4D DRUG DELIVERY SYSTEMS: A SMART APPROACH IN MODERN PHARMACEUTICS

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ABSTRACT:

The 4D drug delivery system is a revolutionary approach to pharmaceuticals, leveraging advanced technologies like 3D printing and smart materials to create devices that change shape or release drugs in response to specific stimuli. This system enables personalized and targeted therapy, improving treatment outcomes and patient compliance. The design and development of 4D printed devices involve careful consideration of materials, shape, and size, as well as simulation and modeling to predict behavior. The 4D drug delivery system has various applications, including cancer treatment, diabetes management, and tissue engineering. Stimuli-responsive materials, such as pH-responsive, temperature-responsive, and light-responsive materials, play a crucial role in these devices. The system also raises regulatory challenges, scalability concerns, and biocompatibility issues, which must be addressed. The future of 4D drug delivery systems looks promising, with potential integration with artificial intelligence, nanotechnology, and other technologies. Personalized medicine and tissue engineering are key areas where 4D printed devices can make a significant impact. As research advances, 4D drug delivery systems are expected to transform the pharmaceutical industry, enabling more effective and efficient treatment options for patients.

Keywords: 4D Printing, Smart Drug Delivery, Stimuli-Responsive Systems, Personalized Therapy, Controlled Release.

INTRODUCTION:

The emergence of 4D drug delivery systems represents a paradigm shift in the field of pharmaceuticals, offering unprecedented opportunities for personalized and targeted therapy. These systems, which leverage advanced technologies such as 3D printing and smart materials, enable the creation of devices that can change shape or release drugs in response to specific stimuli, like pH or temperature changes. This innovative approach has the potential to revolutionize the way medications are administered, providing more effective and efficient

treatment options for a wide range of diseases. By allowing for controlled release, personalized dosing, and targeted delivery, 4D drug delivery systems can improve treatment outcomes, reduce side effects, and enhance patient compliance. [1]

Four-dimensional (4D) printing has emerged as ground breaking advancement in the held of regenerative medicine, building upon the foundational principles of three-dimensional (3D) bioprinting by introducing the dimension of time into material design and function. Conventional 3D printing has significantly advanced the fabrication of architecturally intricate, yet static biomedical constructs such as scaffolds and implants. However, it lacks the ability to impart dynamic responsiveness. [2] In contrast, 4D printing integrates time as a functional dimension by utilizing smart biomaterials that can actively respond to external stimuli—such as temperature, pH, light, or humidity—after fabrication. This enables the production of constructs capable of real-time adaptation, offering behaviors that more closely resemble the dynamic nature of native biological tissues.

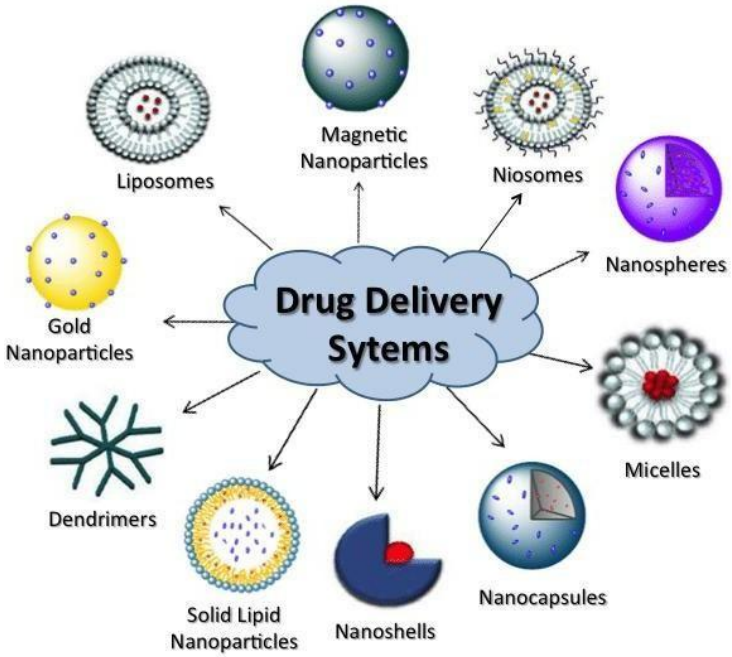

FIGURE NO 01: TYPES OF NANOCARRIERS USED IN DRUG DELIVERY SYSTEM.

