Nano-Frontiers in Oncology: Revolutionizing Anti-Cancer Drug Delivery Systems

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ABSTRACT:
Cancer is a major cause of Obesity and passing away, having a complex pathogenesis. Conventional cancer treatments consist of immunotherapy, targeted therapy, radiation therapy, and chemotherapy. Still, constraints such as lack of selectivity, cytotoxicity and resistance to several drugs provide significant challenges for effective cancer treatment. Nanotechnology has changed cancer diagnosis and treatment. Nanoparticles (1-100 nm) offer advantages in cancer treatment, including precision targeting, enhanced permeability and retention, heightened stability, decreased toxicity, and biocompatibility. The particles known as nanoparticles include divided into numerous groups. The nanoparticle medication delivery method targets tumor and environment features. Nanoparticles improve cancer treatment and conquer resistance to many drugs. In light of recent multidrug resistance pathways emerge, nanoparticles are receiving increased attention for research. The therapeutic potential of formulations has opened up new avenues for cancer treatment. However, most research is limited to in vivo and in vitro trials, and the number of approved nanodrugs has not significantly increased over time. This review covers various nanoparticle kinds, targeting mechanisms, and authorized nanotherapeutics with oncological applications in cancer treatment. We outline the present state of clinical translation, including its advantages and obstacles.

Keywords: Cancer, Nanoparticles, Chemotherapy, Cellular targeting, Multidrug resistance.

Introduction:

Cancer is a broad word for a group of disorders defined by uncontrolled, random cell divisionand invasive behavior. Over the past many years, extensive attempts have been made to identify numerous cancer risk factors. For certain malignancies, the cause has been linked to particular eenvironmental factors that are acquired, such pollution and radiation. On the other hand, a poor diet, smoking, drinking, stress, and inactivity all contribute significantly to an unhealthy lifestyle and increase the risk of cancer. It has been challenging to ascertain the significance of proto-oncogene mutations, tumour suppressor gene expression patterns, and DNA repair genes, despite the fact that these extrinsic factors have been recognised as important cancer drivers. The genetics of the cancer patient accounts for only 5–10% of malignancies. Growing older is a major risk factor for many types of cancer. [1]. Cancer is the world's second largest cause of death and a major public health concern. The American Cancer Society predicts 1.9 million additional cases by 2021. Conventional therapies Cancer environmental factors that are acquired, such pollution and radiation. However, therapeutic options for an unhealthy lifestyle, such as a bad diet, include radiation, chemotherapy, surgery, targeted therapy, and immunotherapy. which is and hormonal treatment. While chemotherapy and radiation treatment have cytostatic and cytotoxic properties, they are generally connected to serious adverse consequences [2].

