NANOPARTICLES IN CANCER THERAPY: ADVANCES, CHALLENGES AND FUTURE DIRECTIONS

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Abstract: Cancer remains one of the leading causes of mortality worldwide, and conventional treatments such as Chemotherapy, radiation, and surgery often face limitations including toxicity, drug resistance, and poor Selectivity. Nanotechnology has emerged as a transformative approach in cancer therapy by enabling Precise drug delivery, enhanced targeting, and reduced systemic side effects. Nanoparticles (NPs) such As liposomes, dendrimers, polymeric nanoparticles, metallic nanoparticles, and quantum dots offer Unique physicochemical properties that improve drug solubility, bioavailability, and controlled release. Their ability to exploit mechanisms like passive targeting through the enhanced permeability and Retention (EPR) effect and active targeting via ligand–receptor interactions significantly enhance Therapeutic efficacy. Despite promising preclinical outcomes, clinical translation remains limited due To challenges in biodistribution, biocompatibility, large-scale synthesis, and long-term safety. Continued research focusing on the optimization of nanoparticle design, toxicity evaluation, and Personalized nanomedicine may pave the way for safer and more effective cancer treatments.

Keywords: Nanoparticles, Cancer Therapy, Drug Delivery, Targeted Therapy, Nanomedicine, Biocompatibility

INTRODUCTION:

Cancer is a complex group of diseases defined by uncontrolled cell division and invasiveness, driven by a combination of environmental factors, unhealthy lifestyle choices, and genetic mutations, though inherited genetics account for only a small fraction of cases [1-3]. Despite being a leading cause of global mortality, conventional treatments like chemotherapy and radiation are frequently hampered by systemic toxicity, severe side effects such as organ damage and bone marrow suppression, and high recurrence rates. While modern advancements like precision and immunotherapy offer more targeted approaches, they face ongoing hurdles including multi-drug resistance, potential autoimmune complications, and varying levels of efficacy between hematological and solid tumors [4-9].

Cancer treatment faces significant obstacles from the unique extracellular matrix (ECM) of tumors, which acts as a physical barrier to immune cells, and the prevalence of dermatological adverse events (DAEs) caused by modern targeted therapies. To overcome these limitations, nanotechnology has emerged as a transformative solution, utilizing nanoparticles to improve pharmacokinetics, enhance targeting precision, and bypass multi-drug resistance (MDR) mechanisms. Since the first medical applications of nanotechnology in the 1960s, and with significant clinical progress since 2010, nanotherapeutics have enabled effective drug combination therapies that minimize systemic toxicity while offering more sophisticated diagnostic and therapeutic tools for precision oncology [10-12].

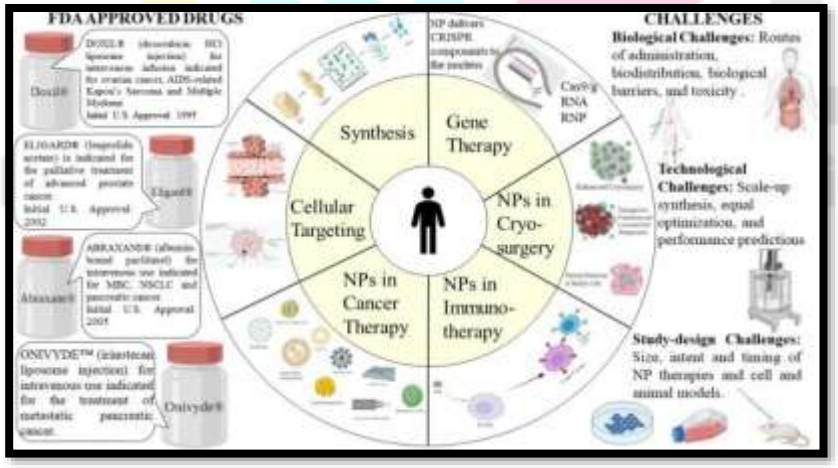


Figure 1: Nanoparticles for Cancer Therapy: Current Progress and Challenges

NANOPARTICLES:

Nanoparticles (NPs) are specialized structures defined by having at least one dimension under 100 nanometers, classified by their dimensionality (0D to 3D) and characterized by a multi-layered architecture consisting of a core, shell, and surface layer. Their exceptionally high surface-to-volume ratio and customizable surface chemistry allow for superior tissue penetration and the

utilization of the enhanced permeability and retention (EPR) effect, which naturally concentrates them within tumor sites. By employing surface modifications—such as polyethylene glycol (PEG) coatings to evade immune detection—these particles can overcome biological barriers, extend circulation time, and provide controlled drug release, making them a cornerstone of modern targeted cancer therapy [13-14].

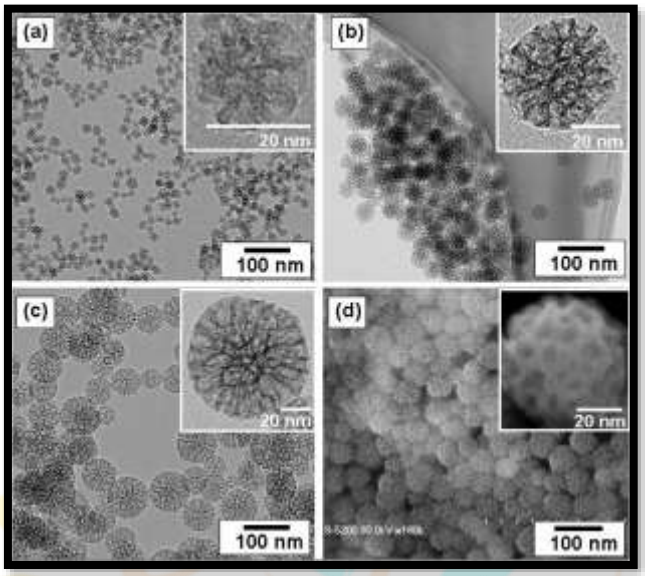
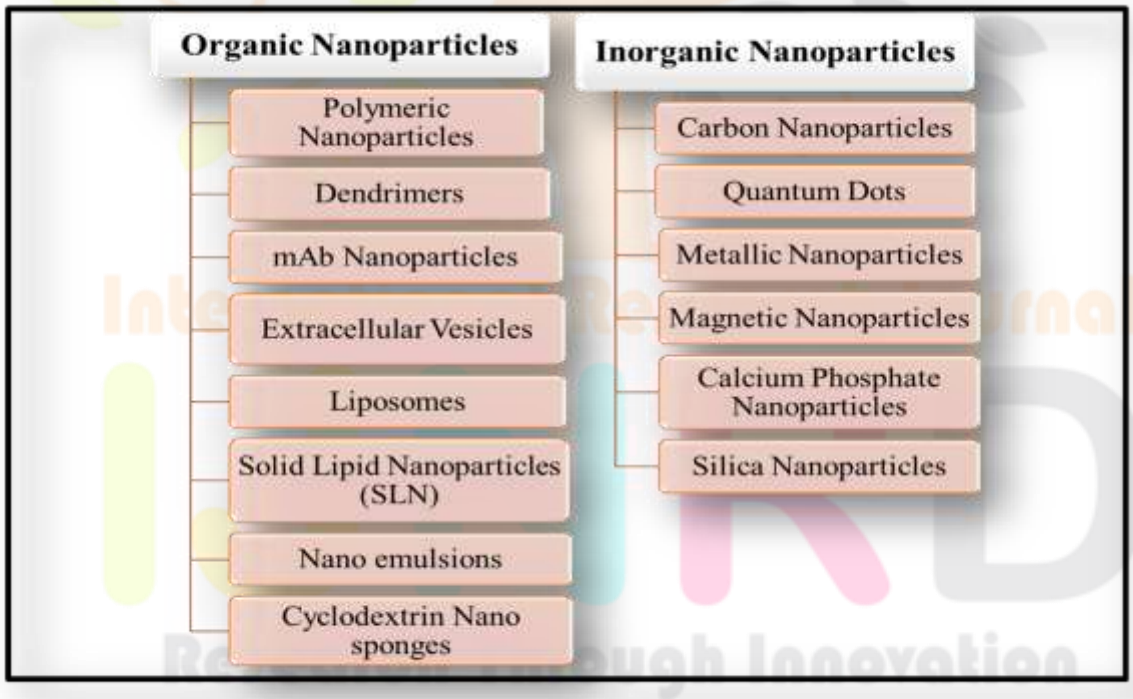


Figure 2: Structure of Nanoparticles

TYPES OF NANOPARTICLES IN CANCER THERAPY:



A. **ORGANIC NANOPARTICLES:**

B. **i) Polymeric Nanoparticles:** Polymeric nanoparticles (PNPs) are "colloidal macromolecules" that function as either nanospheres or Nano capsules to transport drugs through entrapment or surface attachment. While early versions utilized non-biodegradable materials like PMMA,[15] modern research has shifted toward biodegradable polymers such as albumin, chitosan, and polylactic acid to ensure biocompatibility and eliminate the risks of toxic accumulation. These carriers are frequently enhanced with surfactants like poloxamers or specific coatings to cross challenging biological barriers like the blood-brain barrier (BBB) [16]. The clinical relevance of PNPs is demonstrated by the success of indomethacin-loaded Nano capsules in glioma models and the progression of several drug-loaded copolymers, including paclitaxel and doxorubicin variants, into clinical development for various cancers [17].

