Title :

Green Nanoparticles as Cancer Therapeutics

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Introduction

Nanoparticles have emerged as a cutting-edge tool in the fight against cancer, offering a promising avenue for more effective and targeted treatment strategies. Their small size and unique properties make them well-suited for delivering therapeutic agents specifically to tumor sites, revolutionizing the field of oncology.

Objectives

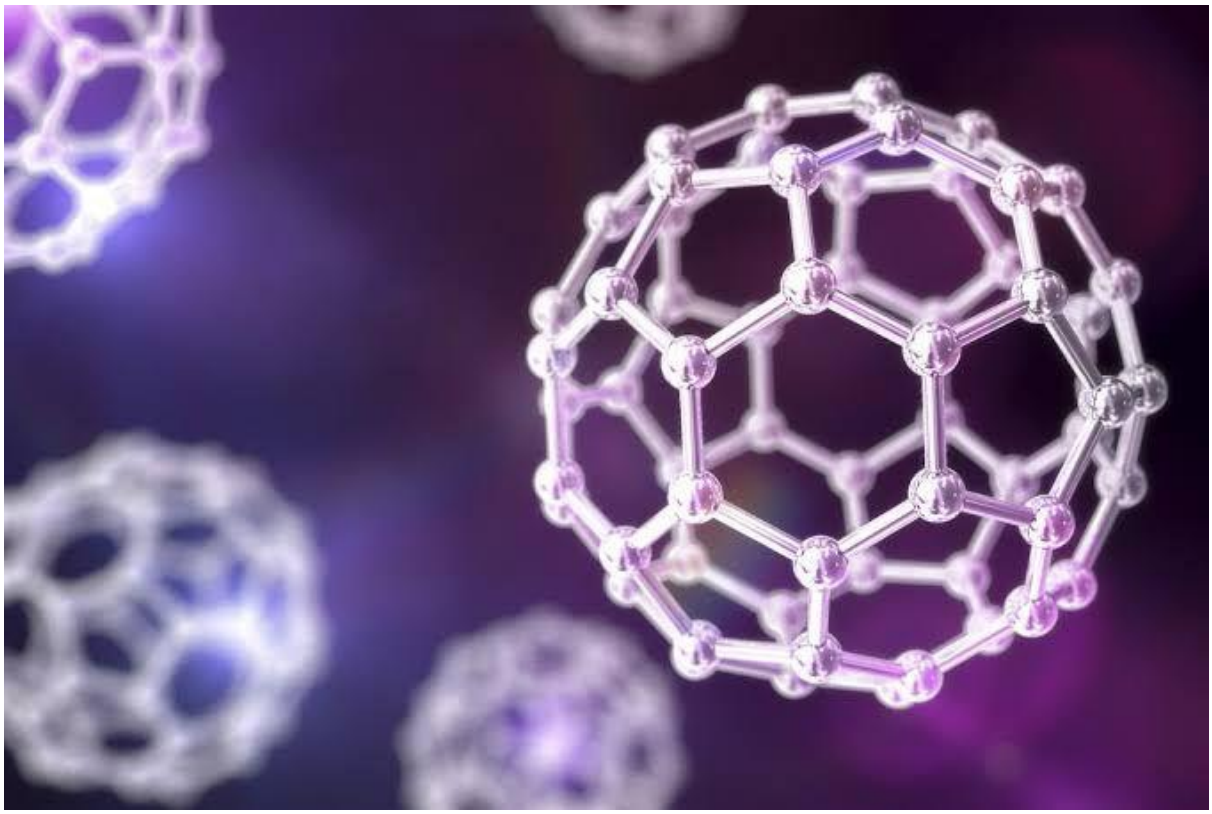
- Compare the efficacy of conventional drugs and nanoparticles in tumor treatment.
- Explore the role of endothelial cell size and VEGF in nanoparticle delivery.
- Enhancing Cancer Treatment Through Nanoparticles
- Evaluate the advantages of green nanoparticles and their therapeutic agents.
- Discuss the capping of nanoparticles to ensure targeted delivery and its effects on tumor treatment.

