ISBN: 978-81-985724-3-1

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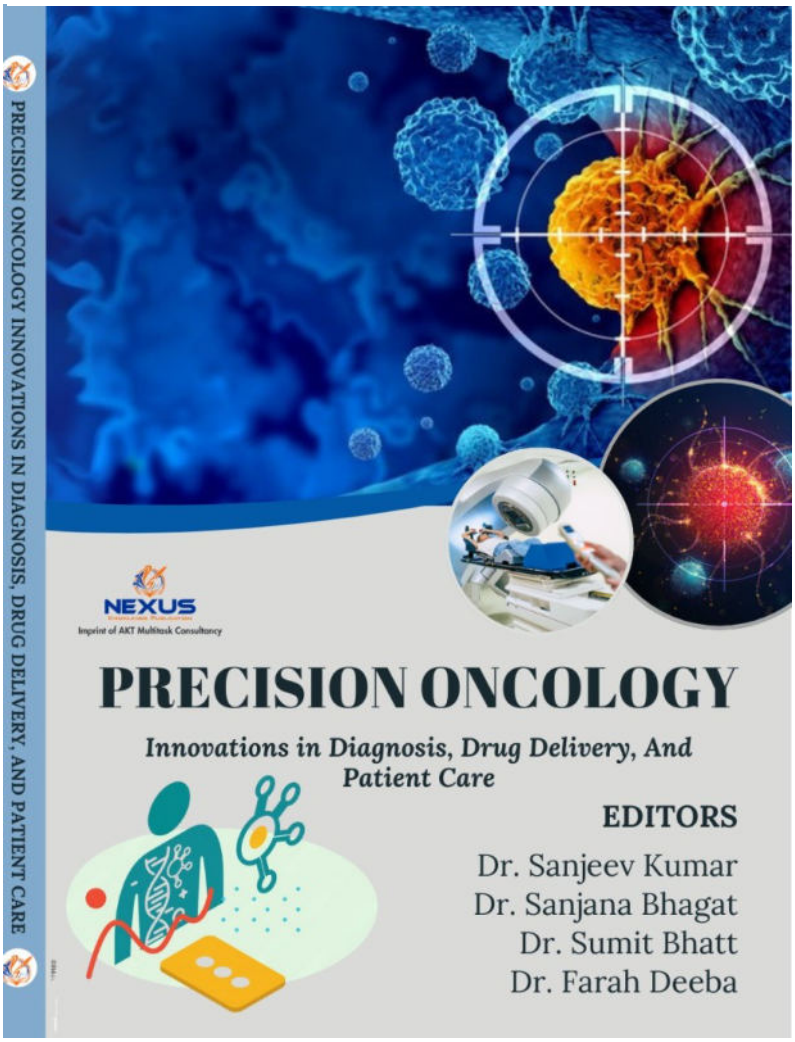
Precision Oncology: Innovations in Diagnosis, Drug Delivery, And Patient Care



Chapter- 5

PRECISION DRUG DELIVERY SYSTEMS

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Published By – Nexus Knowledge Publication

(Imprint of AKT Multitask Consultancy)

Bilaspur, Chhattisgarh, India, 495006

www.aktmultitask.com

DOI 10.5281/zenodo.17199086

ISBN: 978-81-985724-3-1

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PRECISION DRUG DELIVERY SYSTEMS

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Site-specific drug delivery technologies are the modern therapeutic approaches aimed at delivering drugs to the diseased tissues or cells in a direct manner to increase treatment efficacy with the minimum harm to the healthy tissues. Contrary to the traditional systemic therapies where the drug is given to the entire body, and may result in severe toxicity in the patient, these precision delivery mechanisms can deliver more drug to the target site, enhancing the therapeutic index and patient outcome. The major methods are passive targeting where the enhanced permeability and retention (EPR) effect in tumors are exploited, active targeting, in which ligands or antibodies are selectively bound to diseased cells, and the stimuli-responsive system, which involves an exit of drugs in response to a particular internal or external stimulus such as pH, enzymes, heat, or light. In particular, these strategies are crucial in oncology, when the exact targeting minimizes collateral damage and increases anticancer effects.