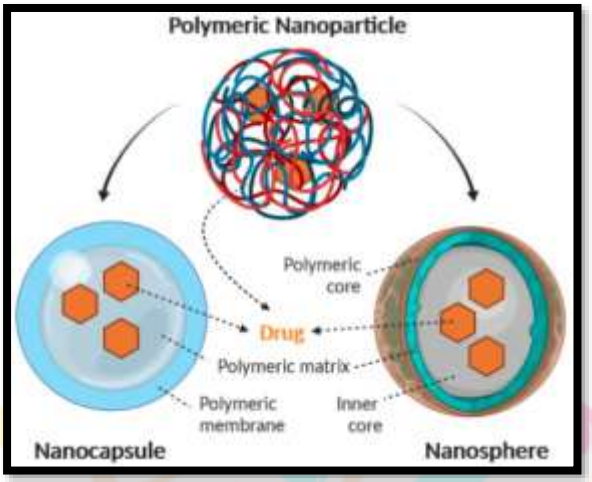


Figure 3. Structure of Polymeric Nanoparticles

ii) Dendrimers:

Dendrimers are highly organized, spherical macromolecules characterized by a unique hyperbranched architecture that typically ranges from 1 to 15 nm in size. Synthesized through a precise stepwise process beginning with a central ammonia core, these structures offer tunable branching and consistent molecular weight, making them exceptionally effective for the delivery of nucleic acids and anticancer agents. Common varieties like PAMAM and PPI dendrimers have demonstrated superior efficacy in overcoming multidrug resistance (MDR); for instance, DNA-assembled PAMAM dendrimers have shown a remarkable ability to inhibit the growth of epithelial cancer xenografts more effectively than traditional single-agent chemotherapy [18].

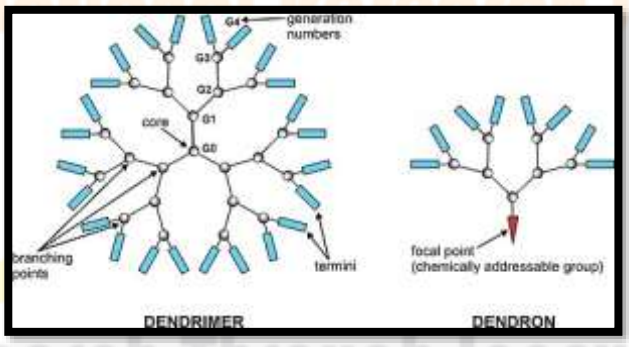


Figure 4: Structure of Dendrimer

iii) mAb Nanoparticles:

Monoclonal antibodies (mAbs) serve as highly specific targeting ligands that, when integrated with nanotechnology, create sophisticated antibody–drug conjugates (ADCs) capable of delivering cytotoxic payloads directly to malignant cells. By combining a nanoparticle core—such as one loaded with paclitaxel—with a surface coating of specific antibodies like rituximab or those targeting HER2-positive receptors, these conjugates achieve superior anti-tumor efficacy while significantly reducing systemic toxicity. This synergistic approach ensures that high concentrations of the therapeutic agent reach the intended site, as demonstrated by the enhanced performance of these hybrids over standalone chemotherapy or immunotherapy treatments in clinical models [19].

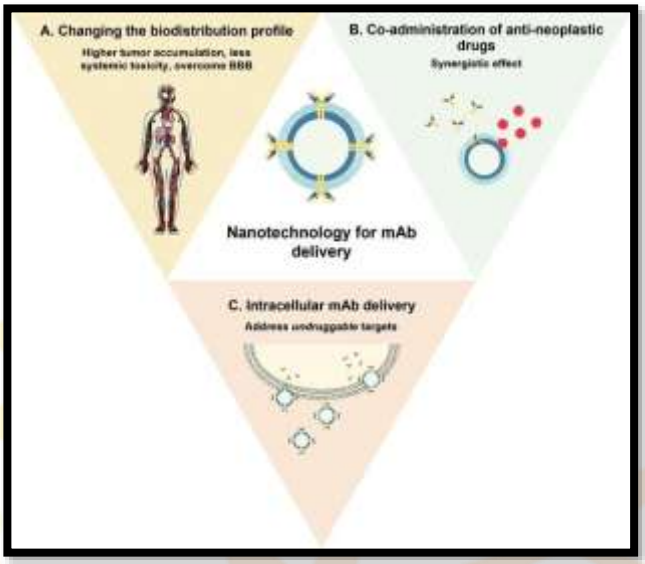


Figure 5: Structure of mAb Nanoparticles

iv) Extracellular Vesicles:

Extracellular vehicles (EVs), particularly exosomes, are natural phospholipid-bilayered vesicles that function as highly efficient drug delivery systems due to their innate biocompatibility and ability to evade immune surveillance. Unlike synthetic nanoparticles, these "nature-made" carriers facilitate seamless cellular communication and entry into malignant cells, significantly improving the therapeutic index of potent drugs; for instance, exosome-loaded doxorubicin (exoDOX) enhances tumor-specific cytotoxicity while mitigating dangerous side effects like cardiotoxicity. Although exosomes offer superior stability and reduced toxicity compared to traditional delivery methods, their widespread clinical application is currently hampered by the technical difficulties associated with standardizing large-scale isolation and purification processes [20].

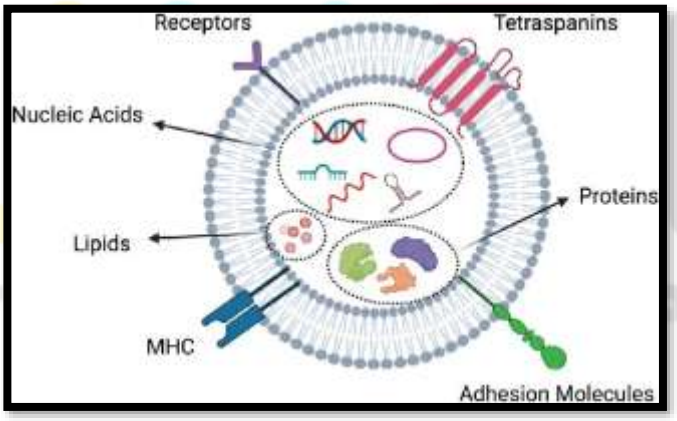


Figure 6: Structure of Extracellular Vesicles

v) Liposomes:

Liposomes are spherical phospholipid vesicles characterized by a unique architecture consisting of a hydrophobic bilayer and a hydrophilic core, enabling them to simultaneously transport both water-soluble and fat-soluble therapeutic agents. As the first FDA-approved nanoscale drug delivery system, liposomes like Doxil® have revolutionized oncology by improving drug stability and bioavailability while significantly reducing systemic toxicity and immunogenicity. Despite their success in treating cancers such as breast cancer, their clinical utility is often constrained by technical hurdles, including low drug encapsulation efficiency, a relatively short shelf life, and rapid clearance from the bloodstream by the body's macrophage system [21].