Conventional Drugs Vs Nanoparticles in Cancer Treatment

1. Application of conventional drug in tumor treatment

Chemotherapy, a common conventional treatment, involves the administration of drugs that target rapidly dividing cancer cells. These drugs can be administered orally or intravenously and work by interfering with the cancer cell's ability to grow and divide.

2. Nanoparticles:



Nanoparticles are tiny particles with dimensions ranging from 1 to 100 nanometers. They can be made from various materials, including metals, polymers, and lipids. Due to their small size, nanoparticles exhibit unique properties that differ from their bulk counterparts.

2(a) Nanoparticles in tumor treatment :

Nanoparticles hold significant promise in tumor treatment due to their unique properties that can improve drug delivery, enhance therapeutic efficacy, and minimize side effects.
Here's how nanoparticles are utilized in tumor treatment:

(i)Targeted Drug Delivery: Nanoparticles can be engineered to encapsulate anti-cancer drugs and deliver them specifically to tumor sites. By functionalizing the nanoparticles with targeting ligands or antibodies, they can selectively bind to receptors or antigens overexpressed on cancer cells, allowing for precise drug delivery while minimizing exposure to healthy tissues.

(ii)Enhanced Permeability and Retention (EPR) Effect:
Tumors often have leaky blood vessels and poor

lymphatic drainage, leading to the accumulation of nanoparticles within the tumor microenvironment. This phenomenon, known as the EPR effect, allows nanoparticles to passively accumulate in tumors, thereby increasing drug concentrations at the target site.

(iii)Controlled Drug Release: Nanoparticles can be designed to release their payload of drugs in a controlled manner, either in response to external stimuli (e.g., light, temperature, pH) or in the presence of specific enzymes or molecules abundant in the tumor microenvironment. This controlled release mechanism can improve drug bioavailability and reduce systemic toxicity.

(iv).Multifunctional Platforms: Nanoparticles can be engineered to carry multiple therapeutic agents, imaging agents, or targeting ligands simultaneously, creating multifunctional platforms for combination therapy and theranostics (therapy and diagnostics). This approach allows for synergistic effects and personalized treatment strategies tailored to the specific characteristics of the tumor.

(v)Overcoming Drug Resistance: Nanoparticles can help overcome multidrug resistance mechanisms commonly encountered in cancer treatment. By encapsulating drugs within nanoparticles and delivering them directly to cancer cells, nanoparticles can bypass efflux pumps and other resistance mechanisms, improving the effectiveness of chemotherapy.

3.What is the difference between conventional drug & nanoparticles in tumor treatment

The primary differences between conventional drugs and nanoparticles in tumor treatment lie in their mechanisms of action, delivery methods, and therapeutic outcomes:

(i). Mechanism of Action:

- Conventional Drugs: Conventional drugs typically exert their effects systemically, circulating throughout the body and interacting with both cancerous and healthy cells. They may target rapidly dividing cells, including cancer cells, but can also affect normal tissues, leading to side effects.

- Nanoparticles: Nanoparticles can be engineered to target specific cells or tissues, such as cancer cells, while minimizing exposure to healthy tissues. They can carry therapeutic payloads directly to tumor sites, enhancing drug efficacy and reducing systemic toxicity.

(ii). Delivery Methods:

- Conventional Drugs: Conventional drugs are usually administered orally, intravenously, or via other routes and distribute throughout the body via the bloodstream. They may require higher doses to achieve therapeutic concentrations at the tumor site.
- Nanoparticles: Nanoparticles can be designed to selectively accumulate in tumors through passive targeting (EPR effect) or active targeting mechanisms. They can be administered intravenously, allowing for precise delivery of therapeutic agents to tumor tissues.

