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A REVIEW OF THE CURRENT STATUS AND PROSPECTS OF NANOTECHNOLOGY IN THE ADVANCEMENT OF CANCER THERAPY

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Article Info

Abstract

Therapy for melanoma, a type of skin cancer, is very challenging due to its tumor microenvironment, resistance, and spread. Advances in nanotechnology have led to the creation of nanocarriers, which decrease systemic toxicity and increase drug delivery precision. These tools address problems like poor tumor penetration and drug resistance. However, there are still problems with regulatory approval processes, manufacturing scalability, and biocompatibility. Continuous interdisciplinary research is necessary to translate scientific discoveries into therapeutic treatment.

Keywords:

Nanotechnology, melanoma, dendrimers, biocompatibility, passive targeting, increased permeability retention (EPR).

Introduction

Melanoma, a severe form of skin cancer, is caused by UV-induced DNA alterations, genetic mutations, excessive UV exposure,[1, 2] and immune system dysfunction. People who have a history of sunburn, fair skin, or immunosuppression are at higher risk.[3] Even though targeted medications like BRAF and MEK inhibitors and early diagnosis have improved treatment, resistance still often arises.[4, 5]

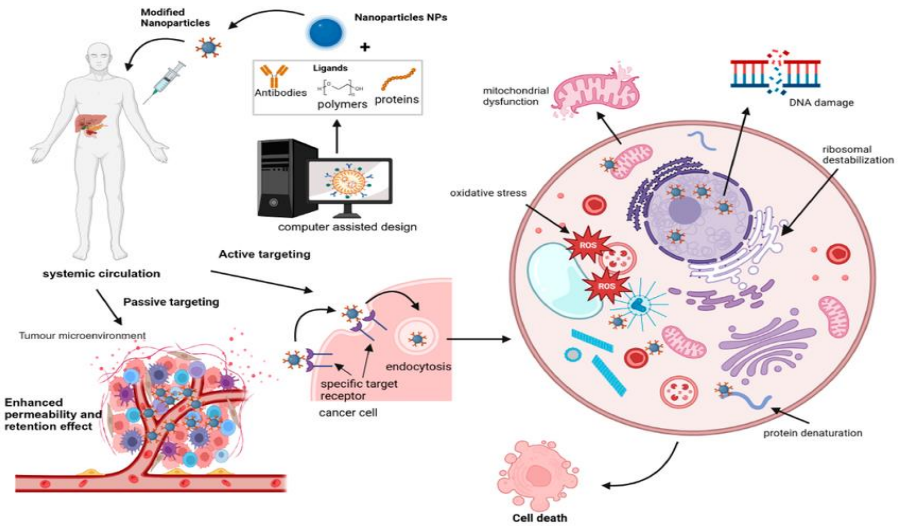
Drugs like PD-1 and CTLA-4 inhibitors can cause joint pain and skin cancer as side effects. Immunotherapies can cause autoimmune issues even though they boost the immune system.[6] Older treatments can be dangerous. Combination therapy improves benefits while increasing negative effects.[7]

Because of its heterogeneity, metastasis potential, and resistance to traditional therapy, melanoma necessitates specialized, cutting-edge therapeutic approaches due to immune-related toxicities, medication resistance, and limited efficacy in specific genetic variants.[8]

Advances in nanotechnology create new opportunities for drug stability, solubility, and bioavailability.[9] Nanocarriers can target cancer-specific labels, overcome resistance, and respond to temperature or pH changes. Multifunctional nanocarriers can also improve chemotherapy efficacy by reducing hypoxia in excrescences.[10] Together, drugs and nanoparticles have the potential to completely transform cancer treatment.[11]

Therapeutic Targeting

Nanotechnology has revolutionized the treatment of cancer by improving drug delivery systems and reducing side effects. Nanoparticles, nanocarriers, and nano formulations are used to address issues such as systemic toxicity, multidrug resistance, and inadequate targeting. They improve drug concentration, control release, and aid in real-time imaging.[12]



The figure No 1 shows how lethal mechanisms like oxidative stress and DNA damage are caused when tailored nanoparticles are delivered to cancer cells selectively using passive and active targeting in nanotechnology.

