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Review Article

A Systemic Review of Smart Drug Delivery Systems

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Abstract: One of the important advancement in pharmaceutical technology that attempts to improve the effectiveness and safety of therapeutic interventions is smart drug delivery systems. To distribute medications in a regulated, focused, and flexible way, these systems combine cutting-edge materials, microelectronics, and responsive mechanisms. The aim to increase patient compliance, reduce side effects, and maximize therapeutic results is what motivates the development of intelligent drug delivery systems. These innovative delivery methods make use of a variety of drug carriers, such as monoclonal antibodies, microspheres, dendrimers, liposomes, lipoproteins, and nanoparticle systems like inorganic nanoparticles (such as magnetic nanoparticles and quantum dots). It is critically examined how smart drug delivery technologies might transform personalized medicine and enhance therapeutic approaches. This study examines current developments in smart drug delivery, emphasizing important technologies as stimuli-responsive delivery platforms, polymeric systems, and carriers based on nanoparticles. The methods of drug release, including pH-sensitive, temperature-sensitive, and physiologically triggered systems, are highlighted. Furthermore, the incorporation of feedback mechanisms and real-time monitoring is examined, demonstrating how these systems can modify drug release rates in reaction to physiological shifts. Through clever and flexible drug delivery options, this review seeks to give a thorough overview of cutting-edge technology and their implications for improving healthcare.

Keywords: Importance, Properties, Route of Administration, Methodologies, Advantages, Limitations, System in Cancer Treatment.

INTRODUCTION

An essential aspect of modern medical practice is drug delivery, which guarantees the safe and efficient transport of therapeutic agents to the intended location within the body [1, 2]. Nonspecific targeting, limited efficacy, and unintended and evident adverse effects are some of the potential problems with traditional drug delivery or systemic administration [3, 4]. The cutting-edge subject of smart medication delivery seeks to solve these shortcomings by designing and developing delivery systems that better target particular cells, tissues, and organs while reducing off-target side effects [5, 6]. New opportunities for targeted medication administration against a variety of diseases, such as cancer, cardiovascular disease, neurological disorders, and infectious diseases, have been made possible by the development of automated drug delivery systems.

Smart drug delivery systems has the ability to completely change healthcare in general and medicine in particular via accurately distributing therapeutic drugs [7]. Several strategies are used by smart drug delivery systems to increase drug delivery's specificity, effectiveness, and safety. These include the use of hydrogels, liposomes, nanoparticles (NPs), hydrogels, and other biomaterials that can enhance the stability, solubility, and bioavailability of drugs. Additionally, intelligently designed medication delivery devices could react to internal or external stimuli and provide regulated drug release at the intended location [8].

One of the most crucial medical treatment modalities, along with surgery, radiation, physical therapy, and psychotherapy, is drug delivery, which is the process of delivering a pharmaceutical substance to produce a therapeutic effect in the prevention of disease

utilizing pharmaceuticals [9]. Serious side effects of such treatments include drug biodistribution changes, repeated treatments, and cell development of multidrug resistance (MDR) [10]. One of the most crucial medical treatment modalities, along with surgery, radiation, physical therapy, and psychotherapy, is drug delivery, which is the process of delivering a pharmaceutical ingredient to produce a therapeutic effect in the prevention of disease by pharmaceuticals [11]. some of the most common medical treatment modalities include drug delivery, surgery, radiation, physical therapy, and psychotherapy. It is the procedure of administering a medication to have a therapeutic effect in the use of medications to prevent illness [12]. Recurrent treatment-induced changes in drug resistance (MDR) are among the severe side effects of such treatments [13]. Among the most important medical treatment modalities include drug delivery, surgery, radiation, physical therapy, and psychotherapy. It is the method by which a pharmacological molecule is administered in order to produce a therapeutic impact in the prevention of disease [14].

Targeted medication administration aims to achieve the same thing. Targeted drug delivery, also known as smart drug administration, is a treatment strategy where a higher dosage of medication is given to one or a small number of body parts than to others. Consequently, it delivers the medication only to the specific areas of the body that it is intended to reach. This increases the effectiveness of therapy while reducing side effects [15]. Although the exact extent and impact of medication on health are difficult to determine, it is undeniable that medication has increased life expectancy when combined with better eating and cleanliness habits. Conventional chemotherapy affects both healthy and diseased cells by distributing drug throughout the body through the circulation [16].

