



## Review Article

# Smart Drug Delivery System

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### ABSTRACT

SDDS is a medicine delivery strategy that attempts to increase dosage in specific body areas while increasing therapeutic efficacy and decreasing adverse effects. It addresses issues such as pharmaceutical solubility constraints, degradation, quick clearance rates, non-specific toxicity, and biological barriers. Smart drug delivery methods include nanoparticles, liposomes, vesicles, implants, polymer-based systems, PH-responsive systems, nanoplastforms, and tailored systems. Nanoparticles contain organic and inorganic features, whereas liposomes are used in cancer therapy, anti-inflammatory therapy, antifungal therapy, and gene therapy. Despite the fact that implantable biomaterials have transformed bone and dentition restoration, surgical methods continue to fail as a result of aseptic loosening and bacterial infections. SDDS aims to minimize adverse effects by regulating active molecule release in response to environmental cues. Recent research has concentrated on the creation of redox-responsive systems, enzyme-cleavable systems, electro-sensitive systems, and dual stimuli-responsive systems. SDDS provides several benefits, including focused therapy, higher bioavailability, fewer adverse effects, controlled releases, and individualized medication. However, concerns with stimulation, biological barriers, size and molecular weight, and toxicity exist. Personalized medication, nanoformulations, implanted devices, biological sensors, gene therapy, responsive administration, biosensors for feedback control, and 3D printing are examples of future methods.


### INTRODUCTION

Drug delivery is the technique of providing a pharmaceutical ingredient to achieve a therapeutic impact in disease prevention via pharmaceuticals, and it is one of the most important ways of medical treatment, alongside surgery, radiation, physical therapy, and psychotherapy. Such treatments have

serious side effects, such as repeated treatments, altered drug biodistribution, and cell acquisition of multidrug resistance (MDR). Drug delivery is the technique of providing a pharmaceutical ingredient to achieve a therapeutic impact in disease prevention using medications, and it is one of the most important ways of medical treatment,

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alongside surgery, radiation, physical therapy, and psychotherapy. <sup>(1)</sup> The goal of targeted medicine delivery is the same. Smart drug delivery, also known as targeted drug delivery, is a therapy strategy that includes increasing the dosage of medication in one or a few body regions compared to others. As a result, it only delivers medication to areas of interest within the body. This improves therapy efficacy while also lowering negative effects. Although estimating the actual extent and influence of pharmacotherapy on health is nearly impossible, there is no doubt that pharmacotherapy, in conjunction with adequate sanitation and a better diet, has enhanced quality of life. <sup>(2)</sup>

Drugs are delivered randomly throughout the body via the bloodstream in conventional chemotherapies, affecting both.

To improve therapy efficiency and reduce side effects, all exciting drug and vaccine candidates must develop suitable drug delivery systems that are appealing methods to allow the effective, safe, and reliable application of bioactive compounds to the patient.

Drug delivery methods, ranging from implantable electronic devices to single polymer chains, must be compatible with the body's functions as well as the dose delivered to the various organs. Furthermore, DDS may solve challenges such as limited drug solubility, degradation (environmental or enzymatic), rapid clearance rates, non-specific toxicity, and difficulty traversing biological barriers, to name a few. <sup>(3)</sup>

The delivery system (DS) is used to localize, preserve drug characteristics, ensure a specific route for drug delivery, target the intended spot solely, limit drug adverse effects, and extend therapeutic contact with diseased tissue. This DT delivery system employs a variety of methodologies for targeting cells, drug delivery mechanisms, drug characteristics, organ-based

targeted sites, illness, and drug-targeted vehicles. <sup>(4)</sup>

## **SMART DRUG DELIVERY SYSTEM**

A smart drug delivery system (SDDS) is a more advanced approach to drug targeting (DT). Active drug molecules should selectively collect in the illness location for a lengthy period of time with excellent controllability to improve therapeutic effects and reduce side effects. Drug delivery refers to the methods, formulations, technologies, and systems for moving treatments in the body as needed to produce their desired therapeutic effects in a safe and effective manner. <sup>(5)</sup>

The smart drug delivered by this system meets the following criteria: increasing the doses of the delivered drug to the targeted body part of interest (tissue, cells, or organs), not being degraded by any of the body fluids, reducing side effects by improving drug treatment efficacy, and absorption of the delivered drug. <sup>(6)</sup>

## **SMART DRUG DELIVERY SYSTEM PROPERTIES**

In contrast to traditional drug delivery systems, SDDS employs the absorption, distribution, metabolism, and excretion (ADME) cycle to accomplish tailored administration. The system must circumvent the host's defensive systems in order to reach its action location. The path followed, the targeted spot, and the drug vehicles are all criteria for a targeted release system. <sup>(11)</sup> The system should ideally be biochemically inert, non-immunogenic, stable in both vivo and in vitro settings, preferentially detect target cells, preserve surface ligand specificity, and have a regulated drug release rate. The technology should be both biodegradable and affordable. <sup>(12)</sup>