(iii). Therapeutic Outcomes:

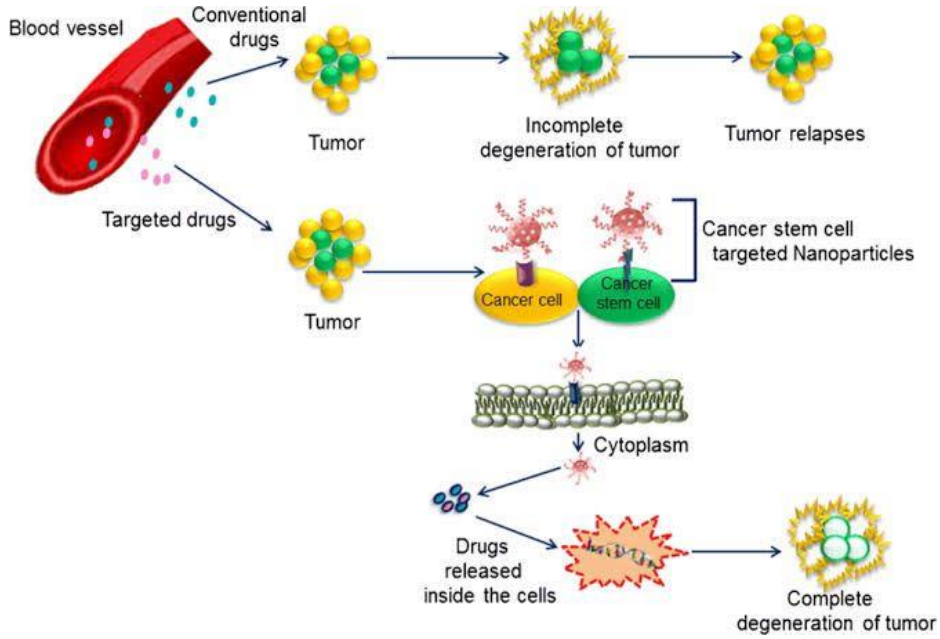
- Conventional Drugs: Conventional drugs may have limited efficacy against tumors due to systemic toxicity, drug resistance, and poor tumor penetration. They can cause significant side effects in healthy tissues.

- Nanoparticles: Nanoparticles can enhance therapeutic outcomes by improving drug bioavailability, increasing tumor penetration, and reducing off-target effects. They have the potential to overcome drug resistance mechanisms and deliver combination therapies for synergistic effects.

(iv).Precision and Personalization:

- Conventional Drugs: Conventional drug therapies are often less precise and may not be tailored to individual patient characteristics or tumor biology.

- Nanoparticles: Nanoparticles offer opportunities for precision medicine by enabling targeted drug delivery and personalized treatment strategies based on the specific characteristics of the tumor and patient.



Overall, nanoparticles represent a promising approach to tumor treatment by addressing limitations associated with conventional drugs, such as poor tumor selectivity, systemic toxicity, and drug resistance. They offer the potential for improved therapeutic outcomes and reduced side effects, making them an exciting area of research and development in oncology.

How Tumor Develops and Grows

Tumors affect people of all ages, including children. Factors that increase the chances of developing a tumor include:

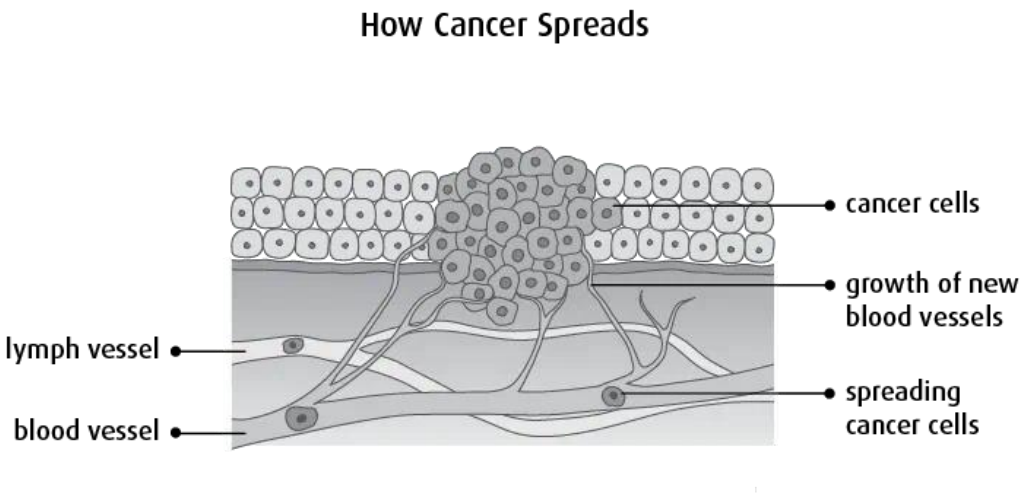
- Gene mutations (changes), such as mutated BRCA (breast cancer) genes.
- Inherited conditions, such as Lynch syndrome and neurofibromatosis (NFS).
- Family history of certain types of cancer like breast cancer or prostate cancer.
- Smoking, including exposure to secondhand smoke.

- Exposure to toxins like benzene or asbestos.
- Previous radiation exposure.
- Viruses like HPV.
- Having obesity.

A tumor cell can have thousands of mutations, but only a certain number of these genetic changes in tumor cells cause the tumor to divide and grow. Mutations that result in the growth of tumor cells are referred to as “driver mutations,” whereas other mutations are considered “passenger mutations.”

Normal genes that help cells grow, called proto-oncogenes, can become “oncogenes” (or those with the potential to cause a tumor) when mutated and drive the growth of the tumor. By contrast, tumor suppressor genes are genes within the cell that tell cells to slow down and stop growing, repair damaged DNA, and they tell cells when to die.As cancer cells divide, a tumour will develop and grow. Cancer cells have the same needs as normal cells. They need a blood supply to bring oxygen and nutrients to grow and survive. When a tumour is very small, it can easily grow,

and it gets oxygen and nutrients from nearby blood vessels.



Size of Endothelial cells in Normal and Tumor Tissue

Size of Endothelial Cells in Normal Tissues:

Uniformity: In normal tissues, endothelial cells typically exhibit a relatively uniform size and shape. They form a continuous monolayer lining the interior surface of blood vessels, known as the endothelium. *The gap between normal endothelial cells measures between 5-10 nm.*

