Pan-African Journal of Health And Psychological Sciences
ISSN: 3093-4737 | www.pajhps.org
Vol.2, No 1 | Jan-March 2026

Targeted Drug Delivery in Oncology: Recent Advances in Nanoparticle-Based Chemotherapeutics

Author(s): Mudasir Majeed [1]*, Shafkat Hussain Malik[2] , Ruhit Ashraf [3] Imtiyaz Hussain[4], Sumairah Qadir[5]

[1,] B.Pharmacy (Student), School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab

[2,] Assistant Professor, School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab

[3]Associate Professor, S. Lal Singh Memorial College of Pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab

[4,] Assistant Professor, School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab

[5] M. Pharm (Student), School of Pharmacy, Desh Bhagat University, Mandi Gobindgarh, Punjab

Corresponding Email: shafkat2016@gmail.com.

Abstract:

Cancer is one such health concern that has been ravaging and taking away many people worldwide in the last four decades despite the four decades of therapeutic progress. Even though traditional chemotherapy is an ancient treatment option, its use is restricted because of its extreme systemic toxicity, nonspecific ablation of normal tissues, and emergence of multidrug resistance. Such a weakness results in making the treatment non-sustainable in the long term and restricting the survival of patients. In order to overcome such barriers, nanoparticle-based drug delivery systems (NDDS) have emerged as a significant and possibly disruptive technology in cancer therapy. The advantages of NDDS are improved aqueous solubility of the poorly water-soluble compounds, prolongation of circulation half-life, improved pharmacokinetics, and passive and active targeting of tumor tissue. Besides this NDDS can be regulated drug delivery, stimulus responsive and therapeutic specificity in off-target effect to the cost. They might also serve as versatile vectors to co-release chemotherapeutics and biomolecules such as nucleic acids, proteins/immune modulators and offer synergistic and personalized therapy. To enhance compatibility and uptake of NDDS by the device, the engineering of flexibility of the structure and surfaces to enable the device to operate in the heterogeneous tumor microenvironment is also enhanced. Moreover, theranostics has been created to have diagnostic and therapeutic capabilities that allow real time therapy monitoring. This review gives a summary on the design strategies and delivery system, targeting, preclinical and clinical outcomes, and approved nanomedicines and emerging nanocarriers technologies.

Majeed, M. et al. (2026).**Targeted Drug Delivery in Oncology: Recent Advances in Nanoparticle-Based Chemotherapeutics .Pan-African Journal of Health and Psychological Sciences. Vol. 2. No. 1. Jan-March 2026. https://doi.org/10.64261/7mtq4k24**.

ISSN: 3093-4737

Keywords:

Targeted drug delivery, Nanoparticles, Oncology, Chemotherapeutics, Cancer therapy, Nanomedicine.

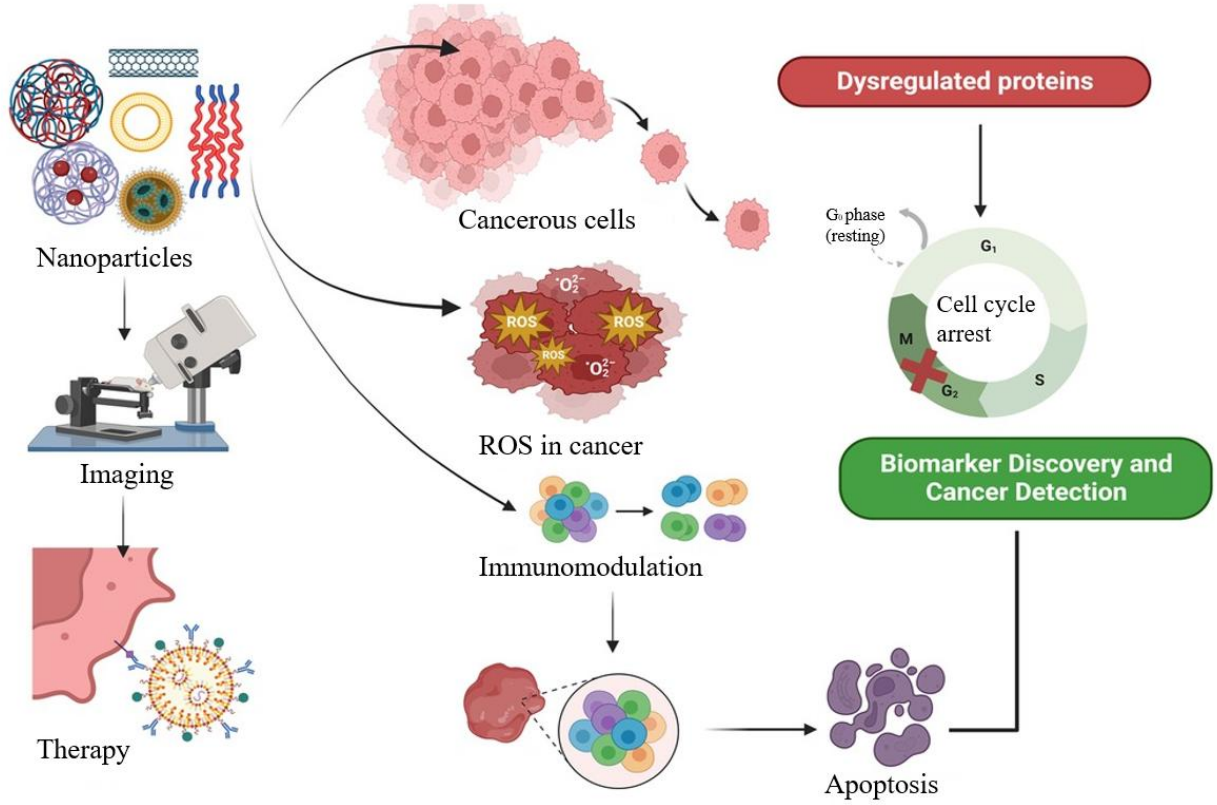

Fig 1*: Graphical overview of nanoparticle-based targeted drug delivery systems in oncology,highlighting enhanced precision, cellular uptake, and therapeutic efficacy.*

1. Introduction:

Cancer is one of the leading threats to the overall health of the world populations, and every year, millions of cases are diagnosed, causing tremendous morbidity and mortality and consuming the healthcare systems globally. Though conventional therapy like surgical excision, radiotherapy, and chemotherapy have

ISSN: 3093-4737

had remarkable contributions in enhancing survival, they have their own disadvantages [1]. In this case, chemotherapy, more specifically, is restrained by a lack of therapeutic selectivity, high rates of systemic toxicity and multidrug resistance developing, all of which diminish its efficacy in the long-term perspective [2]. Chemotherapy drugs administered traditionally are neither specifically targeted but rather delivered indiscriminately and therefore can only destroy healthy tissues but not cancerous cells thus, undermining safety and quality of life of the patient [3]. A groundbreaking alternative to this, nanoparticle-based drug delivery systems (NDDS) circumvents these natural obstacles by taking advantage of the enhanced permeability and retention (EPR) effect of preferential tumour uptake and reduction of systemic exposure to drugs [4]. In addition to passive conjugation, because nanoparticles can undergo functionalisation with aptamers, peptides or antibodies, they can also be functionalised to actively recognise tumour-associated receptors so that enhanced tumour-specific delivery of drugs can occur and on-target interactions can be reduced [5]. Further, electrotransducible surfaces facilitate spatiotemporal drug delivery, programmed to respond to unique tumour microenvironment signals, e.g. acidic pH, hypoxia, redox imbalance, or enzyme overexpression and conduct release into specific regions of action under control. These systems improve the pharmacokinetics, biodistribution of drugs, increase therapeutic indices and reduce toxic side effects [6]. Additionally, NDDS offer the ability of co-delivery of multiple therapeutic agents which would allow synergistic effects like combining chemotherapy with nucleics acids or immunotherapy which beat drug resistance and increase treatment consequences [7]. This is because the incorporation of imaging agents into nanoparticles allows theranostics and both therapeutic and diagnostic functions to be applied in real-time. The same versatility highlights the great clinical potential of nanoparticle-based drug delivery systems (NDDS) in precision oncology [8]. Finally, through simultaneous compliance with principles of personalised medicine, nanoparticle-mediated chemotherapy is positioned to significantly extend therapeutic potential, as well as move forward to remodel the clinical environment of cancer therapy moving forward [9].