## **Types of Smart Drug Delivery Systems**

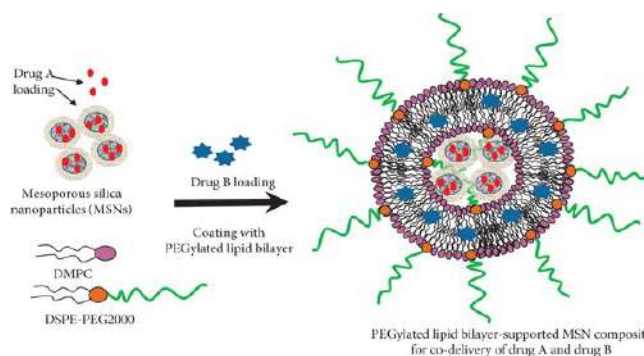
1. Nanoparticle
1. Liposome and vesicle
2. Implants and microspheres
3. polymer-based system
4. PH-responsive systems and nanoplatfoms



## 5. Targeted system.

### 1. Nanoparticle

After hybridization, organic-inorganic hybrid smart biomaterials combine organic and inorganic properties to respond to stimuli. These materials can be created by fusing organic or polymer molecules with nanometal particles or nanooxides like titanium dioxide and silica. Mesoporous silica nanoparticles (MSNPs) have a high loading capacity; however, they are easily released after administration, which could reduce therapeutic efficacy and cause serious side effects. Different organic compounds or polymers are used as clever gatekeepers on the pore outlets to reduce the amount of premature medication release. <sup>(27)</sup> Utilizing various anchoring techniques, two new MSNPs hybridized with poly-L-lysine outer surface systems were created. Gold nanoparticles (AuNPs) have been employed as PTT agents, but they are not biodegradable. Surface modification of organic functional groups can solve this problem. Kojima and colleagues created liposome complexes with AuNPs, encouraging stable dispersions under isotonic circumstances. PEG-attached PAMAM dendrimers were extremely hazardous to HeLa cells. <sup>(28)</sup> Magnetic nanoparticles (MNPs) may be manipulated in an alternating magnetic field (AMF), making them suitable for medication and gene delivery, diagnostics, and therapies. MNPs can be created as synergistic or sequential drug delivery systems when combined with several triggers, boosting efficacy while decreasing negative effects. SPIO Fe<sub>3</sub>O<sub>4</sub> nanoparticles implanted in microbubbles, for example, can be utilized as ultrasonic and magnetic resonance contrast agents, and polymeric double-layer shelled microspheres can be controlled by external magnetic force. <sup>(29)</sup>

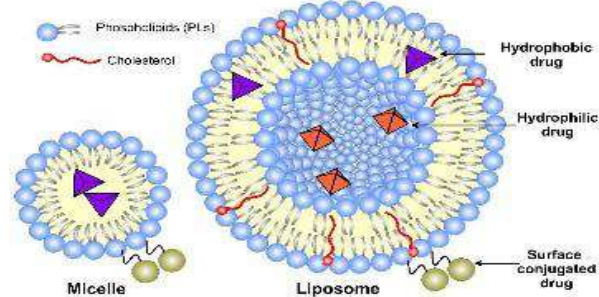


(Figure no. 1) Nanoparticle

### 2. Liposome

Alec Bangham and colleagues originally described liposomes, which are encapsulated phospholipid bilayer structures, in 1965. Gregory et al. employed them as medication delivery systems for the first time in 1971. Liposomes have been extensively used in clinical studies for anti-cancer, anti-inflammatory, antifungal, and gene treatments. Some liposome compositions have received commercial approval. Smart liposomes, which may be activated by a variety of triggers, are a hot issue in nanomedicine with possible therapeutic uses in the future. <sup>(17)</sup> Liposomes are tiny vesicles made of phospholipid bilayers that range in size from 20 to 100nm. They are utilized as medication delivery vehicles to overcome hurdles to cellular and tissue absorption. Liposomes can be opsonized by phagocytic cells because of their increased surface hydrophobicity, making them effective for targeting malignancies in RES organs. The long-circulating characteristic of stealth liposomes created by adding a PEG molecule increases targeting efficiency. <sup>(17)</sup> There are pH-sensitive, heat-sensitive, enzyme-sensitive, and photosensitive liposomes for drug release. At 42°C, thermosensitive liposomes release medicines, resulting in maximum drug accumulation in tissues for focused action. <sup>(19)</sup> To manage medication release, ThermoDox, a smart drug carrier technology, employs temperature-sensitive liposomes. <sup>(21)</sup> Celsion's liposomes have demonstrated increased safety and efficacy in liver cancer trials. To improve drug release,

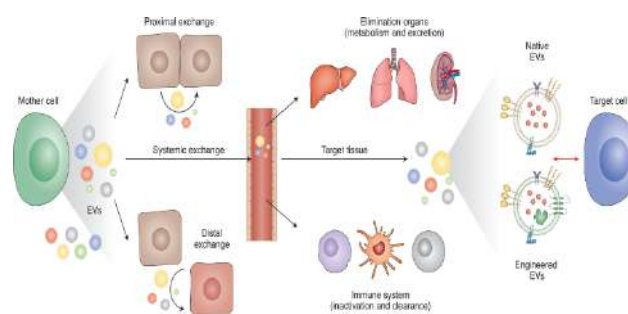
thermosensitive polymers are utilized to alter liposomes, with EOEOVE polymers being the most temperature-sensitive. (20)