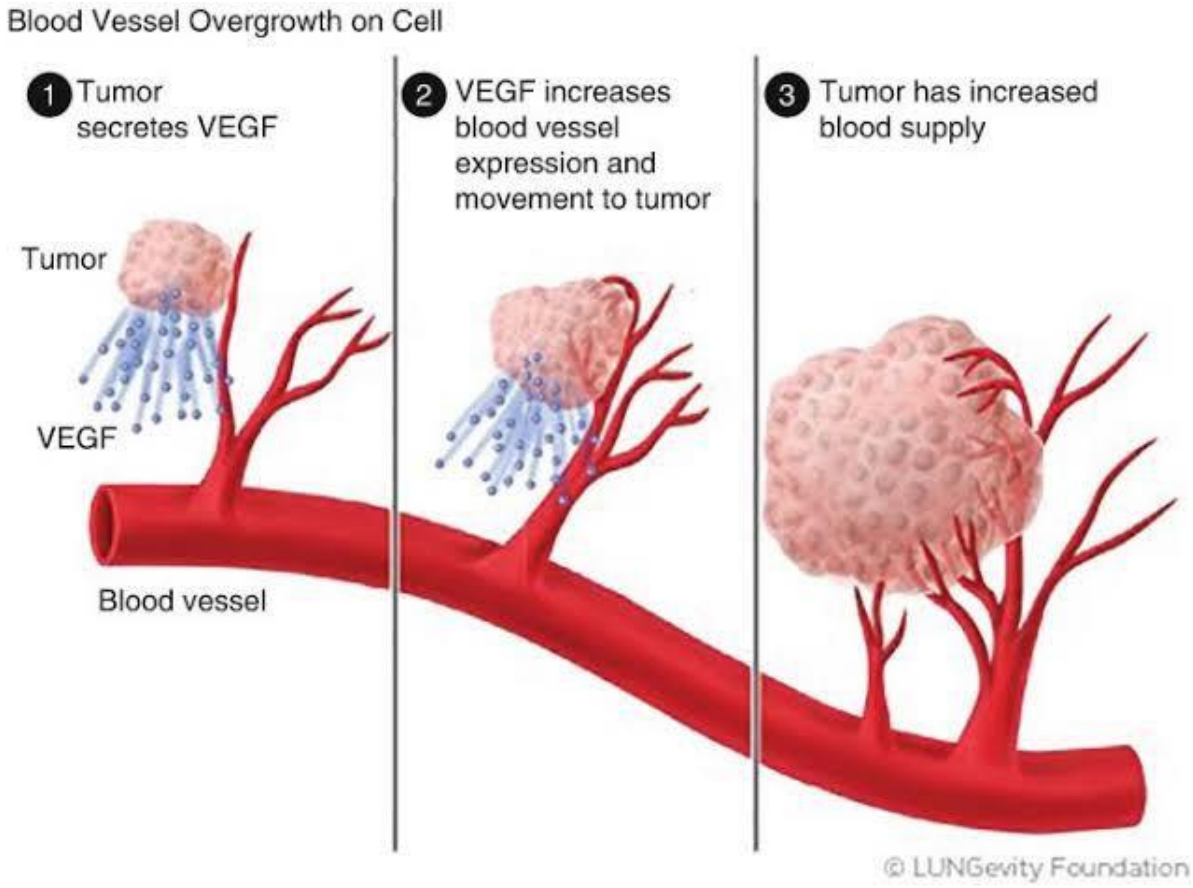
Size of Endothelial Cells in Tumor Tissues:

Alterations: In tumor tissues, the size and morphology of endothelial cells can be significantly altered due to the chaotic nature of tumor angiogenesis, the process by which tumors induce the formation of new blood vessels to support their growth and metastasis. *The gap between endothelial cells measures upto 400 nm*.

Dysregulated Growth: Tumor-derived factors, including growth factors, cytokines, and chemokines, stimulate the proliferation and migration of endothelial cells, leading to the formation of new blood vessels. However, this process is dysregulated in tumors, resulting in the aberrant growth and structure of tumor blood vessels.

Role of Vascular Endothelial Growth Factor (VEGF) in Angiogenesis:

Key Regulator: VEGF is a central regulator of angiogenesis in both normal and tumor tissues. It is a potent mitogen and chemoattractant for endothelial cells, stimulating their proliferation, migration, and survival.



Expression: In tumor tissues, cancer cells and the surrounding stroma often overexpress VEGF and other pro-angiogenic factors in response to hypoxia (low oxygen levels) and other microenvironmental cues. This excessive production of VEGF drives the angiogenic switch, initiating the formation of new blood vessels within the tumor microenvironment.

Signaling: VEGF acts through several signaling pathways to promote angiogenesis. It binds to and activates endothelial cell receptors, primarily VEGF

receptor-1 (VEGFR-1) and VEGF receptor-2 (VEGFR-2). Activation of these receptors triggers downstream signaling cascades that promote endothelial cell proliferation, migration, and tube formation, ultimately leading to the formation of new blood vessels.

Green Nanoparticles in Cancer Treatment

Medicinal nanoparticles are nano-sized particles designed for the diagnosis, treatment, and prevention of diseases, including cancer. They offer several advantages over traditional therapies, such as targeted delivery, controlled release, and reduced side effects. These nanoparticles can be synthesized using various materials, including lipids, polymers, metals, and silica, and can be loaded with therapeutic agents to enhance their efficacy.

