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Development and Evaluation of Nanoparticles - Based Drug Delivery Systems for Targeted Cancer Therapy

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Abstract: *It is believed that drug delivery systems based on nanoparticles (DDS) hold potential for the treatment of cancer. Compared to the traditional DDS, the nanoparticle-based DDS is more effective by:*
1) prolonging the half-life of proteins and medications that are susceptible
2) Making hydrophobic medications more soluble
3) making it possible to distribute medications at the sick spot in a targeted and controlled manner...
The creation of DDS based on nanoparticles using chitosan, silica, and poly(lactic-co-glycolic acid) is the main focus of this paper. They describe how they are made and how they are used to treat cancer. The present constraints and future directions of the DDS based on nanoparticles are examined.

Keywords: Drug resistance, cancer, biomarkers, nanotechnology, nanoformulation, and nanoimaging

I. INTRODUCTION

Humans have been using natural products derived from plants as medicines to treat a variety of illnesses since ancient times. The majority of modern medications are made from herbs using traditional knowledge and methods. Natural resources are the source of around 25% of the main pharmaceutical substances and their derivatives that are now on the market. Novel drug discovery is based on natural molecules with diverse chemical bases. The focus in creating synthetically accessible lead molecules that resemble the chemistry of their counterparts has been a recent trend in the natural product-based drug discovery process. Amazing features of natural products include incredible chemical variety, biological and chemical qualities with macromolecular specificity, and reduced toxicity[1]. These make them favorable leads in the discovery of novel drugs .Moreover, computational research has aided in the development of next-generation drug innovations such target-based drug delivery and discovery as well as the visualization of molecular interactions of pharmaceuticals.

Pharmaceutical corporations are reluctant to spend more in medication delivery and discovery methods based on natural products, despite a number of benefits[2]. Instead, they are looking through the libraries of chemical compounds that are now available to find new treatments. But now, researchers are looking at using natural substances to treat a number of serious illnesses, including as diabetes, cancer, heart disease, inflammatory conditions, and microbial infections. This is mostly due to the special benefits that natural medications offer, including reduced toxicity and adverse effects, affordability, and promising therapeutic outcomes. However, the use of natural chemicals as medication is made more difficult by issues with their toxicity and biocompatibility[3]. As a result of these issues, numerous natural substances are failing to pass the clinical trial stages. In vivo instability, limited solubility and bioavailability, poor body absorption, issues with target-specific delivery and tonic effectiveness, and probably adverse pharmacological consequences are the main barriers to adopting large-sized materials for drug administration. Therefore, the introduction of innovative drug delivery systems that target treatments to specific body locations may be one possible answer to these urgent issues. Nanotechnology is therefore essential to better medicine and drug formulations, reaching the target market, and successfully implementing controlled drug release and distribution[4].

Nanophases and nanostructures in a variety of scientific domains, particularly in nanomedicine and nanobased By using medication delivery methods, where such particles are of great interest, nanotechnology has demonstrated the ability to bridge the gap between the medical and physical sciences . Nanomaterials are materials that range in size from tissue engineering to drug delivery, microarray testing, and biosensor microfluidics. In order to create nanomedicines,

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nanotechnology uses therapeutic substances at the nanoscale level. Starting with nanoparticles, the discipline of biomedicine, which includes drug delivery, tissue engineering, biosensors, and nanobiotechnology, has been able to push the boundaries of nanomedicine. Nanoparticles are typically tiny nanospheres since they are made of materials that are atomic or molecular in nature[5]

They are therefore more mobile than larger elements inside the human body. Particles at the nanoscale have special mechanical, chemical, electrical, magnetic, biological, and structural characteristics. Because nanostructures can be used as delivery vehicles to encapsulate pharmaceuticals or attach therapeutic chemicals to them, they can transport treatments to target tissues more accurately with a controlled release, which is why nanomedicines have gained popularity recently. A new discipline called "nanomedicine" is applying the principles and methods of nanoscience to medical biology, disease prevention, and treatment. It involves the use of nanoscale materials such as actuation materials in living cells, nanorobots, and nanosensors for delivery, diagnosis, and sensory applications. For instance, a technique based on nanoparticles has been created that combines the imaging and therapeutic modalities for the diagnosis of cancer. The FDA has now approved lipid systems including liposomes and micelles, which were used in the first generation of nanoparticle-based therapy. Inorganic nanoparticles such as magnetic or gold nanoparticles may be present in these liposomes and micelles. Because of these characteristics, inorganic nanoparticles are being used more frequently for medicinal, imaging, and drug delivery purposes. Furthermore, nanostructures are said to help distribute scarce water-soluble medications to their intended site and prevent medications from becoming tainted in the gastrointestinal tract. Due to their usual absorptive endocytosis absorption methods, nanodrugs have a higher oral bioavailability[6].