(Figure no. 2: liposome system)

### Vesicle

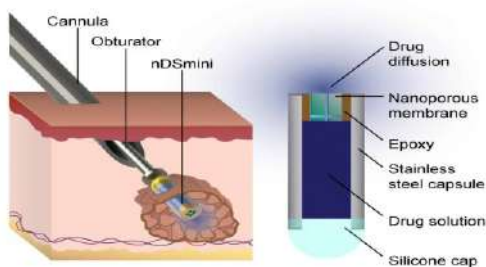
BMVs, or outer membrane vesicles, have been employed as drug carriers since the 1970s and 1980s, although there are still worries about their stability and toxicity. Modifying BMVs to respond to certain environmental signals might boost therapeutic effectiveness while decreasing negative effects. There are three theories for BMV biogenesis: loss of outer membrane and peptidoglycan layer connection, turgor pressure buildup, and conformational alterations. Techniques for purification and characterization include serial ultracentrifugation, ultrafiltration, precipitation, and ultracentrifugation; however, these processes might result in contamination or deformation. BMVs can carry many biomolecules concurrently and across vast distances. Tumor cell growth is essential for metastasis, and the enhanced permeability and retention effect (EPR) in tumor tissues permits nanocarriers to accumulate. Active targeting techniques are required for therapeutic efficacy, and surface modification of BMVs has ushered in new eras in drug delivery systems. Potential solutions include stimuli-based medication delivery systems, dual/multi-responsive targeting, and inverse targeting. BMVs have the potential to be exploited for bioimaging in early cancer detection and treatment efficacy, and fusion proteins can be coupled to membrane-associated proteins for a variety of functions.



(Figure 3): vesicle system

### 3. Implant and microsphere

Although the introduction of implantable biomaterials has revolutionized bone and dentition therapy, surgical treatments still face failure risks owing to aseptic loosening and bacterial infections. Although biomaterials are antibacterial, drug delivery systems (DDSs) can be troublesome because of cytotoxicity, covalent bonding, and the inability to be delivered on demand. Infected microenvironments can be triggered by physical stimuli, pH, temperature, touch, and virulence-factor-responsive systems. Protease-activated systems can provide antibiotics on demand, but further research is needed to determine their duration and sensitivity. Intelligent medication delivery can be initiated via lipase-triggered systems, which use enzymes involved in fat breakdown. Pathogenic bacteria's gelatinases can trigger collagen breakdown, which improves antibiotic treatment. Dual-responsive systems improve stimulus-responsive release while decreasing antibiotic resistance. Host-Immune-Response Systems (DDSs) regulate medication release in response to infections. Inflammatory agents such as matrix metalloproteinases (MMPs) can induce periodontal damage. Degradable hydrogels and biodegradable coatings have shown promise for on-demand antibiotic administration. However, these systems lack specificity for bacterial infections, which might result in unintentional antibiotic release. (25)

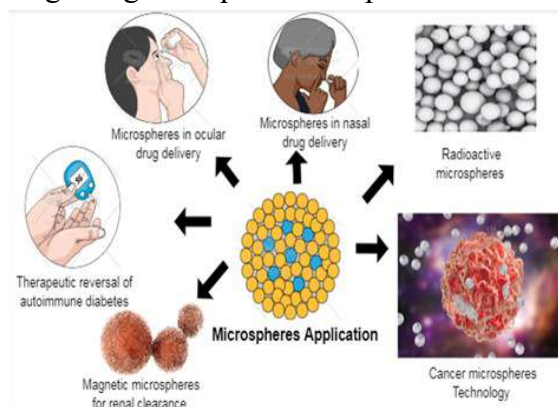


**(Figure no. 4) Implantable**

Microspheres are micron-sized spheres made of mixed polymers used for dispersing drugs and other components. They can be divided into solid, double-layer, hollow, and porous microspheres. Solid microspheres have problems like high initial concentration explosions and long drug release times. Double-layer microspheres use polymers to reduce the initial burst concentration. Porous microspheres have large specific surface areas, low density, and controllable porosity. Microspheres improve patient compliance and are widely used in tissue engineering. Microspheres have attracted attention for their potential in tissue engineering due to their uniform shape and unique characteristics. This systematic study examines numerous processing methods, synthetic materials, and uses in various illnesses, as well as flaws and future prospects. In tissue engineering applications, microspheres are treated using emulsification, microfluidics, template techniques, and electrojet procedures. Droplet formation is controlled by active and passive approaches, with mold methods providing superior analytical performance, lower volume, fewer samples, and low energy usage.

