

Review on Different Types of Nanoparticles in Cancer Treatment and Dignosis

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ABSTRACT

Cancer is a major health problem with complex causes. Common cancer treatments like chemotherapy and radiation have limitations such as harming healthy cells and drug resistance. The use of very tiny particles called nanoparticles, which have unique properties like being safe and precise, has changed how we approach cancer. These nanoparticles can be designed to target cancer cells specifically. They not only help with the limitations of traditional treatments but also overcome drug resistance. Scientists are studying them more to understand how they can combat cancer better. While most of this research is done in labs and animals, not many of these treatments have been officially approved yet. This review explores the different types of nanoparticles, how they target cancer, and the approved treatments that use them to fight cancer.(4)

Keywords: Cancer, Nanoparticles, treatment,dignosis,drug delivery .

I. INTRODUCTION

Cancer is a highly intricate disease characterized by a multifaceted progression, including resistance to cell death (apoptosis), uncontrolled cell proliferation, alterations in cellular signaling, tissue invasion, metastasis, and angiogenesis. Typically, cancer starts as a localized tumor but can metastasize to distant parts of the body, complicating its management. The World Health Organization (WHO) projected even higher figures in 2020, with 19.3 million new cases and 10 million cancer-related deaths.(6)

Several factors contribute to the increased incidence of cancer, including elevated pollution levels, radiation exposure, sedentary lifestyles, imbalanced diets, infections from oncogenic microorganisms, and other variables like genetic predisposition. These factors can inflict damage on

the DNA of host cells, leading to the formation of oncogenes, which drive the development of cancer. Ultimately, cancer results from the uncontrolled growth of cells that evade mortality and replicate at an accelerated rate, eventually overwhelming healthy cells.This review outlines recent advancements in the utilization of nanomaterials for cancer treatment, focusing on synthetic methods, the delivery of therapeutic agents, and tumor imaging. It encompasses inorganic nanomaterials as well.

Nanotechnology, focusing on atomic and molecular properties at the nanoscale upto100 nm, holds promise in addressing cancer. It harnesses the unique attributes of nanoparticles, such as quantum properties, a significant surface-to-mass ratio, and the ability to transport various compounds like probes, proteins, and drugs. Nanotechnology is increasingly integrated with modern biology and medicine to create innovative nanoscale materials for use in biological systems. These nanoparticles can be composed of diverse materials, ranging from natural substances like lipids and chitosan to synthetic materials like silica, carbon, and metals.(22)

Nanoparticles:

Nanoparticles are incredibly small particles, typically less than 100 nanometers in at least one dimension. These tiny particles exhibit special characteristics that are often quite different from those seen in larger quantities of the same material. The specific properties of nanoparticles can vary based on their overall shape. Due to their tiny size, nanoparticles possess unique properties and behaviors, including increased surface area, quantum effects, and enhanced reactivity, which can differ from those of bulk materials. Nanoparticles are extensively used in various fields, including medicine, electronics, materials

science, and environmental science, owing to their potential for targeted drug delivery, improved

imaging, and a wide range of other applications.(21)

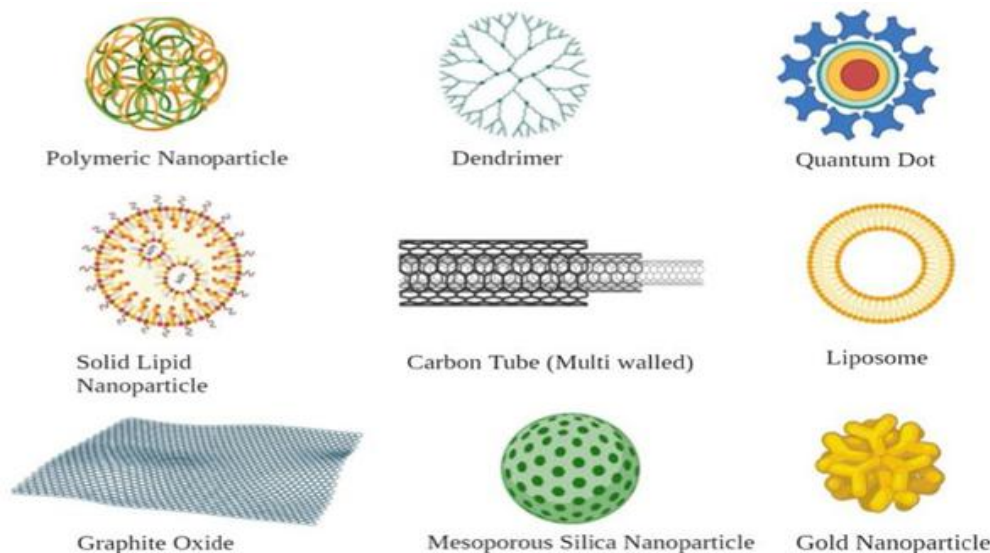


Fig1.1 . Different types of nanoparticles

Properties of nanoparticles:

1.Size of partical:

Nanoparticles are extremely small, typically ranging in size from 1 to 100 nanometers in diameter. Their minute size is a defining characteristic, allowing them to exhibit unique properties and find applications in various fields, from materials science to medicine

2.Surface area :

Nanoparticles have an exceptionally large surface area relative to their volume. This characteristic is a result of their small size and high surface-to-volume ratio. Because of their extensive surface area, The large surface area enhances their reactivity and their ability to interact with other substances, making them valuable in a wide range of scientific application Surface properties can enhance the stability of nanoparticles and extend their presence in the bloodstream, leading to increased accumulation in tumors through the Enhanced Permeability and Retention effect. Furthermore, these surface properties significantly impact electrostatic and hydrophobic interactions.

Classification of nanoparticles:

i) One-Dimensional Nanoparticles: These are nanomaterials that have their special properties in a single dimension, like being ultra-thin films or coatings. They find use in applications like resisting corrosion, preventing wear and scratches,

repelling dirt, and having antibacterial properties, among others.

ii) Two-Dimensional Nanoparticles: These nanoparticles, such as nanotubes, nanowires, nanofibers, and nanopolymers, have unique characteristics in two dimensions. They are used in various applications due to their special properties.

iii) Three-Dimensional Nanoparticles: These are nanomaterials like fullerenes, dendrimers, and quantum dots that exhibit their unique features in all three dimensions. They have diverse applications due to their special properties.

Advantages of nanoparticles:

1. Targeted Drug Delivery nanoparticles can be designed to carry and deliver cancer drugs directly to tumor cells, reducing damage to healthy tissues and enhancing the effectiveness of treatment.
2. Improved Drug Solubility they can improve the solubility of poorly soluble cancer drugs, increasing their bioavailability and therapeutic efficacy.
3. Reduced Side Effects: Targeted delivery minimizes damage to healthy cells, which can result in fewer side effects compared to traditional cancer treatments.
4. Prolonged Drug Release: Nanoparticles can release drugs slowly over time, providing a sustained therapeutic effect

5. Overcoming Drug Resistance: They may help overcome drug resistance in cancer cells by

delivering multiple drugs or using innovative treatment strategies.

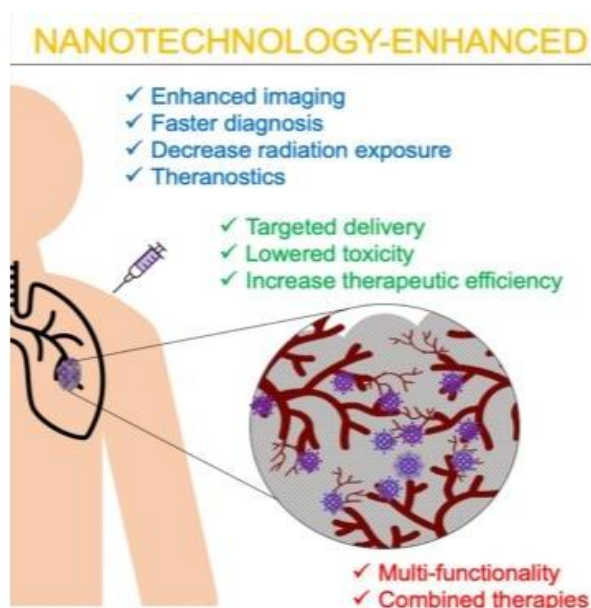


Fig .Different advantages of nanoparticles

6.Enhanced Immunotherapy: Nanoparticles can be used to deliver immunotherapies, boosting the body's natural defense mechanisms against cancer.

7.Reduced Toxicity: By localizing treatment to the tumor site, nanoparticle-based therapies can reduce systemic toxicity.

Nanotechnology in medicine:

Nanotechnology in medicine, often referred to as nanomedicine, presents exciting prospects for enhancing healthcare. The goal is to enable tailored medical treatments that can deliver the right medication, in the correct dosage, precisely when needed, to the specific patient. This approach promises advantages such as precision, effectiveness, safety, and swiftness. While certain techniques remain in the realm of imagination, others are in different phases of experimentation or are currently in practical use. Nanomedicine is a field where tiny robots might fix things in our cells in the future. It could replace some medicines we use today, like chemotherapy. Right now, it's still in the early stages, but the most advanced part is using tiny particles to deliver drugs.

NANOPARTICLES IN DIGNOSIS IN CANCER IMAGINGTECHNOLOGY FOR CANCER DIAGNOSIS:

In the history of cancer diagnosis, imaging has played a pivotal role in understanding cancer stages, tumor size, and location. The evolution of imaging technology has been significant:

1. 16th Century: Microscopes were the primary tools for detecting cancer and diseases in cells.
2. 1895: The X-ray machine was invented, revolutionizing the visualization of internal structures.
3. 1956: The ultrasound machine was introduced, offering a non-invasive way to examine tissues.
4. 1970s: CT (Computed Tomography) and MRI (Magnetic Resonance Imaging) machines were invented, allowing for more detailed and layered imaging.