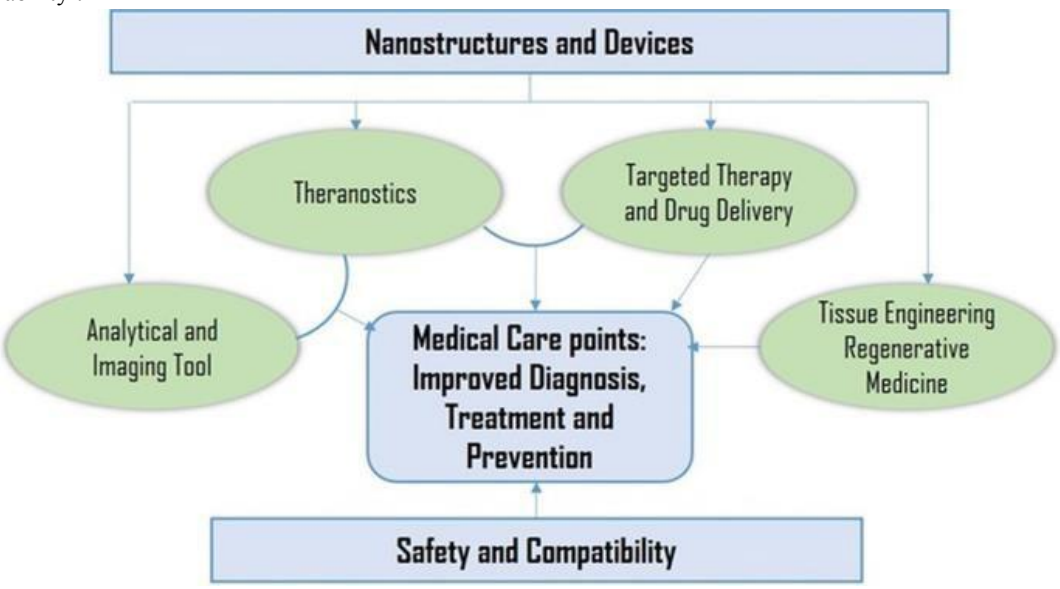

Fig ; -Application and goal of nanomedicine in different sphere of biomedical research

INTRODUCTION

The creation and use of materials at the nanoscale for illness detection, treatment, and prevention is known as nanomedicine. Its indications span from biological devices and nanomaterials used in medicine to electrical biosensors at the nanoscale scale. The mainstay of nanomedicine, nanoparticles have drawn a lot of attention as prospective drug delivery vehicles for the detection and treatment of cancer. 1–3 Submicron-sized (100–1,000 nm) particles, devices, or systems created from a variety of materials, such as polymers (e.g., polymeric nanoparticles, micelles, vesicles, or dendrimers), lipids (liposomes), viruses (viral nanoparticles), and even inorganics, are used as drug delivery systems. 7, 8 Nanoparticles can raise the intracellular concentration of medications in cancer cells while avoiding harm to healthy cells by employing passive or active targeting techniques. After entering tumor cells, nanoparticles are typically encapsulated by endosomes by receptor-mediated endocytosis, avoiding p-glycoprotein recognition, which is one of the primary mechanisms of drug resistance[7]