Different Types of Therapeutic Agents Involved

- Chemotherapeutic Drugs:
- Natural Compounds:
- Immunotherapeutic Agents:
- Gene Therapy Agents:
- Photosensitizers:

- Radiotherapeutic Agents:

Capping of Nanoparticles for Target Delivery

Capping refers to the functionalization or coating of nanoparticles with specific molecules that enhance their stability, solubility, biocompatibility, and targeting ability. This process ensures that nanoparticles can effectively reach and accumulate in tumor tissues while minimizing off-target effects.

Types of Capping Agents

1. **Polyethylene Glycol (PEG):**
2. **Targeting Ligands**:
   - **Examples**: Antibodies, peptides, aptamers, folic acid
3. **Biomolecules**:
   - **Examples**: Proteins, sugars, nucleic acids
4. **Natural Polymers**:
   - **Examples**: Chitosan, alginate

Effects of Capping on Tumor Treatment

1. **Enhanced Targeting and Accumulation**:

- Capping with targeting ligands ensures that nanoparticles preferentially bind to and are internalized by cancer cells, exploiting tumor-specific markers for selective delivery.

2. **Prolonged Circulation Time**:

- PEGylation and other stabilizing caps prevent rapid clearance by the reticuloendothelial system (RES), allowing more nanoparticles to reach the tumor site.

3. **Reduced Immunogenicity and Toxicity**:

- Functionalization with biocompatible materials minimizes the immune response and reduces toxicity to normal cells, improving overall safety.

4. **Improved Stability and Solubility**:

- Capping agents enhance the stability of nanoparticles in biological fluids, preventing

aggregation and improving solubility, which is crucial for effective delivery.

5. **Controlled and Sustained Release**:

- Functional coatings can be designed to release the therapeutic agents in response to specific stimuli in the tumor microenvironment (e.g., pH, enzymes), ensuring that the drugs are released at the right time and place.

❖ Selection of the Best Medicinal Nanoparticle for Tumor Treatment

Considering the unique properties, therapeutic efficacy, and potential for nanoparticle synthesis, **Curcumin from Curcuma longa (Turmeric)**stands out as a highly promising nanoparticle.

Reasons for Selecting Curcumin-Based Nanoparticles

1. **Potent Anticancer Properties**:

- Curcumin has shown significant anticancer activity across various cancer types by inducing apoptosis,

inhibiting cell proliferation, and preventing angiogenesis.

- It modulates multiple signaling pathways involved in cancer progression, such as NF-κB, MAPK, and PI3K/AKT.

2. **Anti-inflammatory and Antioxidant Effects:**

- Its strong anti-inflammatory and antioxidant properties help reduce the inflammatory environment associated with tumors, which can contribute to cancer progression.

3. **Enhanced Bioavailability through Nanoparticles:**

- Curcumin has poor bioavailability when taken orally due to rapid metabolism and elimination. However, encapsulating curcumin in nanoparticles significantly enhances its bioavailability and therapeutic efficacy.

- Nanoparticles protect curcumin from degradation and ensure sustained release at the tumor site.

4. **Targeted Delivery and Reduced Side Effects:**

- Curcumin-loaded nanoparticles can be functionalized with targeting ligands to improve

selective delivery to tumor cells, minimizing exposure to healthy tissues and reducing side effects.

- They exploit the Enhanced Permeability and Retention (EPR) effect for better accumulation in tumor tissues.

5. **Multifunctionality**:

- Curcumin nanoparticles can be co-loaded with other therapeutic agents or imaging agents, providing a multifunctional platform for combination therapy and real-time monitoring of treatment response.

Therapeutic Agents Involved

- **Curcumin**: The primary anticancer agent derived from Curcuma longa, with potent anti-inflammatory, antioxidant, and pro-apoptotic properties.