2. Principles of Nanoparticle-Based Drug Delivery in Oncology

2.1 The Enhanced Permeability and Retention (EPR) Effect

Solid malignancies have their own characteristic pathophysiological features, the most notable ones being grossly distorted and leaky vasculature and broken lymphatic drainage [10]. These circumstances result in a tumor microenvironment that preferentially selectively concentrates nanoscopic particles-usually the 10-200 nm size range-in malignant tissues instead of diffusely distributed throughout the body. This is called the enhanced permeability and retention (EPR) effect; it is the basis of the principle of passive targeting in nanoparticle-mediated therapeutics [11]. Nanocarriers have

ISSN: 3093-4737

the potential to increase the localization in tumors, increase drug concentration at the pathological site, decrease off-target exposure, and eventually improve the therapy effect by exploiting the EPR effect. It is important to note that the extent of the EPR effect may vary by the tumor type and within a tumor due to heterogeneity, i.e. optimization of the nanoparticle properties such as size, surface charge and stability is required [12]. Through these strategies, the drug can be delivered more efficiently, patient tolerability can be enhanced, and even a combination of passive targeting and active targeting strategies can be implemented to obtain the highest treatment benefit attainable [13].

2.2 Active Targeting

Nanoparticles can also be modified using surface functionalization with targeting ligands to be actively targeted along with passive accumulation mediated by the enhanced permeability and retention (EPR) effect. These ligands, antibodies, peptides, aptamers, or small molecules selectively bind tumour associated receptors that are commonly expressed tumor to great fames like folate receptors, HER2 or epidermal growth factor receptors (EGFR) [14]. Interaction of these receptors promotes higher efficacy of endocytosis and thus enhances intracellular drug delivery and increases therapeutic efficacy of the nanoparticles in malignant cells. Active targeting does not only result in improved accuracy in oncology, but also leads to an enhanced level of therapeutic efficacy, less systemic toxicity, and less adverse adverse off-target effects [15]. Moreover, this strategy can allow the administration of keys to lower effective doses of drugs, can increase the capacity of drugs accumulating at the tumor site, and can expand the possibility of combining therapeutic payloads with imaging modalities [16]. Collectively, energetic nanoparticles targeting is a safer and more efficient translationation route to nanomedicine in clinical practice in cancer therapy and facilitates improved approaches to precision treatments [17].

2.3 Stimuli-Responsive Drug Release

Nanocarriers can be actively configured to pursue directional, stimuli-adaptive delivery of drugs, which in turn enables specific delivery of drugs in the tumor microenvironment to spare normal tissues. There are intrinsic tumor-specific initiators such as low pH, increased redox potential, and overexpression of the proteolytic enzymes which allow a selective activation of drugs in the malignant tissue [18]. At the same time, release is space and time controllable by external stimuli (eg. light, heat, ultrasound, magnetic fields and ionizing radiation), increasing the tumor selectivity and minimizing systemic toxicity. The high-level accuracy enhances treatment effectiveness, patient safety, and reduces the negative consequences. Besides, there is increasing novel designs of nanocarriers with dual or multi-stimuli responsiveness that enables synergistic therapeutic effects [19]. As an example, nanoparticles which can react to pH alterations in addition to enzymatic activity can be delivered

ISSN: 3093-4737

to the target cell with improved ability, and photothermal-responsive delivery vehicles could be triggered remotely on command [20]. Importantly, the combination of these approaches with real-time imaging and theranostic systems will provide clinicians with adaptive treatment options, which are beneficial to build personalized and dynamic cancer treatments in the framework of precision nanomedicine [21].

3. Types of Nanoparticles in Cancer Chemotherapy

3.1 Liposomes

Liposomes are tiny vesicles that are a single or many phospholipid bilayers around an aqueous center with any drug encouraging hydrophilic or hydrophobic enveloping the carryer independently of shape variability and offer a core of vast capacity (local utilizing or avoiding structure). Their structural moldability increases solubility of drugs and at the same time, shields therapeutic agents against premature enzymatic breakdowns and quick system clearance [22]. Liposomes dramatically increase the therapeutic index of conventional chemotherapeutics agents by optimizing pharmacokinetics, prolonging the circulation time, and alleviating offchannel toxicity [23]. Liposome stealth properties can be further enhanced by polyethylene glycol (PEGylation), which decreases Quinoline muscle identification with the reticuloendothelial system and elimination by the reticuloendothelial system. In addition, the tumour targeting and increase in concentration at the bizarre concentrated spots of the disease is facilitated by a surface functionalization with antibodies, peptides, or aptamers [24]. Most importantly, liposomal formulations can be designed to be stimuli-responsive carriers, which detach drugs when subjected to tumour-specific microenvironmental factors, which increases safety and efficacy [25]. The clinical effectiveness of using approved formulations like Doxil®/Caelyx® and Myocet 4.0 confirms their translational directly and demonstrates the suitability of liposomes as a strong nanomedicine-based system in precision oncology and can be used prospectively in combination therapy and theranostic development [26].

3.2 Polymeric Nanoparticles

Nanoparticles made of polymer have received significant attention in oncological therapy studies due to their biocompatibility, stability and variety as effective drug delivery vehicles. Such systems, which are produced using biodegradable polymers like poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG) and polylactic acid (PLA), and natural polymers like chitosan, can deliver controlled and sustained release of drugs, which is advantageous, as it allows pharmacokinetics, increasing therapeutic action, and reducing systemic side effects [27]. Their flexible structure allows the functionalization of the surface with ligands, antibodies, peptides or aptamers which enables them to control targeting of specific cellular receptors that are abnormally expressed on tumor cells in a highly specific fashion [28]. This focused delivery type improves uptake

ISSN: 3093-4737

within the cell, accumulation levels within malignant lesions, and high-level therapeutic payload delivery. Moreover, polymeric nanoparticles may also be designed to be stimuli-responsive and respond to changes in pH, redox gradients, or enzymatic activity under the tumor microenvironment to allow Well-controlled release of therapeutics into a specific region and at a specific time. Notably, these nanocarriers can also be co-loaded with more than one therapeutic mouseinfusion - e.g., chemotherapeutics and nucleic acids - to render combinatorial regimens of treatment. The combination of these properties is that polymeric nanoparticles are highly versatile, tunable, and potent precision oncology tools [29].

3.3 Micelles

Polymeric micelles are type of nanoscale drugs delivery vehicles formed upon self-assembly of amphiphilic block copolymers in solution. These are structurally characterized by a hydrophobic central section capable of taking poorly water-soluble chemotherapeutics, such as paclitaxel, doxorubicin and camptothecin, and is enveloped by a hydrophilic outer section which may be polyethylene glycol (PEG) [30]. This structure gives it colloidal stability and stealth properties as well as longer plasma stay. Due to their small sizes, less than 100nm in diameter, the micelles are efficient in exploiting the increased permeability and retention (EPR) effect to accumulate in tumors [31]. In addition, micellar surface may be functionalised with targeting ligands (antibodies, aptamers, or peptides) and in this way active uptake through tumour specific receptors can take place; this leads to selectivity and a reduction in systemic toxicity. Notably, polymeric micelles can be designed as stimuli-responsive, externally activated to release their payload upon tumour-specific stimuli, e.g. acidic pH, enzymatic activity or temperature changes [32]. This regulated drug delivery, coupled with high loadingplicity, excellent solubility and desirable biodistribution, make polymeric micelles highly adaptable and promising as nanocarriers in precision oncologic therapy and combinatorial regimens [33].