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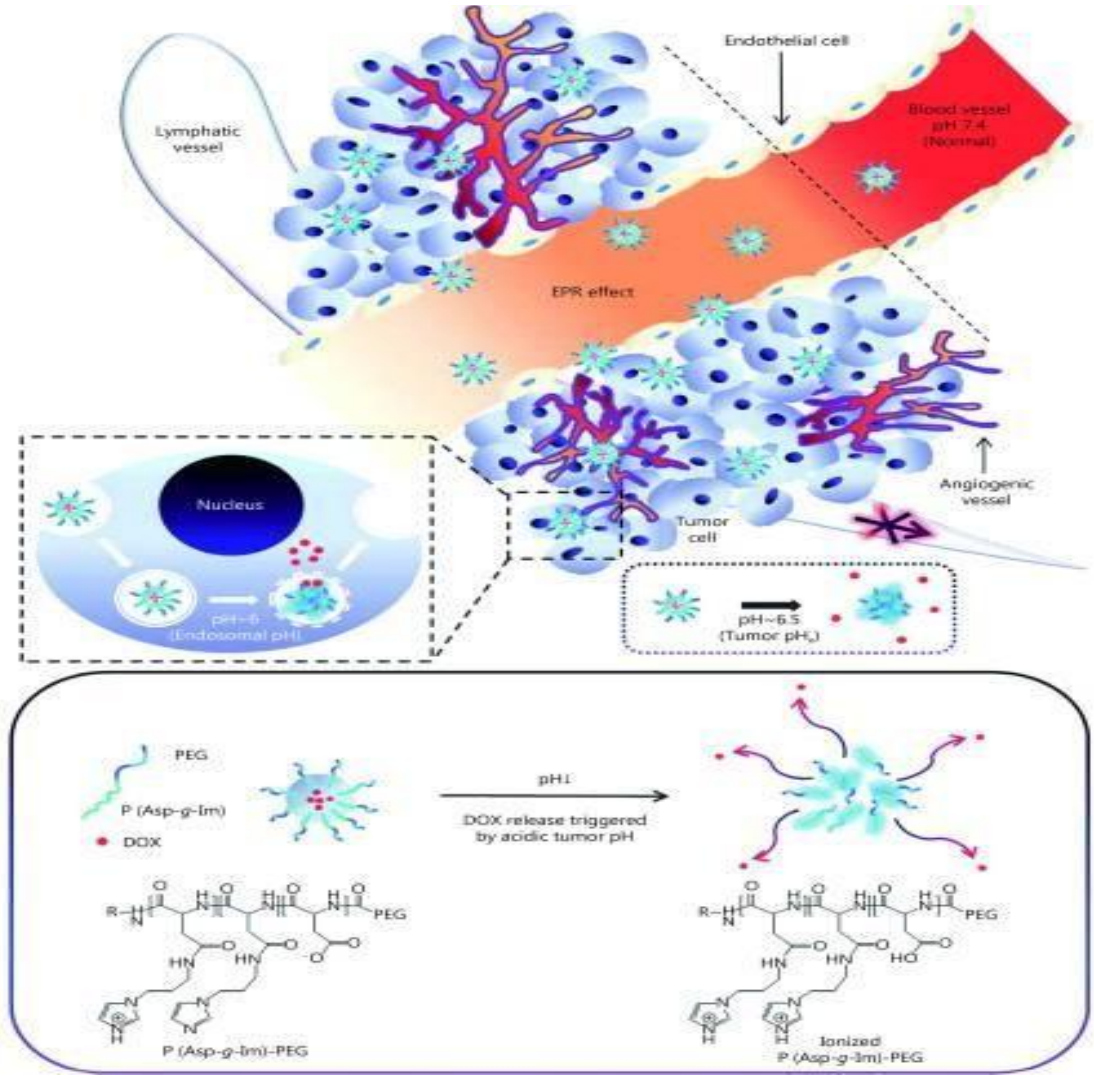

Fig;-Schematic for the proposed in vivo behaviour of Dpharma. reproduced with permission from Ref

II. MECHANISM OF TARGETING

One essential feature of nano-carriers for drug delivery is their ability to preferentially target cancer cells, which improves therapeutic efficacy while shielding healthy cells from damage. The targeting design of NP-based medications has been the subject of numerous investigations. It is essential to first comprehend tumor biology and the relationship between nano-carriers and tumor cells in order to effectively address the difficulties associated with tumor targeting and the creation of nano-carrier systems. One can broadly categorize the targeting mechanisms as follows:

1) Passive targeting
2) Targeting actively
3) Attacking cancerous cells8
4) Endothelium tagging

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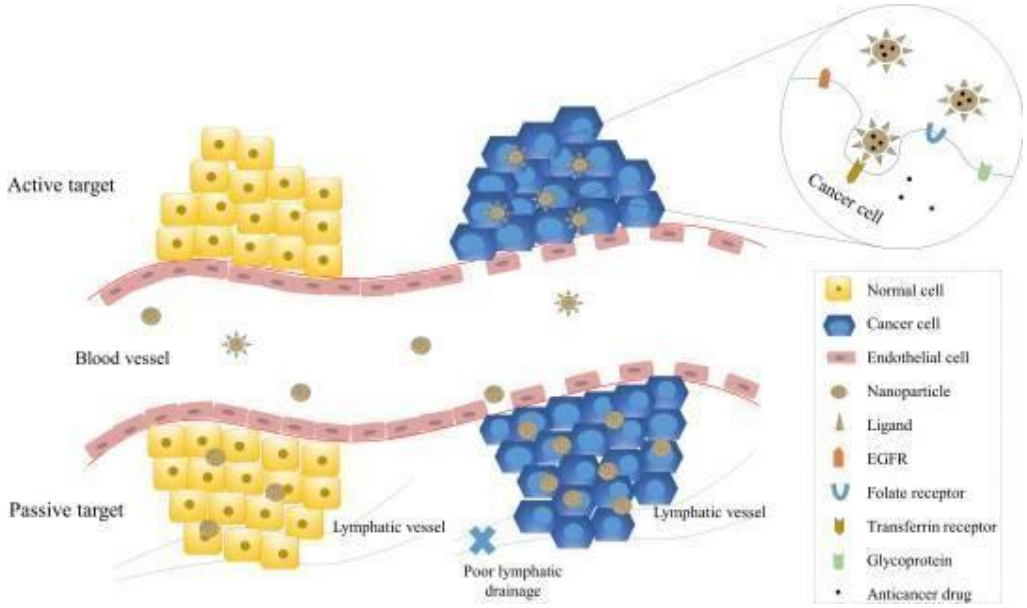

Fig;-Passive and active targeting of NPs to cancer cells.