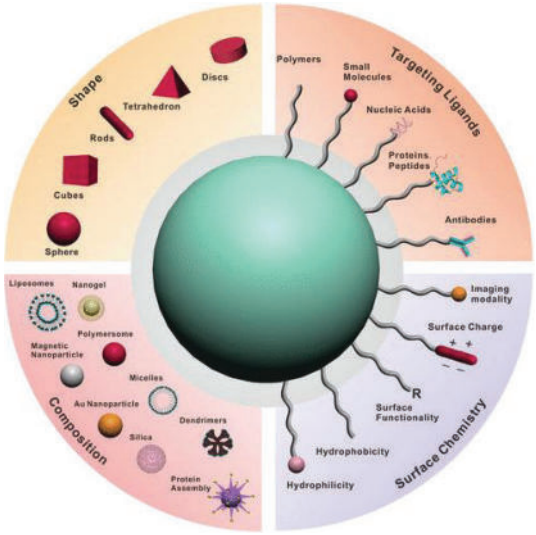

Figure 1: Precision Drug Delivery Systems

Source: (https://journals.physiology.org/doi/full/10.1152/physrev.00015.2016)

Modern delivery systems are liposomes, nanoparticles, and polymers. Liposomes are globular vesicles with the capacity to entrap both hydrophilic and hydrophobic medications, which provide biocompatibility, degradation resistance and specific local delivery by modifying its surface such as PEGylated preparations such as Doxil. Nanoparticles (lipid-based, polymeric, and metallic) offer targeted drug delivery, enhanced biodistribution, and the capacity to traverse biological barriers, and surface functionalization has allowed passive and active targeting. Polymer-based systems such as PLGA nanoparticles and dendrimers enable sustained or stimuli-responsive drug delivery, improved pharmacokinetics and targeted delivery to be

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customized, so they offer versatile vectors to carry chemotherapeutics, nucleic acids and imaging agents.

Precision delivery is further enhanced by ligand-targeted therapies and controlled release platforms in that molecular recognition is coupled with temporal control of drug release. Ligand-targeted systems e.g. antibody-drug conjugate or folate receptor targeted nanoparticles are selective, which selectively binds receptors overexpressed on diseased cells, promoting intracellular drug delivery and reducing systemic toxicity. Diffusion-based and degradation-based carriers, and stimuli-responsive platforms, known as controlled release systems, are systems that retain therapeutic levels of drug over time or in response to biological or external stimuli, leading to less frequent dosing, and enhanced patient compliance.

In general, site-specific drug delivery has a beneficial effect on therapy outcomes, minimizing toxicity, maximizing therapy efficacy, and increasing patient adherence. Targeted systems restrict exposure of the drug to normal tissues and amplify cytotoxic responses on cancerous cells and overcome evasion of the drug through drug efflux pumps. The sustained and stimuli-responsive release guarantees the optimal drug concentrations in the disease microenvironment with increased anticancer activity and reduced adverse effects. These technologies are one of the largest developments in precision medicine, which has created safer and more efficient treatments in a variety of diseases, specifically in cancer therapy.

5.1. OVERVIEW OF SITE-SPECIFIC DRUG DELIVERY TECHNOLOGIES

Site-specific drug delivery technologies are designed to deliver therapeutic agents to diseased cells or tissues, a significant improvement over the traditional systemic therapies. Conventional treatments, including chemotherapy, tend to spread drugs all over the body including normal and cancerous cells. Such unspecific exposure may lead to serious toxicity, restrict the maximum tolerable dose and decrease the total efficacy of treatment. Contrary to this, site-specific delivery systems focus the therapeutic agents on the target site, improving drug efficacy and sparing normal tissues, which increases the therapeutic index and minimizes adverse effects.

These accuracy delivery plans are specifically revolutionary in oncology, where the selective targeting of the tumor cells plays a key role. Site-specific systems allow the accumulation of drugs in tumor tissues and reduced systemic exposure by favoring ligand binding, stimuli-responsive release or molecular recognition of the site. Such specific mode of action leads not

only to increased potency of treatment, but also to higher dosing and combination therapies that would otherwise be too toxic. Altogether, site-specific drug delivery improves patient outcomes, minimizes the complications associated with treatment, and is one of the foundations of contemporary precision medicine in cancer therapy.