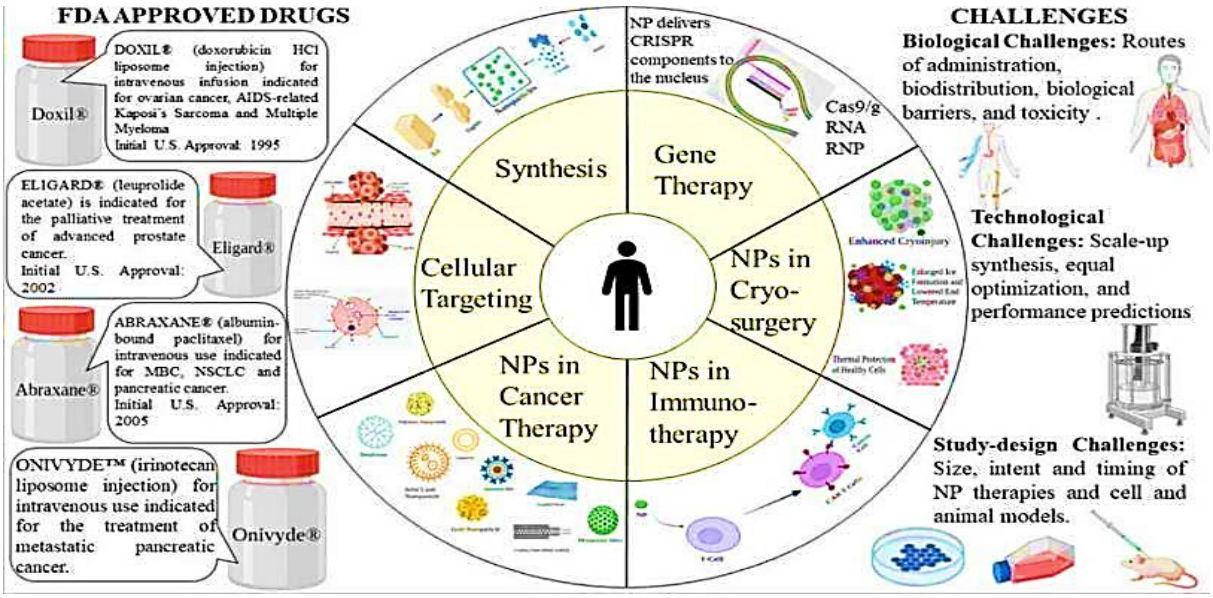

Fig.no. 01 Nanoparticle for Cancer Therapy

Nanoparticles for anti- cancer therapy:

The introduction of tailored therapy has led to an increase in precision therapy. However, undesirable consequences such multi-drug resistance can restrict therapeutic efficacy. Immunotherapeutic drugs have shown promising outcomes in not only treating Primary cancer can be treated by avoiding distant metastasis and reducing recurrence rates. Nonetheless, autoimmune diseases are a common side effect of immunotherapy. Research indicates that immunotherapy may be less effective in treating solid tumors than lymphoma. Cancer cells produce a unique extracellular matrix (ECM) that immune cells struggle to penetrate. New targeted Adverse events (AEs) related to dermatology are caused by medications and immunotherapies that interfere with signalling pathways necessary for both malignant behaviour and normal epidermal homeostasis dermis. Given all of these details, there has been a growing demand in recent years for the creation of novel strategies in the pursuit of precise cancer treatment. There have been recent attempts to use small particles to address the inadequacies of the current therapeutic options. The therapy and management of cancer have benefited from the good pharmacokinetics, precise targeting, fewer side effects, and decreased drug resistance demonstrated by nanoparticle-based drug delivery methods.

The field of medicine has seen advancements with nano therapeutic medicines delivery pathways, anti-tumor multidrug resistance (MDR), and drug resistance mechanisms inhibition by offering the possibility of therapeutic combination therapy. This combination has led to improved diagnostics and treatments. This examination primarily focuses on the fundamental ideas of the This article discusses the use of nanotherapeutics, its limitations and opportunities, and future research directions [3].

Nanoparticle: -

Nanoparticles (NPs) are particles with dimensions less than 100 nm with unique properties that differ from bulk samples of the same substance. The overall shape of the nanoparticle determines whether it is classed as 0D, 1D, 2D, or 3D. Nanoparticles are composed of three layers: surface, shell, and core. The core is the central section of the NP and is sometimes referred to as the NP. These materials are highly valued in several industries due to their unique properties, including high surface-to-volume ratio, dissimilarity, sub-micron size, and increased targeting. Nanoparticles (NPs) penetrate deep tissues, leading to increased permeability and retention. Surface features affect bioavailability and half-life by effectively bridging epithelial fenestration. Coating nanoparticles with PEG, a hydrophilic polymer, can reduce opsonization and prevent it. Immuno system clearance. Modifying particle polymer properties can improve drug or active moiety release rates. The distinct characteristics of nanoparticles impact their therapeutic efficacy in the management and treatment of cancer. [4].

Synthesis of Nanoparticles:

The NPs vary in form, size, and structure. Multiple synthesis approaches are used to achieve this goal. These methods can be broadly classified into two basic categories:

1. Bottom-up and
2. Top-down approaches.

These approaches can be further classified. divided into subclasses based on reaction conditions and operation.