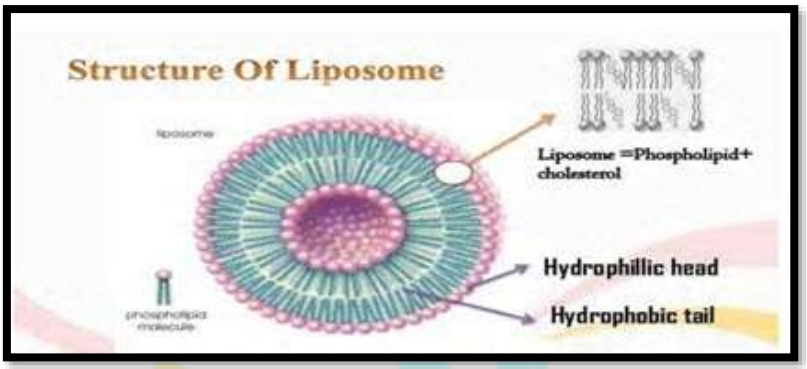


Figure 7: Structure of Liposomes

vi) Solid Lipid Nanoparticles (SLN):

Solid lipid nanoparticles (SLNs) are specialized colloidal carriers ranging from 1 to 100 nm that utilize a solid lipid core—comprised of triglycerides or fatty acids—stabilized by a phospholipid monolayer and emulsifiers. Unlike the aqueous centers of liposomes, SLNs feature a micelle-like, non-aqueous core that provides superior drug stability and improved bioavailability for hydrophobic treatments. These nanocarriers have demonstrated significant therapeutic potential in hematological oncology, with doxorubicin and daunorubicin formulations showing high efficacy against resistant leukemia cell lines and murine models while simultaneously reducing the systemic toxicity typically associated with these potent agents [22].

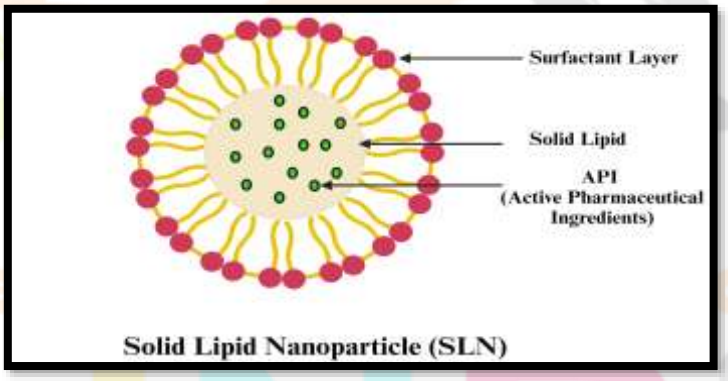


Figure 8: Structure of SLN

vii) Nanoemulsions:

Nanoemulsions are colloidal delivery systems consisting of oil and water droplets ranging from 10 to 1,000 nm, typically stabilized into oil-in-water or water-in-oil configurations. These systems are highly valued in oncology for their optical clarity, biodegradability, and exceptional stability, which allow for the effective transport of potent combinations like spirulina and paclitaxel to trigger anti-tumor signaling pathways. While they have shown clinical promise in treating aggressive conditions such as advanced melanoma using drugs like bevacizumab and rapamycin, their widespread adoption is restricted by the high-cost manufacturing requirements, which necessitate specialized equipment and extreme conditions of pressure and temperature [23].

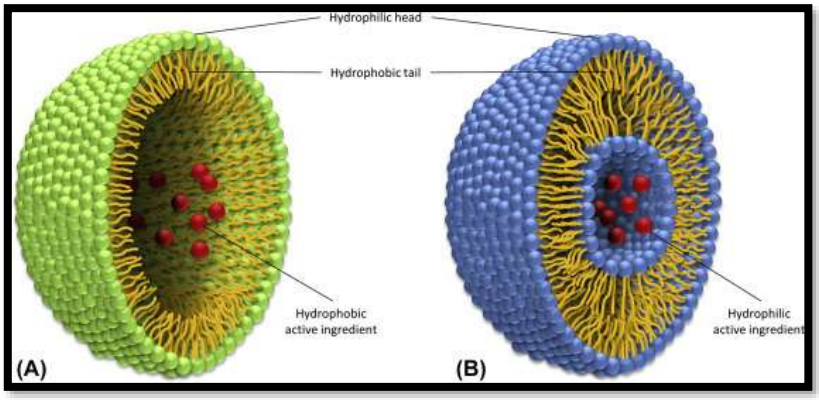


Figure 9: Structure of Nanoemulsions

viii) Cyclodextrin Nano sponges:

Nanosponge carriers are highly porous, mesh-like nanoparticles, often synthesized using cyclodextrins to create a scaffold capable of encapsulating a wide variety of therapeutic agents. This unique architecture significantly improves the solubility and chemical stability of poorly water-soluble drugs, allowing for much higher drug-loading capacities compared to traditional nanocarriers. Research has demonstrated their clinical potential through formulations such as paclitaxel-loaded \beta-cyclodextrin Nano sponges, which exhibit potent cytotoxicity against MCF-7 breast cancer cells, and calprotectin-based versions that resolve common issues with drug degradation, marking them as a versatile tool for precision cancer therapy [24].

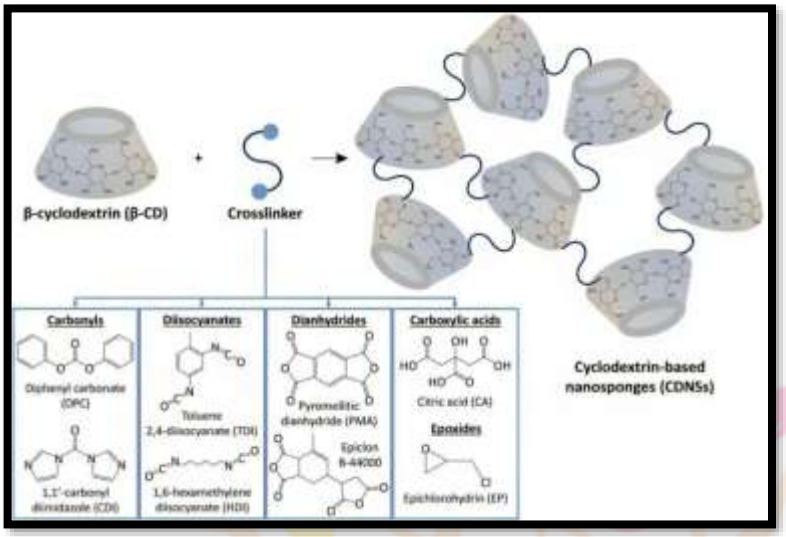


Figure 10: Cyclodextrin Nano sponges

C. INORGANIC NANOPARTICLES:

i) Carbon Nanoparticles:

Carbon-based nanoparticles, such as graphene, carbon nanotubes, fullerenes, and nanoforms, leverage their unique structural diversity and exceptional optical and electrical properties to serve as versatile platforms for oncological applications. Derivatives like graphene oxide (GO) are particularly effective at targeting tumor hypoxia and delivering doxorubicin in breast cancer models, while the cage-like architecture of fullerenes makes them ideal candidates for photodynamic therapy. Additionally, carbon nanotubes (CNTs) provide high surface areas for the targeted delivery of DNA and chemotherapy drugs to specific sites, such as colon cancer cells; however, despite their therapeutic potential and high drug-loading capacity, their clinical integration remains subject to ongoing investigation regarding their long-term safety and potential immune system interactions [25].

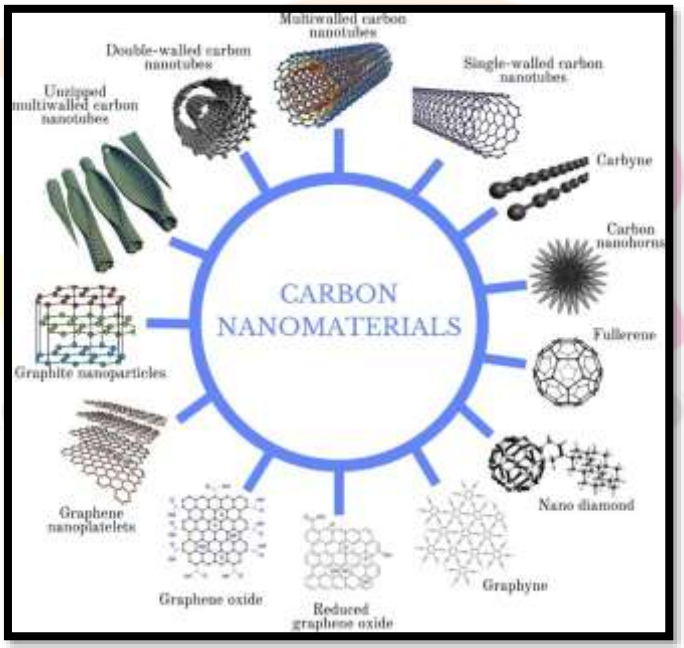


Figure 11: Structure of Carbon Nanoparticles

ii) Quantum Dots:

Quantum dots are nanoscale semiconductor particles valued in oncology for their exceptional optical properties, including high photostability and narrow emission spectra, which facilitate precise biological imaging and targeted therapy. They are categorized into several types, with graphene quantum dots being particularly prominent in research due to their superior biocompatibility and the body's ability to excrete them rapidly. These nanostructures can be engineered into complex conjugates—such as those combining aptamers and doxorubicin—to deliver highly specific treatment to cells like prostate cancer; however, their transition

from laboratory to widespread clinical use is currently restricted by the difficulty of establishing standardized, high-volume production methods that ensure consistent quality and performance [26].