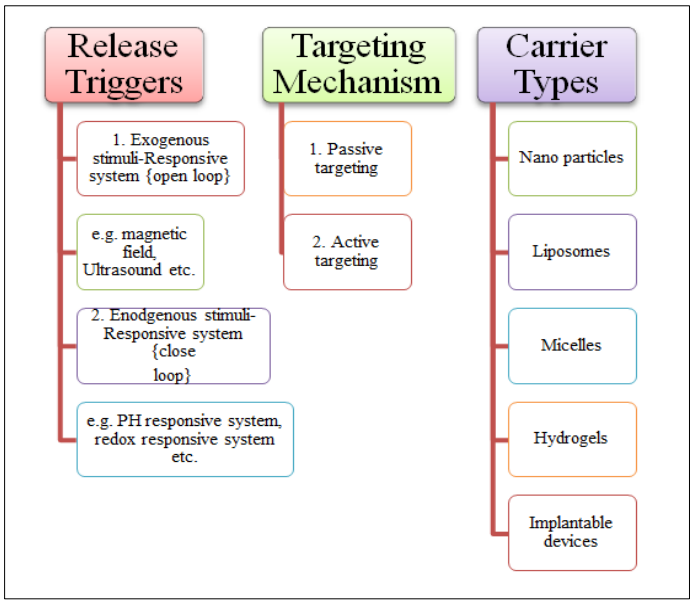
But for all promising drug and vaccine candidates, in order to increase efficacy and reduce side effects, suitable drug delivery systems that are enticing ways to enable the efficient, safe, and reliable application of bioactive compounds to the patient must be developed [17].

Smart Drug Delivery System

Advanced techniques or technologies that administer therapeutic compounds in a controlled, targeted, and intelligent way to improve treatment outcomes are referred to as smart drug delivery systems (SDDS). An SDDS is intended to deliver medication to specific areas at the appropriate time and dose, frequently in response to feedback or stimuli, in contrast to conventional drug delivery, which disperses pharmaceuticals non-specifically in the body [18, 19]. To put it another way, these systems "smartly" modify the release of a medicine in order to enhance effectiveness and reduce adverse effects. For instance, they may do this by identifying a target tissue or by detecting a trigger, such as pH or temperature [20, 21].

Targeted drug delivery, which emphasizes that the drug is intelligently given to a particular organ, cell type, or even intracellular compartment rather than spreading throughout the body, is frequently used interchangeably with smart drug administration [22]. In general, a smart drug delivery system seeks to improve patient outcomes and adherence by minimizing toxicity (by preserving healthy tissues) and optimizing therapeutic impact (by concentrating the drug at the site of need) [23]. On-demand or feedback-regulated drug release, pre-programmed release profiles, stimuli-responsiveness, and spatial targeting ability are important characteristics that commonly define SDDS [24].

CLASSIFICATION



IMPORTANCE

The pharmacokinetic and pharmacodynamic qualities of a medication can be enhanced with the use of smart drug delivery systems [25]. Enhances biocompatibility and cell specificity as well. Systemic drug administration has historically been best described as the "Random Walk" procedure of introducing a medication to every portion of the body in order to produce its therapeutic effect [25]. Along the way, it is likely to come across targets that are more likely to be hazardous to both healthy cells and non-targets. SDDS should be used for the purpose reduce the toxicity given on by conventional application techniques.

The three main reasons are as follows: -

- The first factor is pharmaceutical-related. Traditional medications tend to have lower solubility and greater instability compared to targeted drug delivery systems.
- Secondly, they exhibit poor absorption, a shorter half-life, and require a larger distribution volume, which reflects their pharmacokinetic characteristics.
- Lastly, in terms of pharmacodynamics, traditional drugs show lower specificity and a reduced therapeutic index when compared to targeted drug delivery methods [26].

Properties of Smart Drug Delivery Systems

The absorption distribution metabolism excretion (ADME) cycle, which starts with the absorption across a biological membrane, is followed by API in a traditional drug delivery system. In SDDS, however, the API circumvents this cycle to accomplish effective targeted delivery. Additionally, the system must be able to get past the host's defenses and arrive at its site of action [27]. The following factors must be considered when developing and putting into practice a targeted release system: the medication's delivery route, the intended location, and drug vehicles [28].