- **Targeting Ligands**: Antibodies or peptides that bind specifically to tumor-associated receptors (e.g., folic acid for targeting folate receptors on cancer cells).

- **Polymeric Nanocarriers**: Biocompatible and biodegradable polymers (e.g., PLGA, chitosan) used to encapsulate curcumin, enhance stability, and control release.

Available Nanoparticles for Tumor Treatment

Several types of nanoparticles have been developed and are available for tumor treatment. These include:

- Liposomal Nanoparticle (Doxil)
- Polymeric Nanoparticles (PLGA)
- Gold Nanoparticles (AuNPs)
- Silica Nanoparticles
- Magnetic Nanoparticles(Iron oxide).

Selected Nanoparticle for Tumor Treatment

Curcumin-Loaded PLGA Nanoparticles

Reasoning for Selecting Curcumin-Loaded PLGA Nanoparticles

1. **Biocompatibility and Biodegradability**:

- **PLGA** is a well-studied and FDA-approved polymer known for its excellent biocompatibility and biodegradability, making it safe for clinical use.

- **Curcumin** is naturally derived and has a well-documented safety profile.

2. **Enhanced Bioavailability:**

- Curcumin's bioavailability is significantly enhanced when encapsulated in PLGA nanoparticles. This

protects curcumin from rapid degradation and improves its absorption and distribution in the body.

3. **Controlled and Sustained Release:**

- PLGA nanoparticles provide controlled and sustained release of curcumin, maintaining therapeutic levels in the tumor microenvironment for extended periods.

4. **Targeted Delivery**:

- PLGA nanoparticles can be functionalized with targeting ligands (e.g., folic acid, antibodies) to specifically target tumor cells, enhancing the accumulation of curcumin at the tumor site and minimizing off-target effects.

5. **Enhanced Permeability and Retention (EPR) Effect**:

- The size and surface properties of PLGA nanoparticles enable them to exploit the EPR effect, allowing preferential accumulation in tumor tissues due to the leaky vasculature of tumors.

6. **Multifunctionality**:

- PLGA nanoparticles can co-encapsulate other therapeutic agents, allowing combination therapy. Additionally, they can be loaded with imaging agents for theranostic applications, enabling simultaneous therapy and monitoring.

How Curcumin-Loaded PLGA Nanoparticles Increase Efficacy in Tumor Treatment

1. **Improved Targeting and Accumulation**:

- By exploiting the EPR effect and surface functionalization with targeting ligands, curcumin-loaded PLGA nanoparticles accumulate more efficiently in tumor tissues, increasing local drug concentration and therapeutic efficacy.

2. **Reduced Systemic Toxicity**:

- Targeted delivery ensures that curcumin is released primarily at the tumor site, reducing systemic exposure and minimizing side effects on healthy tissues.

3. **Sustained Therapeutic Levels:**

- Controlled release from PLGA nanoparticles maintains therapeutic levels of curcumin in the tumor microenvironment, enhancing its anticancer effects over time.

4. **Enhanced Cellular Uptake**:

- The nanoparticle form enhances the cellular uptake of curcumin by cancer cells, facilitating more effective intracellular delivery and action.

5. **Synergistic Effects**:

- Curcumin’s anti-inflammatory, antioxidant, and pro-apoptotic properties, combined with the nanoparticle’s ability to deliver other therapeutic agents, provide a multifaceted approach to attacking tumor cells.

Conclusion

In wrapping up the exploration of nanoparticles in cancer therapy, it's evident that these minuscule particles hold immense potential in revolutionizing how we combat tumors. By harnessing the unique properties of nanoparticles to precisely deliver drugs to cancer cells while sparing healthy tissues, researchers

are paving the way for a more targeted and less toxic form of treatment.The application of nanoparticles in cancer therapy represents a significant advancement in the field, offering hope for improved treatment outcomes and enhanced patient well-being. As we continue to unlock the full capabilities of nanoparticles in the fight against cancer.