Microfluidic electrospray technology is a potential way for producing microspheres, which are employed in a variety of therapies such as angiogenic, magnetic, and stem cell microcapsules. It provides effective and straightforward manufacturing processes such as spray drying and membrane emulsification. Because of its biocompatibility, long-acting release, targeting, safety, and non-toxicity, PLGA,

a biodegradable polymer, is widely employed in biomedical and industrial applications. Modified nanocarriers improve tumor-targeted treatment. PLA, a traditional synthetic degradable polymer, can preserve pharmaceuticals while also increasing their therapeutic index. Microspheres hold great promise for treating illnesses such as oncotherapy, skin wounds, bone regeneration, and arthritis. They are biocompatible, have good drug-release capabilities, are safe, and are non-toxic. Microspheres boost bone regeneration and wound healing by inhibiting proteoglycan expression in chondrocytes, decreasing medicine doses, and increasing patient outcomes. Microspheres are used in drug delivery systems to treat disorders such as nerve growth factor-induced peripheral nerve damage, enteritidis, and reproductive difficulties, as well as to promote nerve tissue healing and good reproductive practices. (26)

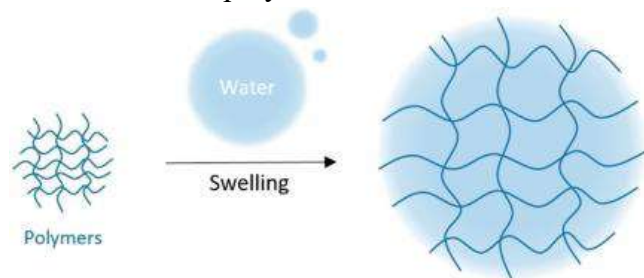


**(Figure No. 5) microsphere**

#### 4. Polymer-based System

Smart drug delivery systems (SDDS) are intended to reduce side effects by controlling the release of active molecules in response to external inputs. These stimuli-responsive polymer-based systems are being studied in cancer, dermatology, and cosmetology, with potential applications in skin problems and external stimuli. (13) Recent studies have concentrated on the development of redox-responsive systems, enzyme-cleavable systems, electro-sensitive systems, and dual stimuli-responsive systems. (14) Disulfide bonds are

incorporated into nanocarriers via redox-responsive devices for smart medicine administration into cancer cells. Based on the biological environment, enzyme-cleavable systems govern active substance distribution. Current amplitude, pulse duration, and pulse interval are all controlled by electro-sensitive mechanisms. Dual stimulus-responsive systems combine characteristics to produce more selective and controllable polymers. <sup>(15)</sup>



(Figure no. 6) polymer system

### 1. Targeted system

#### a. Active drug delivery system

Active targeting entails precise interactions between a medication and target cells, most commonly via ligand-receptor interactions. This improves therapeutic efficacy, decreases adverse effects, and allows for lower therapy dosages. There are three approaches: confining nanoparticle circulation to certain tumor areas, targeting specific malignant cells or tissues, and targeting nanoparticles to the intracellular region of targeted tumor cells. <sup>(30)</sup>

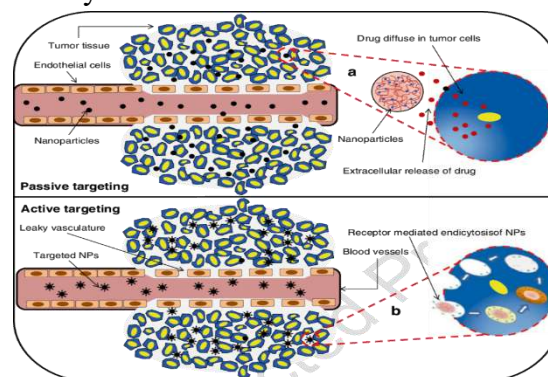
#### b. Passive Targeting Delivery System

Passive targeting entails the accumulation of a drug-carrier system at a specific place that is influenced by the chemical, physical, pharmacological, and biological features of the disease. Few medications can be delivered as inactive or prodrugs, allowing for very active drug exposure to malignant tissue. <sup>(31)</sup>

#### c. Dual-targeting delivery system

Dual targeting systems are being developed in order to activate targeted drug delivery systems that can be triggered by stimuli such as

temperature, pH, and redox. These systems can direct drug delivery vehicles that use several external inputs at the same time. Hyper-branched polymers with dual stimulus amalgamation capabilities have been developed, as have drug-targeted delivery systems with dual stimulus sensitivity. <sup>(32)</sup>



(Figure no; 7) active and passive systems.

### 2. Smart drug delivery systems on nanoplatforms

#### a. PH-responsive system

pH is a typical trigger for drug release, with conventional pH-responsive carriers based on changes in different organs. Eudragit S100-coated citrus pectin nanoparticles may distinguish subtle pH changes in illness areas such as inflammatory, ischemia, and tumor tissues. The pH range is important for creating enhanced drug delivery systems (DDSs) since it can be employed as a specific stimulus in controlled DDSs. However, pH must be paired with other stimuli, such as temperature and redox, to produce an exact and specific release in target areas. <sup>(33)</sup>

#### c. Redox-responsive

Redox-responsive stimuli are increasingly exploited in disease therapy, particularly in intracellular drug delivery systems (DDSs). These methods make use of the multivariate redox potential of microenvironments, making them appealing for targeting specific tumor intracellular locations. Glutathione reduction, a well-known redox pathway within cancer cells, is a promising technique for targeting medication delivery. ROS-

response DDSs can also carefully control targeted drug release, as mucosal ROS concentrations in inflammatory tissues and colon cancer are 10-100-fold higher than in normal tissues.<sup>(33)</sup>

#### d. Enzyme Responsive

Enzymes are utilized as triggers in smart DDSs due to their substrate specificity and great selectivity. They can achieve drug release through biocatalytic activity in cancer or inflammatory tissues, but regulating the first response time is difficult.<sup>(33)</sup>

