various cancers, including ovarian, breast, and multiple myeloma. Liposomal encapsulation of doxorubicin in Doxil improves its pharmacokinetics, prolongs circulation time, and enhances tumor accumulation through passive targeting via the enhanced permeability and retention (EPR) effect. Clinical studies have demonstrated that Doxil reduces cardiac toxicity and improves treatment tolerability compared to free doxorubicin, leading to its approval for several cancer indications. [13]

Fig-05 Doxil

3. **Ferroptosis-Inducing Nanoparticles (FINs):** Ferroptosis is a form of programmed cell death characterized by iron-dependent lipid peroxidation, which can be induced as a therapeutic strategy for cancer treatment. Researchers have developed ferroptosis-inducing nanoparticles (FINs) capable of delivering iron oxide nanoparticles and lipid peroxidation catalysts to cancer cells, triggering ferroptotic cell death selectively. Preclinical studies have shown promising results in various cancer models, including breast, lung, and liver cancers, highlighting the potential of FINs as a novel cancer therapy.

4. **Gold Nanoparticle-Based Photothermal Therapy:** Gold nanoparticles (GNPs) have unique optical properties that enable them to absorb and convert light energy into heat, making them promising agents for photothermal therapy (PTT) of cancer. GNPs can be functionalized and targeted to specific cancer cells or tissues, where they selectively accumulate and induce hyperthermia upon exposure to near-infrared (NIR) laser irradiation, leading to localized tumor ablation. Clinical studies and case reports have demonstrated the efficacy and safety of GNP-based PTT in various cancers, including head and neck cancer, melanoma, and prostate cancer. [13]

9. Conclusion

In conclusion, nanoparticles have emerged as game-changers in the field of cancer treatment, offering innovative solutions to longstanding challenges and revolutionizing the way we approach cancer therapy. Throughout this presentation, we have explored the multifaceted role of nanoparticles in addressing key aspects of cancer management, from targeted drug delivery and imaging to overcoming drug resistance and enabling personalized medicine.

The significance of nanoparticles in cancer treatment lies in their ability to:

1. **Enhance Targeting and Efficacy:** Nanoparticles enable precise delivery of therapeutic agents to cancer cells while sparing healthy tissues, maximizing treatment efficacy and minimizing side effects.
2. **Enable Imaging and Diagnosis:** Nanoparticles serve as versatile contrast agents for enhancing imaging modalities, allowing for early detection, accurate diagnosis, and monitoring of treatment response.
3. **Overcome Drug Resistance:** Nanoparticle-based strategies offer novel approaches to overcome multidrug resistance mechanisms, enhancing the sensitivity of cancer cells to chemotherapy and targeted therapies.
4. **Integrate Therapy and Diagnostics:** Theranostic nanoparticles combine therapy and diagnostics in a single platform, enabling real-time monitoring of treatment response and personalized medicine approaches.

As we reflect on the remarkable progress achieved thus far, it is evident that the journey of nanoparticles in cancer therapy is far from over. A call to action is needed for further research and development in the field, driven by collaboration, innovation, and a commitment to translating scientific discoveries into tangible benefits for patients. Key areas for future exploration include:

- **Addressing Toxicity Concerns:** Continued efforts to understand and mitigate the potential toxicity of nanoparticles, ensuring their safety and biocompatibility for clinical applications.
- **Advancing Clinical Translation:** Accelerating the translation of nanoparticle-based therapies from bench to bedside through rigorous preclinical testing, regulatory approval, and well-designed clinical trials.
- **Exploring Emerging Technologies:** Embracing emerging technologies and interdisciplinary approaches to push the boundaries of nanoparticle research, including artificial intelligence, nanobiotechnology, and precision medicine.

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