The applications of 4D drug delivery systems are vast, ranging from cancer treatment and tissue engineering to pain management and beyond. As research in this field continues to advance, we can expect to see the development of increasingly sophisticated 4D printed devices that can adapt to the complex needs of individual patients. With the ability to tailor treatment regimens to specific patient populations, 4D drug delivery systems hold great promise for improving health outcomes and transforming the future of medicine. [3]

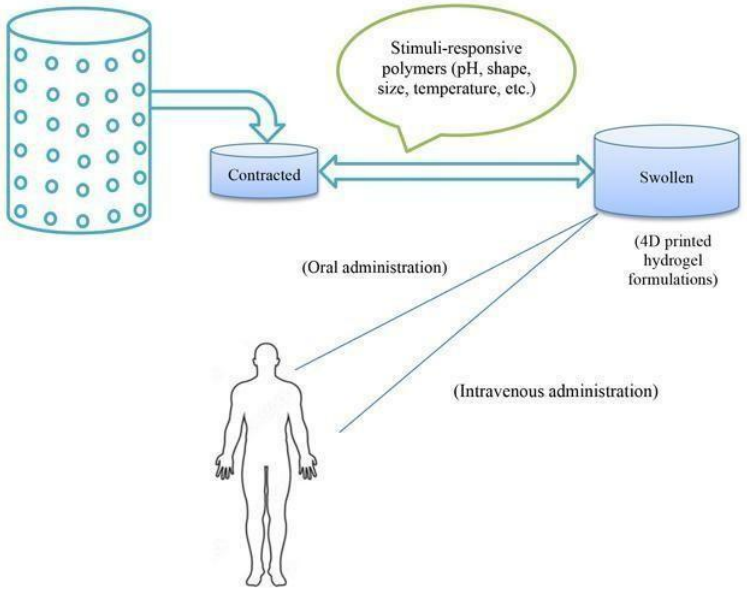

FIGURE NO 02: WORKING PRINCIPLE OF 4D PRINTED SMART DRUG DELIVERY SYSTEM.

The integration of 4D printing technology with pharmaceuticals has opened up new avenues for the development of smart drug delivery systems that can respond to the dynamic environment of the body. These systems have the potential to overcome the limitations of traditional drug delivery methods, providing more precise and effective treatment options for patients. [4] As the field of 4D drug delivery systems continues to evolve, it is likely that we will see the emergence of new and innovative applications that will further transform the way we approach healthcare.

The future of medicine is being shaped by the convergence of advanced technologies, and 4D drug delivery systems are at the forefront of this revolution. With their ability to provide personalized and targeted therapy, these systems are poised to make a significant impact on the treatment of various diseases, improving patient outcomes and enhancing quality of life. [5] The development of 4D drug delivery systems represents a major breakthrough in the field of pharmaceuticals, offering new hope for patients and healthcare providers alike. As we move forward in this exciting era of personalized medicine, it is clear that 4D drug delivery systems will play a critical role in shaping the future of healthcare.

There is always a continuous demand for developing advanced drug delivery systems (DDS) to boost the therapeutic effect of pharmaceutically active ingredients, including large biomolecules (e.g., peptides and proteins) suffering from poor bioavailability, hydrophobicity, or narrow therapeutic window. [6] Conventional DDS demonstrate a restricted ability for adapting to patient to-patient pharmacokinetic behaviors variations. Additionally, conventional DDS are more likely to cause undesirable side effects resulting from over- or underdosing.