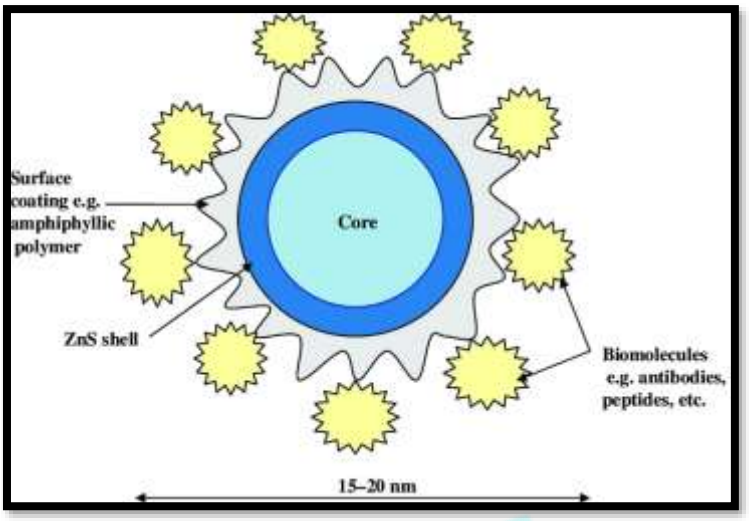


Figure 12: Structure of Quantum Dots

iii) Metallic Nanoparticles:

Metallic nanoparticles, such as gold, silver, copper, and iron-based varieties, utilize their distinct optical, magnetic, and photothermal properties to serve as multifunctional agents for both cancer imaging and drug delivery. Gold nanoparticles are particularly effective as trackable intracellular carriers, with specialized gold–silica nano shells being used to precisely target HER2-positive breast cancer cells. Similarly, iron oxide nanoparticles provide critical diagnostic value, exemplified by the FDA-approved ferumoxytol and the experimental formulation Combi Dex (Combidex®), which facilitate the imaging of nodal metastases and the treatment of iron-deficiency anemia in oncological patients [27].

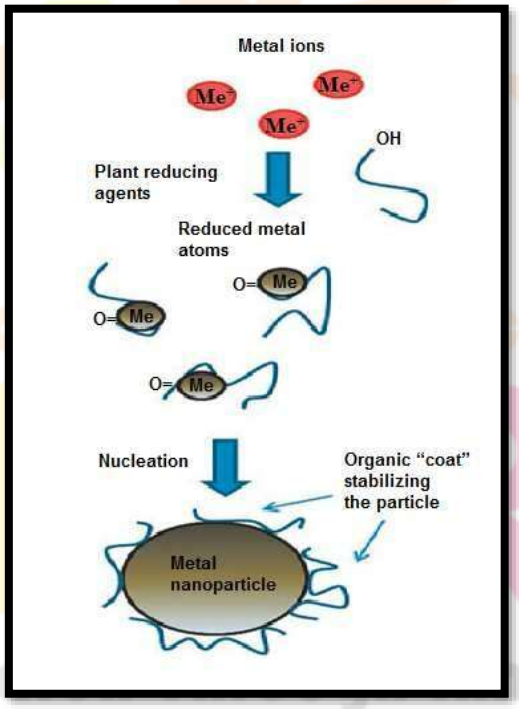


Figure 13: Structure of Metallic Nanoparticles

iv) Magnetic Nanoparticles:

Magnetic nanoparticles, typically composed of iron oxide and stabilized with polymer or fatty acid coatings, serve as dual-purpose agents for both high-resolution MRI imaging and targeted therapy. Their unique magnetic properties allow for the use of magnetic hyperthermia, a process where an external alternating magnetic field generates localized heat to thermally ablate cancer cells without damaging surrounding healthy tissue. Clinically, specialized formulations like LHRH-conjugated superparamagnetic iron oxide nanoparticles are being utilized for precise breast cancer targeting, while other agents such as Feridex® and Resovist® have been developed to enhance the detection and treatment of liver metastases and colon cancer [28].

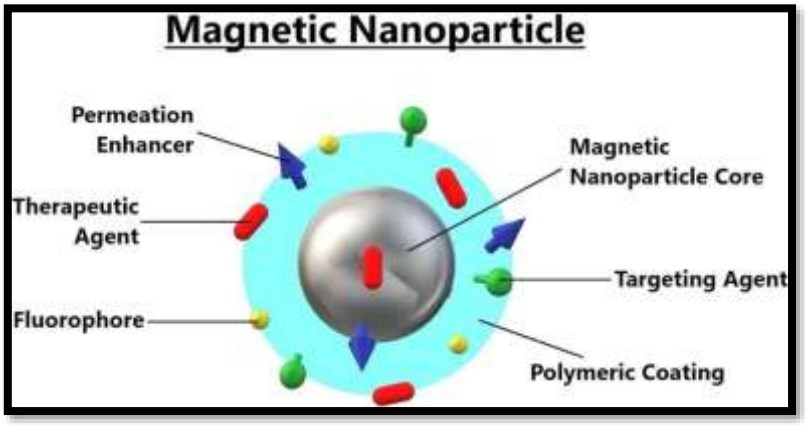


Figure 14: Structure of Magnetic Nanoparticles

v) Calcium Phosphate Nanoparticles:

Calcium phosphate nanoparticles are distinguished by their exceptional biodegradability and biocompatibility, serving as safe and efficient delivery vehicles for a diverse range of therapeutics, including insulin, growth factors, and antibiotics. Their structural affinity for nucleic acids makes them particularly valuable in gene therapy for transporting plasmid DNA and oligonucleotides, often in synergy with viral or non-viral vectors to maximize gene transfer efficiency. Advanced formulations, such as calcium glycerol liposomal nanolipoplexes, have demonstrated the ability to significantly enhance transfection rates while minimizing the cellular toxicity often associated with synthetic carriers, offering a versatile and non-toxic platform for modern precision medicine [29].

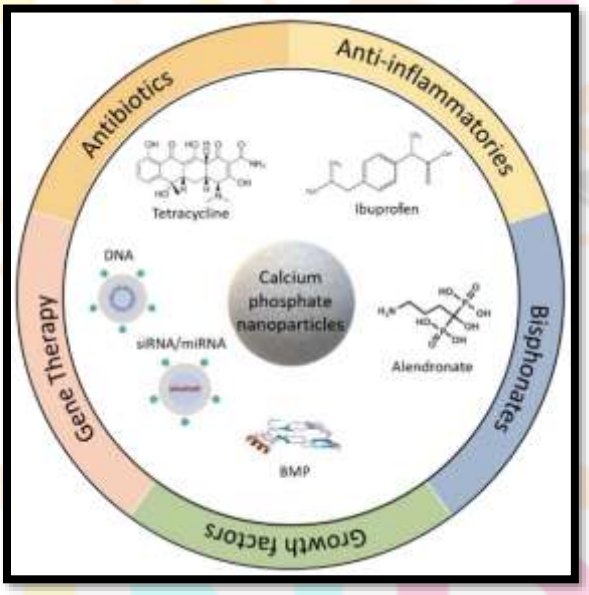


Figure 15: Structure of Calcium Phosphate Nanoparticles

vi) Silica Nanoparticles:

Silica nanoparticles have emerged as highly efficient platforms for drug and gene delivery, characterized by their versatile surface chemistry and low cellular toxicity. When functionalized with amino silanes, such as N-(6-aminohexyl)-3-aminopropyl-trimethoxysilane, they facilitate superior gene transfection with minimal damage to the host cells. Particularly, mesoporous silica nanoparticles are valued for their exceptional pharmacokinetics and high surface area, which allow for substantial drug loading and precise release; this has been effectively demonstrated in immunotherapy studies where calprotectin-loaded particles were successfully internalized by colorectal cancer cells to induce therapeutic effects [30].