- **Key Approaches Include:**
  - **Passive Targeting:** Passive targeting takes advantage of the natural physiology of diseased tissues. Enhanced permeability and retention (EPR) effect is one of the most extensively studied phenomena utilized in the cancer therapy. Tumor vasculature is characterized by irregularity and hyper porosity with big fenestrations enabling nanoparticles and macromolecular drugs to selectively localize into tumor tissues. Besides, tumors are characterised by the poor lymphatic drainage which further enhances retention of therapeutic agents in tumor microenvironment. Passive targeting does not need a particular molecular recognition, and in most cases, size, shape and physicochemical properties of the drug carriers can determine selective accumulation in the diseased site.
  - **Active Targeting:** Active targeting refers to the active use of molecular recognition factors, e.g., ligands, antibodies, aptamers or peptides, designed to specifically bind receptors or antigens that are overexpressed by diseased cells. This will allow delivery of a drug selectively, avoiding normal cells and minimising systemic toxicity. An example is that monoclonal antibodies that have been conjugated to chemotherapeutic agents have the capability of specifically binding tumor-associated antigens to enable internalization and release of the drug specifically in cancer cells. Nanoparticle-based carriers can be used in conjunction with active targeting to increase further stability, circulation time, and accumulation of the drug at its disease location.
  - **Stimuli-Responsive Systems:** The stimuli-responsive drug delivery systems are intended to release their therapeutic cargo based on a certain internal or external stimuli. Internal stimuli are the changes in pH, enzymatic activity or redox potential that are tumor microenvironmental. As an example, pH-sensitive nanoparticles can be engineered to release the drug selectively in the pH-acidic tumor tissues and be stable at normal body physiological pH. Localized drug release may also be induced by external stimuli, which may include heat, light, ultrasound, or magnetic fields, which offers both temporal and spatial control of therapy. These systems increase the

therapeutic effect, reduce off-target effects, and provide solutions to overcome the drug resistance mechanisms.

- **Clinical Relevance:** There are great clinical implications of site-specific drug delivery systems. These technologies enhance therapeutic index by delivering therapeutic agents to the disease site so that higher effective dose levels can be achieved at the minimal adverse effects. They are also able to deal with issues like deficiencies in multidrug resistance by enhancing intracellular levels of accumulation and avoiding efflux pathways. In general, site-specific drug delivery is an urgent breakthrough in precision medicine with more effective and safer treatment approaches in a variety of conditions, especially in cancer.

5.2. LIPOSOMES, NANOPARTICLES, AND POLYMER-BASED SYSTEMS

Advanced drug delivery platforms are liposomes, nanoparticles and polymer-based systems developed to improve the level of therapeutic efficacy and precision. Liposomes are vesicles consisting of phospholipid bi-layers that surround hydrophilic or hydrophobic drugs to provide biocompatibility, degradation protection, and functionalization, such as PEGylated Doxil. Lipid, polymeric, and metallic nanoparticles can be used to provide controlled drug release, enhanced biodistribution, and traversing of biological barriers; surface modifications can be used to passively or actively target nanoparticles as observed in the case of mRNA vaccine delivery. Polymer-based systems, e.g., PLGA nanoparticles and dendrimers, offer sustained or stimuli-responsive release, improved pharmacokinetic properties, and targeted customization, and are therefore flexible carriers of chemotherapeutics, nucleic acids and imaging agents.

Liposomes

Liposomes are vesicles that are spherical in shape, made of one or more bilayers of the phospholipid which surround an aqueous core, to create a structure that resembles natural cell membranes. This distinctive architecture enables multi-purpose encapsulation of therapeutic agents: hydrophilic drugs may be solubilized in the aqueous interior, whereas hydrophobic drugs may become a part of the lipid bi-layer. The dual ability allows the delivery of a broad spectrum of drugs, both small molecule and large biomolecule, such as nucleic acids and proteins.