Advancements in medical imaging continued, with the development of 3D lenses and techniques that improved cancer diagnosis. Modern imaging technology enables clear visualization of living cells deep within the body, aiding in the detection and understanding of cancer.

One notable development involved the use of engineered cells forming air-filled proteins and ultrasound imaging to observe cellular function deep inside the body, offering insights into cancer cells.

Today, doctors use various diagnostic methods, including radiographic imaging such as CT scans, to target specific cancer genes and proteins. These methods help in identifying cancer

types and mutations, as well as assessing cancer risk factors.

For example, breast cancer can be detected early using radiographic imaging methods. In 2014, a significant number of breast and lung cancer cases were diagnosed in the United States.

Imaging technology has also been employed for the detection of lung cancer through annual low-dose CT scans and magnetic resonance imaging (MRI), which utilizes strong magnetic fields to create detailed images of soft tissues. MRI is particularly effective in detecting cancer cells that may be challenging to visualize using other imaging techniques.

Nanoparticles play a significant role in cancer diagnosis for several reasons:-

1. **Improved sensitivity:** Nanoparticles, especially metallic and magnetic ones, can enhance the sensitivity of tumor detection. They can be conjugated with cancer-specific antibodies, allowing them to bind more effectively to cancer cells and improving the accuracy of cancer diagnosis.
2. **Targeted Delivery:** Nanoparticles can remain in the bloodstream for extended periods and target specific cells. They can traverse biological barriers, such as cell membranes, to interact with biological systems and reach the target cells, which is essential for effective diagnosis and treatment.
3. **Multi-Modal Imaging:** Nanoparticles with unique optical, magnetic, and chemical properties enable the development of imaging probes with improved contrast enhancement, increased sensitivity, and the ability to perform multimodal imaging across various techniques like MRI, PET, SPECT, and ultrasound. This enhances the ability to visualize and diagnose tumors.
4. **Nanocomposites:** Combining different types of nanoparticles, such as gold, platinum, silver, copper, and cobalt, in nanocomposites has shown promise in detecting and imaging cancer cells with greater accuracy. These composites can penetrate cancer cells more effectively and produce better signals for diagnosis.
5. **Detection of Biomarkers:** Nanoparticles can be used to detect specific cancer-related biomarkers like methylation patterns and mutations, aiding in cancer diagnosis and monitoring.

6. **Potential for Personalized Medicine:** Nanoparticles and sensors can provide real-time assessment of disease progression, which can lead to personalized medicine approaches tailored to the individual patient's needs.

Overall, nanoparticles have the potential to revolutionize cancer diagnosis by increasing sensitivity, improving imaging, and enabling earlier detection, which can have a profound impact on the effectiveness of cancer treatment and patient outcomes.

Overall, advancements in imaging technology have significantly improved cancer diagnosis and understanding, enabling healthcare professionals to provide more targeted and effective treatments. Nanoparticles are tiny materials that can be used to detect cancer more effectively. They come in different types like quantum dots, carbon nanotubes, and more. By attaching special molecules to these nanoparticles, they can specifically find and signal cancer in the body. Some studies even used gold nanoparticles that give off bright light for cancer detection. These nanoparticles can also help spot cancer markers, and they are especially good at doing it quickly and inexpensively without many side effects. They can be used in simple tests like electrochemical biosensors. To make them work better, scientists can modify these nanoparticles by adding specific antibodies to target cancer cells, making it easier to find them.

1. Magnetic Nanoparticles:-

The use of magnetic nanoparticles for drug delivery is based on a concept developed in the 1970s by a group of scientists led by Widder. This method allows drugs to be directed using magnets. The initial therapeutic application of magnetic nanoparticles for drug delivery was observed in C12S cells in mice by Mah and colleagues. Super paramagnetic iron oxide nanoparticles, mediated by recombinant single-chain FV antibody fragments, are being explored as potential candidates for cancer-specific magnetic resonance imaging. Super paramagnetic iron oxide nanoparticles linked with luteinizing hormone have shown effectiveness in targeting and imaging breast cancers. Several magnetic nanoparticle products have entered clinical trials for various purposes. These include Feridex for liver cancer imaging, Resovist for colon cancer and liver metastasis imaging, and Ferumoxytol for Central Nervous System (CNS) cancer imaging.

2. Calcium Phosphate Nanoparticles:-

Calcium phosphate nanoparticles, used alone or in combination with non-viral and viral vectors, have demonstrated remarkable results in delivering drugs for cellular gene transfer. These nanoparticles are preferred due to their low production costs, biocompatibility, resistance to microbial degradation, and storage stability. They are biodegradable and do not cause significant harm or side effects at the injection site. They are employed to deliver various medications such as contraceptives, growth factors, antibiotics, and insulin. Plasmid DNA and oligonucleotides can also be transported using calcium phosphate nanoparticles. Researchers have found that a formulation called liposomal Nanolipoplex, combining glycerol and calcium, reduces cytotoxicity and enhances transfection capabilities in cells.