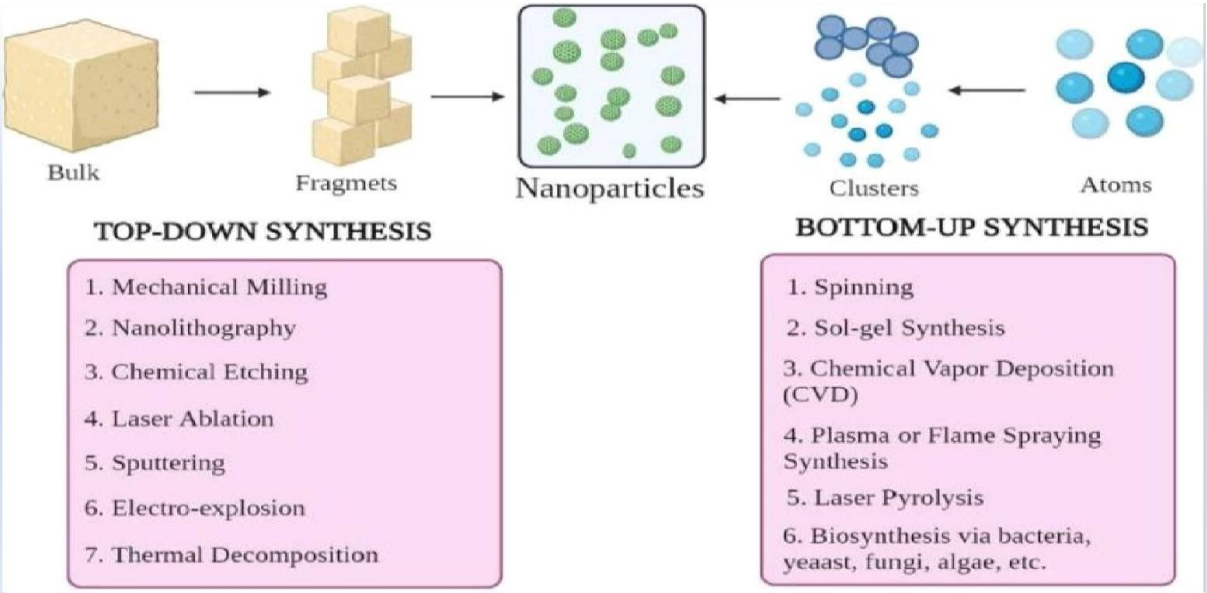

Fig.no. 02 Synthesis of Nanoparticle

Classification of Nanoparticles drug synthesis:

1. Bottom-up approaches:

The constructive technique includes constructing materials from atoms, clusters, and NPs, starting with simpler compounds. Common processes include spinning, sol gel synthesis, CVD, plasma, and flame. Spray synthesis, laser pyrolysis, and biosynthesis.

2. Top-Down Approaches:

The destructive process involves reducing bulk material to produce nanoparticles. Nanoparticles (NPs) are created by disassembling larger molecules into smaller ones. Mechanical milling, chemical etching, laser ablation, sputtering, electro-explosion, thermal breakdown, and nanolithography are some of the methods used. The size, shape, and charge of NPs can be altered by adjusting the synthesis parameters and reaction circumstances. Furthermore, the chemical properties of NPs are influenced by the development method. For this reason, comprehending the growth mechanism is essential to synthesizing the required NPs [4].

Nanoparticles in Cancer Therapy:

The three types of nanoparticles (NPs) that are frequently utilised in drug delivery systems are hybrid, inorganic, and organic.

Polymeric Nanoparticles:

Colloidal macromolecules" with a distinct structure made up of different monomers are what are known as polymeric nanoparticles (PNPs). The drug is encapsulated or attached to the outside of the NPs to achieve controlled drug release in the target, creating a nanosphere or nano capsule. Polyacrylamide, polyethylene glycol (PMMA), and polystyrene were among the non-biodegradable polymers that once made up PNPs. Unfortunately, because they were hard to get rid of, the buildup of them led to toxicity. Currently in use, biodegradable polymers such polylactic acid, poly (amino acids), chitosan, alginate, and albumin have been demonstrated to reduce toxicity while enhancing medication release and biocompatibility. Studies have indicated that the encapsulation of PNPs with polysorbates and their use as surfactants can improve their efficacy. Finishing the outside of NPs enhance their contact with the endothelial cell membrane of the blood-brain barrier. [5].