Targeted drug delivery systems should ideally be non-immunogenic, biochemically inert (non-toxic), physically and chemically stable both in vitro and in vivo, recognized by the target cells specifically and selectively, possess a controlled and predictable rate of drug release, and maintain the specificity of the surface ligands crossing various barriers. After that, it need to be easily and quickly removed from the body or biodegradable. The distribution system should be easy or somewhat simple to prepare, reproducible, and economical [29].

Routes of Smart Drug Delivery System

Drugs can enter the human body through a number of different anatomical paths. They may be intended to have systemic effects, or they may target particular organs and diseases. The route of administration must be chosen based on the disorder, the desired result, and the product that is accessible. Medications can be administered directly to the damaged organ or systemically and precisely to the diseased organ.

Classification of Anatomical Route:

- Oral delivery systems
- Transdermal delivery
- Inhalation systems
- Intravenous delivery
- Ocular delivery
- Vaginal and rectal delivery

Mechanism of Drug Delivery System

"Intelligent therapeutics" are a new class of intelligent, responsive delivery systems designed to do a number of tasks, such as identifying, isolating, and/or releasing therapeutic chemicals to treat illnesses [30]. Stimuli-responsive polymers, which can detect changes in a particular variable and start a reversible administration technique, are used in most intelligent drug delivery systems [31]. The development of open-loop and closed-loop control systems based on stimuli-responsive polymers and their applications as pulsatile, self-regulating drug delivery systems are reviewed in this review [32].

Methodologies of Smart Drug Delivery System

The ability to regulate and target the release of a medicine in response to particular stimuli or conditions is at the heart of smart drug delivery system techniques. The main approaches are as follows:

1. Mechanisms that Respond to Stimuli:

Therapeutic compounds are released in the following system in reaction to particular internal or external stimuli. Currently, one of the most alluring methods for drug administration is stimuli-responsive delivery. This approach, which uses either endogenous or exogenous triggers, is being actively studied to allow for tumor-specific delivery and regulated release of therapeutic medicines.

2. pH-Responsive Systems:

Because every organ or tissue in the body has a different pH, changes in the pH of the body can be used to trigger a reaction [33]. Since pH-responsive biomaterial nanoparticles may deform or dissolve in externally acidic or alkaline conditions, they can be used as DDSs [34]. Additionally, healthy and sick tissues have different pH values. To address this, nanogels have been designed to be sensitive to the particular pH range of interest, allowing for drug release only in the targeted tissue [35]. Use materials that alter their characteristics in response to temperature changes in temperature-responsive systems. It is very intriguing to consider the possibility of a device that can identify this divergence and release a therapeutic drug [33]. The DDSs must be stable and able to keep the cargoes at normal body temperature (up to 37 °C) in order to release them at higher temperatures (such as >40 °C) through significant physico-chemical changes in response to a restricted

temperature rise [36,37]. For instance, when the body temperature rises above a specific threshold, a thermoresponsive hydrogel may release a medication.Using enzymatically degradable linkers or polymers that release medications in response to particular enzymes found in the target tissue or environment is known as an enzyme-responsive system. Tyrosinase, trans-glutaminase, horseradish peroxidase, and elastase are the enzymes that are continuously utilized [38]. For example, Aimetti and colleagues developed human neutrophil elastase (HNE) anovel enzyme-responsive DDS to address local inflammation [34].

3. Magnetic and Light-Responsive Systems:

Using light or external magnetic fields to initiate the release of a medication. Light-sensitive materials can release medications when exposed to specific light wavelengths, while magnetic nanoparticles can release drugs when heated by an external magnetic field. Magnetic fields can be employed for both the viewing of magnetic materials through Magnetic Resonance Imaging (MRI) with a static magnetic field and controlled drug release in combination with Alternating Magnetic Fields (AMF) due to their profound penetration into biological tissues [39].