3. Polymeric Nanoparticles:-

Polymeric nanoparticles, while posing production challenges, are the most promising agents for drug delivery and are extensively investigated in nanotechnology, especially for targeted anticancer drug delivery. These nanoparticles are primarily composed of materials like polylactic acid, polyglycolic acid, and acrylates. Studies have shown that nanoparticles containing anti-human epidermal growth factor receptor 2 and doxorubicin can localize anticancer drugs within human epidermal growth factor 2-overexpressing breast cancer SKBR-3 cells. In addition, research has demonstrated that indomethacin-encapsulated nanocapsules result in a significant reduction in tumor size and increased survival in a rat model with glioma.

4. Gold nanoparticles:-

Gold nanoparticles are tiny particles made of gold that can be used to deliver drugs inside cells. They have special qualities, like their size and surface can be easily changed, and they can be seen under light. Scientists use them to target and treat breast cancer with a specific protein (HER2). They sometimes use a substance called sodium bromohydrate to make these gold particles, but it may not be suitable for certain treatments because it can affect the composition of other important molecules. So, while gold nanoparticles have potential for therapy.

5. Solid Lipid Nanoparticles:- These are like tiny carriers made of fat that can hold drugs. When anticancer drugs like mitoxantrone are put in these carriers, it improves their effectiveness and safety. They also work well for treating leukemia.

6. Fullerenes:- These are unique carbon molecules known as Buckyballs. They're very stable and can be used to deliver drugs to cancer cells. Fullerenes can also absorb light and generate substances that can help with cancer therapy. Some researchers have explored their use in cancer treatment and imaging.

6. Dendrimers:-

Dendrimers are tiny, highly controlled polymers that are incredibly small, ranging from 1 to 100 nanometers. They're crucial for making various small structures in both organic and inorganic materials. They can interact with things like DNA, metal nanoparticles, and nanotubes. For example, a company called Starpharma is developing a product called VivaGel, which uses dendrimers and is in the testing phase. Dendrimers have many uses, including in medicine for drug delivery, and for environmental and water purification.

7. carbon nanotubes:- Carbon nanotubes are tiny structures made of carbon atoms arranged in a special pattern, like a tiny rolled-up sheet of paper. They can be incredibly narrow, about 1/50,000th the width of a human hair, or they can be longer, like tiny tubes. Think of them like really tiny straws, but some can be like a stack of straws inside one another, getting wider as they go.(7)

8. QuantumDot: quantum dots are like tiny balls, really small, just 1 to 10 billionths of a meter wide. They can be made from different materials. People use them to study DNA in cells, make bright lights, and create sensors for finding harmful biological substances.

Gold nanoparticles:-

Gold nanoparticles, which are tiny particles of gold ranging from 10 to 100 nanometers in size, respond to light by vibrating their electrons, a phenomenon called plasmon resonance. This response allows them to both absorb and scatter light. This unique property can be used for two main purposes: heating and destroying specific tissue or releasing important therapeutic substances. Gold nanoparticles can also

be linked to molecules that are active in biology, offering the potential to target them to specific parts of the body.(9)

Even though gold nanoparticles have been used in diagnosing diseases for a while, using them for medical treatments is a relatively new field. What makes them appealing for medical use are their resistance to damage from oxygen, the ability to easily attach biological molecules, and their ability to capture light in a much more efficient way than other substances used for similar purposes.(18)

In one study, researchers found that gold nanoparticles could be inside cells in various forms and provide information about their structure. However, they weren't very good at specifically targeting cancer cells. To improve this, they attached antibodies that recognize a protein called

EGFR to the gold nanoparticles. This made the nanoparticles attach more strongly and specifically to cancer cells compared to healthy cells. This could be useful for diagnosing and studying cancer cells both inside and outside the body.

When these antibody-covered gold nanoparticles were used with cells, they behaved differently. Noncancerous cells didn't interact much with the nanoparticles and were hard to distinguish. In contrast,

cancer cells, especially one type, had the nanoparticles on their surface, specifically on the outer part of the cell. This was because the cancer cells had more of the EGFR protein on their surface, which the antibodies on the gold nanoparticles could recognize. Some of the nanoparticles also ended up on