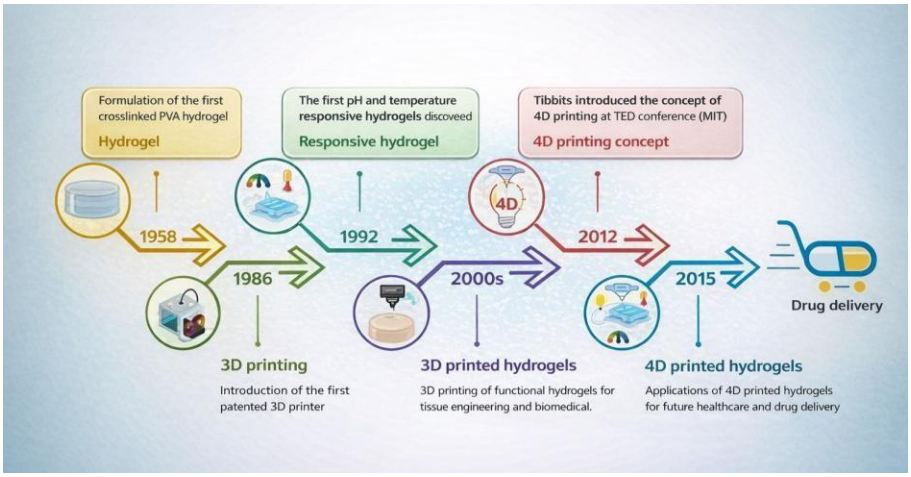

FIGURE NO 03: EVALUATION OF SMART HYDROGELS TO 4D DRUG DELIVERY SYSTEM.

Failure of precisely dose controlling based on individual patient differences can lead to patient incompliance, mainly for pediatrics and geriatrics. More specifically, the use of implantable DDS may rise some safety concerns related to the unfavorable foreign body reactions. Additionally, the presence of different formulations for a certain drug varying the dosage and physical form may affect its in vivo performance. [7] Also, the limitations in size and design of conventional DDS restrict the highest incorporated dosage in a single device, which, in turn, affects the ability and durability for long-term delivery. Accordingly, the need for dosage-controlled DDS has attracted the attention of scientists for the last years.

On the other hand, the more advanced four-dimensional (4D) printing, the smart materials are 3D printed to produce items that alter their shape after production, in a programmed manner over time, when exposed to a Graphical abstract Salama Future Journal of Pharmaceutical Sciences (2025). 4D-printed dosage forms differ from 3D ones in that time is considered as the 4th dimension during their performance. The term “4D printing” describes smart materials manufactured by the additive technique to produce easily achieved, complex-shaped, nonstatic objects that are more advanced than 3D objects. 4D-printed objects can be manufactured with 3D printers.[8]

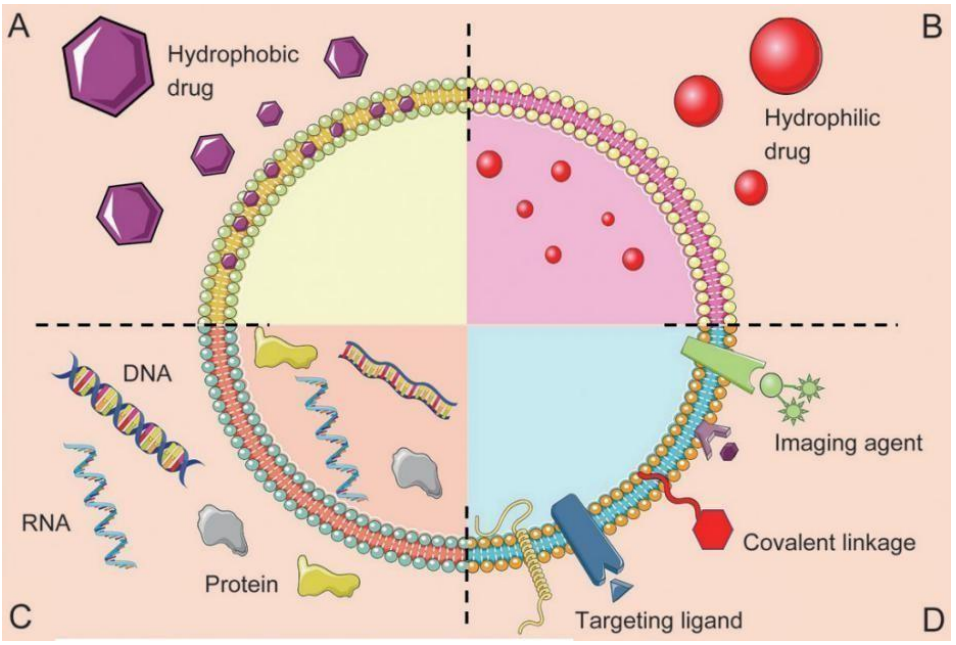

FIGURE NO 04: NANOCARRIER SYSTEM IN 4D DRUG DELIVERY SYSTEM.