SYNTHESIS OF NPS:

Nanoparticle synthesis is fundamentally categorized into top-down and bottom-up strategies, each utilizing different physical or chemical pathways to achieve nanoscale dimensions [31]. Top-down approaches rely on the external breakdown of bulk materials through high-energy physical processes such as mechanical milling, lithography, or laser ablation. Conversely, bottom-up methods involve the precise assembly of nanoparticles from the atomic or molecular level, utilizing chemical synthesis, self-assembly, or biological processes to grow the structures. These methodologies can be further refined into physical, chemical, and hybrid techniques, allowing researchers to exercise meticulous control over the final particle size, shape, and surface functionality required for specific medical applications [32].

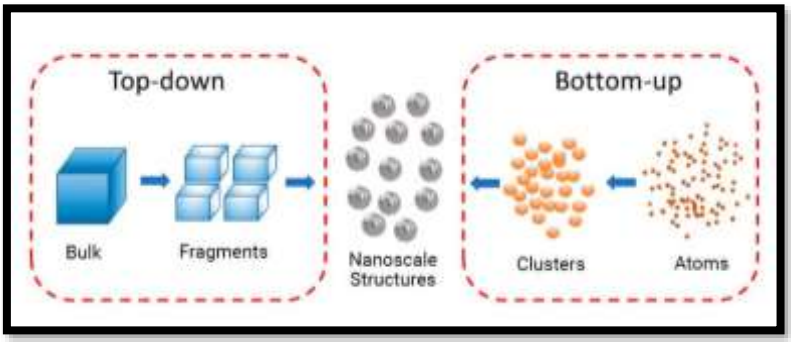


Figure 16: Scheme of top-down and bottom-up synthesis of nanoparticles (NPs)

a) Top-down Approach:

The top-down or destructive synthesis method produces nanoparticles by systematically breaking down bulk materials into nanoscale fragments through high-energy physical and chemical processes. This category encompasses a variety of techniques, including mechanical milling, laser ablation, nanolithography, and thermal decomposition, each of which can be fine-tuned by adjusting parameters like temperature, pressure, and reaction time. By precisely controlling these synthesis conditions, researchers can dictate the resulting nanoparticles' size, geometric shape, surface charge, and chemical reactivity. Mastering the underlying growth and fragmentation mechanisms is critical for ensuring that the final particles possess the specific structural characteristics required for advanced medical and industrial applications [33].

b) Bottom-up Approach:

The bottom-up or constructive synthesis method involves the precise assembly of nanoparticles by building them from the atomic or molecular level, transitioning through clusters until the desired nanoscale structure is achieved. This approach is highly valued for its ability to provide meticulous control over the physical and chemical properties of the resulting material, such as its crystalline structure and surface functionality. Key techniques include Chemical Vapor Deposition (CVD), sol-gel synthesis, and biosynthesis, which utilize chemical reactions or biological systems to "grow" particles with high uniformity. By starting from the smallest building blocks, this method allows for the creation of complex, high-purity nanoparticles that are often more consistent in size and shape than those produced by destructive methods [34].

MECHANISMS OF CELLULAR TARGETING:

Developing an effective cancer therapy requires nanoparticles (NPs) to navigate a rigorous series of biological hurdles, from escaping the reticuloendothelial system (RES) in the bloodstream to penetrating the dense interstitial fluid of the tumor microenvironment (TME). To be successful, these carriers—ideally sized between 10 and 100 nm—must remain stable during circulation, evade immune clearance by the mononuclear phagocyte system, and specifically accumulate within the tumor vasculature [35]. Even after reaching the tumor, the NPs must overcome enzymatic defenses and cross cellular membranes to reach their precise subcellular targets, such as the cytosol or nucleus, which necessitates meticulous engineering of their size, surface chemistry, and biocompatibility to avoid non-specific interactions with healthy tissue.

The efficiency of these systems is largely governed by two primary mechanisms: passive and active targeting. Passive targeting leverages the unique pathophysiological conditions of the tumor, such as the Enhanced Permeability and Retention (EPR) effect, which allows nanoparticles to leak through poorly formed tumor blood vessels and accumulate at the site [36]. In contrast, active targeting involves functionalizing the nanoparticle surface with ligands that bind specifically to receptors overexpressed on cancer cells, facilitating selective interaction and internalization. The success of these mechanisms depends heavily on the interplay between the NPs' physicochemical properties and the specific biology of the tumor, ensuring high therapeutic efficacy while minimizing cytotoxic effects on normal cells [37].

a) Passive Targeting:

The Enhanced Permeability and Retention (EPR) effect is a cornerstone of passive targeting in nanomedicine, first identified through the selective accumulation of macromolecules like SMANCS in cancerous tissues [38]. This phenomenon is driven by the structural flaws of tumor physiology: as tumors grow rapidly, they undergo neovascularization to meet their oxygen demands, resulting in "leaky" blood vessels with large gaps or fenestrations ranging from 200 to 2,000 nm [39]. Unlike healthy tissues that possess a functional lymphatic system for fluid drainage, tumors suffer from disrupted lymphatic flow, which prevents the clearance of extravasated particles. Consequently, nanoparticles that are large enough to avoid rapid renal clearance but small enough to exit these leaky vessels become trapped within the tumor interstitial space, significantly increasing the local drug concentration [40].

Beyond vascular abnormalities, the tumor microenvironment (TME) provides chemical triggers that further refine passive targeting strategies. For example, the high glycolytic rate of rapidly dividing cancer cells creates an acidic environment that distinguishes the tumor from healthy tissue. Researchers exploit this by designing pH-sensitive nanoparticles that remain stable in the bloodstream but release their therapeutic payload only upon encountering the low pH of the TME [41]. While passive targeting is highly versatile because it does not require specific surface markers, its success is heavily dependent on individual tumor biology, including vascular density and interstitial fluid pressure. By encapsulating small-molecule drugs into these nanoscale carriers, scientists can improve pharmacokinetics and ensure the treatment bypasses healthy organs to accumulate precisely where it is needed most [42].

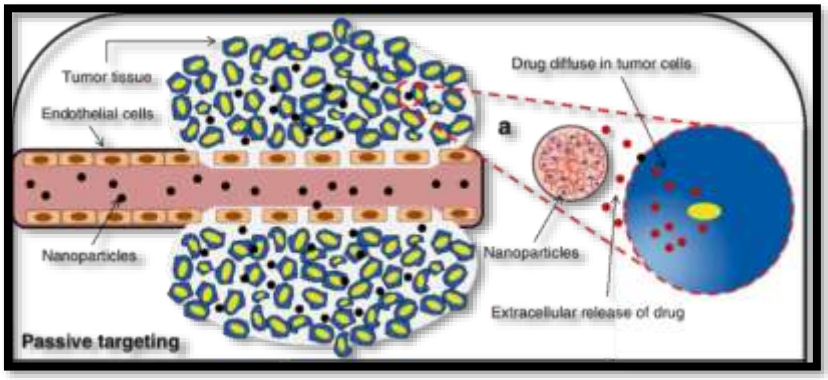


Figure 17: Structure of Passive Cellular Targeting

Example of Passive Targeting:

Taxanes like paclitaxel remain a cornerstone of cancer therapy, with advanced nano-formulations significantly improving their clinical performance. Abraxane®, an albumin-bound nanoparticle, enhances the stabilization of microtubules to halt cell division, while Genexol PM® utilizes polymeric micelles to allow for higher tolerated doses and superior tissue penetration in metastatic breast cancer. Additionally, liposomal systems like DaunoXome® have long been utilized to optimize the delivery of daunorubicin for conditions such as Kaposi's sarcoma. However, the efficacy of these nanomedicines is often hindered by physiological barriers like tumor heterogeneity, irregular vascular networks, and high interstitial fluid pressure; to overcome these, clinicians are increasingly exploring "priming" strategies such as hyperthermia, ultrasound, and nitric oxide to physically open the tumor structure and ensure deeper drug penetration [43].

b) Active Targeting:

Active or ligand-mediated targeting utilizes specific molecules such as antibodies, peptides, folate, or transferrin to "decorate" the surface of nanoparticles, allowing them to bind precisely to receptors that are overexpressed on the surface of malignant cells. This strategic binding facilitates receptor-mediated endocytosis, ensuring that the drug payload is actively pulled into the cancer cell rather than relying solely on random diffusion. For instance, transferrin-modified nanoparticles can specifically seek out ovarian carcinoma cells that have a high demand for iron, while other active strategies target the endothelial cells of tumor blood vessels to starve the tumor of oxygen, leading to necrosis. While this approach significantly enhances the cellular uptake and "crosstalk" between the carrier and the target, its success remains highly dependent on the density of the receptors, the specific design of the nanoparticle, and the chosen route of administration [44].