#### e. Temperature-responsive

Temperature plays an important role in medication release, especially in pathophysiological circumstances such as inflammation and malignancies. While functionalized nanoparticles can improve medication release, ensuring safety is difficult.<sup>(33)</sup>

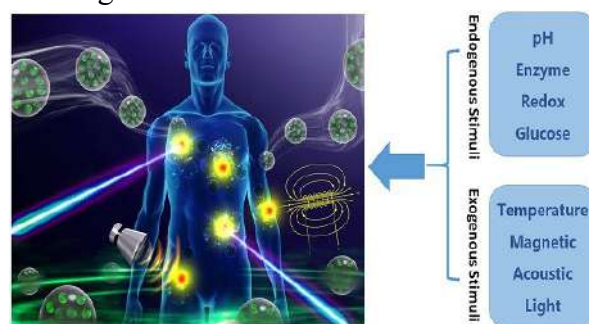
#### f. Light, magnetic, and US-responsive

Light-responsive smart drug delivery systems (SDDSs) make use of both natural and artificial electromagnetic radiation with wavelengths ranging from 2500nm to 380nm. These systems use an on/off medication release mechanism to deliver the encapsulated or conjugated substance to the appropriate spot in a spatiotemporal controlled way. To conjugate pharmaceuticals for light-sensitive release, such as doxorubicin-encapsulated poly(lactic-co-glycolic acid) matrix particles, photo-cleavable bonds can be employed. Light-responsive systems use external light irradiation to initiate medication release at the target. Although photosensitive carriers achieve on-off medication release, the depth of light penetration limits non-invasive applications for deep tissues.

Magnetic-responsive drug delivery systems provide noninvasive control over carrier proximity to targets by exploiting magnetic nanoparticles for accurate design and engineering. Magnetically adjustable BSA particles, magneto-thermally responsive nanocarriers, and CEMNs are now

being investigated for potential applications in cancer therapy, MRI, cell migration control, hyperthermia, and medicine administration. Magnetic stimuli can be used to control carrier movement and medication release in non-invasive ways. MNPs with core or shell magnetic characteristics have active locations for biomolecule conjugation. These nanoscaled MNPs can be encapsulated in colloidal carriers, allowing for multifunctional formulations for diagnostic and therapeutic reasons. This enables long-term circulation, target specificity, and therapeutic administration.<sup>(33)</sup>

Ultrasound, a high-frequency sound wave, can influence drug release in sick areas, and its strength can be adjusted for imaging and permeability. It is popular for clinical research because of advantages such as tissue penetration, control, and safety. Ultrasonic sensitivity in nanocarriers has expanded ultrasound operations, such as medication administration in conjunction with micelles. Because of its great safety and intrinsic tissue penetration, ultrasonography (US) is frequently utilized in clinics for diagnosis and therapy, and ultrasonic-sensitive nanocarriers are increasing its effectiveness.<sup>(33)</sup>



(Figure no. 8) target system

### ADVANTAGES OF A SMART DRUG DELIVERY SYSTEM

- Target therapy: delivery of the drug directly through the affected area, reducing systemic exposure.
- Improved bioavailability: enhance drug solubility and absorption.

- Reduced side effects: minimized damage to healthy tissues
- Controlled Releases: administer the drug gradually, reducing the need for frequent dosing.
- Personalized Medicine: Tailoring of drugs for delivery to individual patient needs

## **ROUTES DRUG ADMINISTRATION**

The method of delivery of medications is critical for illness cure. Despite the development of promising therapeutic moieties, ineffective medication targeting by tablets or injection in the proper region of the body restricts therapeutic values to a greater extent.

### ***Parenteral drug administration***

Bio-nanotechnology has been used in parenteral administration procedures, giving painless, patient-friendly alternatives to injections. Microneedles are shallow needles that penetrate superficial skin layers, reducing the discomfort associated with normal hypodermic needles. Jet injectors distribute high-velocity liquid jet streams into different skin layers. Micronization of medicines enhances dose form and therapeutic efficiency. Microspheres of appropriate particle size can be delivered directly to tissue or concentrated in specified locations via intravenous injection. These devices provide painless and patient-friendly alternatives to standard injections.<sup>(34)</sup>

### ***Oral Administration***

Because of its ease of use, cost-effectiveness, and painlessness, oral medication administration is the recommended approach. It is not, however, appropriate for medications that degrade readily in the gastrointestinal system, such as proteins and peptides. Barriers such as the epithelial cell lining, mucus layer, and gut lumen proteolytic enzymes can all have an effect on delivery. Drug-loaded nanoparticles, on the other hand, can protect against degradation in the gastrointestinal system,

increasing absorption at M-cell-containing patch patches.<sup>(35)</sup>

### ***Topical Administration***

Several commentators have addressed the viability of using nanoparticles in topical or cosmetic treatments. In any case, this dosage form takes advantage of nanoparticle benefits such as controlled drug release, the ability of solid lipid nanoparticles to act as occlusives to increase skin water content, and the ability of nanoparticles to serve as physical barriers on the skin to block UV light.<sup>(36)</sup>

## **APPLICATION**

1. Cancer Treatment
2. Chronic disease management
3. Neurological disorder
4. Vaccines and immunotherapy

### **1. Cancer treatment**

Smart drug delivery methods use nanoparticles with a high surface area-to-volume ratio, which allows them to attach to tumor cells. Light is used in photodynamic treatment to spotlight a particle, heating it and the surrounding tissue. This treatment is intriguing because, unlike chemotherapy, it does not leave a hazardous trail of reactive chemicals.