Moreover, 3D printing can be exploited in the biomedical research fields represented in regenerative medication, tissue engineering, cancer research, and drug screening. The term "Bioprinting" describes this emerging, potent, and multipurpose bio fabrication technique which demonstrated promising applications in this field. In bioprinting process, depositing solutions or hydrogels of cell-laden polymer on a podium constructed using a computer-aided design (CAD) model is performed

Smart biomaterials for 4D bioprinting [9]

pH-Responsive materials are particularly advantageous for targeted drug delivery in pathological environments characterized by abnormal acidity. For instance, the tumor microenvironment and intracellular compartments such as endosomes and lysosomes typically exhibit a lower pH than normal physiological tissues. Materials designed to undergo structural changes or degrade in response to acidic conditions can enable site-specific release of therapeutic agents, enhancing efficacy while minimizing systemic toxicity. This makes pH sensitive polymers and hydrogels highly suitable for cancer therapy and intracellular delivery systems. The foundation of 4D bioprinting lies in the strategic use of smart biomaterials engineered substances capable of responding to specific environmental cues. These materials enable printed constructs to undergo controlled, time-dependent changes in shape, mechanical properties, or bio functionality. In the context of regenerative pathology, such adaptability is critical for achieving seamless integration with dynamic biological systems.

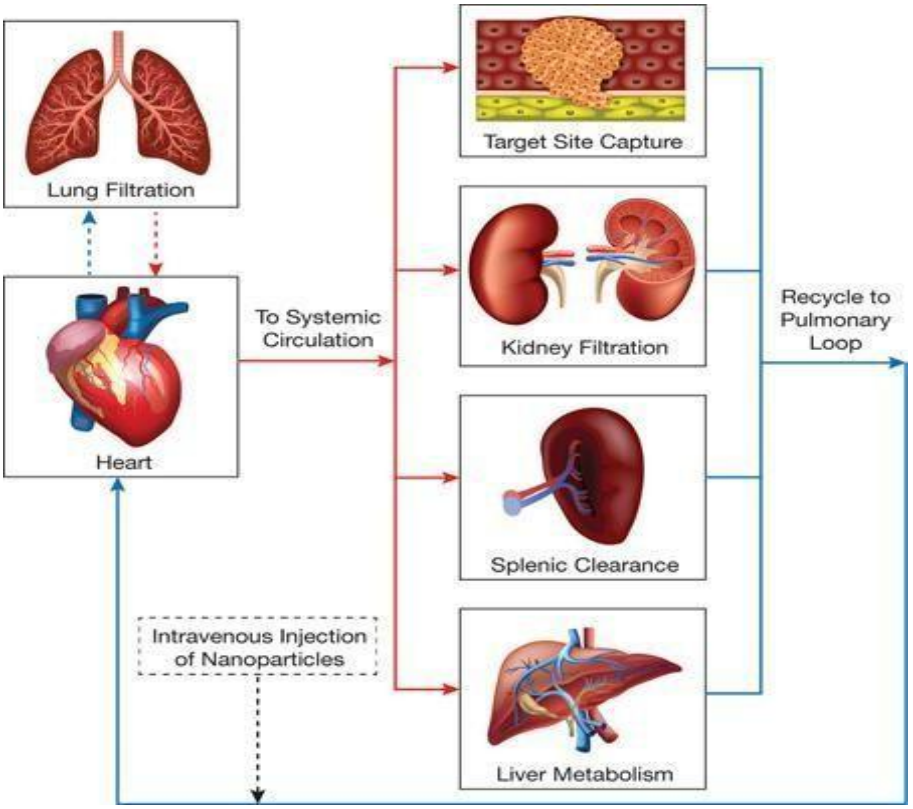

FIGURE NO 05: IN *VIVO* DRUG TRANSPORT AND ORGAN DISTRIBUTION.