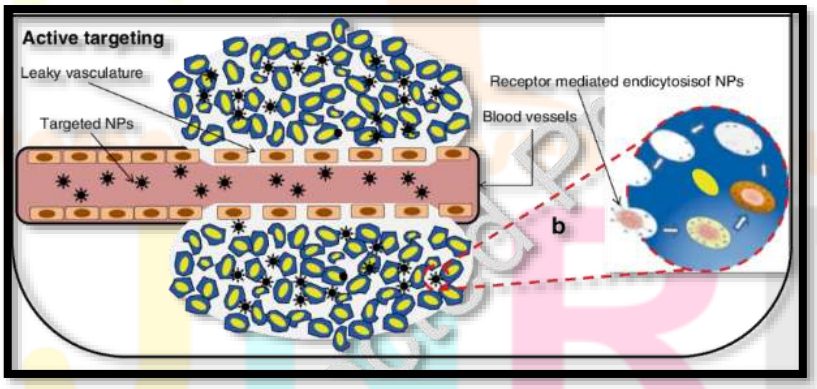


Figure 18: Pictorial Representation of Active Cellular Targeting

Example of Active Targeting:

Receptors such as EGFR and HER2 serve as critical molecular "anchors" for nanoparticle-based therapies due to their significant overexpression in various malignancies. By functionalizing carriers with specific antibodies, treatments like anti-EGFR gold nanoparticles can be directed toward squamous cell carcinomas, while HER2-targeted PEGylated liposomal doxorubicin effectively treats breast cancer while minimizing dangerous side effects like cardiotoxicity [45]. Beyond these growth factor receptors, researchers are targeting the folate receptor (FR), which is highly prevalent in solid tumors (FR-\alpha) and liquid cancers (FR-\beta), as well as VCAM-1 to disrupt tumor-induced angiogenesis. These ligand-receptor interactions transform nanoparticles into precision tools that can distinguish between healthy and cancerous tissues based on their unique protein signatures [46].

ADVANTAGES OF NANOPARTICLES IN CANCER THERAPY:

Nanotechnology has fundamentally transformed oncology by providing sophisticated platforms that ensure high therapeutic concentrations at tumor sites while shielding healthy tissues from systemic toxicity. By meticulously engineering the physical properties of nanoparticles—such as size, shape, and surface chemistry—researchers can create "smart" carriers that are sensitive to specific triggers like pH or temperature for controlled drug release. These systems are uniquely capable of surmounting formidable biological obstacles, utilizing PEGylation to evade the reticuloendothelial system (RES), and employing mechanisms like transcytosis or ultrasound to penetrate the blood–brain barrier (BBB) [47]. Practical successes, such as glutathione-PEGylated

liposomes for enhanced methotrexate delivery and gold nanoparticles for inducing targeted apoptosis, highlight how these carriers significantly improve the stability and bioavailability of potent drugs compared to conventional chemotherapy [48].

Nanoparticles In Immunotherapy:

Nanotechnology significantly amplifies the potential of immunotherapy by providing a platform for the precise delivery and activation of the body's natural immune defenses against tumor cells. Rather than just attacking cancer directly, nanoparticles can be engineered to support CAR-T cell therapy, stabilize cancer vaccines, or deliver immune checkpoint inhibitors and modulators directly to the immune cells within the tumor microenvironment [49]. This targeted approach helps to overcome the immunosuppressive nature of tumors, ensuring that the immune system remains "switched on" and capable of recognizing and destroying malignant cells while reducing the risk of systemic autoimmune side effects [50].

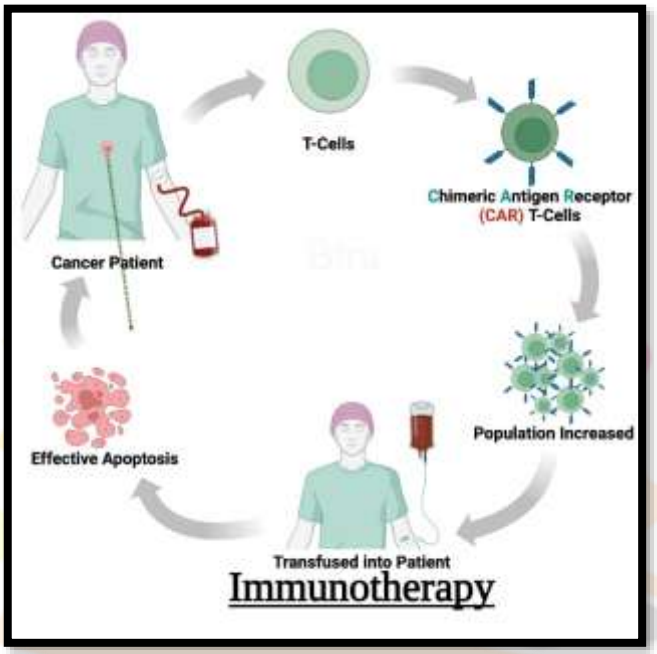


Figure 19: Structure of Immunotherapy

Nanoparticles In Cryosurgery:

Cryosurgery is a minimally invasive technique that eliminates tumor tissue through localized freezing; however, its clinical efficacy is often hindered by insufficient freezing depth and the risk of collateral damage to adjacent healthy structures. Nanoparticle-assisted cryosurgery overcomes these limitations by introducing nanoparticles with exceptionally high thermal conductivity into the tumor site, which accelerates and intensifies ice crystal formation within the cancer cells [51]. This "Nano cryosurgery" approach grants surgeons superior control over the cooling rate, the expansion of the ice ball, and the direction of the freeze, ensuring the thermal ablation is more precise and destructive to the malignancy while sparing the surrounding healthy tissue [52].

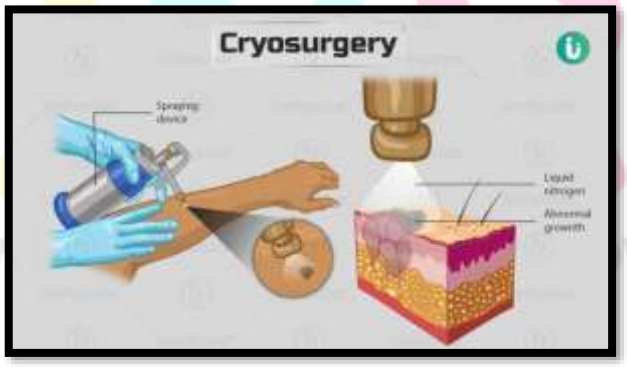


Figure 20: Structure of Cryosurgery

DISADVANTAGES OF NANOPARTICLES IN CANCER THERAPY:[53]

- ✓ Highly reactive in the cellular environment due to their small size and large surface area.
- ✓ Risk of accumulation of non-biodegradable particles at the delivery site, causing persistent Inflammation.
- ✓ Limited targeting capabilities make it difficult to stop therapy once started.
- ✓ Development and application of nanotechnology are often very costly.
- ✓ Potential misuse concerns, as advancements in nanotechnology could contribute to more
- ✓ Powerful and destructive weapons.

SIGNIFICANT CHALLENGES IN THE CLINICAL APPLICATION OF NANOPARTICLES:

Despite the rapid expansion of nanotechnology research, the transition from the laboratory to clinical practice remains a significant hurdle, with only a small percentage of nanoparticles successfully progressing to human trials. This "translational gap" is largely due to biological complexities—such as unpredictable biodistribution, premature degradation, and long-term toxicity—and a reliance on animal models that often fail to accurately replicate the human tumor microenvironment [54]. Furthermore, because nanomedicines are frequently tested as a last resort in patients with advanced, drug-resistant cancers rather than as first-line treatments, their true therapeutic potential may be underestimated in clinical data. To address these issues, researchers are increasingly turning to advanced predictive tools like computational modeling and organs-on-chips to better simulate human physiological responses before beginning expensive clinical trials.