Liposomes have a number of pharmacological benefits: they are highly biocompatible so drugs are not lost due to enzymatic degradation or premature clearance to increase bioavailability and

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circulation time. Furthermore, they can be loaded with other molecules, including ligands, antibodies or polyethylene glycol (PEG) to enable targeted delivery to a given tissue or tumor cell and to minimize reticuloendothelial system (RES) recognition.

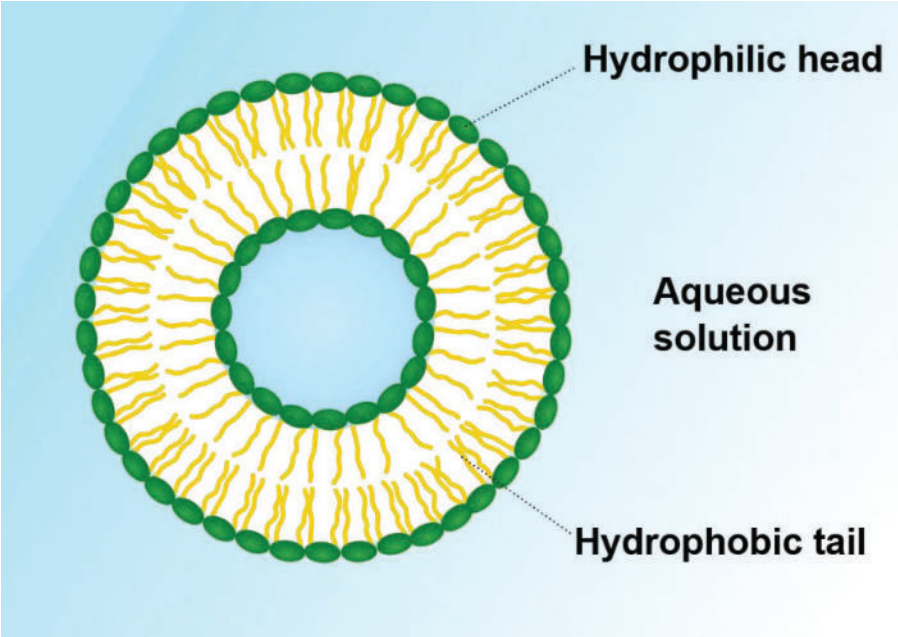

Figure 2: Liposomes

Sources: (https://en.wikipedia.org/wiki/Liposome)

One example of this is the PEGylated liposomal doxorubicin, Doxil, which is a clinically relevant example. This development shows lower cardiotoxicity with conventional doxorubicin, which retains and or improves therapeutic value. Doxil emphasizes the opportunities of liposomes to offer a controlled pharmacokinetics, reduce off-target effects, and prevent patient outcomes in the field of oncology. Moreover, liposomes have been discussed in delivering anti-inflammatory drugs, antibiotics, and gene therapies, demonstrating how wide they can be used.

- ***Nanoparticles (NPs)***

Nanoparticles are solid colloidal particles that are 1-100 nanometers old, and which are intended to wrap, adsorb or conjugate drugs to achieve control over drug release, biodistribution, as well as, pharmacokinetics. NPs can be divided into polymeric, metallic, and lipid-based nanoparticles and are specific in their characteristics according to their therapeutic purposes.

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As an example, lipid nanoparticles (LNPs) have become a leading option in the delivery of mRNA vaccines, such as COVID-19 vaccines. The lipid matrix shields the delicate mRNA against enzymatic destruction, enables cellular intake and allows evasion of the endosome, all of which underscores the clinical viability of nanoparticle-mediated delivery. Another advantage of nanoparticles is that the drug loading is high, an increase or slow release, and that nanoparticles bypass biological barriers, including the blood brain barrier that is vital in treating neurological diseases.