Passive Targeting

EPR improves drug delivery and lessens side effects by passively targeting nanoparticles in tumor tissue. However, tumor heterogeneity, high fluid pressure, and a large extracellular matrix can all reduce efficacy. Researchers are changing the shape, size, and surface of nanoparticles.[13]

Controlled release technologies, such as pH-sensitive or enzyme-responsive nanoparticles, enhance drug delivery by releasing medications directly into the tumor environment.[14] Passive targeting has limitations, such as reduced efficacy in non-solid or poorly vascularized tumors and patient-to-patient variability in the EPR effect,

despite being widely applicable and effective for many solid tumours .[15]To address these issues, new techniques are being developed, including the use of stimuli-responsive materials, combining passive and active targeting, and tumour priming. Despite its drawbacks, passive targeting remains a crucial tactic in cancer nanomedicine and is necessary to develop safer and more effective cancer treatments.[16]

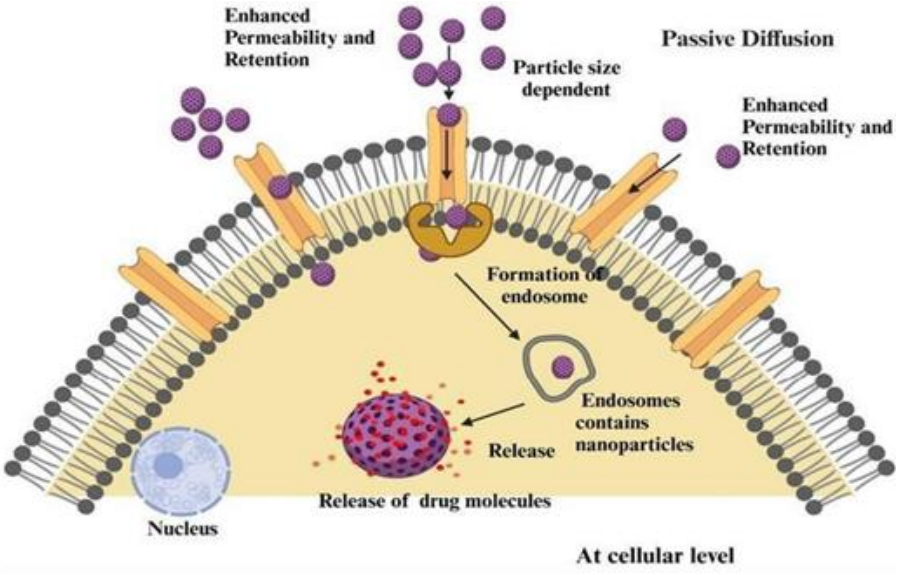


Figure 2 shows The Enhanced Permeability and Retention (EPR) effect demonstrates the passive targeting mechanism of nanoparticles while highlighting size-dependent endocytosis, endosomal encapsulation, and intracellular drug release at the tumour cell level.

Active Targeting

Active targeting in cancer nano therapy marks a major advancement by enabling precise delivery of medicines directly to cancer cells, minimizing damage to healthy apkins. This approach involves functionalizing nanoparticles with specific ligands similar as antibodies, peptides, aptamers, or small motes — that bind to receptors overexpressed on cancer cells. By feting unique molecular labels (e.g., folate receptors, transferrin receptors, epidermal growth factor receptors), active targeting allows largely picky medicine delivery.[17] This not only boosts the remedial effectiveness of anticancer agents but also reduces side goods generally associated with conventional chemotherapy. Exemplifications include Folic acid- functionalized nanoparticles targeting folate receptors in ovarian, bone, and lung cancers.

Trastuzumab- conjugated nanoparticles targeting HER2-positive bone cancer cells.[17, 18]

Active targeting ensures that the therapeutic payload is focused in cancer tissue, resulting in better treatment outcomes and reduced systemic toxicity. It represents a promising technique for increasing the precision, safety, and efficacy of cancer treatments.[19]

STIMULUS- RESPONSIVE TARGETING: Stimulus-responsive targeting enhances drug delivery and the effectiveness of nanomedicine, particularly in cancer treatments, by limiting side effects during circulation and only activating systems in response to particular triggers.[20]

Mechanisms of Stimulus-Responsive Targeting

Stimulus Types: Systems can respond to external triggers (like light, magnetic fields, ultrasound, and temperature) or internal cues (like pH, redox state, enzymes, and hypoxia) to release drugs or activate imaging agents at the disease site.[21-23]

Activation Process: Nanocarriers are made to be inactive while in circulation and then change or activate when they come into contact with their target environment, such as an acidic or enzyme-rich tumor microenvironment.[24, 25]