### **2. Chronic Disease Management**

These systems can help manage chronic conditions like asthma by releasing the medication needed to control the system.

### **3. Neurological disorder**

These systems can target specific regions of the brain, providing more effective treatment for conditions like Parkinson disease.

### **4. Vaccines and immunotherapy**

Smart drug delivery systems can improve the efficacy of vaccines by providing sustained-release medication when needed to control symptoms. A smart drug delivery system can release immunosuppressive drugs in response to immune system activity, helping manage conditions like rheumatoid arthritis.





## 5. Glucose sensor

PH-sensitive polymers are commonly employed in diabetic insulin delivery devices. In a glucose-rich environment, the built-in glucose sensor can be triggered by glucose oxidase. This enzyme enables the use of pH-sensitive hydrogels for regulated insulin administration.

## 6. Birth control

Implantable devices can release contraceptives at controlled rates, offering long-term birth control options for women.

## 7. Gene therapy

Some gene therapies use viral vectors as delivery systems to introduce therapeutic genes into cells.

## 8. Pediatrics medicine

A smart drug delivery system can be particularly useful for children, ensuring they receive the right dose of medication at the right time.

## 9. Hormone replacement therapy

A smart patch and implant can deliver hormones in a precise and controlled manner, benefiting menopausal women and transgender individuals.

## 10. Antibiotic Therapy

Infections can be treated with targeted antibiotic delivery systems, reducing the risk of antibiotic resistance.<sup>(37)</sup>

## CHALLENGES AND CONSIDERATIONS

### Stimulus

To accomplish smart drug release, environment-sensitive drug carriers are impacted by internal and external stimuli such as pH, glucose, and low oxygen concentrations. In clinical therapies, these vehicles provide self-regulated delivery and excellent targeting. Externally activated nanoparticles have great repeatability and may be delivered remotely. Exogenous stimulus-responsive systems are easier to manage, but tissue damage and penetration depth must be addressed.

### Biological Barriers

The drug-loaded vehicles encounter a range of intricate biological hurdles that severely impede site-specific targeting. Biological barriers such as

opsonization and enzyme breakdown of mucosal membranes not only reduce the buildup of nanocarriers at target areas but also the therapeutic results. In general, to increase the therapeutic impact Drug-loaded cars should be able to breach physical obstacles using SDDS, such as extracellular matrix (ECM) and cell membrane endosomes, to reach the cell's nucleus.

### Size and Molecular Weight

Smaller nanoparticles have a higher surface area, leading to quicker drug release. Larger particles, on the other hand, disperse slowly, leading smaller particles to congregate during storage and transportation. Polymer degradation is also affected by particle size, with bigger particles degrading faster. Polymer molecular weight can alter organ distribution, potentially compromising patient clearance.

Toxicology, cost-effectiveness, heterogeneity, and a lack of regulatory requirements are all concerns for smart drug delivery systems (SDDSs). Nanocarriers are hazardous and have limited clinical efficacy, whereas ligands need selection, conjugation techniques, and characterization. SDDS formulation necessitates additional stages, including quality control and regulatory oversight. Drug release in the cellular milieu and functional group complementarity are significant problems. SDDSs, on the other hand, have the potential to be used in translational medicine by merging diagnostic and targeted therapy into a centralized system. Future research should concentrate on clinical translation in order to make more stimulus-sensitive nanomedicine available in clinical settings.<sup>(38)</sup>

### FUTURE DIRECTION

1. "Personalized Medicine": Tailoring drug delivery to individual patient needs based on their genetics, metabolism, and disease profile for more effective treatments.
2. Nano formulations: Developing nanoscale drug carriers like liposomes and nanoparticles



to improve drug solubility stability, and targeted delivery to specific cells or tissues.

3. **Implantable Devices:** Advancing implantable devices that can continuously release drugs, monitor patient health, and adjust dosages in real-time.
4. **Biological Sensors:** Integrating sensors within drug delivery systems to monitor biomarkers and adjust drug release accordingly, ensuring precise therapy.
5. **Gene Therapy:** Combining drug delivery with gene therapy techniques to target and modify genetic elements offers potential cures for genetic diseases.
6. **Responsive Delivery:** Creating systems that respond to external stimuli like pH, temperature, or light to release drugs at the right time and place in the body.
7. **Biosensors for Feedback Control:** Developing biosensors that can detect changes in a patient's condition and provide feedback to regulate drug delivery autonomously.
8. **"3D Printing":** Utilizing 3D printing technology to create custom drug delivery devices and formulations for personalized treatment.
9. **Artificial Intelligence:** Implementing AI algorithms for predictive modeling of drug release, optimizing dosing regimens, and improving treatment outcomes.
10. **Remote Monitoring:** Enabling remote monitoring of drug delivery and patient health through IoT-connected devices for telemedicine applications.
11. **Biodegradable Materials:** Advancing biodegradable materials for drug carriers to minimize side effects and reduce the need for device removal.
12. **Drug-Device Combinations:** Integrating drugs with delivery devices, such as inhalers or

patches, for more convenient and targeted administration.