4. Targeted Delivery:

Intelligent medicine delivery devices can reduce side effects and boost effectiveness by precisely delivering prescription drugs to the right place. Ligand-Receptor Binding: Ligands are added to nanoparticles or carriers so they can bind to receptors that are overexpressed on target cells, such as cancer cells. This guarantees the drug's targeted distribution to the intended site. Both ligand-based active targeting techniques and local administration are used in the development of targeted drug delivery systems (DDS). Drugs, including bio-macromolecules (such as growth factors or genes) and small molecules, can be precisely localized to their intended target areas thanks to hydrogel-based local delivery and ligand-mediated interactions [40].

5. Antibody-Drug Conjugates:

These provide targeted delivery by conjugating drugs with antibodies that selectively target antigens on the surface of disease cells. Glycoproteins called antibodies, or immune globulins (Ig), are present on the surface of B cells and function as antigen receptors. A signaling cascade is set off when a particular antigen attaches to these receptors, activating and differentiating B cells into plasma cells, which then release antibodies into the circulation or other bodily fluids. Antibodies that are joined to other molecules by a chemical linker are known as antibody-drug conjugates, or ADCs. Targeting osteoclasts with an anti-RANK receptor monoclonal antibody and the peptide calcitonin, which has been demonstrated to inhibit osteoclast growth, is one instance of the use of ADC.

6. Controlled Release System:

This system is designed to keep the drug's concentration within the range that is therapeutically effective. By modifying its release rate, a controlled release device controls the target chemical's concentration [41]. A number of issues are resolved by this novel method, such as low solubility, poor bioavailability, poor absorption in the body, and instability in vivo [33, 34].

7. Matrix System:

The drug is mixed with a slowly dissolving carrier and compressed to form a matrix system [38]. A polymeric membrane disperses a medicinal molecule in this kind of controlled release device. These systems use both diffusion- and dissolution-controlled methods to continually distribute medication. 8. It has often been demonstrated that matrix technologies are appealing because to their convenience of use, ease of manufacturing, high degree of reproducibility, stability of the raw materials and dosage form, and ease of process validation and scaling up [39]. Glucotrol XL and Procan SR are two of the few commercially available formulations of these kinds.

8. Reservoir System:

A polymeric membrane encloses the drug core in the reservoir system [42]. The drug may exist in the drug reservoir compartment as a solid polymer matrix, gel, suspension, or solution, among other forms. The non-biodegradable polymers that make up the polymeric membrane. The physicochemical features of the drug being contained, such as solubility, particle size, and molecular weight, as well as the polymer's composition, molecular weight, and film thickness, control the rate of drug release in this system [43, 44]. Nico-400 and Nitrospan are two of the few commercially available reservoir system preparations.

Recent Drug Delivery Systems and Applications

In recent years, there has been a major advancement in the effective creation of drug delivery systems based on organic, inorganic, and hybrid nanoparticles as drug carriers for active targeting, particularly in chemotherapy. Better properties such as stability, toxicity, prolonged delivery, targeted specificity, enhanced permeability, increased solubility, and smaller particle sizes are developed into newer drug delivery systems (DDS). They can significantly improve the effectiveness of medicinal drugs when compared to conventional dosage forms [45, 46].

The most recent developments and innovative insights into the pharmacokinetic and pharmacodynamic behavior of medicines in the creation of the perfect drug delivery system are recognized as recent drug delivery systems. Being transporters, these DDS are able to transfer materials to the site of action and sustain drug concentrations within the therapeutic range for prolonged periods of time. Adoption of the delivery

system is directly related to the commercial and therapeutic success of the innovation. This would entail determining any problems, ensuring that patients receive the most benefit from the device, and incorporating them early in the development process. improving delivery strategies that reduce toxicity and increase efficacy. Different types of drug delivery systems are depicted in Figure No. 1.