Targeting of NPs enhance therapeutic efficiency and reduce systemic toxicity. Passive targeting of NPs is mainly achieved by the enhanced permeability and retention (EPR) effect, which exploits the increased vascular permeability and weakened lymphatic drainage of cancer cells and enables NPs to target cancer cells passively. Active targeting is achieved by the interaction between ligands and receptors.The receptors on cancer cells include transferrin receptors, folate receptors, glycoprotein (suchaslectin), and epidermal growth factor receptor (EGFR)[9]

III. MECHANISMS OF NPS IN OVER COMING DRUG RESISTANCE

Despite an increase in cancer therapeutic techniques, drug resistance remains a significant issue in cancer treatment. When different cancer treatments fail due to multidrug resistance, the cancer progresses and the prognosis deteriorates. Cellular and physiological factors, such as overexpression of ATP binding cassette (ABC) transporters (e.g., efflux transporter) (Litman et al., 2000), malfunctioning apoptotic machinery, interstitial fluid pressure, and an acidic and hypoxic tumor microenvironment, are among the mechanisms of tumor drug resistance. It has been demonstrated that using nanotechnology to deliver drugs for the treatment of cancer significantly helps to overcome drug resistance.

1. Targeting transporters of efflux
2. Apoptotic pathway targeting
3. Aiming for hypoxia

IV. THE ROLE OF NPS IN CANCER IMMUNOTHEROPY

A new era in cancer treatment has begun with the development of immunotherapy. NPs have demonstrated significant promise for use in immunotherapy in addition to their crucial function in chemotherapy delivery. Activating the anti-tumor immune response is the primary method of cancer immunotherapy. Nanovaccines, artificial antigen-presenting cells (aAPCs), and targeting the immunosuppressed tumor microenvironment (TME) are all components of NP-associated immunotherapy. Tumor-associated antigens (TAAs) and adjuvants are delivered to APCs, including dendritic cells (DCs), via nanovaccines. Furthermore, NPs themselves can be utilized as adjuvants to enhance APC antigen presentation and encourage DC maturation, which will activate cytotoxic T cells' anti-tumor function. The cytoplasmic transport of TAAs into DCs by NPs, including liposomes, gold NPs, PLGA NPs, micelles, and dendrimers, can strengthen the immune response against tumor cells. Among the various NP types, it has been demonstrated that inorganic NPs like mesoporous silica and polymers like acetylated dextran (AcDEX) work as adjuvants in immunotherapy, stimulating the immune response. In contrast to nanovaccines, artificial APCs work by binding to T cell receptors (TCRs) and co-stimulatory receptors on T cells directly through MHC-antigen complexes and co-

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stimulatory molecules, respectively, activating T cells. Targeting tumor associated macrophages (TAMs), myeloid derived suppressor cells (MDSCs), and regulatory T cells (Tregs), three crucial cell types in the TME, is the primary method of addressing the immunosuppressive TME. Additionally, NPs are typically treated with PEG to reduce interactions with the reticuloendothelial system10

V. TYPES OF NANOPATICALES IN THERAGONISTIC

1) Gold nanoparticles - Gold nanoparticles have emerged as a promising tool in ther agnostics due to their versatility and numerous potential biological ap plications. Their high surface-to-volume ratio and unique optical features make them valuable for noninvasive imaging. These nanoparticles can be loaded with a myriad of chemicals, including tar geting or imaging moieties and therapeutic medications. Gold nano particles integrate targeting, diagnostics, treatment, and monitoring, overcoming limitations associated with traditional diagnosis and ther apeutic techniques. This allows for the simultaneous administration of imaging and therapeutic molecules at the same location while simulta neously monitoring their effects in real-time. In addition, targeted molecular imaging and the enhanced retention of therapeutic agents at specific locations may lead to reduced levels of nanoconjugates in cir culation, thereby reducing systemic toxicity.

2) Iron oxide nanopaticales- A mutation or cellular aberration that favors tumor formation in humans is the initial step in a complex chain reaction that culminates in cancer. The presence of distinct sets of cellular receptors in normal and cancer cells opens the possibility of imaging probes targeting specific receptors.Adding ligands, such as antibodies, peptides, or small compounds that target receptors prevalent in tumor cells to the surface of iron oxide nanoparticles is a common and established practice. Numerous tumor imaging approaches using targeted iron oxide nano particles have been explored in both in vitro and animal studies.