3.4 Albumin-Based Nanoparticles

An example of nanoparticles utilizing endogenous transporter processes to promote site-specific delivery of therapeutic agents in the oncologic environment is referred to as albumin-conjugated nanoparticles, exemplified by the FDA-approved analogue Abraxaneversolutions (nabABPA). These nanostructures enhance levels of solubility, physicochemical stability, and systemic bioavailability significantly through covalent or non-covalent interactions of hydrophobic chemotherapeutic agents and albumin, and result in high concentrations in tumor cells [34]. Albumin interacts with gp60 receptors on monitor the luminal surface of the endothelial cells and with secreted protein acidic and rich in cysteine (SPARC) expressed in the tumor microenvironment, thereby causing a receptor-mediated transcytosis and pretarget nanoparticles to the tissues of the neoplasm [35]. Such a policy therefore eliminates the need to consist of toxic solubilizing agents like

ISSN: 3093-4737

Cremophor EL thereby suppressing both hypersensitivity responses as well as systemic toxicity profiles. Moreover, compared to the traditional drug carriers, albumin-based formulations possess superior pharmacokinetic properties, greater intratumoral delivery, and enjoy superior safety margin. These nanoparticles are very versatile platforms that can be engineered to co-delivery of various therapeutic constructs, integration of imaging intelligences and support of combinatorics regimens [36]. Being multifunctional nanocarriers, they open possibilities to see any combination of chemotherapy with immunotherapy, nucleic acid therapeutics, and other targeted modalities, which will consolidate their position as a potentially useful tool to enhance precision and personalized oncology [37].

3.5 Dendrimers

Dendrimers and hyperbranched polymers Both dendrimers and hyperbranched polymers have provided the unique opportunities of drug delivery due to their specifically controlled structures, nanoscale dimensionality, and controllable surface chemistries. These multifunctional folded architectures provide a wide range of application-specific properties that can be chemically customized to obtain controlled release kinetics, augmented aqueous solubility and enhanced biocompatibility [11]. Thus, such carriers demonstrate significantly high drug loading capacities due to the capacity to bind therapeutic agents to them in terms of host-guest interactions or covalently bonded to surface functionalities. Further, the surface can be targeted with functional ligands--monoclonal antibodies, peptides or aptamers--to specifically accumulate in tumorous tissues through receptor-mediated endocytosis [38]. Image probes can also be conjugated to dendrimers to add theranostic properties, thus allowing therapeutic delivery and diagnostic readout into a single system. Moreover, reaction to particular environmental stimuli, like changes in pH or enzymatic activity inducement, can allow stimulus-controllable dendrimers to release encapsulated drugs to ensure local actuation [39]. The dendrimer-based nanomedicine platforms provide a system with effective and developing potential to achieve precision targeted oncology therapy to optimize therapeutic effects with reduced systemic toxicity [12].

3.6 Metallic and Inorganic Nanoparticles

Nanoparticles made of gold, iron oxide and hafnium oxide have come to the forefront in cancer diagnostics, and therapy because of their unique physicochemical properties [40]. Gold nanoparticles, especially, exhibit strong surface plasmon resonance that has served in numerous optical imaging, photothermal therapy applications and as radiosensitizers to enhance the efficacy of radiotherapy. The most common nanoparticles, which are iron oxide nanoparticles, as clinically approved contrast agents in magnetic resonance imaging provide high-resolution diagnostic information and at the same time can generate localised heating when subjected to alternating magnetic fields that can be exploited to develop magnetic

ISSN: 3093-4737

hyperthermia therapies that are capable of ablating malignant cells selectively [41]. Hafnium oxide nanoparticles are viable radiosensitizers; they increase the sensitivity of tumor tissues to ionizing radiation and at the same time increase the damage in the malignant cells; sparing the adjacent healthy tissues. All of these inorganic and metallic nanomaterials comprise a route between diagnostic and therapeutic methods, providing real-time visualization, increased therapeutic accuracy, and better patient outcomes [42]. Therefore, current research continues to expand on its multifunctional integration by supramolecularly coupling them with chemotherapeutics, immunotherapies, and agel delivery vehicles, which is slowly centralizing their role in modern oncological nanomedicine [43].

3.7 Hybrid Nanoparticles

Hybrid nanoparticles offer an opportunity of multifunctional nanoplatforms of organic and inorganic configurations, as such, preserving a high degree of application in oncologic therapeutics and diagnostics. The organic constituents e.g. lipids, dendrimers, or bio degradable polymers give ideal biocompatibility, stability and effective encapsulation of therapeutic agents whereas the inorganic constituents e.g. gold, silica, or iron oxide provide definite optical, magnetic or structural properties. Such synergistic combination will help to simultaneously incorporate pharmaceutical preparation, diagnostics and treatment methods into one system, which will allow monitor the progress of the treatment in real-time [44]. The flexibility in surface chemistry of such nanoparticles allows the functionalization (PEG, antibody or peptide) and thereby enables active targeting, release control, and minimal off-target toxicity to be achieved. Moreover, it is possible to design stimuli-responsive behavior into hybrid nanoparticles, which emit therapeutic agents in response to particular stimuli like change of pH, hyperthermia, or enzymatic activities [45]. Equipping with common therapeutic and diagnostic assistance, these advanced nanosystems provide great capabilities as potent theranostic agents, which enable significant prospects of precision nanomedicine enhancement, patient-specificated outcomes, and consequently accelerate clinical translation of nanotechnology in the field of oncology [46]. **Fig. 2** Shows types of Nano particles in Chemotherapy.