Applications and Effectiveness

Cancer Treatment: These systems, which are commonly used to target tumors, enhance cellular uptake, promote drug accumulation in tumors, and allow for precise, on-demand drug release, all of which reduce harm to healthy tissues.[26-28]

Other Diseases: Stimulus-responsive systems are also being developed to treat bacterial infections and inflammatory diseases like IBD by concentrating on specific microenvironmental features.[29-32]

By using a range of internal or external stimuli to release medication in a targeted manner, stimulus-responsive drug delivery systems improve therapeutic accuracy.[33] pH-responsive systems target infections, tumors, and inflammatory bowel disease (IBD) by activating under acidic conditions.[22] Enzyme-responsive systems are used to treat cancer and osteoarthritis because they can more accurately target overexpressed enzymes.[32] With a primary focus on tumor targeting, redox-responsive systems respond to the elevated glutathione levels commonly seen in tumor microenvironments.[34] Lastly, by facilitating precise drug release and imaging, light-responsive devices offer external control and spatial accuracy in therapeutic applications.[28]

Enzyme-responsive nanoparticles, which are activated by enzymes specific to tumors, provide targeted distribution and therapeutic control.[35] External stimuli like light, magnetic fields, and ultrasound cause the release of medication, improving treatment precision and reducing systemic toxicity.[36] However, issues like stability, sensitivity, and production scalability remain critical for future research.[37]

Mechanisms and Effectiveness Targeted Drug Release: These nanoparticles are made to release medications exclusively in the tumor microenvironment by reacting to enzymes specific to tumors, such

as matrix metalloproteinases, cathepsin B, or hyaluronidase.[38, 39] This approach increases drug accumulation at the tumor site while lessening the effect on healthy tissues.[40, 41]

Dual or Multi-Responsive Systems:

Some nanoparticles combine enzyme responsiveness with other triggers (such as pH, redox conditions, or external stimuli like light) to create even more control over drug release and synergistic therapeutic benefits[42, 43]

Increased Cellular Absorption Targeting ligands (such as concanavalin A and hyaluronic acid) and other surface modifications increase specificity and increase uptake by cancer cells.[39, 44]

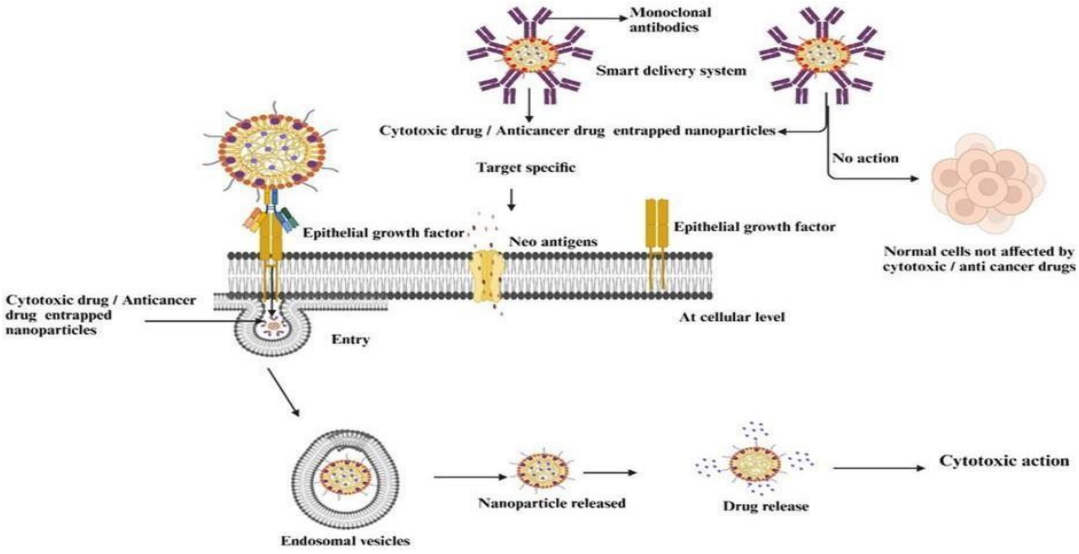


Figure 3 illustrate monoclonal antibodies for targeted cytotoxic action in a drug delivery system based on intelligent nanoparticles. By binding preferentially to tumor-specific epithelial growth factor receptors, the mechanism protects healthy cells from negative effects while ensuring medication release at the cellular level.