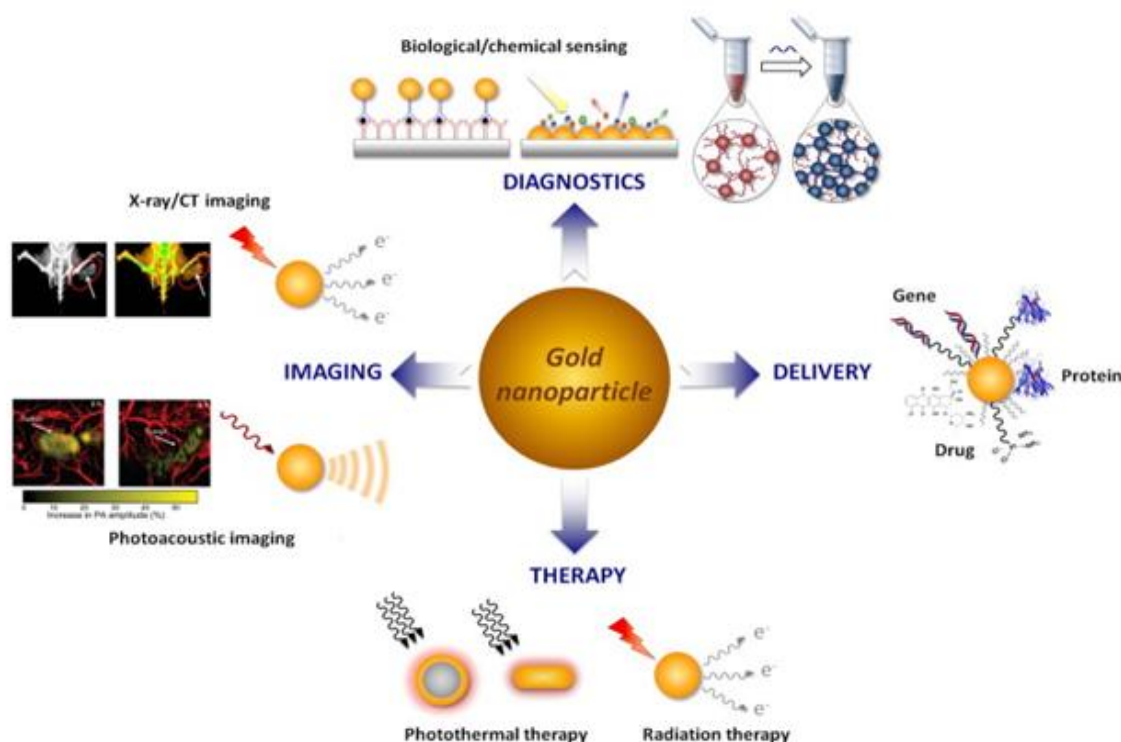


Fig. Gold nanoparticles in cancer

noncancerous cells, but this was mostly due to random interactions rather than any specific targeting. There were also interactions with the collagen matrix, creating a reddish appearance in the background.

NANOTECHNOLOGY IN CANCER TREATMENT:-

Cancer is a serious disease that causes a lot of deaths around the world. Cancer is usually treated by surgery to remove tumors, along with chemotherapy or radiation. But these treatments have problems. They often spread throughout the body, making them less effective, and it's hard to know if they're working. This can lead to issues

like tumors not responding to treatment. Nanoparticles are tiny particles that can be made from different materials, like natural fats or man-made substances. They interact differently with things from our bodies compared to man-made stuff. When it comes to treating cancer, traditional methods like surgery, chemotherapy, and radiation can harm both cancer and healthy cells.

Lately, scientists are really interested in using nanotechnology and nanoparticles to make cancer treatment better. The problem with regular chemotherapy is that it often doesn't get the medicine to the cancer cells very well and can cause drug resistance. This happens because of barriers in our bodies and the way tumors are structured. Nanoparticles can help by delivering drugs more effectively to the cancer cells.

The main goals of using nanotechnology in drug delivery are to make sure the medicine goes where it's needed, reduce side effects, and create new and safer drugs. To do this, scientists need to understand how the drugs and nanoparticles work, how long they last, whether they're safe, where they go in the body, and how they work.(12)

Many different nanotechnology products are used to deliver drugs in cancer treatment. Some examples are liposomes, dendrimers, carbon nanotubes, tiny fat particles, magnetic

nanoparticles, solid lipid particles, and quantum dots. Dendrimers are very tiny round particles. They can hold a lot of medicine. Using dendrimers can change the way cancer tumors look and behave, making them less dangerous. Dendrimers are made by starting with ammonia and mixing it with acrylic acid. Chemists create dendrimers by starting with a special molecule that turns into a smaller molecule, and this process continues until they get the result they want. These dendrimers, especially the ones based on PAMAM, have been studied a lot and are commonly used for medical purposes. Some researchers have made DNA-based dendrimers to target specific cancer cells. They've also developed dendrimers with folic acid and fluorescein to reduce drug side effects. In lab tests, these dendrimers were found to attach to cancer cells that have a particular receptor. Scientists have used dendrimers loaded with paclitaxel, folic acid, and fluorescein isothiocyanate to target cancer cells with overactive folate receptors. These multifunctional dendrimers, made from ethylenediamine, were used to study their effect on cancer cells with folate receptors. Another group of scientists created dendrimers loaded with methotrexate for intravenous use to target cancer cells with folate receptors, effectively inhibiting the growth of epithelial cancer.(19)