3) Silica nanoparticales- Silica has earned a positive reputation for being completely safe due to its historical use as a surgical implant. Moreover, the ability to pre cisely control the size and shape of silica nanoparticles during manufacturing is well- documented. the coag ulated silica nanoparticles precursors facilitate the incorporation of various imaging and therapeutic functions, forming the basis for ther agnostic applications. Silica nanoparticles are synthesized through the hydrolysis and condensation of tetraethyl orthosilicate, commonly achieved by transferring amine or thiol groups to the particles' surfaces within the tetraethyl orthosilicate matrix. A convenient method involves injecting a functional molecule pre-coupled with APS/MPS into the nano system during particle creation. Utilizing this technique, organic dyes and Gd-DTPA complexes have been coupled and integrated into a silica particle matrix, resulting in agents with optical or magnetic activity.

4) Carbon nanoparticales - Biomedical researchers are interested in the distinctive characteris tics of carbon nanotubes (CNT), such as their stable nanoscale size, vast surface area, high aspect ratio, and various surface chemical functions. find CNTs intriguing as potential carriers and mediators for cancer therapy. Functionalized CNTs have been investigated for their effectiveness in delivering various chemotherapeutic agents, including doxorubicin, camptothecin, carboplatin, cisplatin, paclitaxel. The unique optical characteristics of CNT make them valuable in photoacoustic imaging. When illuminated wth a laser, CNTs pro duce ultrasonic sounds. This may in turn enable the obtaining of high- resolution images of deeper tissues. This feature allows us to monitor cancers without having to perform invasive surgery. CNTs can be enhanced with protein or fluorescent dyes for fluorescence imaging, providing a higher probability of detection in cancer cells and other environments. Additionally, Raman photography takes advantage of the unique Raman scattering features of the CNTs, offering genomic data for sensitive and accurate characterization of cancer cells and tissues.

5) Quantum dots- Quantum dots provide a wide surface area for drug conjugation due to their inflexible structure. The two most common functional groups used for medicine binding are carboxylic acid groups and free amine groups. Ranging in diameter from 100 to 200 nm, quantum dots are nanoparticles with size-ranging microscopic and targeting capabilities.The primary objective is to develop small, stable, and selective probes capable of penetrating cells and organelles. Quantum dots emit energy in water, influencing brightness in the ultraviolet-near infrared range through the emission of blue and red luminescence from larger and smaller nanocrystals, respectively. Their electrical and optical properties, sustained luminescence and drastically reduced photo sta bility distinguish them from traditional organic

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dyes. Toxic effects are difficult to detect in living organisms due to the short testing durations and protective sophisticated polymer coating of the quantum dots.

6) Liposomes- The distinctive round shape of liposomes allows them to encapsulate hydrophilic chemicals in the central aqueous compartment and hydro phobic compounds in the lipid bilayers, shielding them from destruction. In clinical trials, liposomes outperform many other carriers for the pharmacokinetics and biodistribution of theragnostic agents due to their superior agent-loading efficiency, biocompatibility, stability in biolog ical environments, and controllable release kinetics. Thus, lipo somes have emerged as a leading delivery mechanism for the diagnosis and treatment of several disorders. the potential of li posomes for targeting, diagnosis as well as theranostics11

VI. APPLICATIONS OF CHITOSAN NANOPARTICALES IN DRUG DELIVERY

1) Passive and active targeting of tumors using chitosan nanoparticles-Jain and Jain used ionotropic gelation to create chitosan nanoparticles linked with hyaluronic acid (HA). 5-fluorouracil (5FU) was selected as the medication to treat colon cancer. Because there are more HA receptors near tumor tissues, HA was added to the DDS chito san nanoparticles. As a result, colon cancers can be targeted by nanoparticles through both the EPR effect and HA binding to HA receptors. The diameter of the chitosan nanoparticles loaded with 5FUs produced in this study was around 135 nm. The particle size increased to approximately 150 nm following the conjugation of HA with free amino groups on chitosan (Scheme 1). Because of the twofold barrier that an extra HA layer on the nanoparticles formed, HA coupled nanoparticles demonstrated decreased drug release in 24 hours when compared to uncoupled chitosan nanoparticles. The HA-conjugated chitosan nanoparticles are potential vehicles for targeted drug delivery to colon tumors, as evidenced by the increased cell uptake rate by cancer cells during 4 hours of incubation at 37 C.

2) Stimuli-sensitive targeting of tumors using chitosan nanoparticles- In cancer treatments, stimuli-sensitive chitosan nanoparticles are also frequently employed. Since inflammatory or malignant tissues will show signs of acidosis or hyperthermia, pH and temperature are frequently selected as physiological indicators. A pH-mediated chito san-based microgel drug delivery method for cancer treatments was designed and described by Zhang et al. [19]. N-[(2-hydroxy-3-trimethylammonium)propyl]chitosan chloride (HTCC) was produced by reacting chitosan powder with glycidyltrimethylammonium chloride after it had been first dissolved in water at 85 C. HTCC nanoparticles were created with TPP using the ionotropic gelation technique. Chitosan nanoparticles' width grew from less than 200 nm to about 400 nm (a 2.2-fold increase) and their relative volume increased by 11 times when the pH dropped from
7.4 to 5.0. It is suggested that the microgels will exhibit significant swelling following internalization into the cell, which will allow them to remain in the sick area and release the medication. The loading efficiency, release kinetics, and cell viability/mortality were assessed following loading with methotrexate disodium (MTX). While around 30% of the medication was held in microgel after 5 days at pH ¼7.4, microgels demonstrated a quicker drug release rate at pH ¼5.0 (93% after day 1). When MTX-loaded HTCC was compared to the pure drug group and the non- conjugated MTX-chitosan nanoparticle group in cell viability tests, it demonstrated the maximum mortality on HeLa cells12.