MULTI-STAGE TARGETING

Multi-stage targeting enhances precision and effectiveness in areas like manufacturing, immunotherapy, drug discovery, nanomedicine, and tracking systems by directing treatments through a series of steps.[45]

Applications in Medicine and Drug Development

Nanomedicine: By first building up at tumor sites and then specifically targeting subcellular components like mitochondria, two-stage targeting nano systems can greatly increase the effectiveness of drug delivery and reduce dosages. This enhances imaging, therapy, and tumor recurrence in cancer treatment.[46]

Discovery of New Drugs: Multi-omics integration enables the discovery of stage-specific druggable targets in diseases such as T-cell acute lymphoblastic leukemia, enabling more precise and effective treatments that are tailored to the progression of the illness.[47]

Protacs: A two-stage method for developing proteolysis targeting chimeras (PROTACs) streamlines the process and permits rapid screening and optimization of substances that degrade disease-related proteins, as shown in estrogen receptor targeting.[48]

Immunizations: Multi-stage targeting in vaccine design, such as in multi-peptide conjugate vaccines, can enhance protection against variations and increase immune activation by focusing immune responses on numerous significant viral protein regions.[49]

Focusing on Several Phases in Monitoring and Management Systems

Target Tracking: Multi-stage data association and feature extraction improve the accuracy and reliability of tracking multiple targets in complex environments, such as video synthetic aperture radar (ViSAR) and multi-target localization using compressed sensing.[50, 51]

Systems for Control: Dual-stage control strategies ensure stability and optimal performance in multiagent systems by enabling coordinated actions, such as encircling a moving target with scattered agents.[52]

Manufacturing Processes and Optimization in Manufacturing:

Multi-stage Bayesian optimization accounts for all process stages and uncertainties in intricate manufacturing processes such as turbine disc forging, leading to the reliable and precise attainment of desired results.[53]

Cancer Immunotherapy Immunotherapy:

Immunotherapies are more effective when T cells that target multiple epitopes are able to recognize and attack cancer cells in multiple ways simultaneously.[54]

NANOTECHNOLOGY PLATFORMS

Nanotechnology platforms are revolutionizing various fields through precise manipulation of nanoscale materials, enhanced drug delivery, diagnostics, imaging, and therapeutic interventions in both industry and medicine.[55]

Platform Types for Nanotechnology and Their Applications

Multifunctional Platforms for Therapy: Nanoplatforms can be used for imaging, therapy, and drug delivery. For example, persistent-luminescence nanoparticle technologies enable imaging and continuous photodynamic and photothermal therapy for tumors without constant external excitation.[56-58]

Systems Based on Exosomes and Biohybrids: Combining biological and synthetic components, such as exosome-based carriers and biohybrid nanocarriers, enhances biocompatibility, immune evasion, and targeted delivery for next-generation theragnostic.[58]

Sensor and biosensor platforms: Advanced nanomaterials are used to create tiny, highly sensitive, and

selective electrochemical sensors and biosensors for environmental monitoring, food safety, and medical diagnostics.[59, 60]

Table No.01 Applications in Medicine and Industry

Application Area	Example Uses
Cancer Therapy	Targeted drug delivery, multimodal imaging, triggered release systems. [56, 57, 61]
Neurology	Drug delivery across the blood-brain barrier, neural interfaces.[62, 63]
Ophthalmology	Site-specific drug delivery, bio-imaging, disease detection.[64]
Industrial Modernization	Enhanced efficiency in manufacturing, agriculture, environmental management.[65, 66]

Liposomes

Liposomes, which are nanoscale vesicles made from phospholipid bilayers, are useful drug delivery vehicles used in food, pharmaceutical, and medical applications because they can encapsulate both hydrophilic and hydrophobic molecules.[67]

Types and structure of liposomes

Basic Structure: Made of synthetic or natural phospholipids, liposomes are a type of cell membrane that mimics natural cell membranes.[68] Liposomes often include cholesterol for stability.[69, 70]

Types: Originally designed to address specific therapeutic needs, liposomes have evolved from conventional forms to more complex ones such as immune-liposomes, long-circulating (PEGylated), targeted, and stimuli-responsive liposomes.[71, 72]

Application and Effectiveness

Drug Delivery: Liposomes increase the solubility, control release, and target delivery of medications, reducing toxicity and enhancing therapeutic benefits in cancer treatment, immunotherapy, vaccinations, antibiotics, and diseases that affect specific organs.[73-75]