MACHANISUM OF CELLULAR TARGETING :-

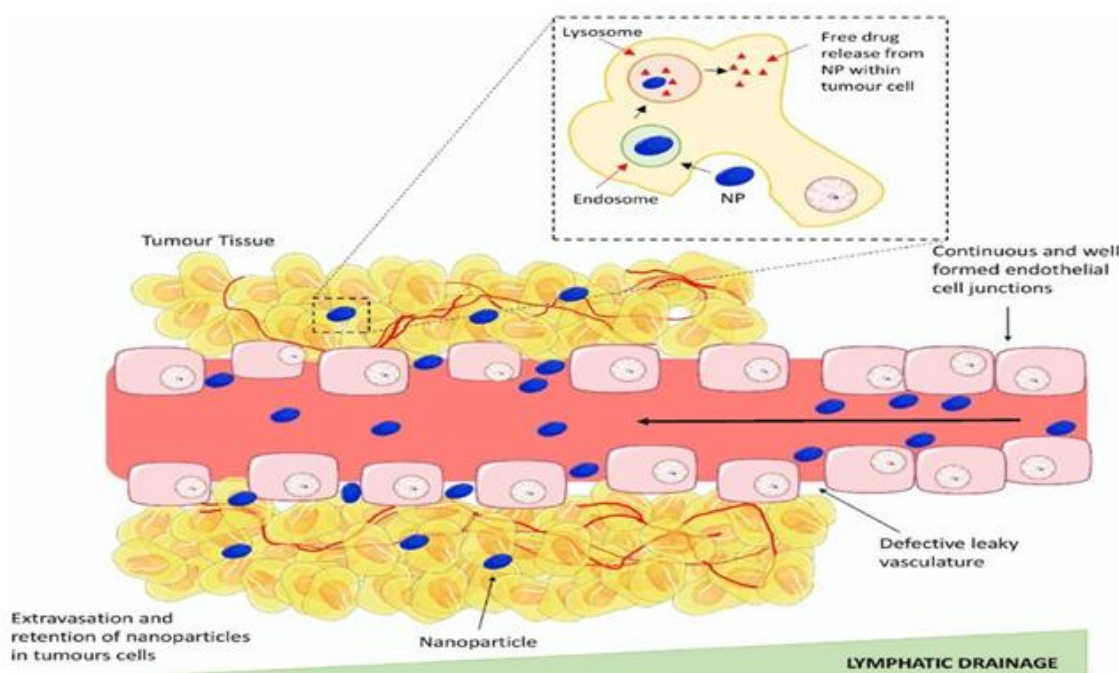


Fig. Cellular targeting

To make cancer treatment better, we need a way to create drugs or gene delivery systems that can precisely target and attack only the cancer cells, leaving the healthy cells unharmed. This makes the treatment more effective and protects the normal cells from harmful side effects. This indirect targeting of cancer cells involves overcoming various barriers in the body, including complex layers and components like epithelium, endothelium, and cellular membranes. Specifications for NP size, biocompatibility, and surface chemistry are crucial to avoid unintended targeting. However, just getting NPs inside the cell doesn't guarantee they'll reach the specific target within the cell. Specific engineering and optimization are necessary for precise targeting within the cell or nucleus. Several studies have been conducted, with more in progress, to design NP-based drug targeting. These nanocarriers should have key characteristics like stability in the blood until they reach the tumor microenvironment (TME), escaping clearance systems, and accumulating in TME via tumor vasculature. Understanding the surface features, chemical properties, and body conditions is vital in the process of NP drug targeting.

To comprehend how NP carriers interact with cancer cells and tumor biology, it's crucial to explore targeting mechanisms. These mechanisms can be broadly categorized into two groups: passive targeting (allowing particles to naturally accumulate in tumors) and active targeting (specifically guiding particles to the tumor).⁽⁸⁾

PASSIVE TARGETING:-

In the late 1980s, scientists noticed that certain large molecules, like poly(styrene-co-maleic acid)-neocarzinostatin (SMANCS), tend to gather more in cancer cells. This accumulation is due to damaged blood vessels in tumors and poor drainage, creating what's known as the "enhanced permeation and retention effect." In specific conditions like low oxygen or inflammation, the layer of cells lining blood vessels becomes more porous. In low-oxygen situations, fast-growing tumor cells trigger more blood vessel formation, resulting in leaky vessels with large pores. These pores, ranging from 200 to 2000 nm, allow nanoparticles (NPs) to easily diffuse from blood vessels into cancer cells.

In normal tissues, fluids typically flow into lymphatic vessels at a steady rate. However, in tumors, this process is disrupted, leading to minimal fluid uptake. This disruption contributes to

NP retention in tumors, known as the enhanced retention part of the effect. This feature doesn't work well for molecules with short circulation time, which are quickly washed out from cancer cells. To address this, small molecules are often enclosed in nanosized drug carriers to improve their pharmacokinetics, focus on tumors, and reduce side effects.