Stimuli-responsive polymers (SRPs) are a unique class of so materials that can change their shape or behavior when exposed to specific environmental cues—such as light, heat, pH, moisture, electric or magnetic held, or even solvents. Because of this remarkable adaptability, they've become central to the development of flexible actuators, so robotics, wearable technology, sensors, and biomedical devices. In recent years, the integration of SRPs with 3D printing—commonly referred to as 4D printing—has opened up exciting possibilities. This technology allows researchers to create smart, personalized structures that don't just sit passively but actively transform over time by bending, expanding, twisting, or reshaping in response to their surroundings. As a result, 4D printing with SRPs is drawing growing interest across engineering, healthcare, and materials science.

pH-Sensitive polymers in 4D printing [10]

pH-Sensitive polymers are integral to 4D printing, enabling constructs to undergo controlled transformations in response to the pH variations within biological environments. These polymers contain functional groups that ionize or deionize at specific pH levels, leading to changes in their physical properties such as swelling, solubility, or mechanical strength This responsiveness is particularly valuable in biomedical applications where pH gradients are prevalent, such as in the gastrointestinal tract, tumor microenvironments, and sites of inflammation. pH-Sensitive polymers can be broadly classified into two categories—anionic and cationic-based on the nature of their ionizable functional groups. Anionic polymers contain

acidic groups, such as carboxylic acids, which undergo deprotonation at elevated pH levels.

This results in an increased negative charge density, leading to polymer chain expansion and swelling. Common examples include polyacrylic acid (PAA), polymethacrylic acid (PMAA), and alginate. These materials are particularly advantageous for drug delivery systems designed to release therapeutic agents in alkaline environments, such as the intestines. In contrast, cationic polymers possess basic groups, like amines, which become protonated under acidic conditions.

This protonation imparts a positive charge and promotes polymer swelling. Chitosan, a naturally derived polysaccharide, examples this class and demonstrates solubility and swelling behavior in acidic media, making it well-suited for targeted delivery in acidic environments such as the stomach or tumor microenvironments. Representative chemical structures of several pH-responsive polymers utilized in 4D printing—such as alginate, Poly (N, N dimethyl aminoethyl methacrylate) (PDMAEMA), chitosan, poly (acrylic acid), and poly (methacrylic acid)

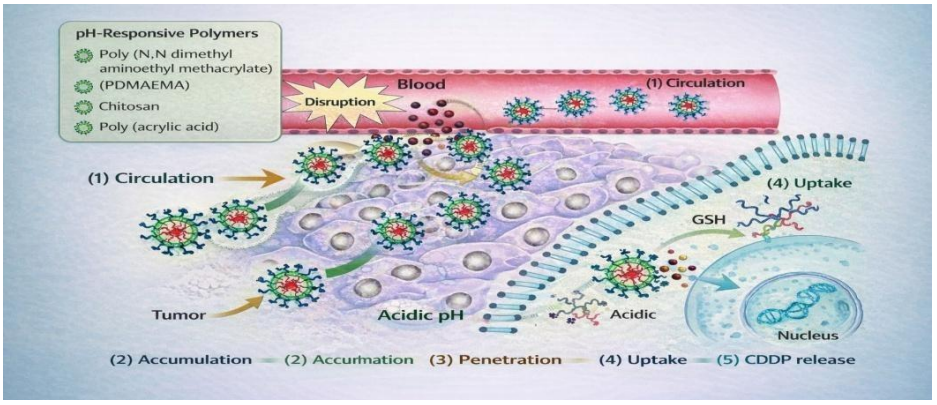

FIGURE NO 06: STIMULI -RESPONSIVE 4D DRUG DELIVRY FOR TARGETED CANCER THERAPHY

Light-sensitive polymers for 4D printing [11]

Light-responsive materials offer precise spatial and temporal control over activation, making them ideal for externally triggered therapies. Upon exposure to specific wavelengths—such as ultraviolet, visible, or near-infrared light—these systems can undergo conformational changes, bond cleavage, or generate heat or reactive species. Such responses enable controlled drug release, photothermal therapy, or photodynamic action, particularly useful in localized cancer treatments and wound healing. Their non-invasive trigger mechanism adds versatility, especially when minimal disturbance to surrounding tissues is desired.