ISSN: 3093-4737

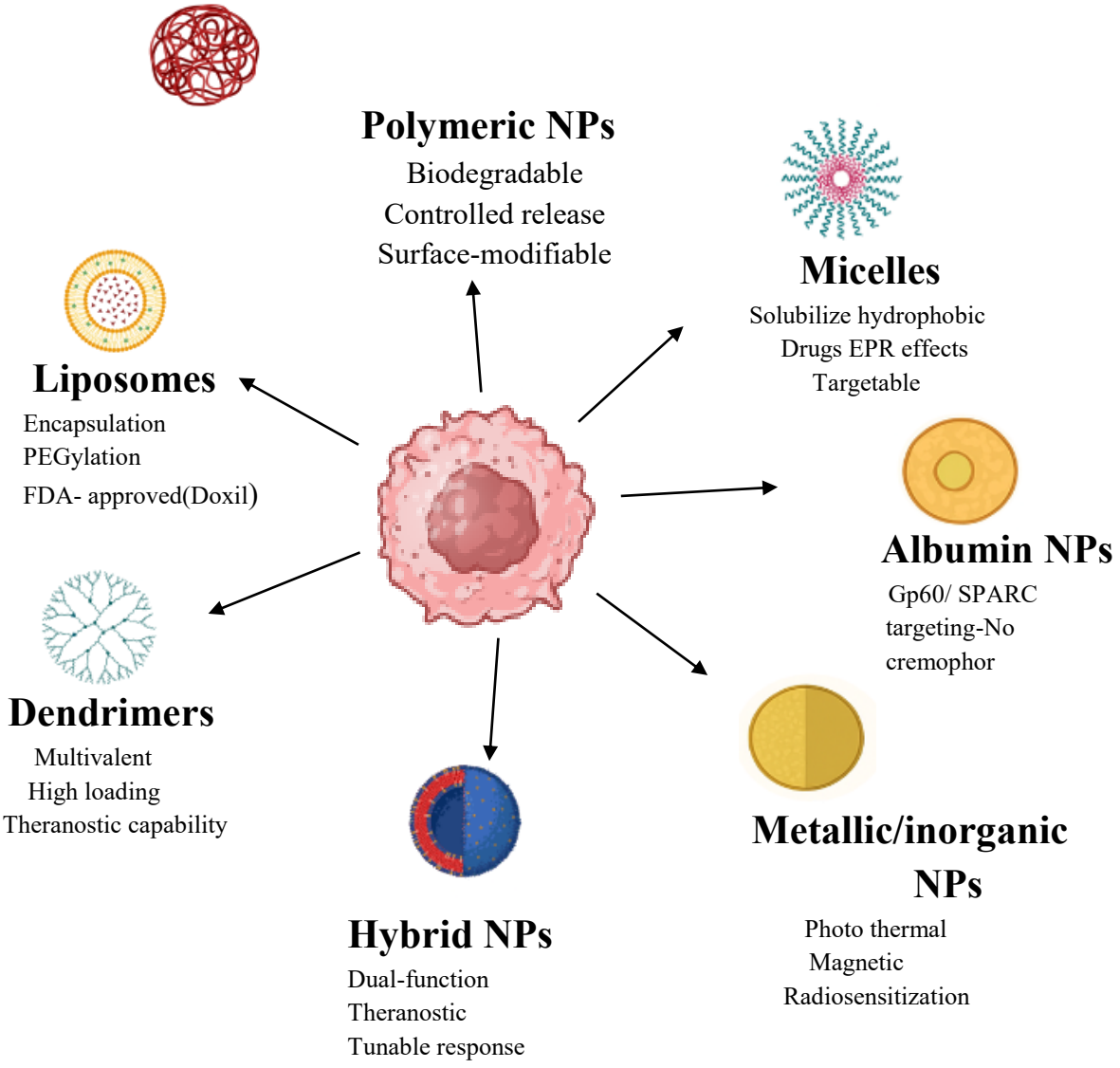

Fig 2: *Types of nanoparticles used in cancer chemotherapy, illustrating diverse nanocarrier platforms and their key therapeutic features.*

ISSN: 3093-4737

4. Clinically Approved Nanoparticle-Based Chemotherapeutics

Several nanoparticle-based chemotherapeutic agents have been progressed to clinical practice, which highlights the clinical translatability of nanomedicine in cancer and other fields [47]. The very first FDA-approved nanomedicine Libosomal doxorubicin (Doxil 2 -/Caelyx) decrease cardiotoxicity without lowering its potent antitumor properties [48]. Likewise, (-)-qvthe paclitaxel/ computer-aided)-qvth albumin (Abraxane) increased solubility and tumour penetration and, through this, prevented the necessity of using harmful solvents like Cremophor EL . Superparamagnetic iron-oxide nanoparticles have been similarly applications in the clinic as MRI contrast agents, thereby leading to better diagnostic possibilities and allowing real-time follow-up of treatment response to therapy [49]. Lipid nanoparticles (LNPs) were even more recently recognized on the global medical stage throughout the COVID-19 pandemic due to their application to vaccine delivery of mRNA, the success of which confirmed their potential in general therapies Lesson [50]. Newer clinically tested nanoparticle design is now being set up upon these successes to use in combination therapeutics, co-deliveries of drugs and biologicals and in theranostics [4]. Not only do these eliminate the lack of safety and efficacy, but they enable nanoparticles to become a flexible component of both precision oncology and contemporary medicine, which subsequently drives future advancements in both therapeutic and diagnostic spheres in addition to personalization of care [39].

Table 1. Clinically Approved Nanoparticle-Based Chemotherapeutics in Oncology

Nanoparticle Formulation	Drug Payload	Indication	Approval Status	Refrences
Doxil®/Caelyx®	Doxorubicin	Ovarian cancer, multiple myeloma, Kaposi's sarcoma	FDA, EMA approved	[51]
Myocet®	Doxorubicin	Metastatic breast cancer	EMA approved	[52]
Abraxane®	Paclitaxel (albumin-bound)	Breast, pancreatic, NSCLC	FDA, EMA approved	[53]

ISSN: 3093-4737

Onivyde®	Irinotecan liposome	Metastatic pancreatic cancer	FDA, EMA approved	[54]
Vyxeos® (CPX-351)	Cytarabine + daunorubicin (liposomal)	Acute myeloid leukemia	FDA, EMA approved	[55]
Genexol-PM®	Paclitaxel (polymeric micelle)	Breast and lung cancers	Approved in South Korea	[56]
Hensify® (NBTXR3)	Hafnium oxide nanoparticles	Radiotherapy enhancer for soft tissue sarcoma	CE Mark (EU)	[57]

5. Recent Advances in Targeted Nanoparticle Systems

5.1 Stimuli-Responsive Nanoparticles

Stimuli-responsive nanoparticles are advanced nanocarriers that have been designed to deliver the therapeutics selectively in the tumour microenvironment (TME). These systems exploit the tumoural conditions that are characteristic to enable targeted therapy. PH-responsive nanoparticles can release their cargo in the acidic environment that is characteristic of the TME, and redox-responsive carriers can be used to gain controlled drug release by using high levels of intracellular glutathione [58]. Enzyme-activatable nanoparticles have the capability to react to the upregulation of tumour-associated proteolytic enzyme and thus promote site-selective activation. In addition, under conditions of increased oxidative stress, ROS-reactive systems are activated, and the delivery of drugs is launched [59]. Taken together, these smart nanocarriers can improve the precision of therapy delivery, reduce systemic toxicity, and improve the effectiveness of cancer therapy by a significant increase [60].

5.2 Ligand-Targeted Nanoparticles

The precise nature of nanocarrier in drug delivery and overall treatment effects is grossly magnified once a targeting ligand is inserted into the nanocarrier by allowing it to be functionalized. By conjugation of nanoparticles with monoclonal antibodies, including trastuzumab, conditional delivery of drugs has been achieved through specific and efficient attachment to overexpressed receptors on the cancerous cell tumor mass or in tumor cell plasma [61]. Likewise, integrin-binding molecules found in short peptides such as the RGD sequence can be target-specifically localized to tumors and enhance targeting of tumor vessels and concentration of drugs in tumor niche areas [62]. Aptamers Aptamers are highly stable high-binding affinity synthetic oligonucleotides also make an active form of

ISSN: 3093-4737

targeting powered to selectively target tumors. These functionalization strategies reduce off-target toxicity, enable increased tumor-specific payload delivery in a one dose administration and maximize the therapeutic responses because of improved cellular internalization, biocompatibility and biomembrane translocation [63]. Additionally, nanoparticles targeted to ligands are under development together with theranostics, allowing therapeutic functionality as well as real time imaging capabilities in a single system [64]. They allow the further evolution of customized nanomedicine, simplify cancer treatment, minimize the risk of recurrence, and help to develop individualized treatment options based on developing patient-specific molecular profiles [65].

5.3 Theranostic Nanoparticles

Theranostic nanoparticles represent a new category of advanced nanosystems, which combine therapeutic as well as diagnostic functionalities into a virtual platform. They are oncologic nanocarriers designed to deliver pharmacologic agents with high specificity to neoplastic tissues and subsequently contain imaging moieties that allow responsible tumor sighting and clarification [66]. Particular producing nanoparticles are designed to allow a type of imaging that can be magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), or fluorescence imaging. These modalities enable real time study of the nanoparticle distribution and tumor accumulation, hence providing clinicians with actionable information on the progress of therapeutic [67]. The dual-response performance allows monitoring the drug delivery, biodistribution, and therapeutic response. The outstanding feature of theranostic nanoparticles is that it is able to increase the therapeutic selectivity of the nanoparticles through its ability to target therapeutic agents on tumor tissues [19]. Shows low systemic toxicity and moderates the unwanted adverse reactions which is the primary therapeutic benefit over traditional treatment regimens. Theranostic systems represent one of the most important developments in the direction of individualized oncology through a combination of therapeutic and diagnostic capabilities [68]. They help create more unique therapeutic regimens that can improve upon the unique biological aspects of every patient. Theranostic nanoparticles have the potential to revolutionize the sphere of precision oncology, in which more studies on these platforms are made over time, revealing a potential unprecedented access to personalized interventional approaches and improved clinical performance [21].