Dendrimers:

Dendrimers are spherical polymeric macromolecules having a specified hyperbranched structure. Dendrimers are characterized by their highly branching architectures. Typically, the production of dendrimers begins with the reaction of an ammonia core with acrylic acid.

This process forms a "tri-acid" molecule, which then combines with ethylenediamine to produce "tri-amine," a GO product. This substance interacts with acrylic acid, resulting in hexa- acid and "hexa-amine" (Generation 1). Typically, dendrimers range in size from 1 to 10 nm. However, the size can reach up to 15 nm. Because of their unique structure, such as defined molecular weight, modifiable branching, bioavailability, and charge, they are utilized to target nucleic acids. Dendrimers commonly employed include poly amidoamine (PAMAM), polyethylene glycol (PEG), poly propylenimine (PPI), and triethanolamine (TEA) [6].

mAb Nanoparticles:
monoclonal antibodies have such specific targeting capabilities, they are frequently used in cancer treatment. To make antibody-drug conjugates, mAbs are combined with nanoparticles (ADCs). Compared to monoclonal antibodies or cytotoxic medications, these treatments are more successful. An antibody-drug NP with a trastuzumab surface and paclitaxel core showed better anti-tumor effectiveness and less toxicity in HER2 positive breast epithelial cell control than either drug alone. [7].

Extracellular Vesicles:
Extracellular vehicles (EVs) are phosphor-lipid vesicles with two layers that range in size from 50 to 1000 nm. Different cell types continuously release extracellular vesicles (EVs), which vary in origin, size, and composition. Three categories are used to group EVs:1) Exosomes, 2) Micro vesicles, and 3) Apoptotic Bodies. NPs and exosomes are commonly used because to their identical lipid and molecular composition to the original cells. Furthermore, they bypass immune surveillance and readily incorporate within cancer cells. They serve as natural vehicles for delivering cytotoxic and anti-tumor medicines to target sites. Exosomes containing doxorubicin (exoDOX) are the greatest example. Exo DOX is an effective treatment for breast cancer, outperforming doxorubicin in terms of cytotoxicity while minimizing cardiotoxicity. Exosome nanoparticles are more biocompatible, chemically stable, and allow for intracellular communication than manufactured nanoparticles. However, limitations such as the lack of standard conditions for exosomal isolation and purification must be addressed [8].

Liposomes:
Spherical vesicles made of phospholipids, which can be unit- or multi-lamellar, are used to encapsulate pharmacological molecules. Liposomes are distinguished by properties characteristics as biological inertness, low immunogenicity, and low intrinsic toxicity. Liposomes, the first medication at the nanoscale, were licensed in 1965. The "hydrophilic core" and the hydrophobic phospholipid bilayer are the two main components of liposomes. Because of the peculiar construction, both hydrophilic and hydrophobic medicines, successfully protecting them from degradation during circulation. Liposomes are effective for delivering drugs including doxorubicin, paclitaxel, and nucleic acid, with increased anti-tumor activity and bioavailability. Doxil and Myocet are approved liposome-based daunorubicin bioavailability and antitumor activity. formulations for treating MBC. Liposome-based nanoparticles have limited use due to issues such as poor encapsulation,rapid removal by MP, cell adsorption, and short shelf life [9].

Solid Lipid Nanoparticles (SLN):
These Phospholipid monolayers, an emulsifier, and water make up colloidal nanocarriers, which range in size from 1 to 100 nm. We call these nanoparticles zero-dimensional. Triglycerides, fatty acids, waxes, steroids, and PEGylated lipids are examples of the lipid component. Since SLNs have a "micelle-like structure" and contain the drug in a non-aqueous core, distinguishing them from traditional liposomes. Mitoxantrone-loaded SLN has been found to be less toxic and more bioavailable. SLN treatment with doxorubicin and idarubicin in "P388/ADR leukemia cells" and the "murine leukemia mouse model" yielded positive results [10].