APPLICATION OF NANOPARTICLES IN CANCER THERAPY:

Photodynamic therapy (PDT) utilizes a photosensitizing dye that, when triggered by a specific laser wavelength, generates singlet oxygen ($O^{2\wedge 1}$) and other reactive oxygen species to induce localized cell death. A major clinical drawback of traditional PDT is the systemic distribution of the dye, which can linger in the skin and eyes, leading to severe photosensitivity for several weeks [55]. To solve this, researchers utilize porous nanoparticles, such as mesoporous silica or polymeric nanocarriers, to encapsulate these hydrophobic dyes. This containment ensures that the dye remains sequestered within the nanoparticle framework during circulation preventing accumulation in healthy tissues while still allowing the toxic oxygen molecules to diffuse out through the pores to destroy the tumor upon laser activation [56].

CONCLUSION:

Nanoparticle (NP)-mediated cancer therapies have revolutionized treatment by offering targeted, less harmful alternatives to traditional methods like chemotherapy and radiation. NPs can precisely Attack cancer cells while minimizing side effects, and ongoing research aims to enhance their Specificity, efficacy, and biocompatibility. There's a growing focus on developing personalized NP-based therapies tailored to individual patients, potentially transforming oncology. Current Efforts also address challenges such as improving NP stability and delivery within the body, paving the way for more effective, less invasive cancer treatments in the future.

FUTURE PERSPECTIVE:

Despite the promising applications of nanoparticles (NPs), their small size, high reactivity, and Unique properties raise concerns about potential risks to human health and the environment. While NPs are not inherently toxic, certain materials like carbon nanotubes and silver-based Nanoparticles have shown harmful effects, including tissue damage, DNA interaction, and organ Toxicity in animal studies. Some NPs, such as silicate-based and heavy metal-containing particles, may accumulate in organs, causing conditions like fibrosis. Although biocompatible options like Liposomes are used clinically, they too can affect liver and kidney functions. Limited studies have Explored the long-term impact of NP exposure in humans and surrounding tissues, highlighting an urgent need for further research into their safety, mechanisms of action, and environmental impact.

REFERENCES

1) WuS,ZhuW,ThompsonP,HannunYA(2018)Evaluatingintrinsicandnointrinsiccancerriskfactors.NatCommon9(1):3490. https://doi.org/10.1038/s41467-018-05467-z.
2) Quasit S (2021) Telomerase gene therapy: a remission towards cancer.Preprints2021,2021100407. https://doi.org/10.20944/preprints202110.0407.v1.
3) Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, Sung B, Aggarwal BB (2008) Cancer is a preventable disease that requires major Lifestyle changes. Pharm Res 25(9):2097–2116. https://doi.org/10.1007/s11095-008-9661-9.
4) Park W, Heo YJ, Han DK (2018) New opportunities for nanoparticles Incancerimmunotherapy.BiomaterRes22:24. https://doi.org/10.1186/S40824-018-0133-y.
5) Jovčevska I, Muyldermans S (2020) The therapeutic potential of Nano bodies. Bio Drugs Cline Immunotherapy Biopharma Gene Therapy 34(1):11–26. https://doi.org/10.1007/s40259-019-00392-z.
6) Chan H-K, Ismail S (2014) Side effects of chemotherapy among cancer patients in a Malaysian general hospital: experiences, perceptions and informational needs from clinical pharmacists. Asian Pac J Cancer Prev 15(13):5305–5309. https://doi.org/10.7314/apjcp.2014.15.13.5305.
7) Quasit S (2021) Artificial intelligence and machine learning in precision and genomic medicine. Preprints 2021, 2021100011. https://doi.org/1020944/preprints202110.0011.v1.
8) Mahapatro A, Singh DK (2011) Biodegradable nanoparticles are excellent vehicle for site directed in-vivo delivery of drugs and vaccines. J Nanobiotechnol 9:55. https://doi.org/10.1186/1477-3155-9-55.
9) Miler I, Rouault A, Metz GT, Coukos G (2014) T-cell and NK-cell infiltration into solid tumors: a key limiting factor for efficacious cancer immune therapy.CancerDisco4(5):522–526. https://doi.org/10.1158/2159-8290.CD-13-0985.
10) LA couture M, Sibaud V (2018) Toxic side effects of targeted therapies and immunotherapies affecting the skin, oral mucosa, hair, and nails. Am JClan Dermatology 19(Supple 1):31–39. https://doi.org/10.1007/S40257-018-0384-3.
11) Dawdle A, Bald A, Nearing RK (2018) Nanoparticles as carriers for drug delivery in cancer. Art if Cells Nano med Biotechnology 46(sup2):295–305. https://doi.org/10.1080/21691401.2018.1457039.

12) Palazzo S, Banda S, Hilda M, Algieri I, Corona G, Tofoli G, Rizzoli F (2018) The clinical translation of organic nanomaterials for cancer therapy :a focus on polymeric nanoparticlesmicelles, liposomes and exosomes.CurryMedChem25(34):4224–4268. https://doi.org/10.2174/0929867324666170830113755.
13) Bissau P, Lou baton B (2011) Nano medicine, nanotechnology in medicine. ScienceDirect. https://www.sciencedirect.com/science/articLe/pii/S1631070511001538.
14) Shin WK, Cho J, Kannan A et al (2016) Cross-linked composite gel polymer electrolyte using mesoporous methacrylate-functionalized SiO2 nanoparticles for lithium-ion polymer batteries. Sic Rep 6:26332 https://doi.org/10.1038/srep26332.
15) Shafer A (2020) Green synthesis of metal and metal oxide nanoparticles from plant leaf extracts and their applications: a review. Green Process synth 9(1):304–339. https://doi.org/10.1515/gps-2020-0031.
16) Omari Y, Barra J (2014) Targeting tumour microenvironment: crossing tumour interstitial fluid by multifunctional Nano medicines. Bio impacts 4(2):55–67. https://doi.org/10.5681/bi.2014.021.
17) Barra J, Omidi Y (2013) Deregulated pH in tumour microenvironment checkmatescancertherapy. Bioimpacts3(4):149–162. https://doi.org/10.5681/bi.2013.036.
18) Bates DO, Hillman NJ, Williams B, Neal CR, Peacock TM (2002) Regulation of microvascular permeabilitybyvascularendothelialgrowthfactors. Janta200(6):581-597. https://doi.org/10.1046/j.14697580.2002.00066.x.
19) Hobbs SK, Minsky WL, Yuan F, Roberts WG, Griffith L, Torching VP, Jain RK (1998) Regulation of transport pathways in tumour vessels: role of tumour type and microenvironment. Pros Natl Accad Sic USA 95(8):4607–4612. https://doi.org/10.1073/pnas.95.8.4607.
20) Pad era TP, Stoll BR, Too Redman JB, Capon D, di Tomas E, Jain RK (2004) Pathology: cancer cells compress intramural vessels. Nature 427(6976):695. https://doi.org/10.1038/427695a.
21) Pelican H, Martin DS, Xu RH, Huang P (2006) Glycolysis inhibition foranticancertreatment. Oncogene25(34):4633–4646. https://doi.org/10.1038/sj.onc.1209597.
22) Lim EK, Chung BH, Chung SJ (2018) Recent advances in pH-sensitive polymeric nanoparticles for smart drug delivery in cancer therapy. CurDrugTargets19(4):300–317. https://doi.org/10.2174/1389450117666160602202339.
23) Mile E, Spinally GP, Mile E, Tomato F, Tomato S (2009) Albumin-bound formulation of paclitaxel (Abraxane ABI-007) in the treatment of breastcancer. Int J Nano med 4:99–105. https://doi.org/10.2147/ijn.s3061.
24) Kim DW, Kim SY, Kim HK, Kim SW, Shin SW, Kim JS, Park K, Lee MY, Heo DS (2007) Multicentre phase II trial of Genexol-PM, a novel Chromophore-Free, polymeric micelle formulation of paclitaxel, with cisplatin in patients with advanced non-small-cell lung cancer. Retrieved July 29, 2021, from https://www.annalsofoncology.org/article/S0923-7534(19)40408-0/fulltext.
25) Peer D, et al (2007) Nano carriers as an emerging platform for cancer therapy.NatNanotechnology2(12):751–760. https://doi.org/10.1038/Nnano.2007.387.
26) 26)Byrne JD, Betancourt T, Brannon-Pappas L (2008) Active targeting schemesfornanoparticlesystemsincancertherapeutics.Adv.DrugDeliRev60(15):1615-1626. https://doi.org/10.1016/j.addr.2008.08.005.
27) Saha RN, Vasanthakumar S, Bende G, Snehalatha M (2010) Nanoparticle.latedrugdeliverysystemsforcancerchemotherapy.MollMemberBoil27(7):215–231. https://doi.org/10.3109/09687688.2010.510804.
28) Amr eddy N, Muralidharan R, Babe A, Mehta M, Johnson EV, Zhao YD, Mushy, Ramesh R (2015) Tumour-targeted and pH controlled delivery of doxorubicin using gold Nano rods for lung cancer therapy. Int J Nano med 10:6773–6788. https://doi.org/10.2147/IJN.S93237.
29) WarburgO(1956)OntheoriginofcancercellsScience123(3191):309–314. https://doi.org/10.1126/science.123.3191.309.
30) Jiang W, Kim BY, Rutka JT, Chan WC (2008) Nanoparticle-mediated cellular response is size-dependent. Nat Nanotechnology 3(3):145–150. https://Doi.org/10.1038/nnano.2008.30.
31) Reuven T, Meitei M, Roman Z, Popover A, Popover R (2011) Targeted gold nanoparticles enable molecular CT imaging of cancer: an in vivo study. Int J Nano med 6:2859–2864. https://doi.org/10.2147/IJN.S25446.
32) Muralidharan R, Babe A, Amr eddy N, Basalingappa K, Mehta M, Chen A, Zhao YD, Kampala UB, Mushy A, Ramesh R (2016) Folate receptor-targeted nanoparticle delivery of HuR-RNAi suppresses lung cancer cell proliferation and migration. J Nanobiotechnol 14(1):47. https://doi.org/10.1186/s12951-016-0201-1.
33) Masood F (2016) Polymeric nanoparticles for targeted drug delivery system for cancer therapy. Mater Sic Eng. C Mater Biol Appl 60:569–578. https://doi.org/10.1016/j.msec.2015.11.067.
34) Elisabeth M, Wooley KL (2012) Design of polymeric nanoparticles for biomedical delivery applications. Chem Sock Rev 41(7):2545–2561. https://doi.org/10.1039/c2cs15327k.
35) Bernard A, Bagnold E, Jagger E, Figueroa F, Edelweiss MI, Pullman AR, Gutierrez SS, Attesting AM (2009) Indomethacin-loaded Nano capsules treatment reduces in vivo glioblastoma growth in a rat glioma model.CancerLett281(1):53–63. https://doi.org/10.1016/j.canlet.2009.02.018.
36) Wang X, Yang L, Chen ZG, Shin DM (2008) Application of nanotechnology in cancer therapy and imaging. CA 58(2):97–110. https://doi.org/10.3322/CA.2007.0003.
37) Lim J, Cotinine M, Mali J, da Costa VC, Annunziata O, Pavan GM, Simanek EE (2013) Synthesis of large dendrimers with the dimensions of smallviruses.JAmChemSock135(12):4660–4663. https://doi.org/10.1021/ja400432e.