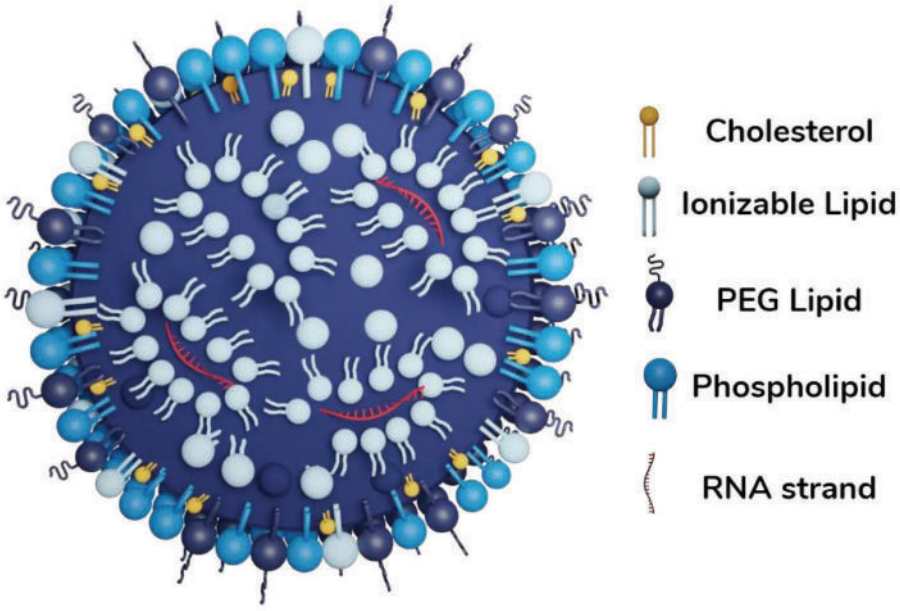

Figure 3: Lipid Nanoparticles

Source: (https://insidetx.com/review/complete-guide-to-understanding-lipid-nanoparticles/)

One of the strategies of nanoparticles targeting is surface modification. Passive targeting takes advantage of the increased permeability and retention (EPR) phenomenon in tumors where leaky vasculature permits accumulation to favorably occur. Active targeting entails the conjugation of nanoparticles to antibodies, peptides, or small molecules to target a cellular surface receptor to enhance specificity of delivery and reduce off-target toxicity.

- ***Polymer-Based Systems***

Medical drug delivery systems are polymer-based systems that employ biocompatible and biodegradable polymers (PLGA; poly lactic-co-glycolic acid) and PEGylated polymers and dendrimers to entrap or conjugate therapeutics. The systems allow sustained or controlled

release, enhance the pharmacokinetics through increased circulation time and decrease immunogenicity and rapid clearance in the body.

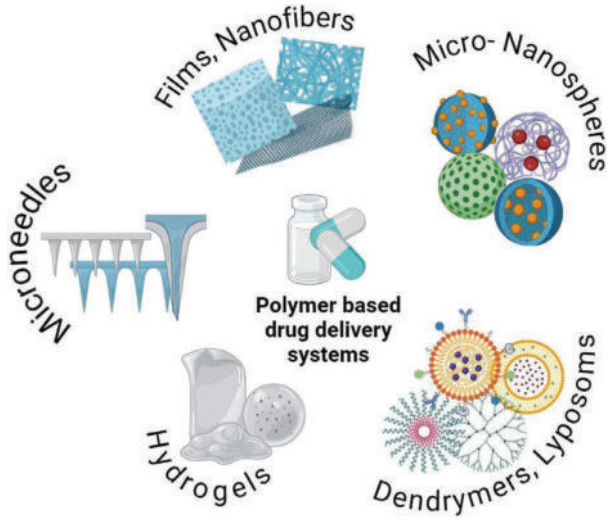

Figure 4: Polymer-Based Drug Delivery Systems

Source: (https://www.researchgate.net/figure/Basic-polymer-based-drug-delivery-systems_fig1_381966432)

Both passive and active targeting Polymer-based carriers can be adapted. As an example, antibodies or peptides that specifically target tumor-specific receptors can be surface-functionalized onto PLGA nanoparticles to enhance therapeutic efficacy, and reduce systemic side effects. Dendrimers are highly branched polymers whose architecture can be well-controlled, can be loaded with drugs, release can be tuned, and can be multivalent to enable targeted functionalization, and thus dendrimers are ideal in the delivery of chemotherapeutic agents, nucleic acids, and imaging contrast agents.