Other Applications: Due to their biocompatibility and ability to protect sensitive materials, liposomes are utilized not only in pharmaceuticals but also in food, cosmetics, diagnostics, and analytical chemistry.[76-78]

Developments in Manufacturing and Preparation

Among the preparation methods are ultrasonication, microfluidics, thin-film hydration, and supercritical fluid techniques. Recent developments have focused on processes that are scalable, repeatable, and

industrially friendly.[79, 80]

Challenges: Important considerations include stability, charge and size control, and efficient drug encapsulation and release.[81]

Advantages and Drawbacks

Benefits: Benefits include minimal immunogenicity, high biocompatibility, biodegradability, and the capacity to encapsulate a variety of compounds.[69, 73]

Limitations: Stability, immunological reactions, possible toxicity, and large-scale production continue to be issues, particularly for oral administration and long-term use.[82]

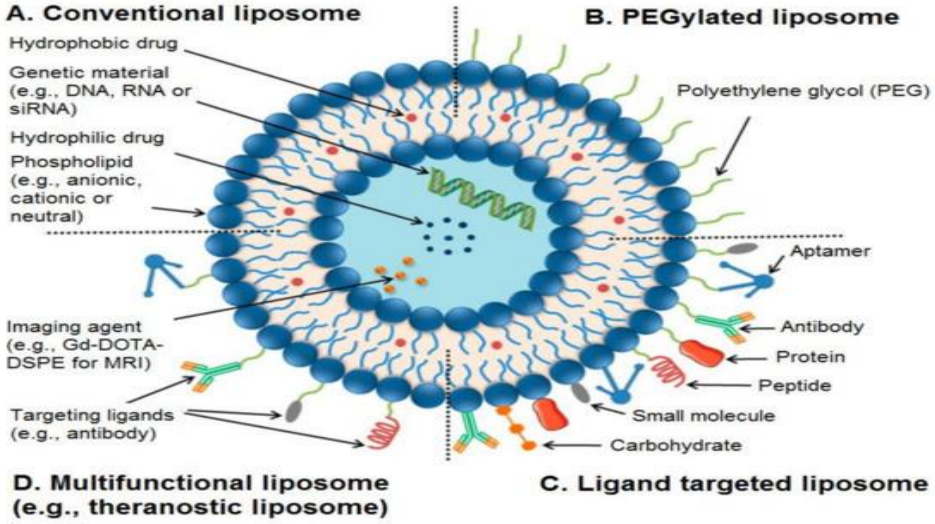
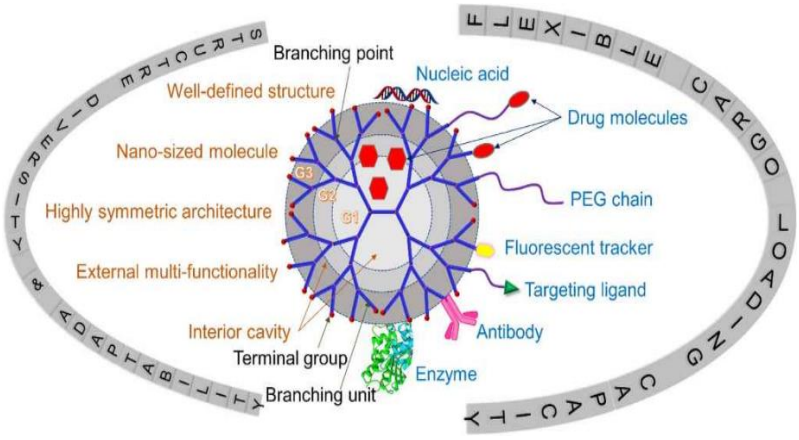


Figure 4 shows both conventional and functionalized liposomes with various properties for solid tumor diagnosis and treatment as well as cancer site targeting. Phospholipid-based, PEGylated/stealth, targeted, and multifunctional types are among them.