Nano emulsions:
Nano emulsions are heterogeneous mixes of oil droplets in aqueous mediums ranging from 10to 1000 nm. There are three forms of nano emulsions: oil-in-water, water-in-oil, and bi- continuous. Study on membrane-modified nano emulsions is quite broad. Via the TLR4/NF-kB signalling pathways, paclitaxel and spirulina nano emulsions improve anti-tumor immunity. A rapamycin, bevacizumab, and temozolomide nano emulsion is effective in treating metastatic melanoma. Nano emulsions exhibit distinct advantages over liposomes, including improved optical clarity, stability, and biodegradability. Clinical applications of nano emulsions face hurdles due to high temperature and pressure requirements, as well as the high cost of instruments like [11].

Cyclodextrin Nano sponges:
Cyclodextrins are commonly utilized as stabilizers to enhance the drug loading capabilityof NPs. Nano sponges are small, mesh-like structures. B-cyclodextrin nano sponges loaded with paclitaxel demonstrated strong cytotoxic effects in MCF-7 cell line culture. Formulating camptothecin with cyclodextrin-based nano sponges improves its solubility and stability [12].

Mechanism of Nanoparticles in Overcoming Drug Resistance:
A significant problem in the management and treatment of cancer is drug resistance. This applies to all cancer kinds and s. Drug resistance occurs when diseases develop tolerance to medicinal therapies.Drug resistance can be divided into two types:
1) Intrinsic
2) Acquired

Gene mutations associated with cell division or death usually cause innate resistance. Acquired resistance refers to resistance that develops after anti-tumor treatment, which might be caused by new mutations or changes in the tumor microenvironment. Nanoparticles have the unique potential to encapsulate several therapeutic compounds, making them

effective in combating cancer medication resistance [13].

Targeting Efflux Transporters:

Efflux transporters are classified as "ATP-binding cassette (ABC) transporters." These are essential to MDR. These transporters' primary function is to pump medications out of cells and reduce their concentration. Drug-resistant cancer cells overexpress the efflux transporter P-gp. Poor treatment response has been associated with overexpression of P-gp, especially in cases of ovarian and breast cancer. It is possible to target efflux pumps with NPs. By internalizing the cell by "endocytosis" and releasing the drug in the "perinuclear site," which is away from active pumps, NPs can avoid efflux pumps. By managing drug release through triggers like low pH and redox, NPs can circumvent efflux pumps. Combination therapy is an additional strategy for beating MDR. NPs are able to hold many medicines in a single carrier. Instead of simply avoiding efflux transporters, inhibiting their expression could be a viable alternative. To do this, nanoparticles can be designed to entrap both efflux pump inhibitors and chemotherapeutic drugs. A recent study found that utilizing NPs that transport COX-2 inhibitors and doxorubicin can effectively reverse MDR in breast cancer cells. Similarly, silica nanoparticles encapsulating miRNA-495 and doxorubicin have successfully overcome treatment resistance in lung cancer cells. A study demonstrated that targeting KDR receptors with nanoparticles in tumor neo-vasculature is more successful than combining P-gp inhibitors for anti-tumor treatment. One method for Depleting the ATP source is the key to beating drug resistance since ATP is required for ABC transporters to operate correctly. Targeting mitochondria will enable you to do this, which decreases ATP synthesis [14].