External or internal stimuli can also be utilized to release drugs in a polymers-based system, where the release is triggered by a stimulus e.g. pH, temperature, or enzymatic activity at the disease site, increasing further therapeutic precision.

5.3. LIGAND-TARGETED THERAPIES AND CONTROLLED RELEASE PLATFORMS

Ligand-targeted therapies Ligand-targeted therapies are an advanced method of targeted drug delivery and involve the use of antibodies, peptides, aptamers or small ligands to identify and target overexpressed receptors on diseased cells. This specific binding has been used to deliver

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drugs straight to tumor or pathological cells producing greater cytotoxic effects on malignant cells and avoiding healthy cells, decreasing the systemic toxicity. This is also achieved by such strategies to overcome resistance mechanisms by making sure that there are increased intracellular concentrations of the drug at the disease site. Examples are antibody-drug conjugates such as T-DM1 and folate receptor-targeted nanoparticles, which are examples of how ligand-directed delivery can be used to enhance efficacy and safety in cancer treatment.

Controlled release platforms complement targeted approaches by regulating the timing, location, and rate of drug release, often in response to specific physiological or external stimuli such as pH, enzymes, or temperature. These systems, which include diffusion-controlled, degradation-controlled, and stimuli-responsive carriers, maintain optimal therapeutic drug concentrations over extended periods, minimize off-target effects, and reduce the need for frequent dosing, thereby improving patient adherence. By combining ligand targeting with controlled release strategies, these advanced delivery platforms maximize treatment precision, enhance therapeutic outcomes, and provide a more patient-friendlier and effective approach to modern oncology care.

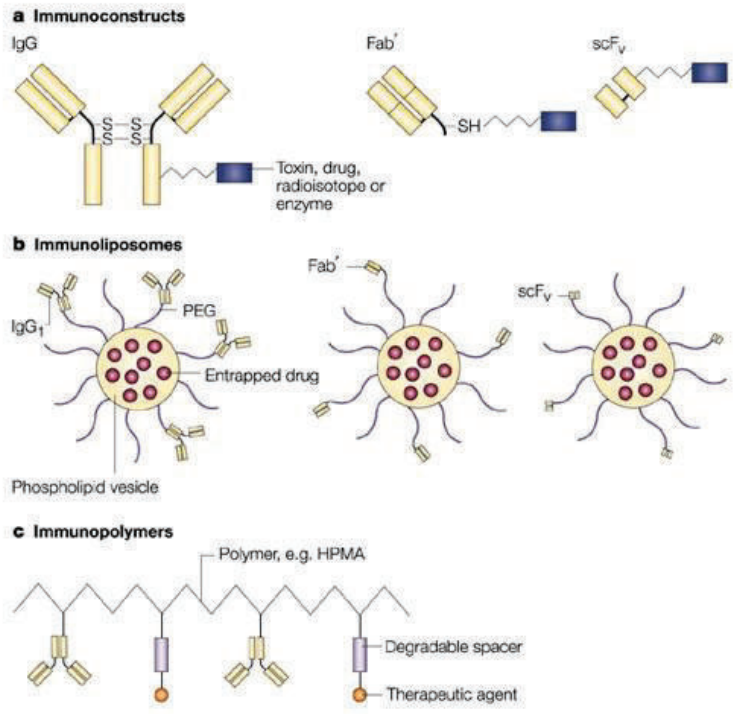

Figure 5: Ligand-Targeted Therapies in Anticancer Therapy

Source: (https://www.nature.com/articles/nrc903)

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❖ ***Ligand-Targeted Therapies***

Ligand-targeted therapies an example is a family of precision drug delivery systems whereby therapeutic agents are attached to ligands that can selectively identify and react with receptors or antigens that are overexpressed on diseased and especially tumor cells. The common ligands are monoclonal antibodies, peptides, aptamers and small molecules, all of which are directed to do selective targeting. As the drug-ligand complex is bound, it is internalised by the tumor cell, facilitating the intracellular delivery of the therapeutic payload and increased cytotoxicity and sparing of healthy tissues.