DENDRIMERS

Dendrimers are unique synthetic polymers with nanoscale architectures that have the potential to be used as tools in advanced applications, drug delivery, medicine, and diagnostics. Research is improving their safety and effectiveness.[83]



The figure NO 5 illustrates the nanoscale, symmetrical, and multifunctional architecture of dendrimers to show how versatile they are in loading therapeutic and diagnostic chemicals for targeted drug delivery and imaging applications.[84]

Types and Characteristics of Structures

Architecture: Dendrimers are globular, monodisperse nanostructures with a central core, multiple terminal groups, and repeating branching layers (generations).[85, 86]

Types: PAMAM, PPI, Janus, supramolecular, and shape-persistent dendrimers are common types of dendrimers, each with unique characteristics and applications.[87]

Surface Modification: For particular uses, their surfaces can be modified with medications, targeted ligands, or imaging agents.[88, 89]

Applications in Biomedicine

The solubility, stability, and targeted delivery of medications, genes, and nucleic acids are improved by dendrimers, which also lessen adverse effects and improve therapeutic results.[90-92]

Diagnostics & Imaging: Dendrimers increase the specificity and efficiency of imaging by acting as contrast agents and carriers for diagnostic compounds.[93, 94]

Additional Uses: These include dental biomaterials, tissue engineering, regenerative medicine, and vaccine administration.[95-97]

Table 02 Benefits and Limitations

Advantage	**Restrictions/Difficulties**	**References**
High capacity for medication	Possible cytotoxicity, particularly with high-generation and cationic dendrimers	(83, 98, 99)
Controlled release and targeting	Not biodegradable in certain kinds	(100)
Multipurposeness	Surface modification is required to low toxicity.	(83, 98)

Safety and Biocompatibility

Cytotoxicity: Dendrimer formation, terminal groups, and surface charge all influence toxicity. More dangerous are cationic and higher-generation dendrimers.[98]

Mitigation: Reduction Surface alterations like PEGylation and Acetylation, as well as the development of biodegradable dendrimers, reduce toxicity and improve safety.[100]

Micelles

Micelles are nanostructures based on amphiphilic molecules that improve the solubility, stability, and targeted delivery of hydrophobic drugs used to treat melanoma. Because they lessen systemic toxicity and target markers unique to melanoma, they are safe carriers.[101] In addition to chemotherapy, micelles are used in combination antidotes and photodynamic therapies. Current research is addressing issues such as physiological stability and manufacturing scalability.[102]

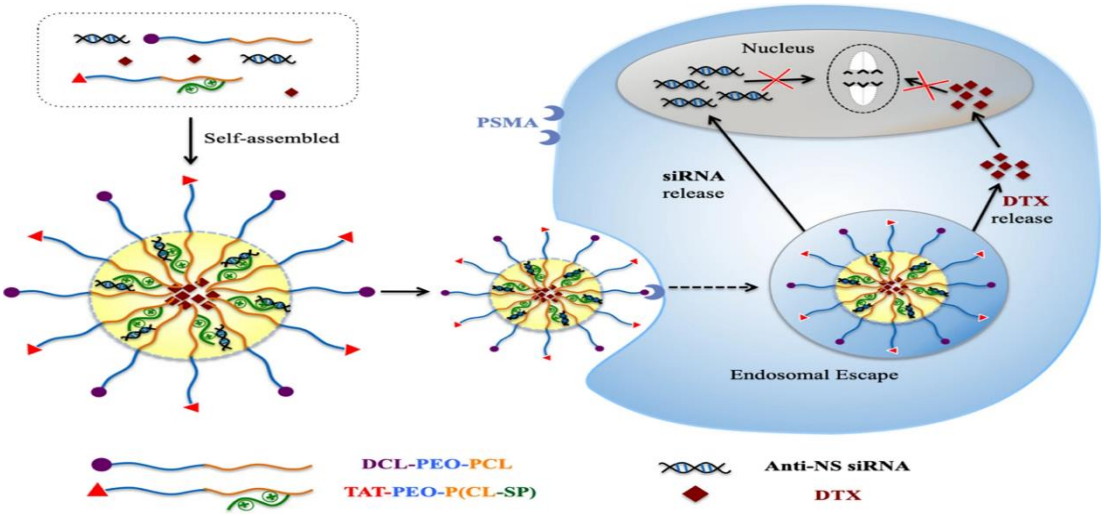


Figure No 5 shows Diagrammatic processes for co-delivery micelles that, after self-assembling and undergoing modification by spermine ligand, DCL ligand, and TAT peptide, carried docetaxel and anti-nucleostemin siRNA