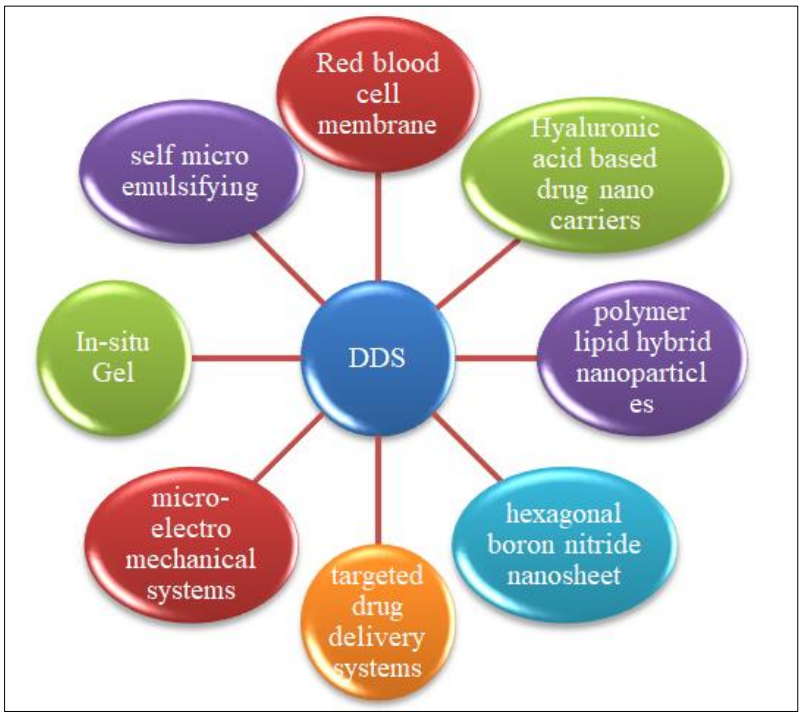


Fig. 1: Several types of recent drug delivery systems for different therapeutic purposes

Since technologies might improve effectiveness of treatment while reducing side effects, smart drug delivery systems have drawn a lot of interest in the field of drug delivery. Smart drug delivery systems have benefits and drawbacks, just like any other technology. Some significant, broader, and crucial parts of this are touched with in this section.

ADVANTAGES

1. Improved therapeutic efficacy: To improve therapeutic efficacy, intelligent drug delivery systems can be made to target particular tissues or cells. The ability of designed NPs to target onco-cells minimizes off-target side-effects and permits larger medication concentrations at the tumor location [47].
2. Controlled drug release: In addition to improved drug targeting, intelligent drug delivery systems can guarantee controlled drug release at predetermined rates or in reaction to predetermined stimuli, giving exact control over the profile and medication release/delivery time. This could lessen side effects and increase treatment efficacy [48].
3. Increased patient compliance: IT-enabled smart medicine delivery systems might be made to allow the consulting clinician to monitor dosage from a distance. By delivering medications across longer time periods, smart delivery systems can improve patient compliance and eliminate the need for frequent dosage [49].

LIMITATIONS

1. Complex design: A thorough understanding of drug pharmacokinetics, illness pathophysiology, and drug-delivery system interactions is necessary for the design and optimization of smart drug delivery systems. The outcome can be intricate and time-consuming design procedures [50].
2. Limited drug loading capacity: The therapeutic efficacy of certain smart drug delivery systems may be impacted by their limited drug loading capacity. Additionally, the drug's release kinetics may be impacted by its loading capacity [50, 51].
3. Biocompatibility and toxicity issues: Smart drug delivery systems' biocompatibility and toxicity must be carefully taken into account. NPs and other materials used to create intelligent drug delivery systems may be cytotoxic, which could have unanticipated negative consequences [50]. Before a potential material is qualified for use in the design of a drug delivery system, this must be handled with due diligence and several in vitro and in vivo compatibility and toxicity tests.

SMART DRUG DELIVERY SYSTEM IN TREATMENT OF CANCER

Rapid cell growth and division, which can infiltrate neighboring tissues and spread to other parts of the body to form tumors (metastasis), are characteristics of cancer. It ranks as the second leading cause of mortality globally. Cancer is a major and unresolvable worldwide health concern despite years of research and conclusions [51]. The main obstacles to effective cancer treatment are chemotherapy-resistant cancer cells, impaired drug transport inside the cells, inactivation of therapeutic medications, and significant organ and body damage. Drug transporters such as hydrogels and nanogels have been employed as a solution.

Compared to other carriers, they are better suited for cancer therapy because of their decreased toxicity, focused drug release in tumor locations, and sensitivity to particular stimuli. The precise drug administration in cancer treatment is made possible by these smart nanogels' ability to react to a variety of stimuli in the tumor environment, including variations in pH, temperature, light, redox, and more.