VII. APPLICATIONS OF SILICA NANOPARTICALS IN DRUG DELEVERY

1) Application of MSNs in gene delivery for cancer treatment-MSNs have been investigated as a possible gene delivery vehicle. In contrast to conventional drug delivery methods, MSNs' mesoporous structure allows for a uniform drug distribution throughout the matrix system. Additionally, the pore size of MSNs can be adjusted to accommodate medications with varying molecular sizes. Additionally, MSNs can load more drugs than chitosan and other polymers. Since gene molecules are buried deep within mesopores, they can evade nuclease destruction before they reach the intended location when utilized in gene delivery.

2) Application of MSNs to achieve zero premature release in the treatment of cancer-Many of the medications used to treat tumors are harmful to other tissues or organs. Therefore, ensuring "zero premature release," or nearly zero medication dispersion in non-targeted areas, is crucial. first altered MSNs with coumarin groups to use UV light to actively photo-control the pore accessibility. The substituents for coumarins are referred to as "hinged double doors." The coumarin groups photopolymerize to form cyclobutane coumarin dimmers when the MSNs are exposed to UV light with a wavelength of 310 nm. This closes the doors and prevents any medication absorption into the pores. Photocleavage of the dimers and the opening of the doors to the interior of the MSNs can occur when they are exposed

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to UV light with a wavelength of 250 nm. After washing with n-hexane, 28 weight percent of the steroid cholestane was absorbed in the irradiated coumarin modified MSNs, whereas no cholestane remained in the coumarin modified MSNs without irradiation, according to a controlled release study of coumarin modified MSNs with cholestane (because of its small molecular size, which allows it to be stored in the pores of MSNs). Other stimuli, including pH, enzymes, and magnetic fields, have been investigated to get 0% premature release in MSNs in spite of photo-stimulation.

3) Applications of PLGA nanoparticles in cancer treatment- The majority of PLGA nanoparticle applications use an active targeting method to administer chemotherapeutic agents in the treatment of cancer because passive delivery via EPR effects was found to be insufficient in delivering nanodrugs into tumors. The surface of PLGA nanoparticles is frequently coated or grafted with targeting ligands. The selected ligands offer a particular affinity to receptors that tumoral endothelial cells or cancer cells frequently overexpress.

4) Obstacles of nanoparticles for clinical use - Only a small number of nanoparticle medications are currently on the market for the treatment of cancer, despite the fact that they provide numerous benefits as drug delivery methods (Table 1). There are still numerous restrictions and drawbacks using DDS nanoparticles13

VIII. FACTORS DRIVING NANOPARTICALES-BASED CANCER DRUG DELIVERY SYSTEM

1) Multifunctionality- Encapsulation of biomolecules for duel function
2) Lower distribution volume
3) Targeted delivery- Ability to locate and target specific tissues and organs
4) Suceesful drug release
5) Enhanced permeability and retention (EPR) effect-Unique accumulation in tumors
6) Controlled dug release-Efficient control of drug releas to prevent tissue damage
7) Biocompatibility
8) Reduced clearance rates –Prolonged retention and reduced clearance ratrs
9) Overcoming drug resistance
10) Improved pharmacokinetics and biodistribution-Optimized metabolism and drug distribution
11) Improved drug solubility-Efficient encasulaion ofhydrophbic drugs or drugs with side effect
12) Delivery to difficult sites-Efficient delivery to areas like the brain or retina14

IX. CLINICAL SETTING

1) Preclinical evaluation-Prior to clinical trials, extensive preclinical evaluations are necessary to investigate the safety profile of smart nanoparticles. This involves in vitro and in vivo studies to assess their biocompatibility, potential toxicity, and any adverse effects on cells, tissues, and organs.

2) Systemic toxicity- Smart nanoparticles should undergo rigorous evaluation to determine their systemic toxicity. This includes examining their distribution in the physiological functions. It is crucial to ensure that the nanoparticles do not induce systemic toxicity or harm the overall health of the patient.

3) Immunotoxicity assessment- The immune response trig gered by smart nanoparticles is a critical aspect to consider. Immunotoxicity studies are essential to evaluate any immune reactions, including inflammation or immunosup pression, caused by the nanoparticles Determining the nanoparticles' compatibility with the immune system and their potential for immunomodulatory applications requires an understanding of the immunological implications.