A number of clinically practical examples demonstrate the usefulness of this method. Trastuzumab-emtansine (T-DM1) is an antibody-drug conjugate to which trastuzumab, a monoclonal antibody against the HER2 receptor, has been conjugated to the cytotoxic drug emtansine. This conjugation enables targeted transfer of the drug to an overexpressing cancer, which by virtue of HER2 is present in the breast cancer, greatly lowering the toxic effects of the systemic toxicity of the drug as compared to normal chemotherapy. The other example is folate receptor-targeted nanoparticles, which take advantage of folate receptors overexpression on ovarian and breast cancer cells to improve the uptake and accumulation of drugs in the tumor tissues selectively. Ligand-targeted therapies have the following advantages: they are more specific, have fewer side effects in the body, have superior uptake by target cells and can potentially circumvent resistance mechanisms of standard therapies.

❖ ***Controlled Release Platforms***

The controllable release platform is the drug delivery system designed to deliver therapeutic agents at a specified rate within a specified time frame or in response to particular physiological or external stimuli. These systems aid in avoiding excessive drug concentration at target site, decrease dosing regimen and enhance compliance in patients. The controlled release can be attained in a number of ways:

- **Diffusion-controlled systems:** Drug molecules slowly leave the carrier matrix with time.
- **Degradation-controlled systems:** The release of drugs can be achieved by means of the degradation of the carrier material (biodegradable polymers) by hydrolysis or enzymatic activity.

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- **Stimulus-responsive systems:** The release of drugs is activated by internal (e.g., pH, enzymes, redox conditions) or external (e.g., temperature, light, magnetic fields) stimuli.

Controlled release sites include hydrogel-based depots, capable of maintaining localized drug delivery over a long duration; pH-sensitive nanoparticles, capable of releasing drugs selectively to acidic tumor microenvironment; and thermo-responsive micelles, capable of releasing their cargo in temperature gradients. Those platforms have relevant therapeutic benefits as they ensure stable drug concentrations at the disease site, thereby limiting variability that may limit efficacy or raise the risk of toxicity, and low drug administration frequency.

5.4. ROLE IN REDUCING TOXICITY AND IMPROVING EFFICACY

Accurate drug delivery systems are necessary in order to promote the therapeutic index of anticancer agents by ensuring they achieve their maximum efficacy at the site of delivery and reduce toxicity to normal tissues. This twofold benefit assists in enhancing patient outcomes, lowering adverse effects and enhancing patient treatment tolerability.

1. **Less Toxicity:** Systemic toxicity is one of the key issues of traditional chemotherapy and this is the case because the drug diffuses across the whole body and targeting healthy tissues as well as cancer cells. Accurate delivery methods, including liposomes, nanoparticles, and ligand targeted therapies, can severely reduce how much drugs get to normal tissues. As an example, liposomal doxorubicin wraps the chemotherapeutic agent in a lipid bilayer and minimizes free drug circulation in the blood. The specificity ensures that the cardiac toxicity that is usually accompanied by the use of conventional doxorubicin is not experienced, thus sparing the heart but preserving anti-cancer capacity. Likewise, nanoparticles and polymer-based carriers can be designed to release drugs selectively in the tumor microenvironment, avoiding such undesirable side effects of drugs on organs as the liver, kidneys and gastrointestinal tract.
2. **Better Efficacy:** Precision drug delivery adds to therapeutic efficacy by raising the concentration of drugs at the target site. Increased local concentrations of drugs enhance the cytotoxic action of malignant cells and may overcome the frequent resistance mechanisms. Indicatively, several cancer cells carry efflux pumps which are active in eliminating chemotherapeutic agents, lowering intra cellular drug concentrations. Nanoparticle-based systems and ligand-targeted systems can circumvent these pumps by enabling direct intracellular delivery so that sufficient accumulation of drug is

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produced to cause cell death. Moreover, sustained-release and stimuli-responsive carriers keep therapeutic drugs in the tumor microenvironment at long-term levels, which increase anticancer activity and reduce the risk of subtherapeutic exposure.