Enzyme levels in tumor cells are frequently unbalanced and significantly different from those in healthy cells, which upsets cellular homeostasis. Proteolytic enzymes and MMPs are released into the extracellular matrix by tumor cells, which causes it to degrade and permits tumor growth. Like the MMP-2 responsive hydrogel created by Li *et al*., utilizing hyaluronic acid and an MMP-2-sensitive peptide, MMP sensitive hydrogels use peptide-bound amino acid fragments to generate a matrix responsive to MMP activity. This hydrogel demonstrated a reactive trend in the release of medicine under laboratory settings [52].

In vivo testing demonstrated faster hydrogel disintegration at the tumor site, resulting in enhanced drug release and tumor growth reduction without compromising organ integrity. Furthermore, the pH of tumor tissues is typically lower than that of normal tissues [53, 54]. Anti-tumor medications can be precisely delivered and dispersed at tumor areas by using the pH difference to create pH-sensitive hydrogels. Liu created a pH-responsive peptide nanogel that can transport gemcitabine and paclitaxel to the tumor site at the same time in order to increase the efficacy against cancers and avoid drug resistance. In-vivo investigations demonstrated that the nanogel could reach the tumor location, enabling the two medications to release gradually and steadily into the tumor microenvironment.

Challenges for Smart Drug Deliv Ery Systems

Notwithstanding their potential benefits, smart drug delivery systems (SDDS) still have obstacles to overcome before they can be widely adopted and reach their maximum potential in clinical settings. The fields of material science, engineering, clinical practice, regulation, and economics are all affected by these difficulties. The following are the most important issues that need to be addressed:

1. Safety and Biocompatibility:

For advanced drug devices and carriers to fulfill their intended purposes without producing harmful immune responses or toxicity, they must be biocompatible. Certain nanomaterials have shown immunogenic or toxic effects in biological systems, including metals like gold and silver, carbon nanotubes, and certain polymers. For instance, despite their ability to effectively transport medications or DNA, carbon nanotubes have raised concerns about potential negative effects on the immune system, liver, kidneys, and lungs. Their safety must be guaranteed by extensive preclinical testing. Additionally, nanoparticles may be recognized as foreign by the body's natural defenses, particularly the liver and spleen mononuclear phagocyte system, which may remove them, decreasing their effectiveness and perhaps causing buildup in detoxifying organs [55, 56]. Implants for devices are also affected by this biocompatibility problem. Implant materials must not result in immunological rejection, fibrosis, or persistent inflammation. Because it can be difficult to balance function and biocompatibility, scientists are looking on biodegradable polymers that resorb after administering the medication. To help nanoparticles avoid immune detection, biomimetic coverings that resemble cell membranes are also being investigated [57].

2. Manufacturing Complexity:

Since intelligent drug delivery systems use advanced carriers, electronics, and even sensors, their construction is usually more complicated than that of conventional drug delivery systems. For example, creating stable nanoparticles with precise medication loading and size is much more difficult than creating conventional pills. Pharmaceutical and microelectronics fabrication are two separate processes that must ideally be linked in order to fabricate implanted micro-devices [58]. Maintaining consistency and quality control on a wide scale is challenging. The behavior and effectiveness of the nanoparticle can be altered by minor formulation modifications. New manufacturing paradigms are needed for some of the more recent distribution modalities, which also need for the sterile assembly of drug reservoirs and electrical components. Automation can also be challenging when dealing with fragile materials or novel processes. These issues can slow down the process from prototype to large-scale manufacture and increase production costs. The field is still working on solutions including scale-up techniques for nano-carriers, modular manufacture of combination goods, and 3D printing of intricate drug delivery devices [59, 60].

3. Regulatory and Approval Challenges:

Navigating regulatory processes is one of the largest SDDS issues. The approval of these products is complicated since they frequently need for the

integration of pharmacological, device, and occasionally biologic properties. Combination product paths are established by regulatory bodies such as the FDA and EMA. However, obtaining permission takes time and necessitates proving the safety and effectiveness of both the medication and the device components. It might be difficult to demonstrate the dependability of any software or hardware used in the delivery system, such as the requirement that devices operate as intended throughout the duration of their use [61]. Regulations for new technologies, like ingested pill sensors or AI algorithms that modify dosage (which are considered software as a medical device), are still being developed.