Targeting an Apoptotic Pathway:

Ineffective apoptotic machinery encourages the growth and survival of cancer cells, which results in resistance to treatment. The apoptotic pathway's flaw is initiated by dysregulation of Bcl-2 and NF-κB. These anti-apoptotic proteins have been extensively studied and may serve as targets for conquering the resistance to medication. MDR can be defeated by delivering "Bcl-2 siRNA and chemotherapeutics" via NPs. Curcumin and "pyrrolidine dithiocarbamate (PDTC)" have been used with NF-κB inhibitors. To fight "apoptotic pathway-mediated drug resistance," both decreasing anti-apoptotic and activating pro-apoptotic proteins can be used. Ceramide regulates alternative pre-mRNA splicing to increase the expression of p53, a key tumor suppressor. Ceramide nanoparticles can effectively repair the p53 missense mutation. Ceramide and paclitaxel have demonstrated remarkable therapeutic efficacy in cancer treatment resistance models. Cationic SLNs have been shown to transfect the p53 gene in lung cancer patients. Transfecting the p53 gene with PLGA in breast cancer cell models has been demonstrated to induce apoptosis and decrease tumor development [15].

Nanoparticles and Proteomics:

In the biological system, NPs are surrounded by cellular and serum proteins, forming a structure known as the protein corona (PC). Proteins are characterized as hard or soft Depending on their interaction with nanoparticles. Corona and soft corona. A "hard corona" is created when proteins attach strongly to NPs. Loose protein binding to NPS results in "soft corona" formation. Proteins with stronger affinities will gradually replace those that compose the majority of a PC. This is known as the Vroman effect. Developing technology to produce NPs with required characteristics is critical. Proteomic techniques include MS, LC-MS, SDS- PAGE, and isothermal microcalorimetry (ITC). PC impacts how nanoparticles interact with the biological environment, influencing their use in medicine. Cancer proteomics analyzes the quantity of proteins in cancer cells and serum to identify biomarkers for diagnosis, therapy, and prognosis. It also helps to understand cancer development and treatment Resistance mechanisms PTMs play a crucial role in incidence, recurrence, and metastasis. In addition to chemotherapy and kinase inhibitors, new therapies like as siRNA, mRNA, and gene editing are commonly employed with nanoparticles [16].

Nanotechnology for Small Interfering RNA (siRNA) Delivery:

siRNAs are tiny dsRNA molecules (about 21 nucleotides long) that decrease gene expression in their target. This mechanism is referred to as "RNA interference." Clinical trials are underway for siRNA-based NPs, including ALN-TTR01, which targets the transthyretin gene to treat transthyretin-mediated amyloidosis, and Atu027, a liposomal siRNA that targets protein kinase N3 and TKM-ApoB to reduce ApoB expression [17].

Nanotechnology for Tumor microRNA Profiling and Delivery:

MicroRNAs are endogenous "single-stranded non-coding RNA" molecules that regulate gene expression by inhibiting translation or destabilizing mRNA. These biomarkers are key targets for cancer detection, therapy, and treatment. Nanotechnology relies on the base priming characteristic of nucleic acids, including miRNA profiling approaches. Various profiling methods combine biosensors or surface plasmon resonance imaging with molecular biology enzymatic activities. Nanotechnology can be utilized to distribute microRNAs. Biodegradable polycationic prodrugs have shown promising results in regulating polyamine metabolism. MicroRNA-loaded polycation-hyaluronic acid nanoparticles containing single-chain antibody fragments reduced "survivin expression" in the lung of mouse B16F10 melanoma with high metastatic cancer load [18].

Some nano medicines for cancer therapy approved by Food and drug administration(FDA)

Table Number: 01 List of nanomedicines for cancer therapy approved by FDA [19].

Trade name	Material	Drug	Company	Indication	Year (s) approved
Doxil®	Liposome-PEG	Doxorubicin	Janssen	MBC, metastatic ovarian cancer	1995
Eligard	PLGA	Leuprolde acetate	Tolmar	Prostate Cancer	2002
Abraxane	Albumin	Paclitaxel	Celgene	Metastatic breast cancer	2005
Genexol PM	mPEG-PLA	Paclitaxel	Samyang Corporation	Metastatic breast cancer	2007
Onivyde®	Liposome	Irinotecan	Merrimack	Pancreatic cancer	2015

Advantages of Nanoparticles in Cancer Therapy:

Nanotechnology's use in cancer detection, therapy, and management has revolutionized the field. Nanoparticles (NPs) can increase drug concentrations within cells without causing harmin healthy tissue, either through active or passive targeting. The Targeted nanoparticles can be pH- or temperature-sensitive, regulating medication release. The pH-sensitive drug delivery device delivers medications within the acidic TME. Temperature-sensitive nanoparticles release medications at the target region in response to temperature variations caused by magnetic fields or ultrasonic waves. The form, size, molecular mass, and surface chemistry of nanoparticles have a crucial role in drug delivery effectiveness. nanoparticles can be modified according to the target and used to target a particular moiety' Conventional chemotherapy and radiation therapy have limitations in terms of efficacy and adverse effects due to unequal distribution and cytotoxicity. To successfully eliminate cancer cells while Minimizing harm judicious dosing is necessary. reach the intended spot, the medicine must pass through many fortifications. Drug metabolism is a highly complex process. MPS in the liver, spleen, or lungs react with medicines, activating "macrophages or leukocytes" to quickly remove them [20].

The brain-blood barrier (BBB) protects the central nervous system from dangerous and poisonous chemicals. "Brain capillary endothelial cells" build a wall to deliver nutrition to the brain. As the primary role of The BBB prevents hazardous chemicals from reaching the brain. Chemotherapy options for brain cancer are limited to intraventricular or intracerebral infusions.

However, it is known that nanoparticles can pass the blood-brain barrier. NPs can now be delivered via several methods, including EPR effect, targeted ultrasound, peptide-modified endocytosis, and transcytosis. Glutathione PEGylated liposomes encapsulated withmethotrexate enhanced its absorption in rats. Au-NPs are commonly employed for drug delivery and apoptosis induction. NPs, as carriers, also improve medication stability by avoiding degradation. enclosed cargo. Additionally, vast amounts of pharmaceuticals can be encapsulated without any chemical reactions. Dry solid dose formulations have higher stability than nano liquid compounds. Stabilizers can improve stability. Using porous nanoparticles can also improve stability [21]

AcDEX nanoparticles enhanced cytotoxic CD8+ T cell growth and activation. Immune reaction. "Programmed cell death protein 1 (PD-1)" or "programmed cell death ligand 1 (PD-L1)" are some of the most important immunological checkpoints. Hence, immune checkpoint inhibitors. These are targeted utilizing NPs. According to one study, traditional immune checkpoint Inhibitors of PD-L1/PD-1 demonstrated variable results. Multivalent poly(amidoamine) dendrimers were employed to improve the binding of immune checkpoint inhibitors to immune checkpoints. The application of these dendrimers not only demonstrated boosted PD-L1 inhibition, but also demonstrated improved drug accumulation at the tumor location [22].

Significant Challenges in the Clinical Application of Nanoparticles:

With the advancement of nanotechnology, there has been a significant increase in study on nanoparticles. However, only a small percentage make it to clinical trials. Most of them stop at the in vivo and in vitro stages. Every nano formulation Most NPs confront comparable problems in clinical translation, categorized as biological, technological, and research design- related. Biological problems for NPs include limited delivery routes, poor biodistribution, degradation, and toxicity. Intravenous injections of NPs into the bloodstream reduce their ability to interact with the target site.

This results in a high concentration of the medication. In vivo and in vitro investigations have shown that magnetic NPs can effectively control their movement against blood flow. However, the impact of magnetic fields on the human body, cross-talk between magnetic areas, and a huge number of NPs need to be investigated. Controlling the biological fate of NPs is difficult and requires a lot of concentration. Despite being built with biosafety materials and modified to enhance retention duration and half-life, nanoparticles can still cause lung, liver, and kidney damage.