A wide range of light-sensitive (photosensitive) functional groups have been reported in the literature, each exhibiting specific photo responsive behaviors such as photoisomerization,

photocleavage, or photodimerization. In the context of 4D printing, particular attention has been given to photosensitive moieties that enable spatiotemporal control over material properties in response to light stimuli. This section focuses on the photosensitive groups that have already been successfully integrated into 4D printing systems. [12] These include, but are not limited to, azobenzene derivatives (photoisomerization), spiropyrans (reversible switching between hydrophobic and hydrophilic states), coumarins (photodimerization and photocleavage), and o-nitro benzyl esters (photodegradation). Their incorporation allows for light triggered changes in shape, mechanical properties, or chemical functionalities, enabling dynamic behavior in smart materials tailored for biomedical, so robotics, and tissue engineering applications.

Thermo-responsive polymers in 4D printing [13]

Thermo-responsive materials exploit temperature fluctuations to trigger functional changes such as sol–gel transitions, swelling or deswelling. These systems are designed to respond near physiological or slightly elevated temperatures, enabling applications in controlled drug release, injectable hydrogels, and tissue engineering. In the context of 4D printing, these polymers play a pivotal role by enabling printed structures to transform their shape, functionality or mechanical properties over time when subjected to specific thermal stimuli.48–50 The integration of thermo-responsive polymers into 4D printing not only enhances the adaptability of printed structures but also expands their applicability in fields like tissue engineering, wearable electronics, and responsive implants.

Multi responsive: [14]

Multi-responsive materials in 4D printing represent a significant advancement in smart manufacturing, enabling printed structures to dynamically adapt to multiple environmental stimuli. By integrating materials that respond to various triggers—such as temperature, pH, light, magnetic fields, or reactive oxygen species—researchers have developed constructs capable of complex, programmable transformations. For instance, a study introduced a nanocomposite combining poly pyrrole-coated iron oxide nanoparticles within a shape memory polymer matrix, resulting in structures that can be remotely actuated using near-infrared light and magnetic elds. Another research effort focused on protein-based hydrogels that respond to temperature, pH, and enzymatic activity, showcasing autonomous shape changes suitable for biomedical applications. These innovations highlight the potential of multi-responsive 4Dprinted materials in creating adaptive systems for fields ranging from so robotics to personalized medicine.

ADVANTAGES: [15]

1. Personalized and Targeted Therapy: 4D drug delivery systems can be tailored to individual patient needs, providing personalized and targeted therapy.

2. Improved Efficacy: The controlled release of drugs can improve efficacy and reduce side effects.

3. Enhanced Patient Compliance: 4D drug delivery systems can improve patient compliance by providing a convenient and easy-to-use device.

4. Reduced Healthcare Costs: The system can reduce healthcare costs by improving treatment outcomes, reducing hospitalizations, and minimizing the need for repeated dosing.

5. Increased Bioavailability: 4D drug delivery systems can increase bioavailability by releasing drugs in a targeted and controlled manner.

6. Reduced Toxicity: The system can reduce toxicity by releasing drugs in a controlled and targeted manner, minimizing exposure to healthy tissues.

7. Improved Patient Outcomes: 4D drug delivery systems can improve patient outcomes by providing more effective and efficient treatment options.

DISADVANTAGES: [16]

1. Complexity: 4D drug delivery systems can be complex and difficult to manufacture, requiring specialized equipment and expertise.

2. Regulatory Hurdles: The regulatory framework for 4D drug delivery systems is still evolving, and there may be uncertainty around approval and reimbursement.

3. Cost: The development and production of 4D drug delivery systems can be expensive, which may limit their adoption.

4. Scalability: Scaling up the production of 4D drug delivery systems can be challenging, which may limit their widespread adoption.