5.4 Combination Therapies

Nanoparticles represent a very versatile system that can simultaneously absorb a variety of therapeutic agents and, therefore, provide synergistic regimens of therapy, which would not be possible with standard drug preparations. An example of such effect is that these carriers can be able to deliver both chemotherapeutic and siRNA or miRNA and, in this way, suppress simultaneously oncogenic signaling pathways

ISSN: 3093-4737

and induce apoptotic effects [69]. In line with this, the combined approach of tumor ablation through chemotherapeutic or immunotherapeutic modalities provokes multiplied anti -tumor immune responses and simultaneously produces a direct reduction in tumor burden in a synergistic manner. This multi-drug paradigm has hence improved both therapeutic efficacy, reduced resistance of drugs, reduced systemic toxicity and allowed company to have controlled drug release at the tumor thereby becoming more effective and personalized oncological therapies [70]. In addition, co-delivery systems in fun of nanoparticle technology allow tuning of the targets of drugs, time or sequential release, and improved pharmacokinetics, providing maximum therapeutic synergy. Such developments highlight the potential of nanoparticles as versatile tools to enable multimodal cancer therapy to become embedded in the process of precision medicine [71].

Table 2. Recent Advances in Smart and Stimuli-Responsive Nanoparticles

Stimuli Type	Mechanism	Example	Potential Clinical Application	Refrences
pH-sensitive	Drug release in acidic TME	pH-labile polymeric micelles	Breast and colon cancer	[72]
Redox-responsive	High glutathione triggers drug release	Disulfide-bonded nanoparticles	Ovarian and lung cancer	[73]
Enzyme-responsive	MMPs degrade protective coating	MMP-sensitive liposomes	Invasive cancers	[74]
ROS-responsive	ROS cleavage activates release	ROS-cleavable polymer NPs	Pancreatic cancer	[75]
External (heat)	Hyperthermia-induced release	Thermosensitive liposomes	Solid tumors	[76]
External (radiation)	Radiation enhances ROS for drug activation	Hafnium oxide NPs	Soft tissue sarcoma	[77]

ISSN: 3093-4737

6. Clinical Translation and Challenges

6.1 Pharmacokinetics and Biodistribution

Nanomedicine The heterogeneity of the enhanced permeability and retention (EPR) effect is a decisive challenge in nanomedicine because it is highly variable not only between different types of tumours but also among people with the same malignancy [78]. Some neoplasms contain vessels with increased permeability thus enabling a significant number of nanoparticle to build up; others have dense stromal, inadequately vascularised, or increased interstitial fluid-filled stroma (which are also associated with limited nanotherapy uptake). Such inter-individual and inter-tumoural variability jeopardizes predictability, reproducibility and overall consistency of therapeutic outcomes within clinical settings [79]. This has prompted an expedient pool of innovative solutions to these problems, including active targeting modalities to utilise ligand-mediated receptor uptake, stimulus-responsive nanoparticle platforms to be developed to release therapeutics in response to certain tumour microenvironmental signatures, and even personalised treatment regimens based on the patient-specific tumour profiles [80]. Furthermore, combining imaging-guided surveillance with flexible dosing regimens has the potential to develop further on biodistribution, increase tumour concentration, and boost therapeutic effect and reduce systemic unwarranted consequences, with nanomedicine evolving toward the overall aim of precision oncology [81].

6.2 Immunogenicity and Safety

Whereas a significant nature of engineered nanoparticles is envisioned as biocompatibility and biodegradability as its fundamental features, there are still high concerns on their safety and persistence in the human body over an extended duration. Unexpected location of nanostructures in vital organs like liver, spleen, and kidneys may initiate toxicological aftermath that sequentially disadvantage organ functions [82]. In addition, some nanomaterials can lead to the immune response or inflammation which can compromise patient care and erode their effectiveness. The clearance kinetics and their extended retention in tissues are also uncertain and increase the chances of chronic sequelae, bioaccumulation and cumulative toxicity after repeated settings [83]. Strong pharmacokinetic, biodistribution, immunogenicity and chronic toxicity profiling is hence essential to the safe clinical translation of nanomedicines. The management of these risks requires use of advanced in vivo models, longitudinal safety surveillance, and predictive toxicology platforms that have the ability to predict the risks even before their clinical implementation. At the same time, regulatory systems should advance to evaluate such unique nanosystems leading to their safe evolution [19]. More current work on designing immuneevasive, biodegradable and has focused on stimulus responsive nanoparticles to reduce side effects and also add

ISSN: 3093-4737

real time imaging modalities of long term safety testing of nanoparticles [84]. Taken together, these approaches will enable developing the next generation and safer nanoparticle systems in oncology and other medical applications without jeopardizing the health of patients [85].

6.3 Large-Scale Manufacturing

The transfer of nanoparticles production in laboratories to large scale industrial manufacturing is not an easy task. The high level of quality control, reproduction and inter-lot consistency is a major issue of concern, as it is essential to maintain the therapeutic efficacy and safety of nanomedicine products. At an industrial level, changes in the particle size, surface chemistry, or colloidal stability on a marginal scale can significantly impact biological performance and threaten clinical performance [86]. This means synthesis protocols need to be optimized to achieve a well-defined particle-size distribution, accurately defined surface properties and physicochemical stability. Moreover, the considerable scale processes have to be both cost-effective and efficient in terms of operations and meet high regulatory requirements [87]. The targeted results normally require the use of sophisticated process engineering, implementation of powerful in-process monitoring systems, and implementation of Good Manufacturing Practices (GMP) all over the entire process of production. The complexity of manufacturing process, in its nature, increases the cost of production and at the same time, slows down the rate of clinical translation and market commercialization [88]. As a result, there is a dire need to overcome such challenges to ensure nanomedicine-related therapeutics are effectively translated out of research laboratories into scalable and effective clinical interventions [89].

6.4 Regulatory Considerations

Obtaining regulatory clearance over the nanoparticle-based therapeutics is a multidimensional and daunting task, and a whole body of evidence is required to support both safety and efficacy [90]. Unlike traditional pharmacological substances, nanoparticles possess unique physicochemical properties that significantly affect their biological relationships and hence the need to have standardized set of characterization [91]. The most paramount parameters, i.e., particle size and morphology, surface charge, stability and drug release kinetics should be strictly evaluated to guarantee reproducibility and quality of the products obtained during one manufacturing batch and the other. The regulators also demand a lot of preclinical and clinical studies to determine biodistribution, pharmacokinetics, immunogenicity, accumulation, and organ-specific properties of the nanotherapeutic [26]. The long-term safety and toxicity tests are also impossible to ignore because the adverse effects can strike without any warning [92]. These cumulative requirements help in minimizing the risk but do not decrease the therapeutic reliability. Good Laboratory Practices (GLP) and Good Manufacturing Practices (GMP) are therefore used to strengthen the regulatory

ISSN: 3093-4737

infrastructure [93]. Therefore, adherence to such high standards will be not merely the key to building trust in nanomedicine, but also the next step in advancing laboratory research to the point of clinical approval to produce benefits to the patients [90].

6.5 Clinical Efficacy

The array of promising preclinical results made by nanoparticles notwithstanding, numerous nanoparticle-based therapeutics have not replicated the same degree of success in the clinic due to the natural complexity and heterogeneity of human malignancies. Unlike in vitro and in animal models, tumors of patients are highly heterogeneous, not only in genomic mutations, proliferative capacity, or stromal cell content [79]. The heterogeneity, in combination with the variability of vascularization and unequalities in the microenvironmental features, imposes a strong effect on the biodistribution and pharmacokinetics of nanoparticles, as a result, reducing therapeutic efficacy. Besides, resistance goals constitute a major obstacle since they come to reality. Up-regulation of drug efflux pumps, rearrangement of intracellular signal-transduction pathways, metabolic reorganization or the expression of evasive defence strategies against immunotherapy can lead to tumor cell resistance, which decreases survival following long-term therapeutic treatments [94]. These constraining factors create a strong difference between the positive results of preclinical studies and the rather imprecise clinical results. The solution to such challenges implies the use of advanced methods, such as personalized nanomedicine, fine-tuning targeting systems, and responsive clinical systems [95]. The element of stringent clinical evaluation is indefinable in ensuring the effectiveness and safety of the translation of nanotherapeutics into clinical practice of oncology [96].