38) Kukowska-Latallo JF, Candida KA, Cao Z, Nigavekar SS, Majors IJ, Thomas TP, Baker JR (2005) Nanoparticle targeting of anticancer drug improves therapeutic response in animal model of human epithelial cancer.Retrievedfrom https://cancerres.aacrjournals.org/content/65/12/5317.

39) Abedin MR, Powers K, Aiardo R, Barua D, Barua S (2021) Antibody-drug nanoparticle induces synergistic treatment efficacies in HER2 positivebreastcancercells.SicRep11(1):7347. https://doi.org/10.1038/S41598-021-86762-6.

40) Gorgy B, Szabo TG, Pasto M, Pal Z, Mistake P, Arad B, Laszlo V, Ballinger E, Pap E, Kittel A, Nagy G, Flus A, Buzzes EI (2011) Membrane vesicles, current state-of-the-art: emerging role of extracellular vesicles. CellMollLifeSicCMLS68(16):2667–2688. https://doi.org/10.1007/S00018-011-0689-3.

41) 41)ReposeG,SorboseW(2013)Extracellularvesicles:exosomes,macrovesicles,andfriends.JCellBiol200(4):373–383. https://doi.org/10.1083/jcb.201211138.

42) Wei W, Ao Q, Wang X, Cao Y, Liu Y, Zheng SG, Tian X (2021) Mesenchymal stem cell-derived exosomes:apromisingbiologicaltoolinNanomedicine.FrontPharmacology11:590470. https://doi.org/10.3389/Fphar.2020.590470.

43) Visit S, Awash R, Rai R, Srivastava P (2014) Development of dehydration-rehydration liposomal system using film hydration technique followed by sonication. Curry Drug Deli 11(6):763–770. https://doi.org/10.2174/1567201811666140910122945.

44) Ferrari M (2005) Cancer nanotechnology: opportunities and challenges.NatRevCancer5(3):161–171. https://doi.org/10.1038/nrc1566.

45) 45)JaiswalM,DudeR,SharmaPK(2015)Nanoemulsion:anadvancedmodeofdrugdeliverysystem.3Biotech5(2):123–127. https://doi.org/10.1007/s13205-014-0214-0.

46) Ali ES, Shirker SM, Islam MT, Khan IN, Shaw S, Rahman MA, Uddin SJ, Shill MC, Rahman S, Das N, Ahmad S, Shelli JA, Tripathi S, Mishra SK, Mubarak MS (2021) Targeting cancer cells with Nano therapeutics and Nano diagnostics: Current status and future perspectives. Semen Cancer Biol 69:52–68. https://doi.org/10.1016/j.semcancer.2020.01.011.

47) Dianzani C, Monger C, Muglia G, Serape L, Martina K, Cinema L, Batali L. (2020) Nano emulsionsasdeliverysystemsforpolychemotherapyaimingatmelanomatreatment. https://www.mdpi.com/2072-6694/12/5/1198.

48) Krishnamurthy K, Raja pan M (2012) Nano sponges: a novel class of drug delivery system—review. J Pharm Pharm Sic 15(1):103–111. https://Doi.org/10.18433/j3k308.

49) Ou L, Song B, Liang H, Liu J, Feng X, Deng B, Shao L (2016) Toxicity of graphene-family nanoparticles: a general review of the origins and mechanisms.RetrievedJuly29,2021,from https://doi.org/10.1186/S12989-016-0168-y.

50) Zhang X, Tian W, Cain X, Wang X, Dang W, Tang H, Cao H, Wang L, Chen T (2013) Hydrazinocurcumin Encapsulate nanoparticles “re-educate” tumour-associated macrophages and exhibit anti-tumour effects on breast cancer following STAT3 suppression. Plops ONE 8(6):e65896. https://doi.org/10.1371/journal.pone.0065896.

51) Fierily M, Vere AF, Ilium M, Perspires M, Ossuary B, Gadara R, Capella AR, Stogie F, Vijayaraghavan A, Isanti MP (2015) Graphene oxide Selectively targets cancer stem cells, across multiple tumour types: Implications for non-toxic cancer treatment, via differentiation-based Nano-therapy.Onstage6(6):3553-3562. https://doi.org/10.18632/Oncotarget.3348.

52) Mors P, Tegus GP, Gail H, Wharton T, Sara T, Hamblin MR (2007) Photo-Dynamic therapy with fullerenes. Photo hem Photobook Sic 6(11):1139–1149. https://doi.org/10.1039/b711141j.

53) Tabatha Y, Murakami Y, Cicada Y (1997) Photodynamic effect of poly-Ethylene glycol-modified fullereneontumour.JonJCancerResGann88(11):11081116. https://doi.org/10.1111/j.13497006.1997.tb00336.x.

54) 54)Jamieson T, Bakhsh R, Petr ova D, Peacock R, Imani M, Seminarian AM(2007)Biologicalapplicationsofquantumdots.Biomaterials28(31):4717–4732. https://doi.org/10.1016/j.biomaterials.2007.07.014.

55) Zhao X, Hilliard LR, Lechery SJ, Wang Y, Bag we RP, Jinn S, Tan W (2004) A rapid bioassay for single bacterial cell quantitation using bio conjugated nanoparticles. Pros Natl Accad Sic USA 101(42):15027–15032. https://doi.Org/10.1073/pnas.0404806101.

56) Moussa SA, Bareli DJ (2011) Nanotechnology-based detection and targetedtherapyincancer: Nanobioparadigmsandapplications.Cancers3(3):2888–2903. https://doi.org/10.3390/cancers3032888.