5. Biocompatibility: The biocompatibility of 4D printed devices is a critical concern, and there may be risks associated with their use in humans.

6. Degradation: The degradation of 4D printed devices can be unpredictable, which may affect their performance and safety.

7. Limited Understanding: There is still limited understanding of the long-term effects of 4D drug delivery systems, which may limit their adoption.

METHODOLOGY:

Step 1: Design and Development

- Computer-Aided Design (CAD): The design of the 4D drug delivery device is created using CAD software, taking into account the specific requirements of the device, such as shape, size, and material properties.
- Simulation and Modeling: The design is simulated and modeled using computational tools to predict the behavior of the device under various conditions, such as temperature, pH, and mechanical stress.

Step 2: Material Selection

- Smart Materials: The selection of smart materials that can respond to specific stimuli, such as temperature, pH, or light, is critical for the development of 4D drug delivery systems.
- Biocompatible Materials: The materials used must be biocompatible and non-toxic to ensure safe use in the body.

Step 3: 3D Printing

- 3D Printing Techniques: The 4D drug delivery device is fabricated using 3D printing techniques, such as stereolithography (SLA), fused deposition modeling (FDM), or selective laser sintering (SLS).
- Printing Parameters: The printing parameters, such as temperature, pressure, and speed, are optimized to achieve the desired device properties.

Step 4: Drug Loading

- Drug Incorporation: The drug is incorporated into the 4D printed device using various techniques, such as solvent casting, melt extrusion, or supercritical fluid technology.
- Drug Distribution: The distribution of the drug within the device is controlled to achieve the desired release profile.

Step 5: Stimulus-Responsive Behavior

- Stimulus-Responsive Materials: The 4D printed device is designed to respond to specific stimuli, such as temperature, pH, or light, which triggers the release of the drug.
- Shape-Memory Effect: The shape-memory effect of the smart materials is utilized to achieve the desired shape change or deformation of the device.

Step 6: In Vitro and In Vivo Testing

- In Vitro Testing: The 4D drug delivery device is tested in vitro to evaluate its drug release profile, biocompatibility, and mechanical properties.
- In Vivo Testing: The device is tested in vivo to evaluate its efficacy, safety, and pharmacokinetics in animal models.

Step 7: Clinical Trials

- Clinical Trials: The 4D drug delivery device is evaluated in clinical trials to assess its safety and efficacy in humans.
- Regulatory Approval: The device must receive regulatory approval before it can be marketed and used in clinical practice.

OBJECTIVES:

1. To develop a personalized and targeted drug delivery system: The 4D drug delivery system aims to provide a personalized and targeted approach to drug delivery, allowing for tailored treatment regimens and improved patient outcomes.
2. To improve drug efficacy and safety: The system aims to improve the efficacy and safety of drugs by releasing them in a controlled and targeted manner, reducing side effects and improving patient compliance.
3. To enhance patient compliance: The 4D drug delivery system aims to improve patient compliance by providing a convenient and easy-to-use device that can be tailored to individual patient needs.
4. To reduce healthcare costs: The system aims to reduce healthcare costs by improving treatment outcomes, reducing hospitalizations, and minimizing the need for repeated dosing.
5. To advance the development of novel biomaterials: The 4D drug delivery system aims to contribute to the development of novel biomaterials that can be used in medical devices and implants.

CHALLENGES AND LIMITATIONS:

1. Complexity of 4D Printed Devices: The complexity of 4D printed devices can make them difficult to manufacture and regulate.
2. Biocompatibility and Biodegradability: The biocompatibility and biodegradability of 4D printed devices are critical concerns that must be addressed.
3. Scalability and Cost-Effectiveness: The scalability and cost-effectiveness of 4D printed devices are important factors that will influence their widespread adoption.
4. Regulatory Hurdles: Regulatory hurdles may slow the development and approval of 4D drug delivery systems.