ISSN: 3093-4737

Challenges in Nanomedicine Clinical Translation

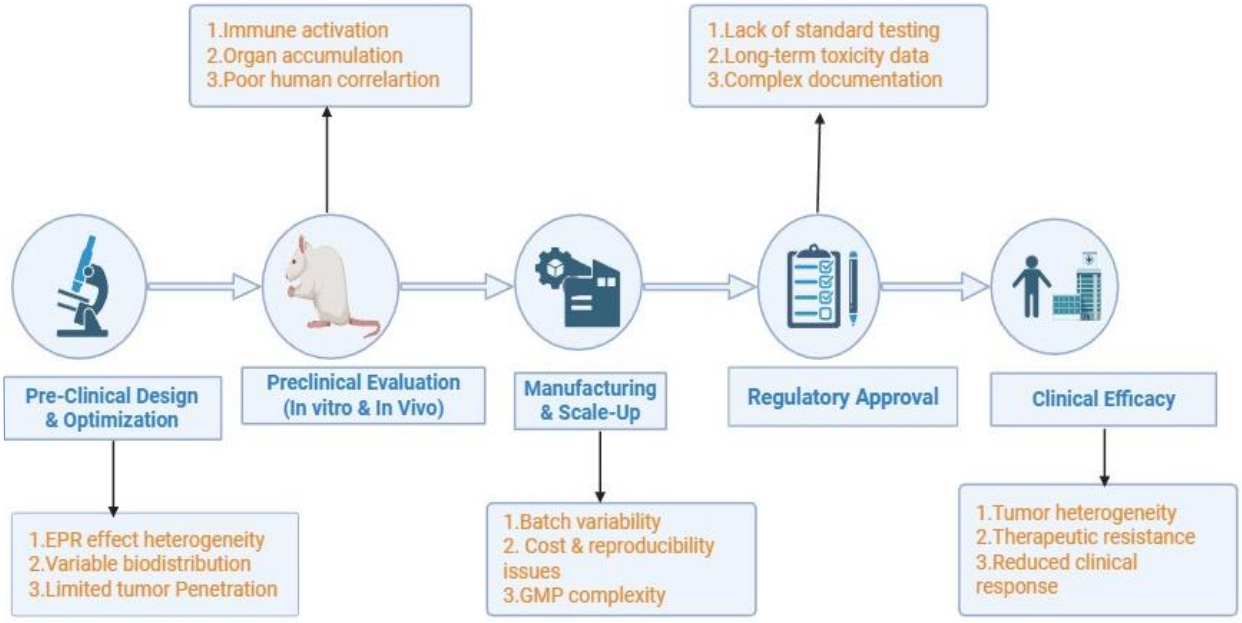

Fig 3 : *Key challenges in the clinical translation of nanomedicine, highlighting barriers related to heterogeneity, manufacturing, immunogenicity, regulation, and clinical efficacy.*

7. Future Perspectives

The future of nanoparticle based chemotherapeutics lies in precision oncology, which entails the development of complex drug delivery systems in accordance with one-on-one tumouric profile of individual patients utilizing the tenets of personalised medicine. The stratification patterns that are under biomarker guidance will enable the separation of patient groups and in so doing, the alignment of the therapeutic interventions with the unique biologic features of a particular malignancy and in the end, the promotion of improved clinical outcomes. Multivalent nanoparticle delivery systems, with the ability to deliver imaging probes, therapeutic agents, and biosensing devices simultaneously will be expected to revolutionize oncologic practice by making treatment much more flexible and dynamically responsive. Advances in artificial intelligence and machine learning are likely to further streamline the design of nanoparticles enabling predictive modelling of tumour nanomaterial nanoparticle interactions. Besides, the next generation biodegradable and immune-evasive materials will tend to improve safety profiles, whereas the combination of nanoparticles with

ISSN: 3093-4737

immunotherapeutic options, such as checkpoint inhibitors or therapeutic vaccines, can significantly enhance anti-tumour immunity.

8. Conclusion

Nanoparticles that deliver targeted drugs to their therapeutic target of interest is a paradigmatic change in oncology with potential to achieve increased drug efficacy, reduced systemic toxicity, and new therapeutic opportunities.The promise of nanomedicine in a clinical practice can be summarized by the authorization of formulations like liposomal doxorubicin and albumin functionalized paclitaxel, thus, highlighting the potential of nanomedicine in clinical practice.The further development of interface systems, stimuli-responsive systems, ligand-directed functionalisation, and theranostic systems which combine diagnostic and therapeutic systems have moved nanoparticles to the centre of stage when it comes to precision medicine. Such innovations allow the easier targeting of tumours, the better pharmacokinetic control of drugs release and eventually patient outcomes.The wide and effective application of nanotherapeutics, however, depends on the overcoming of a row of obstacles. The issues include tumour heterogeneity, inter-patient variability, long-term safety issues, and treatment of large-scale lesions, which remain major obstacles.There is also a necessity to ensure the course of regulatory standards maintenance without affecting the cost-effective clinical translation.Such limitations have to be met with interdisciplinary studies and stringent clinical verification in order to enable the sphere of nanomedicine to continue the development and allow integrating it into new oncological paradigms in the future.

References:

1. Sung, H., et al., *Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries.* CA Cancer J Clin, 2021. **71**(3): p. 209-249.

2. Zafar, A., et al., *Advancements and limitations in traditional anti-cancer therapies: a comprehensive review of surgery, chemotherapy, radiation therapy, and hormonal therapy.* Discov Oncol, 2025. **16**(1): p. 607.

3. Mollaei, M., et al., *Chemotherapeutic drugs: Cell death- and resistance-related signaling pathways. Are they really as smart as the tumor cells?* Transl Oncol, 2021. **14**(5): p. 101056.

4. Yao, Y., et al., *Nanoparticle-Based Drug Delivery in Cancer Therapy and Its Role in Overcoming Drug Resistance.* Front Mol Biosci, 2020. **7**: p. 193.

5. Park, S., et al., *Nanoparticle-Based Delivery Strategies for Combating Drug Resistance in Cancer Therapeutics.* Cancers (Basel), 2025. **17**(16).

6. Singh, R., et al., *Smart nanomaterials for cancer diagnosis and treatment.* Nano Converg, 2022. **9**(1): p. 21.

7. Bishoyi, A.K., et al., *Nanotechnology in leukemia therapy: revolutionizing targeted drug delivery and immune modulation.* Clin Exp Med, 2025. **25**(1): p. 166.

8. Graham, W., et al., *Magnetic Nanoparticles and Drug Delivery Systems for Anti-Cancer Applications: A Review.* Nanomaterials (Basel), 2025. **15**(4).

9. Li, X., et al., *Multifunctional nanoparticle-mediated combining therapy for human diseases.* Signal Transduct Target Ther, 2024. **9**(1): p. 1.

10. Leong, S.P., et al., *Molecular mechanisms of cancer metastasis via the lymphatic versus the blood*

vessels. Clin Exp Metastasis, 2022. **39**(1): p. 159-179.

11. *World Molecular Imaging Congress 2022*. Mol Imaging Biol, 2022. **24**(Suppl 2): p. 63-480.

12. Abdullah, K.M., et al., *Nanomedicine in Cancer Therapeutics: Current Perspectives from Bench to Bedside*. Mol Cancer, 2025. **24**(1): p. 169.

13. Rinoldi, C., et al., *Nanotechnology-Assisted RNA Delivery: From Nucleic Acid Therapeutics to COVID-19 Vaccines*. Small Methods, 2021. **5**(9): p. e2100402.

14. Spada, A. and S. Gerber-Lemaire, *Surface Functionalization of Nanocarriers with Anti-EGFR Ligands for Cancer Active Targeting*. Nanomaterials (Basel), 2025. **15**(3).

15. Gu, X. and T. Minko, *Targeted Nanoparticle-Based Diagnostic and Treatment Options for Pancreatic Cancer*. Cancers (Basel), 2024. **16**(8).

16. Cheng, H., et al., *Advances in targeted therapy for tumor with nanocarriers: A review*. Mater Today Bio, 2025. **31**: p. 101583.