4) Targeted toxicity- Smart nanoparticles designed for targeted drug delivery or specific therapeutic purposes should undergo evaluations to assess their toxicity at the target site. This involves investigating if the nanoparticles induce any cytotoxicity or unwanted effects in the vicinity of the target area. Ensuring localized safety is crucial for successful clinical applications

5) Pharmacokinetics and biodistribution- Understanding the pharmacokinetics (absorption, distribution, metabolism, and excretion) and biodistribution of smart nanoparticles is essential for predicting their behavior in the human body. This information helps assess potential accumulation in critical organs, elimination pathways, and the overall clearance of the nanoparticles, minimizing the risk of toxicity and ensuring safe clinical use.

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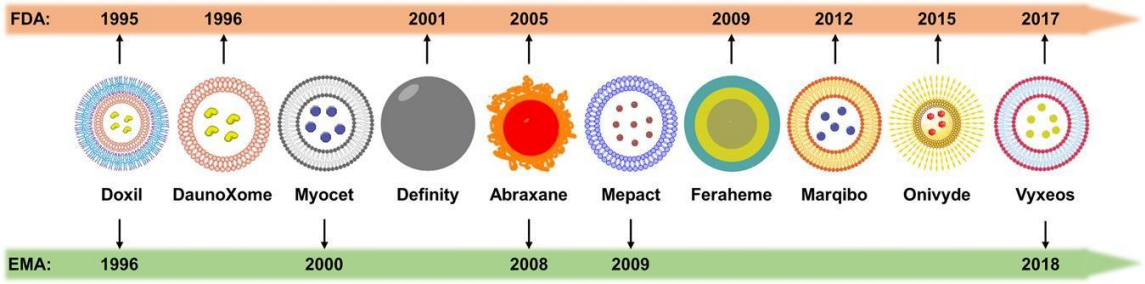
6) Long-term safety- Long-term safety assessments are vital for the clinical translation of smart nanoparticles. These evaluations involve prolonged exposure studies to monitor any chronic toxicity, including the nanoparticles' potential to induce tumorigenic effects or chronic inflammation.

7) Regulatory compliance- Compliance with regulatory guidelines is paramount to facilitate the clinical translation of smart nanoparticles. Regulatory authorities, such as the FDA, require comprehensive safety data to support the approval of nanoparticle-based therapies. Meeting the regulatory stan dards ensures that the nanoparticles are safe for human use and paves the way for their successful clinical implementation15



Fig;- Timeline of the development of smart nanoparticles for cancer diagnosis and treatment.

By addressing these safety considerations, researchers and clinicians can establish a solid foundation of evidence regarding the safety and toxicity of smart nanoparticles. This information not only promotes the responsible development of these innovative technologies but also instills confidence in their potential for clinical applications.

Several clinically approved nanoparticle formulations either by the FDA in the United States or the European Medicines Agency (EMA) in the European Union are used to treat a variety of cancers at different stages (Table 2). The timeline and basic structure of smart nanoparticles for cancer diagnosis and treatment in the clinical setting are shown in Fig. 5. Doxil, a PEG functionalized liposomal doxorubicin, was the first nanomedicine that has been approved for anticancer medications (FDA in 1995). .292 Rapid clearance is a ubiquitous challenge for nanoparticle-based drug delivery. To increase circulation time, chemical modification with a variety of compounds, including PEG and its derivatives can be utilized to alter the surface of a nanoparticle. Except for Doxil and Onivyde, most of these formulations are non-PEG.345 CPX-351 (Vyxeos) is a gel-phase bilamellar liposome nanoparticle with a mean diameter of 107nm and a strong negative surface potential, which is based on the principle of 'ratiometric' dosing of the cytarabine/daunorubicin combination with a molar ratio of 5:1 provides the greatest synergistic effect with the lowest antagon ism in vitro and in vivo. 346 This liposomal nanoparticles are approved from US FDA for the for the treatment of adults with newly diagnosed acute myeloid leukemia (AML) with myelodysplasia-related changes (AML-MRC) and therapy-related AML (t-AML).347 Non- liposomal nanoparticle systems that have been approved for cancer treatment include Abraxane and NBTXR3 Hensify.348 These agents are either actively or passively targeted to enhance anticancer efficiency to reduce side effects. The reduced toxicity results from their ability to preferentially accumulate at the tumor site and limit off-target side effects.