Beyond the enhanced permeation and retention effect, the tumor microenvironment (TME) plays a crucial role in passive targeting. Rapidly growing tumor cells rely on glycolysis for energy, creating an acidic TME. This lower pH can be utilized with pH-sensitive NPs that release drugs in low-pH conditions. Passive targeting doesn't involve specific molecules for particular tumor cells; it relies on different tumor characteristics (vascular structure, leakiness) and carrier properties (size and circulation time). The effectiveness of this targeting depends on factors like angiogenesis, lymphangiogenesis, tumor invasion, and intratumor pressure, combined with the physical and chemical traits of NPs, influencing the efficiency of NP drug delivery systems.

Example:-

1. Genexol PM® is a new way of delivering paclitaxel, a cancer-fighting substance, using special nanoparticles. It was found to have a higher tolerated dose in mice, and it's approved in South Korea for a type of breast cancer. In the USA, it's still being studied for pancreatic cancer.

2. DaunoXome® is a medicine that fights cancer by reducing tumor cell growth. It uses a unique form of daunorubicin, approved by the USFDA in 1996, mainly for treating Kaposi's sarcoma.

In cancer, the irregular growth of tumor cells and their proximity to blood vessels can make drug delivery challenging. Scientists are exploring ways to overcome these challenges, using methods like nitric oxide, ultrasound, and radiation to enhance drug delivery, but there are still limitations and considerations in using these approaches.

ACTIVE TARGETING:-

Active targeting involves using specific molecules or ligands, like transferrin and folate, that attach to receptors found on target cells, such as diseased organs or tissues. This method, known as ligand-mediated targeting, aims to improve the connection between nanoparticles (NPs) and the target without changing their overall distribution in the body. Ligands can include proteins, peptides,

antibodies, nucleic acids, sugars, or small molecules like vitamins.

Commonly studied receptors include transferrin receptor, folate receptor, glycoproteins, and the epidermal growth factor receptor (EGFR). The interaction between ligands and receptors triggers the folding of the cell membrane, leading to the internalization of NPs through receptor-mediated endocytosis.

Active targeting has various mechanisms, with a significant focus on targeting tumor cells. For instance, transferrin, a glycoprotein that transports iron into cells, is often overexpressed in tumor cells, making it a target. NPs can be modified with ligands specific to these receptors to enhance their targeting.

An alternative approach involves targeting cells near cancer cells, such as angiogenic endothelial cells. These cells have close contact with tumor blood vessels, creating hypoxia and necrosis by reducing blood supply to cancer cells. Tumor tissues are also more acidic, and this acidity can be exploited using pH-sensitive liposomes in drug delivery systems.

Example:- 1. Herceptin® for Breast Cancer: Herceptin® is a drug designed to target HER2, a receptor overexpressed in breast cancer cells. PEGylated liposomal doxorubicin, targeted at HER2, was developed to reduce the side effect of cardiotoxicity associated with anthracyclines.

1. VCAM-1 Targeting for Breast Cancer: The surface of tumor blood vessels expresses VCAM-1, a glycoprotein involved in angiogenesis (blood vessel formation). Nanoparticles targeting VCAM-1 show promise in breast cancer models.

Consequences and Where We're Headed Next:-

Nanoparticles hold great promise for the next wave of cancer treatments. Additionally, advancing multifunctional nanoparticles could enable them to identify and eliminate cancer cells simultaneously. Therefore, delving deeper into nanotechnology research is likely to result in the more strategic creation of enhanced nanoparticles, improving their targeting precision, effectiveness, and safety.

REFERENCE:-

[1]. Soma CE, Dubernet C, Bentolila D, Benita S, Couvreur P (2000) Reversion Of multidrug resistance by co-encapsulation of doxorubicin and cyclosporin A in polyalkylcyanoacrylate nanoparticles.

Biomaterials 21(1):1-7. [https://doi.org/10.1016/s0142-9612\(99\)00125-8](https://doi.org/10.1016/s0142-9612(99)00125-8)

[2]. Tran S, DeGiovanni PJ, Piel B, Rai P (2017) Cancer nanomedicine: a review of recent success in drug delivery. *ClinTransl Med* 6(1):44. <https://doi.org/10.1186/s40169-017-0175-0>

[3]. Nikolova M, Slavchov R, Nikolova G. Nanotechnology in medicine. In: *Drug Discovery and Evaluation: Methods in Clinical Pharmacology*.