Toxic factors include surface area, particle size and shape, solubility, and agglomeration. NPs have demonstrated higher deposition. Increased lung deposition can lead to inflammation, oxidative stress, and cytotoxicity. Research suggests that nanoparticles (NPs) can cause free radicals in healthy cells. Fabricating NPs with more friendly compounds, such as

chitosan Materials that degrade when exposed to near infrared light could offer viable answers [23].
Another tough problem is to prevent the "mononuclear phagocytic system (MPS)." In biological fluids, NPs adsorb proteins, causing PC to fight MPS and absorb NPs. To avoid this, NPs are coated with compounds that hinder the production of protein coronas. However, they have not produced any meaningful outcomes.
Designing nanoparticles (NPs) that target "macrophages" and use them as drug vehicles can address this issue. Currently, regularly employed techniques include inhibiting macrophage recruitment, depleting and reprograming TAMs, and blocking "CD47-SIRPα pathways. "NPs present technological issues such as scaling up synthesis, equal optimization, and predicting performance. These are critical in ensuring the clinical success of NPs. NPs utilized in vivoand in vitro investigations are often manufactured in small batches, making large-scale production challenging due to instrumentation and other constraints [24].

The most effective clinical candidates in animal models are not routinely optimized. To address this issue, we can test multiple nano formulations and select the best one through selective iterations. However, such hits should not be directly tested in humans. It is challenging to predict nanoparticle efficacy and performance, and reproducing in vivo outcomes in human trials is even more difficult. Computational or theoretical modeling, together with experimental results, can simulate physiological tissue and surroundings.
Challenges in research design, including size, intent, and scheduling of NP medicines, have a substantial impact on clinical studies. Most research use "cell and animal models," which may not produce clear findings in human trials. Using a single model makes it difficult to mimic genuine reactions in the human body. Research into "models of cancer metastasis" is crucial as it is a key feature of cancer.

Personalized medicine requires N = 1 clinical studies. Multiple factors, including genetics, environment, and medical history, must be considered. One important difficulty is that nanoparticles are not employed as first-line therapy. Although nano formulations have been approved, they are often reserved for future treatment if disease progression occurs. Located in the clinical trial scenario. Most patients have either progressed through many therapies or developed medication resistance. These conditions can bias clinical trial results, limiting the effectiveness of NP treatment for people who are still curable. [25]

Conclusion and Future Perspective:
Nano technology offers a promising approach to cancer treatment by delivering small molecules for detection, diagnosis, and therapy. Nanoparticle treatments are widely used in
cancer treatment due to their unique properties. types. NP-based DDS offers improved pharmacokinetics, biocompatibility, tumor targeting, and stability compared to traditional medicines. Furthermore, NPs offer a promising platform for combination therapy, which aids in overcoming MDR. Research indicates that several forms of NPs, including polymeric, metallic, and hybrid NPs, can enhance medication delivery efficacy.
Researchers must consider both the nanoplatform features and therapeutic drug properties. However, there are certain drawbacks, such as the lack of precise in vitro models. Reproduce in vivo, immunotoxicity, long-term toxicity, and neurotoxicity. While "nano vaccines" and “artificial APCs" have shown enhanced potency compared to traditional immunotherapy, their clinical efficacy remains subpar.
Safety and Tolerance These new modalities should be inspected. Developing "immunomodulatory factor-loaded NPs" could improve the effectiveness of vaccinations for immunotherapy. Proteomics study on the "mechanism of cancer origin, MDR, and occurrence" is expected to lead to increased use of nanoparticle-based medicines. Despite extensive research, only a few NP-based medications are now in use, with the majority in clinical trials or in the exploratory stage. To build rational nanotechnology, it's important to consider the toxicity, cellular and physiological aspects that affect NP-based medication delivery, EPR, and PC mechanisms in humans. Our results suggests that nanotechnology and cancer therapy development will lead to a breakthrough in clinical translation for NP-based cancer therapy.

Abbreviations:
- ECM - Extracellular Matrix
- MDR - Multidrug Resistance
- NPs - Nanoparticles
- PNPs - Polymeric Nanoparticles
- PMMA - Polymethyl methacrylate
- PPI - Polypropylenimine
- TEA - Triethanolamine
- PEG - Polyethyleneglycol
- ADCs - Antibody Drug Conjugates
- EVs - Extracellular Vesicles
- ABC - ATP Binding Cassette
- BBB - Brain Blood Barrier
- aAPCs - Artificial Antigen Presenting Cells

- DCS – Dendritic Cells

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