Additionally, as the number of linked devices rises, there are additional regulatory considerations, such as protecting cybersecurity and data privacy, since the devices may be compromised or suffer data breaches. It is very important to follow regulations in several areas, including cybersecurity, software validation, pharmaceutical GMPs, and medical device quality systems. These challenges necessitate interdisciplinary regulatory affairs experience and can slow down development times. The FDA's Digital Health Innovation Action Plan, which is working to clear the clearance process for innovative medicines, is one example of how regulatory authorities are attempting to provide more specific guidelines [62].

4. Economic Viability and Prohibitive Costs:

The design and implementation of smart medicine delivery systems are expensive. Such sophisticated systems demand costly manufacturing techniques and iterative research and development. As a result, a lot of SDDS products are expensive, and there are questions about their economic feasibility and cost-effectiveness. For instance, closed-loop pumps and sophisticated wearable injectors can cost hundreds to thousands of dollars, which can be a major deterrent to the widespread adoption of these technologies by patients and healthcare systems, especially in environments with limited resources [63]. According to a recent report, a major obstacle to industry participation in the SDDS market is the high costs associated with development, manufacture, and adoption. These solutions must clearly enhance health outcomes or produce savings, such avoiding hospitalization, in order to justify these costs.

Reimbursement presents another financial obstacle since insurance must choose whether and under what circumstances to fund these devices. Adoption of patients will be impeded in the absence of insurance reimbursement. Unit costs should drop when production scales are increased and technologies develop over time. Nonetheless, proving cost-effectiveness continues to be a crucial obstacle to commercialization. To promote the financial sustainability of goods, developers are advised to consider value-based pricing or health economic studies and to include cost modeling into development early on [64, 65].

5. Adoption and Adherence of Patients:

Enhancing patient adherence to recommended treatments is one of the main goals of SDDS. However, the effectiveness of such systems depends on the patients' willingness and ability to use them appropriately. A primary concern is usability. If a wearable injector is uncomfortable or bulky, or if connecting a smart inhaler to a smartphone is too challenging, patients may stop using the gadget. Human considerations also come into play; some patients may not charge their devices or may find technology uncomfortable [66]. Approximately 50–60% of patients with chronic illnesses have not taken their prescriptions as prescribed in the past, and non-adherence has been linked to almost 69% of hospitalizations for medication-related reasons.

Through automated dosage or reminding the patient, smart gadgets try to decrease forgetfulness. However, they also present new adherence issues, like device maintenance. Clinical research have shown that patients' adherence problems with devices are similar to those with pills. Developers make user interfaces simpler, offer training, and provide continuing assistance in order to lessen this. To reduce human mistake, certain wearable injectors, for instance, are made to start immediately upon application. Studies on patient acceptability also highlight how crucial it is for patients to feel comfortable both physically and mentally while using implants or electronics in their therapy. Last but not least, patient-focused design and education are necessary to maximize patient compliance with smart medication delivery systems and make them seem like a benefit rather than a burden [67].

6. Digital Infrastructure Integration:

Delivering interoperability, data security, and privacy is a challenge as intelligent delivery devices create data and communicate with health IT systems. Although different devices may be on different platforms and standards, and integration may be complicated, providers seek smooth data integration from smart pumps or inhalers into electronic health records (EHRs). In order for data from devices, such as an oncology medication implant, to be examined alongside lab findings within the hospital system, standard processes are required [68].

FUTURE PROSPECT OF SMART DRUG DELIVERY SYSTEM:

The healthcare industry is undergoing a change because to smart drug delivery systems (SDDSs), which provide individualized, regulated, and targeted treatment alternatives. SDDSs have enormous promise to solve unmet medical needs and enhance patient outcomes as technology develops [69].