Polymeric Nano particles

Polymeric nanoparticles are adaptable, biodegradable carriers produced from polymers like as PLGA, PLA, and chitosan that encapsulate both hydrophilic and hydrophobic medicines, allowing for effective melanoma therapy.[103] Nanoparticles improve drug stability, reduce toxicity, and boost therapeutic efficacy. Immune clearance is inhibited and circulation times are prolonged by PEGylation and other surface modifications. improving the treatment of melanoma to address drug resistance, systemic toxicity, and inadequate tumor response.[104]

Hydrogels

Hydrogels, which are biocompatible networks of polymers, are ideal for treating melanoma because they can encapsulate various drugs and biomolecules for controlled release, enhancing their efficacy and reducing systemic toxicity.38 Recent advancements in hydrogels include functionalization with tumor-targeting ligands for melanoma research, formulations loaded with nanoparticles for improved tumor penetration, and injectable formulations for less invasive delivery.[105]

METALLIC NANO PARTICLES

Metallic nanoparticles like gold, silver, and iron oxide enhance melanoma treatment by facilitating accurate drug delivery, enhancing the effects of chemotherapy, and facilitating early MRI diagnosis.[106]

Additionally, MNPs are being studied as adjuvants for immunotherapy to increase T-cell responses and target resistant cancer cells. Ongoing research aims to improve their biocompatibility, enhance tumor selectivity by surface modification, and integrate therapeutic modalities such as photothermal and photodynamic therapy.[107] Although it is still challenging to understand MNPs' long-term safety and biodistribution, they have the potential to provide precise, multifunctional melanoma theragnostic.[108]

PEPTIDE-BASED NANO PARTICLEs

Peptide-based nanoparticles (PNPs), self-assembling nanostructures that are highly biocompatible and tumor-specific, are used to treat melanoma. When combined with tumor-targeting peptides, they improve therapeutic outcomes, reduce toxicity, and improve selective drug delivery.[109] PNPs can be trained to release drugs in response to stimuli specific to tumors, like an acidic pH or enzyme activity. By administering adjuvants that trigger anti-tumor immune responses, checkpoint inhibitors, or peptide vaccines, they make a substantial contribution to immunotherapy in addition to drug delivery. It has been demonstrated that immune checkpoint blocking has synergistic effects when used in combination therapy.[110] Despite problems with stability and scalability, PNPs are still being improved by nanotechnology, which makes them a promising foundation for successful and individualized melanoma treatment.[111]

Hurdles In Nanotechnology

Among the challenges faced by nanotechnology-based drug delivery systems for melanoma therapy are complex manufacturing, high production costs, and issues with precise targeting due to tumor heterogeneity and receptor expression.[112]Nanoparticles must also maintain their stability throughout storage and circulation, but many materials can degrade or aggregate, decreasing their efficacy.[113] It is still very difficult to maintain biocompatibility in order to reduce toxicity and immunological reactions, particularly for complex or synthetic formulations. Clinical translation is also hampered by regulatory approval, as many novel devices necessitate rigorous safety, efficacy, and repeatability testing.[113] Due to difficulties maintaining batch consistency and therapeutic efficacy, especially in resource-constrained settings, greater access is limited when production is scaled from laboratory to industrial scale.[114]

The tumor microenvironment (TME) and patient variability add to the complexity. The TME's hypoxic, acidic, and immunosuppressive characteristics make it difficult to administer drugs effectively, necessitating the development of flexible and dynamic materials.[115] The requirement for tailored nanoparticle designs because of patients' immune systems, genetic makeup, and disease progression complicates therapeutic development and application.[116] Long-term safety is still an issue because non-biodegradable nanoparticles can build up in organs and result in chronic toxicity. Social and ethical concerns, like fair access, the environmental impact of manufacturing, and potential abuse, must also be addressed.[117] To effectively incorporate nanotechnology into treatment, an interdisciplinary team comprising materials science, clinical research, and policymaking is required.[118]

Conclusion

Nanotechnology holds promise for cancer therapy, particularly in difficult-to-treat cancers like melanoma, because it enhances drug delivery and reduces systemic toxicity through nanocarriers. These nanocarriers ensure targeted delivery to cancer cells with minimal damage to healthy tissues by enhancing drug stability, solubility, and bioavailability. Issues such as complex manufacturing processes, high production costs, and precise targeting due to tumor heterogeneity prevent widespread adoption. Multidisciplinary research involving materials science, clinical research, and policymaking is needed to integrate nanotechnology into conventional cancer treatment.

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