[4]. Sharifi M, Avadi MR, Attar F, et al. Cancer diagnosis using nanomaterials based electrochemical nanobiosensors. *BiosensBioelectron.*2019

[5]. Tran S, DeGiovanni PJ, Piel B, Rai P (2017) Cancer nanomedicine: a review of recent success in drug delivery. *ClinTransl Med* 6(1):44. <https://doi.org/10.1186/s40169-017-0175-0>

[6]. Krishna KV, Ménard-Moyon C, Verma S, Bianco A (2013) Graphenebased nanomaterials for nanobiotechnology and biomedical applications. *Nanomedicine (Lond)* 8(10):1669-1688. <https://doi.org/10.2217/nnm.13.140>

[7]. Mousa SA, Bharali DJ (2011) Nanotechnology-based detection and targeted therapy in cancer: nano-bio paradigms and applications. *Cancer*3(3):2888-2903. <https://doi.org/10.3390/cancers3032888>

[8]. Masood F. (2016). Polymeric nanoparticles for targeted drug delivery system for cancer therapy. *Materials science & engineering. C, Materials for biological applications*, 60, 569-578. <https://doi.org/10.1016/j.msec.2015.11.067>

[9]. Samadian, H., Hosseini-Nami, S., Kamrava, S. K., Ghaznavi, H., & Shakeri-Zadeh, A. (2016). Folate-conjugated gold nanoparticle as a new nanoplatform for targeted cancer therapy. *Journal of cancer research and clinical oncology*, 142(11), 2217-2229. <https://doi.org/10.1007/s00432-016-2179-3>

[10]. Gurunathan, S.; Jeyaraj, M.; Kang, M.-H.; Kim, J.-H. Anticancer Properties of Platinum Nanoparticles and Retinoic

- Acid:Combination Therapy for the Treatment of Human Neuroblastoma Cancer. *Int. J. Mol. Sci.* 2020, 21, 6792. [CrossRef]
- [11]. Ma H, Liu J, Ali MM, et al. Nucleic acid aptamers in cancer research, diagnosis and therapy. *ChemSoc Rev.* 2015;44(5):1240–1256. Doi:10.1039/C4CS00357H
- [12]. NektarTherapeutics. Study to Evaluate the Safety and Efficacy of NKTR-102 (PEGIrinotecan) in Patients With Metastatic or Locally Advanced Breast Cancer. *ClinicalTrials.gov* web site 2008 [online], <http://clinicaltrials.gov/ct2/show/NCT00802945>
- [13]. ShreelaxmiGavas, Sameer Quazi and Tomasz M. Karpiński. Nanoparticles for Cancer Therapy: Current Progress and Challenges <https://doi.org/10.1186/s11671-021-03628-6>
- [14]. Kumar BishwajitSutradhar and Md. LutfulAmin.Nanotechnology in Cancer Drug Delivery and SelectiveTargeting <http://dx.doi.org/10.1155/2014/939378>
- [15]. SomaiaAbdEl-Karim,Manal M Anwar.Nanotechnology in Cancer Diagnosis and Treatmentn *Journal of Pharmacy and Pharmacology* · July 2015 <https://www.researchgate.net/publication/282351768>
- [16]. Kumar BishwajitSutradhar and Md. LutfulAmin.Nanotechnology in Cancer Drug Delivery and SelectiveTargetingHindawi Publishing CorporationISRN NanotechnologyVolume 2014, Article ID 939378, 12 pages <https://doi.org/10.3390/pharmaceutics15031025>
- [17]. Y. Liu, K. Li, J. Pan, B. Liu, and S.-S. Feng, “Folic acid cconjugatenanoparticles of mixed lipid monolayer shell and biodegradablepolymer core for targeted delivery of Docetaxel,” *Biomaterials*, vol. 31, no. 2, pp. 330–338, 2010.
- [18]. National cancer institute ,Nanodilivary system and device.Cancer and Nanotechnology <https://www.cancer.gov/nano/cancer-nanotechnology>
- [19]. NavedulHaque,SanjayYadav,Nagiat T Hwisa,Shukri Al-sharifNanotechnology in Cancer in Therapy *Journal of Drug Targeting* · January 2010 <https://www.researchgate.net/publication/216089054>
- [20]. <http://www.physorg.com/news65705979.html>
- [21]. DeepaMundekkad William C. Cho.Nanopartical clinical translation for cancer therapy <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8835852/>
- [22]. A Hett. Nenotechnology : small matter, many unknowns, 2004, <http://www.swissre.com>
- [23]. Noor Alrushaid ,FirdosAlam Khan ,Ebtasam Abdullah Al-SuhaimiandAbdelhamidElaissari Nanotechnology in Cancer Diagnosis and Treatment *Pharmaceutics* 2023, <https://doi.org/10.3390/pharmaceutics15031025>
- [24]. Chang P-Y, Kuo Y-B, Wu T-L, et al. Association and prognostic value of serum inflammation markers in patients with leukoplakia and oral Cavity cancer. *ClinChem Lab Med.* 2013;51(6):1291–1300. Doi:10.1515/cclm-2012-0504
- [25]. Jaiswal M, Dudhe R, Sharma PK (2015) Nanoemulsion: an advanced Mode of drug delivery system. *3 Biotech* 5(2):123–127. <https://doi.org/10.1007/s13205-014-0214-0>