13. **"Regulatory Considerations":** Addressing regulatory challenges to ensure the safety and efficacy of smart drug delivery systems, including approval pathways for innovative technologies

These future directions hold the potential to revolutionize drug delivery, making treatments more effective, convenient, and tailored to individual patient needs. However, they also come with challenges related to safety, ethics, and regulatory approval. That needs to be carefully addressed. <sup>(39)</sup>

## CONCLUSION

Traditional ways of administering therapeutic substances for disease treatment or prevention influence both sick and normal cells of the body and are linked with significant side effects. To improve therapeutic agent efficiency and decrease unfavorable side effects, additional safe and appropriate medication delivery methods, such as smart drug delivery, have been created. The procedure is a clever medication delivery method. method of delivering a medicinal chemical to a specific target or ailment in a spatially controlled manner. It is intended to improve drug biodistribution and cellular compound communication in certain bodily areas without damaging the natural tissue. Generally, the smart medicine delivery system offers various advantages and is significantly more cost-effective than utilizing Smart drug delivery systems (SDDS) have the potential to replace existing approaches in the pharmaceutical and biotechnology sectors. These systems have a long shelf life, are efficient at intracellular delivery, and are tolerable. Liposomes and nanoparticles, which respond to stimuli, are critical for anti-cancer medicine delivery. These technologies have the potential to enhance patient compliance and quality of life, making them the future of translational medicine.



## REFERENCES

1. Allen, T. M., & Cullis, P. R. (2013, January). Liposomal drug delivery systems: From concept to clinical applications. *Advanced Drug Delivery Reviews*, 65(1), 36–48. <https://doi.org/10.1016/j.addr.2012.09.037>
2. Brigger I, Dubernet C, and Couvreur P (2002). Nanoparticles in cancer therapy and diagnosis. *Advanced Drug Delivery Review* 54: 631-651.
3. Panchagnula, R. (1997). Transdermal delivery of drugs. *Indigenous Journal of Pha Perspective* 161: 152-163
4. Gupta M, Sharma V (2011) Targeted drug delivery system: A Review *Res J Chem Sci* 1: 135–138.
5. Hruby M, Filippov SK, Štěpanek P (2015) Smart polymers in drug delivery systems are at a crossroads: which way deserves following? *European Polymer Journal* 65: 82–97
6. Muller R., Keck C. (2004). Challenges and solutions for the delivery of biotech drugs—a review of drug nanocrystal technology and lipid nanoparticles. *Journal of Biotechnol* 113: 151–170
7. Grund S., Bauer M., Fischer D. Polymers in drug delivery—state of the art and future trends *Advanced Engineering Materials*. 2011; 13:B61-B87.
8. Annabi N, Tamayol A, Uquillas JA, Akbari M, Bertassoni LE, Cha C, et al. 25th anniversary article: rational design and applications of hydrogels in regenerative medicine. *Advanced Materials*. 2014;26:85–124.
9. Chang H-I, Yeh M-K. Clinical development of liposome-based drugs: formulation, characterization, and therapeutic efficacy. *International Journal of Nanomedicine*, 2012, 7:49–60.
10. Kumari A, Yadav SK, and Yadav SC Biodegradable polymeric nanoparticle-based drug delivery systems *Colloids and Surfaces B: Biointerfaces*. 2010;75:1–18.
11. Liu D., Yang F., Xiong F., and Gu N. (2016) The smart drug delivery system and its clinical potential *Theranostics* 6: 1306.
12. Bertrand N, Wu J, Xu X, and Kamaly N (2011) The journey of a drug carrier in the body: an anatomo-physiological Cancer nanotechnology: The impact of passive and active targeting in the era of modern cancer biology *Advanced Drug Delivery Review* 66: 2–25
13. Mura S., Nicolas J., and Couvreur P. Stimuli-responsive nanocarriers for drug delivery *Nature Materials*. 2013;12:991-1003
14. Cheng R, Meng F, Deng C, Klok H-A, and Zhong Z. Dual and multi-stimuli responsive polymeric nanoparticles for programmed site-specific drug delivery. *Biomaterials*. 2013;34:3647-57
15. Gao W, Chan JM, Farokhzad OC. pH-responsive nanoparticles for drug delivery. *Molecular Pharmaceutics*. 2010;7:1913–20.
16. Deamer DW. From “Banghasomes” to Liposomes: A Memoir of Alec Bangham, 1921–2010. *The FASEB Journal*, 2010, 24:1308–10.
17. Gregoriadis G., Ryman B. Liposomes as carriers of enzymes or drugs: a new approach to the treatment of storage diseases. *Biochemical Journal*. 1971; 124:58P.
18. Mikhaylov G, Mikac U, Magaeva AA, Itin VI, Naiden EP, Psakhye I, et al. Ferri-liposomes are an MRI-visible drug delivery system for targeting tumors and their microenvironment. *Nature Nanotechnology*. 2011;6:594-602.
19. Mori A, Klibanov A, Torchilin V, Huang L (2005) Influence of the steric barrier activity of amphipathic poly (ethylene glycol) and ganglioside GM on the circulation time of liposomes and on the target binding of immunoliposomes in vivo, *FEBS Lett* 284: 263-266.