3. **Better Adherence to drug therapy:** Controlled-release and targeted drug delivery systems enhance patient compliance, as well, as the frequency and severity of dosing-side effects are minimized. The sustained-release system is based on the use of hydrogel depots, biodegradable polymeric systems to enable the sustained drug delivery over days or weeks, thus avoiding repeated high-dose deliveries. By reducing off-target toxicity, targeted therapies increase tolerability and allow patients to more comfortably accomplish prescribed treatment regimens.

REFERENCES

1. Ezike, T. C., Okpala, U. S., Onoja, U. L., Nwike, C. P., Ezeako, E. C., Okpara, O. J., ... & Nwanguma, B. C. (2023). Advances in drug delivery systems, challenges and future directions. *Heliyon*, *9*(6).
2. Wang, X., Li, C., Wang, Y., Chen, H., Zhang, X., Luo, C., ... & Wang, J. (2022). Smart drug delivery systems for precise cancer therapy. *Acta Pharmaceutica Sinica B*, *12*(11), 4098-4121.
3. Manzari, M. T., Shamay, Y., Kiguchi, H., Rosen, N., Scaltriti, M., & Heller, D. A. (2021). Targeted drug delivery strategies for precision medicines. *Nature Reviews Materials*, *6*(4), 351-370.
4. GBARABA, S. V., MUSTAPHA, A. Y., OLAMIDE, B., TOMOH, A. O., & FORKUO, A. Y. (2025). Smart Drug Delivery Systems: The Future of Precision Medicine. *IRE Journals*, *8*(9), 821-829.
5. Mitchell, M. J., Billingsley, M. M., Haley, R. M., Wechsler, M. E., Peppas, N. A., & Langer, R. (2021). Engineering precision nanoparticles for drug delivery. *Nature reviews drug discovery*, *20*(2), 101-124.
6. Gao, J., Karp, J. M., Langer, R., & Joshi, N. (2023). The future of drug delivery. *Chemistry of Materials*, *35*(2), 359-363.
7. Sivakumar, M., Muthu, Y., & Elumalai, K. (2025). Advancements in drug delivery systems: a focus on microsphere-based targeted delivery. *Biomedical Materials & Devices*, *3*(2), 1030-1057.
8. Waheed, S., Li, Z., Zhang, F., Chiarini, A., Armato, U., & Wu, J. (2022). Engineering nano-drug biointerface to overcome biological barriers toward precision drug delivery. *Journal of Nanobiotechnology*, *20*(1), 395.
9. Qu, J., Liang, Y., Shi, M., Guo, B., Gao, Y., & Yin, Z. (2019). Biocompatible conductive hydrogels based on dextran and aniline trimer as electro-responsive drug delivery system for localized drug release. *International Journal of Biological Macromolecules*, *140*, 255-264.
10. Wang, P., Jin, Z., Song, G., & Zhang, X. B. (2021). Recent progress and strategies for precise framework structure-enabled drug delivery systems. *Materials Today Sustainability*, *13*, 100065.

ISBN: 978-81-985724-3-1

11. Liu, J., Liu, W., Zhang, K., Shi, J., & Zhang, Z. (2020). A magnetic drug delivery system with “OFF–ON” state via specific molecular recognition and conformational changes for precise tumor therapy. *Advanced Healthcare Materials*, *9*(3), 1901316.
12. Safarkhani, M., Ahmadi, S., Ipakchi, H., Saeb, M. R., Makvandi, P., Ebrahimi Warkiani, M., ... & Huh, Y. (2024). Advancements in aptamer-driven DNA nanostructures for precision drug delivery. *Advanced Science*, *11*(26), 2401617.
13. Glassman, P. M., & Muzykantov, V. R. (2019). Pharmacokinetic and pharmacodynamic properties of drug delivery systems. The Journal of pharmacology and experimental therapeutics, 370(3), 570-580.
14. Hu, M., Ge, X., Chen, X., Mao, W., Qian, X., & Yuan, W. E. (2020). Micro/nanorobot: a promising targeted drug delivery system. *Pharmaceutics*, *12*(7), 665.
15. Durán-Lobato, M., Niu, Z., & Alonso, M. J. (2020). Oral delivery of biologics for precision medicine. *Advanced Materials*, *32*(13), 1901935.