17. Wang, X., et al., *Harnessing glucose metabolism with nanomedicine for cancer treatment*. Theranostics, 2024. **14**(17): p. 6831-6882.

18. Majumder, J. and T. Minko, *Multifunctional and stimuli-responsive nanocarriers for targeted therapeutic delivery*. Expert Opin Drug Deliv, 2021. **18**(2): p. 205-227.

19. Wang, B., et al., *Current advance of nanotechnology in diagnosis and treatment for malignant tumors*. Signal Transduct Target Ther, 2024. **9**(1): p. 200.

20. Sun, Y. and E. Davis, *Nanoplatforms for Targeted Stimuli-Responsive Drug Delivery: A Review of Platform Materials and Stimuli-Responsive Release and Targeting Mechanisms*. Nanomaterials (Basel), 2021. **11**(3).

21. Şerban, M., C. Toader, and R.A. Covache-Busuioc, *CRISPR and Artificial Intelligence in Neuroregeneration: Closed-Loop Strategies for Precision Medicine, Spinal Cord Repair, and Adaptive Neuro-Oncology*. Int J Mol Sci, 2025. **26**(19).

22. Lin, L.L., et al., *Surface-Enhanced Raman Spectroscopy for Biomedical Applications: Recent Advances and Future Challenges*. ACS Appl Mater Interfaces, 2025. **17**(11): p. 16287-16379.

23. Izadiyan, Z., et al., *Advancements in Liposomal Nanomedicines: Innovative Formulations, Therapeutic Applications, and Future Directions in Precision Medicine*. Int J Nanomedicine, 2025. **20**: p. 1213-1262.

24. Koshmanova, A.A., et al., *Aptamer's Structure Optimization for Better Diagnosis and Treatment of Glial Tumors*. Cancers (Basel), 2024. **16**(23).

25. Garello, F., et al., *Micro/Nanosystems for Magnetic Targeted Delivery of Bioagents*. Pharmaceutics, 2022. **14**(6).

26. *ISEV2025 Abstract Book*. J Extracell Vesicles, 2025. **14**(S1): p. e70157.

27. Abdulsalam, L., et al., *Advanced Biocompatible and Biodegradable Polymers: A Review of Functionalization, Smart Systems, and Sustainable Applications*. Polymers (Basel), 2025. **17**(21).

28. Ramaraj, P.K., et al., *Covalent Attachment of Functional Proteins to Microfiber Surfaces via a General Strategy for Site-Selective Tetrazine Ligation*. ACS Appl Mater Interfaces, 2024. **16**(46): p. 63195-63206.

29. Beach, M.A., et al., *Polymeric Nanoparticles for Drug Delivery*. Chem Rev, 2024. **124**(9): p. 5505-5616.

30. Liu, H., et al., *Structural Determinants of Stimuli-Responsiveness in Amphiphilic Macromolecular Nano-assemblies.* Prog Polym Sci, 2024. **148**.

31. Atanase, L.I., *Micellar Drug Delivery Systems Based on Natural Biopolymers.* Polymers (Basel), 2021. **13**(3).

32. Adams, C.A., et al., *Shifts in avian migration phenologies do not compensate for changes to conditions en route in spring and fall.* Ecology, 2025. **106**(5): p. e70110.

33. Turnovská, A. and T. Etrych, *Polymeric micelles in advanced photodynamic therapy: Design, delivery and translational prospects.* Int J Pharm X, 2025. **10**: p. 100439.

34. Jarak, I., et al., *The Many Faces of Cyclodextrins within Self-Assembling Polymer Nanovehicles: From Inclusion Complexes to Valuable Structural and Functional Elements.* Int J Mol Sci, 2024. **25**(17).

35. Hu, H., et al., *Deciphering albumin-directed drug delivery by imaging.* Adv Drug Deliv Rev, 2022. **185**: p. 114237.

36. Dal-Fabbro, R., et al., *Recent Advances in Injectable Hydrogel Biotherapeutics for Regenerative Dental Medicine.* Macromol Biosci, 2025. **25**(10): p. e00096.

37. Azimizonuzi, H., et al., *A state-of-the-art review of the recent advances of theranostic liposome hybrid nanoparticles in cancer treatment and diagnosis.* Cancer Cell Int, 2025. **25**(1): p. 26.

38. Yan, Y., et al., *Advances in RNA-based cancer therapeutics: pre-clinical and clinical implications.* Mol Cancer, 2025. **24**(1): p. 251.

39. Zeng, J., et al., *Engineered GLP-1R-targeting nanoplatforms: multimodal therapeutics in human diseases.* J Nanobiotechnology, 2025. **23**(1): p. 682.

40. Ke, W., et al., *Trends and patterns in cancer nanotechnology research: A survey of NCI's caNanoLab and nanotechnology characterization laboratory.* Adv Drug Deliv Rev, 2022. **191**: p. 114591.

41. Singh, P., et al., *Advanced Nanomaterials for Cancer Therapy: Gold, Silver, and Iron Oxide Nanoparticles in Oncological Applications.* Adv Healthc Mater, 2025. **14**(4): p. e2403059.p

42. Chehelgerdi, M., et al., *Progressing nanotechnology to improve targeted cancer treatment: overcoming hurdles in its clinical implementation.* Mol Cancer, 2023. **22**(1): p. 169.

43. Li, M., et al., *Advancements in Tumor-Targeted Nanoparticles: Design Strategies and Multifunctional* Therapeutic *Approaches.* Nanomaterials (Basel), 2025. **15**(16).

44. Joseph, T.M., et al., *Nanoparticles: Taking a Unique Position in Medicine.* Nanomaterials (Basel), 2023. **13**(3).

45. O'Hagan, M.P., et al., *Photocleavable Ortho-Nitrobenzyl-Protected DNA Architectures and Their Applications.* Chem Rev, 2023. **123**(10): p. 6839-6887.

46. Andoh, V., et al., *The Advancing Role of Nanocomposites in Cancer Diagnosis and Treatment.* Int J Nanomedicine, 2024. **19**: p. 6099-6126.

47. Liu, Y., et al., *Recent advances in the bench-to-bedside translation of cancer nanomedicines.* Acta Pharm Sin B, 2025. **15**(1): p. 97-122.

48. Sarkar, M., et al., *Pharmacokinetic behaviors of soft nanoparticulate formulations of chemotherapeutics.* Wiley Interdiscip Rev Nanomed Nanobiotechnol, 2023. **15**(2): p. e1846.

49. Murar, M., L. Albertazzi, and S. Pujals, *Advanced Optical Imaging-Guided Nanotheranostics*

towards Personalized Cancer Drug Delivery. Nanomaterials (Basel), 2022. **12**(3).

50. Wilson, B. and K.M. Geetha, *Lipid nanoparticles in the development of mRNA vaccines for COVID-19.* J Drug Deliv Sci Technol, 2022. **74**: p. 103553.

51. Fulton, M.D. and W. Najahi-Missaoui, *Liposomes in Cancer Therapy: How Did We Start and Where Are We Now.* Int J Mol Sci, 2023. **24**(7).

52. Taléns-Visconti, R., et al., *Nanoliposomes in Cancer Therapy: Marketed Products and Current Clinical Trials.* Int J Mol Sci, 2022. **23**(8).

53. Okunaka, M., et al., *Retrospective cohort study of nanoparticle albumin-bound paclitaxel plus ramucirumab versus paclitaxel plus ramucirumab as second-line treatment in patients with advanced gastric cancer.* BMC Cancer, 2020. **20**(1): p. 1111.

54. Liu, P., G. Chen, and J. Zhang, *A Review of Liposomes as a Drug Delivery System: Current Status of Approved Products, Regulatory Environments, and Future Perspectives.* Molecules, 2022. **27**(4).p

55. Pagano, L., et al., *The Role of CPX-351 in the Acute Myeloid Leukemia Treatment Landscape: Mechanism of Action, Efficacy, and Safety.* Drugs, 2025. **85**(7): p. 855-866.