20. Anderson T., Jensen S., and Jorgensen K. (2005) Advanced strategies in liposomal cancer therapy problems and prospects of active and tumor-specific drug release *Journal Progress in Lipid Research* 44: 68–97
21. Li L., Tenhagen T., Schipper D., Wijnberg T., Vanrhoo G., et al. (2010). Triggered content release from optimized stealth thermosensitive liposomes using mild hyperthermia *Journal of Control Research* 143: 274–293.
22. Deatherage BL, Cookson BT. Membrane vesicle release in bacteria, eukaryotes, and archaea: a conserved yet underappreciated aspect of microbial life *Infect Immun* 2012; 80:1948–1957. Doi: 10.1128/IAI.06014-11.
23. Zaborowski MP, Bajaj L, Breakefield XO, and Lai CP Extracellular Vesicles: Composition, Biological Relevance, and Methods of Study *Bioscience* 2015;65:783-797.
24. McConnell MJ. Extracellular vesicles and immune modulation *Immunol Cell Biol* 2018; 96:681-682.
25. Stewart S, Domínguez-Robles J, Donnelly R, Larrañeta E. Implantable Polymeric Drug Delivery Devices: Classification, Manufacture, Materials, and Clinical Applications. *Polymers* [Internet]. MDPI AG; 2018; 10(12):1379. Available from: <http://dx.doi.org/10.3390/polym10121379>.
26. Lengyel M., Kállai-Szabó N., Antal V., Laki AJ., and Antal I. Microparticles, Microspheres, and Microcapsules for Advanced Drug Delivery. *Scientia Pharmaceutica* [Internet] MDPI AG; 2019; 87(3):20. Available from: <http://dx.doi.org/10.3390/scipharm87030020>.
27. Sun T-M, Wang Y-C, Wang F, Du J-Z, Mao C-Q, Sun C-Y, et al. Cancer stem cell therapy uses doxorubicin conjugated to gold nanoparticles via hydrazine bonds. *Biomaterials*. 2014; 35:836-45.
28. Wang F, Wang Y-C, Dou S, Xiong M-H, Sun T-M, and Wang J. Doxorubicin-tethered responsive gold nanoparticles facilitate intracellular drug delivery for overcoming multidrug resistance in cancer cells. *ACS Nano*. 2011; 5:3679–92.
29. Dykman L., Khlebtsov N. Gold nanoparticles in biomedical applications: recent advances and perspectives *Chemical Society Reviews*, 2012, 41:2256–82.
30. Kirpotin D, Drummond D, Shao Y, Shalaby M, Hong K, et al. (2006) found that antibody targeting of long-circulating lipidic nanoparticles does not increase tumor localization but does increase internalization in animal models. *Cancer Research* 66: 6732–6740
31. Stefanadis C, Chrysochoou C, Markou D, Petraki K, Panagiotakos D, et al. (2001). Increased temperature of malignant urinary bladder tumors in vivo: The application of a new method based on a catheter technique *Journal of Clinical Oncology* 19: 676–681.
32. Pang Y, Zhu Q, Zhou D, Liu J, Chen Y, et al. (2011) Synthesis of backbone thermo and pH dual-responsive hyperbranched poly (amine-ether) through proton-transfer polymerization. *Journal of Polymorphism Science* 49: 966–975.
33. Liu D, Yang F, Xiong F, and Gu N. The Smart Drug Delivery System and Its Clinical Potential. *Theranostics* [Internet]. Ivyspring International Publisher; 2016; 6(9):1306–23. Available from: <http://dx.doi.org/10.7150/thno.14858>.
34. Lu B., Zhang J., and Yang H. (2003) Lung-targeting microspheres of carboplatin *International Journal of Pharmacology*, 265: 1–11.
35. Martins E., John-Africa L., Yetunde I., Olobayo K., and Sabinus O. (2012) Eudraginated polymer blends: a potential oral controlled drug delivery system for theophylline *Acta Pharmaceutica* 62: 71–82.

36. Majuru S. and Oyewumi M. (2009) Nanotechnology in drug development and life cycle management M. de Villiers (eds.), *Nanotechnology in Drug Delivery*, Chapter 20: 597–619
37. Chan A, Orme R, Fricker R, and Roach P (2013). Remote and Local Control of Stimuli-Responsive Materials for Therapeutic Applications. *Advanced Drug Delivery Reviews* 65: 497–514.
38. Nakayama M., Okano T., Miyazaki T., Kohori F., Sakai K., et al. (2006) Molecular Signs of Biodegradable Polymeric Micelles for Temperature-Responsive Drug Release *Journal of Controlled Release* 115: 46–56
39. Adepu S., Ramakrishna S., *Controlled Drug Delivery Systems: Current Status and Future Directions*. *Molecules* [Internet]. Multidisciplinary Digital Publishing Institute, 2021 Available from: <https://doi.org/10.3390/molecules26195905>.

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