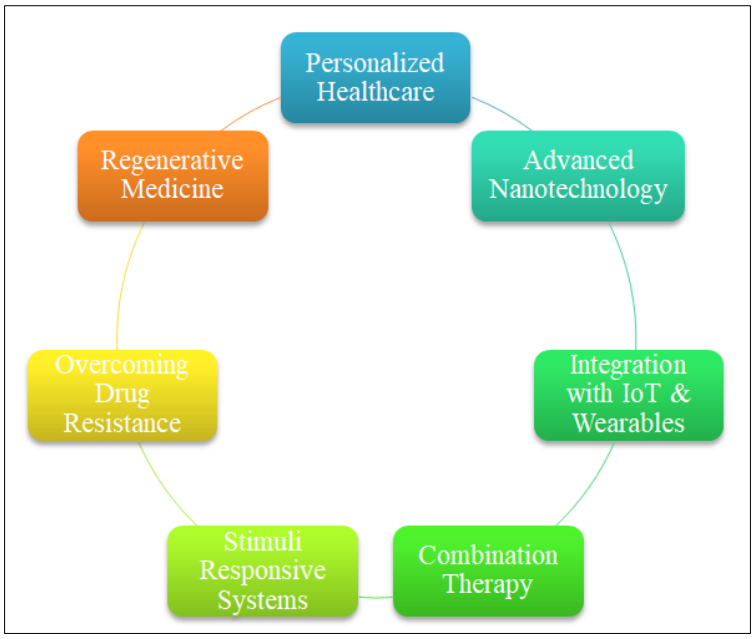


Fig. 2: Key Future Trends the Evolution of Smart Drug Delivery System

The following are some of SDDSs' main potential for the future:

Personalised Healthcare:
Personalized Treatment Programs:

Depending on the demands and genetic composition of each patient, SDDSs can be made to administer precise drug dosages at precise timings. Enhanced Efficacy: SDDSs can reduce adverse effects and increase therapeutic efficacy by directing medications directly to the afflicted location [70].

Advancements in Nanotechnology:
Drugs Nanoparticles: Their tissue penetration, bioavailability, and solubility can all be improved by using nanoparticles as carriers.

Targeted Delivery: Nanoparticles can be engineered to recognize specific cells or tissues, allowing for highly targeted drug delivery [71].

Integration with IoT and Wearables:
Real-time Monitoring:
IoT-enabled SDDSs can track patient data, such as vital signs and medication adherence, providing valuable insights for healthcare providers.

Remote Monitoring: Wearable devices can be integrated with SDDSs to enable remote monitoring and adjustments to treatment plans [72].

Stimuli-Responsive Systems:
Controlled Release: SDDSs can be engineered to release medications when triggered by certain stimuli, like alterations in pH, temperature, or enzymes.

On-Demand Delivery: This approach can ensure that drugs are released only when needed, reducing side effects and improving patient outcomes [73].

Combination Therapies:
Synergistic Effects: SDDSs can be used to deliver multiple drugs simultaneously, potentially enhancing therapeutic effects and reducing the need for multiple administrations.

Personalized Treatment: By combining different drugs in a controlled manner, SDDSs can offer more personalized treatment options [74].

Overcoming Drug Resistance:
Novel Delivery Methods: SDDSs can help overcome drug resistance by delivering drugs in a way that bypasses resistance mechanisms. Enhanced Drug Penetration: By improving drug penetration into resistant cells, SDDSs can increase the effectiveness of existing treatments [75].

Regenerative Medicine:
Stem Cell Delivery: SDDSs can be used to deliver stem cells to damaged tissues, promoting regeneration and repair.

Tissue Engineering: SDDSs can also be employed to deliver growth factors and other molecules to support tissue engineering and regeneration [76].

With the ongoing advancement of research and development in SDDSs, we anticipate witnessing further innovative and efficient applications in the coming years. These systems have the potential to revolutionize healthcare by providing personalized, targeted, and

efficient treatment options for a wide range of diseases and conditions [77].

CONCULSION

Future smart DDSs will use a variety of controlled-releasing nanomaterials as material science, pharmaceutical research, and biomedical science advance. Before smart DDSs are used in clinics, potential drug ability must be assessed, despite the fact that smart nano-DDSs have proven to be far more effective in diagnosis and treatment. Improving preclinical research of advanced DDSs to produce reproducible and transferable output to clinical-trial success would be a huge challenge for researchers. However, we must remember that the ultimate goal of all our efforts is to treat people. To guarantee that more stimulus-sensitive nanomedicine can be deployed in clinical settings, future research on smart DDSs for controlled drug delivery should concentrate on clinical translation.

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