Due to the success of these smart nanoparticles in the clinic and commercial field, enormous efforts continue to explore nanome dicines and developing new smart nanoparticles for clinically disquisitive trials.287 Therefore, the current clinical trials of smart nanoparticles for cancer diagnosis and treatment are also reviewed (Table 3). The list shows a variety of representative nanoparticle systems that have already been active or working in clinical trials. Some of these systems are liposomes, many of which have similar design characteristics to approved liposome systems (e.g., nontargeted, PEGylated, non-PEGylated, or encapsulate of a single drug). For example, VYEXOS/CPX□351 is a combination therapy that encapsulates a synergistic ratio of two anticancer drugs (cytarabine and daunorubicin). There are also many other smart nanoparticle delivery systems in clinical trials for cancer therapy, such as nanoparticle systems that target and stimulate responses. Despite the massive potential of nanoparticles for future cancer diagnostic and treatment, they are still at the relatively preliminary stages of clinical applications. A large number of challenges remain to be addressed to accelerate their further translations16

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X. PERSONALIZED CANCER NANOMEDICINE

A single patient or single-disease unique profile, including clinical genomic and environmental information, as well as the nature of diseases, including their onset, progression, and response to treatment, are all taken into consideration in personalized medicine, a strategy to achieve individualized and improved health care decisions through disease diagnosis, treatment, and monitoring. Personalized medicine is particularly prevalent in personalized oncology, a type of cancer treatment. The main obstacle to achieving successful cancer diagnosis and therapy is the significant intra- and intertumoral heterogeneity. To assess these various individual tumors and cancer cells, as well as therapy characteristics, as thoroughly as possible, versatile and adaptable materials and techniques (such as image-guided nanomedicine and targeted therapies) have been developedTo find cancers that are receptive to nanomedicine treatment, image-guided nanomedicine tracking drug delivery, drug release, and drug efficacy prescreens patients. Target site accumulation and nanomedicine biodistribution appear to be very helpful in tailoring tumor treatment. demonstrated the levels of EPR-mediated tumor accumulation in indium 111-labeled PEGylated liposomes varied considerably amongst tumor types, including breast, lung, and neck cancers. According to clinical case studies, a patient with Kaposi sarcoma responded favorably to Doxil treatment with extremely leaky, enhanced permeability, and retention after radiolabeled PEGylated liposomes accumulated highly efficiently in the patient's primary tumor mass as well as in several secondary and/or metastatic lesions. Personalized nanomedicine based on nab-PTX has also been effectively used to increase response rates in patients with breast cancer in other clinical trials. Additionally, nab-PTX improved survival in pancreatic cancer patients when used in conjunction with gemcitabine. The creation of NP- based individualized cancer therapies transforms the field of cancer treatment by greatly extending and enhancing a patient's life expectancy17

XI. CONCLUSION

People's knowledge of cancer is growing as medical detection and treatment technologies advance, and nanoparticles made of different materials have been created as drug carriers for drug delivery systems that target the membranes of cancer cells. Here, we highlight some recent developments in nano carriers as a cutting-edge delivery and controlled release platform. The surface of nanocarriers can be modified with different receptor-targeting ligands (FR, TfR, HA, etc.) to specifically bind to the receptors on the surface membrane of cancer cells, improving intratumor delivery and active targeting of drugs, especially for drugs that target cancer cells. Among them, nanomaterials comprising biocompatible polymers, liposomes, or inorganic materials coupled with targeting components exhibit significant promise for delivering potent medications to specific locations to improve therapeutic outcomes. Despite significant current investment in targeted nano-delivery system research, numerous issues remain in its clinical use, including biological dispersion, pharmacokinetics, the interaction of the nano-biological interface, and the lack of mass production technology. Furthermore, clinical transformation is severely hampered by the possible toxicity of nanoparticles when administered to patients. The discrepancy between clinical and preclinical results is caused by the continued lack of reliable in vitro and in vivo models to assess actual patient treatment. Therefore, additional assessment in these areas is urgently needed for designing, optimizing, and developing nanoparticles in the preclinical stage. It is important to note that additional positive news regarding the active targeting field of anticancer drug nanomaterials in the future can be brought about by the collaboration of scientists and physicians.

Abbreviations

BBB- blood-brain barrier CPT- camptothecin
DT-A- diphtheria toxin suicide gene
DOX- doxorubicin enhanced permeability and retention PEO-PPO- ethylene oxide-propylene oxide block copolymer C60- fullerenes
GBM- glioblastoma multiforme GCS- glucosylceramide synthase
HER2- anti-human epidermal growth factor receptor 2 MRI- magnetic resonance imaging
MAbs- monoclonal antibodies
MPS- mononuclear phagocyte system MDR- multidrug resistance
PspA- pneumococcal surface protein A

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C32- polybutane diol diacrylate co amino pentanol PCA- poly cyanoacrylate
PLG- poly(D,L glycolide
PEO-PCL- poly epsilon-caprolactone PEG- polyethylene glycol
PLA- poly lactic acid
PLGA- poly lactide-co-glycolide Tween 80- polysorbate 80
SWCNT- single-walled carbon nano-tube SSM- sterically-stabilized micelles
TLR- toll-like receptor

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