56. Jeong, H., et al., *Gemcitabine and Cisplatin Plus Polymeric Micellar Paclitaxel and Survival in Advanced Biliary Tract Cancer: A Randomized Clinical Trial.* JAMA Netw Open, 2025. **8**(10): p. e2534560.

57. Zarić, M., et al., *The Three Musketeers in Cancer Therapy: Pharmacokinetics, Pharmacodynamics and Personalised Approach.* J Pers Med, 2025. **15**(11).

58. Wang, Y., et al., *Smart Nanoplatforms Responding to the Tumor Microenvironment for Precise Drug Delivery in Cancer Therapy.* Int J Nanomedicine, 2024. **19**: p. 6253-6277.

59. Sharma, A., et al., *Theranostic Fluorescent Probes.* Chem Rev, 2024. **124**(5): p. 2699-2804.

60. Keerikkadu, M., et al., *An Overview on Lipid Nanocapsules: Exploring the Role in Precision Cancer Treatment and Lymphatic Drug Distribution.* Adv Pharm Bull, 2025. **15**(2): p. 248-267.

61. Sharma, G., et al., *Impact of pathological factors on survival in patients with upper tract urothelial carcinoma: a systematic review and meta-analysis.* Int Braz J Urol, 2022. **48**(3): p. 406-455.

62. Wang, X., et al., *From Mechanoelectric Conversion to Tissue Regeneration: Translational Progress in Piezoelectric Materials.* Adv Mater, 2025. **37**(33): p. e2417564.

63. Sun, L., et al., *Smart nanoparticles for cancer therapy.* Signal Transduct Target Ther, 2023. **8**(1): p. 418.

64. Aghanwa, C.I., et al., *Radiotherapy-chemodynamic cancer therapy using bismuth-based nanoparticles: a synergistic approach for enhanced cancer treatment.* RSC Adv, 2025. **15**(40): p. 32956-32994.

65. Tufail, M., et al., *Predictive, preventive, and personalized medicine in breast cancer: targeting the PI3K pathway.* J Transl Med, 2024. **22**(1): p. 15.

66. Ahmed, A.A.A., et al., *Interfacing with the Brain: How Nanotechnology Can Contribute.* ACS Nano, 2025. **19**(11): p. 10630-10717.

67. Abhinav, V., et al., *Advancements in Wearable and Implantable BioMEMS Devices: Transforming Healthcare Through Technology.* Micromachines (Basel), 2025. **16**(5).

68. Guo, Z.H., et al., *Role of Nanomedicine-Based Therapeutics in the Treatment of CNS Disorders.* Molecules, 2023. **28**(3).

69. Zamanian, M.Y., et al., *Curcumin and Resveratrol as Dual Modulators of the STAT3 Pathway in Lung Cancer: A Comprehensive Review.* Food Sci Nutr, 2025. **13**(9): p. e70829.

70. Longo, J.F., S.N. Brosius, and S.L. Carroll, *Defining Gene Functions in Tumorigenesis by Ex vivo Ablation of Floxed Alleles in Malignant Peripheral Nerve Sheath Tumor Cells.* J Vis Exp, 2021(174).

71. Prakashan, D., et al., *Sustainable Nanotechnology and Artificial Intelligence to Empower Image-Guided Therapy for Precision Healthcare.* BME Front, 2025. **6**: p. 0150.

72. Zhu, R., et al., *Nano drug delivery systems improve metastatic breast cancer therapy.* Med Rev (2021), 2021. **1**(2): p. 244-274.

73. Yu, Z., et al., *Smart Polymeric Nanoparticles in Cancer Immunotherapy.* Pharmaceutics, 2023. **15**(3).

74. Telkoparan-Akillilar, P., et al., *Integration of MicroRNAs with nanomedicine: tumor targeting and therapeutic approaches.* Front Cell Dev Biol, 2025. **13**: p. 1569101.

75. Fu, X. and X. Hu, *Ultrasound-Controlled Prodrug Activation: Emerging Strategies in Polymer Mechanochemistry and Sonodynamic Therapy.* ACS Appl Bio Mater, 2024. **7**(12): p. 8040-8058.

76. Yaramiri, A., et al., *A Comprehensive Review of Smart Thermosensitive Nanocarriers for Precision Cancer Therapy.* Int J Mol Sci, 2025. **26**(15).

77. Wang, J., et al., *Advances of hafnium based nanomaterials for cancer theranostics.* Front Chem, 2023. **11**: p. 1283924.

78. Wu, J., *The Enhanced Permeability and Retention (EPR) Effect: The Significance of the Concept and Methods to Enhance Its Application.* J Pers Med, 2021. **11**(8).

79. Vanbilloen, W.J.F., et al., *Nanoparticle Strategies to Improve the Delivery of Anticancer Drugs across the Blood-Brain Barrier to Treat Brain Tumors.* Pharmaceutics, 2023. **15**(7).

80. Zhang, H., et al., *Inflammation-modulating polymeric nanoparticles: design strategies, mechanisms, and therapeutic applications.* EBioMedicine, 2025. **118**: p. 105837.

81. Cheng, Z., et al., *Lipid-based nanosystems: the next generation of cancer immune therapy.* J Hematol Oncol, 2024. **17**(1): p. 53.

82. Ma, X., et al., *Nanotechnology in healthcare, and its safety and environmental risks.* J Nanobiotechnology, 2024. **22**(1): p. 715.

83. Hardefeldt, L., et al., *Antimicrobial prescribing guidelines for horses in Australia.* Aust Vet J, 2025. **103**(12): p. 781-889.

84. Parvin, N., S.W. Joo, and T.K. Mandal, *Biodegradable and Stimuli-Responsive Nanomaterials for Targeted Drug Delivery in Autoimmune Diseases.* J Funct Biomater, 2025. **16**(1).

85. Aboul-Ella, H., et al., *Monoclonal antibodies: From magic bullet to precision weapon.* Mol Biomed, 2024. **5**(1): p. 47.

86. Bas, T.G., *Innovative Formulation Strategies for Biosimilars: Trends Focused on Buffer-Free Systems, Safety, Regulatory Alignment, and Intellectual Property Challenges.* Pharmaceuticals (Basel), 2025. **18**(6).

87. Desai, N., et al., *Nanoparticle Therapeutics in Clinical Perspective: Classification, Marketed Products, and Regulatory Landscape.* Small, 2025. **21**(29): p. e2502315.

ISSN: 3093-4737

88. Correa, S., et al., *Translational Applications of Hydrogels.* Chem Rev, 2021. **121**(18): p. 11385-11457.

89. Đorđević, S., et al., *Current hurdles to the translation of nanomedicines from bench to the clinic.* Drug Deliv Transl Res, 2022. **12**(3): p. 500-525.

90. Rodríguez-Gómez, F.D., et al., *Regulatory pathways and guidelines for nanotechnology-enabled health products: a comparative review of EU and US frameworks.* Front Med (Lausanne), 2025. **12**: p. 1544393.

91. Duman, H., et al., *Gold Nanoparticles: Multifunctional Properties, Synthesis, and Future Prospects.* Nanomaterials (Basel), 2024. **14**(22).

92. Wimmelbücker, L. and A. Kar, *A history of thalidomide in India.* Med Hist, 2023. **67**(3): p. 228-246.

93. Dhaiban, S., et al., *Clinical translation of human iPSC technologies: advances, safety concerns, and future directions.* Front Cell Dev Biol, 2025. **13**: p. 1627149.

94. Nicolaou, N., et al., *Emerging insights into the immunosuppressive tumor microenvironment and its implications for glioblastoma immunotherapy.* Front Immunol, 2025. **16**: p. 1665742.

95. Gangadhar, L., et al., *Recent Trends in Biomedical Applications of Cu(2)MX(4)-Based Nanocomposites: An Updated Review.* Int J Nanomedicine, 2025. **20**: p. 11895-11939.96.

Parodi, A., et al., *Anticancer Nanotherapeutics in Clinical Trials: The Work behind Clinical Translation of Nanomedicine.* Int J Mol Sci, 2022. **23**(21).