APPLICATIONS:

4D printing for developing drug-loaded implants for breast cancer treatment

Although breast-conserving surgery is performed as a primary approach to treat breast cancer in its early-stage, the chance of recurrence and body image alteration adversely influence patient by the emotional distress. It is advised also to complete the treatment with either radiotherapy or systemic therapies to increase the patient's survival chance, and also to avoid possible recurrence. [17] This leads to longer treatments durations, and undesirable systemic adverse effects. A patient-centered approach is essential to eradicate the heterogeneity between tumors and individuals. To achieve this aim, a multipurpose 4D-printed doxorubicin-loaded implant was developed by Moroni et al. by blending carboxymethyl cellulose sodium salt and cellulose nanocrystals. Full rheological investigation was performed in order to expect the printability accomplishment. [18]

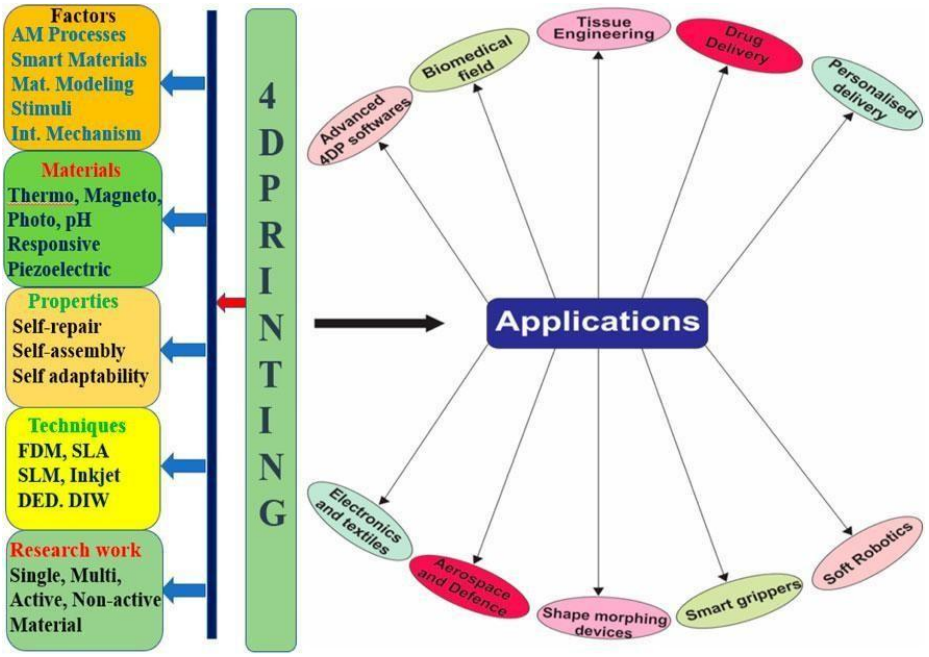

FIGURE NO 07: SCHEMATIC ILLUSTRATION OF 4D PRINTING FOR SMART DRUG DELIVERY APPLICATION.

Herein, by swelling, the designed smart device was programmed to change size for exact fitting in the intended tissue cavity. This fitting is highly desirable for personalization of treatments and improves the esthetic results. The effect of the printing as well as formulation parameters on shape conversion was tested by conducting a swelling test, to prove the possibility of programming a 4D shape. The assessment of the anticancer efficacy was performed in vitro using MDAMB-231 cells, where the designed 4D-printed implant displayed an excellent anticancer efficacy. The results of the in vitro studies as well as the morpho-transformation suggested the potential of the designed implants as a promising treatment approach for breast

cancer after resection, by filling the surgery-left void and providing an anticancer influence to prevent recurrence, as well. [19]

The authors suggested performing comprehensive investigations for the technical aspects for the fruitful translation of 4D printing technology into biomedical applications. This necessitates proficiency regarding material selection, including their availability and smart properties, as well as a thorough understanding of how printing parameters and design could influence responsiveness to specific stimuli. [20] Moreover, exploring other trigger stimuli that could increase other potential applications of 4D printing. However, in spite of these prospects, lack of clear regulatory guidelines for additive manufacturing technologies, and inadequate focus on scalability, hinders further progression from research to clinical use. Therefore, foregrounding regulatory strategies for large-scale production is fundamental.

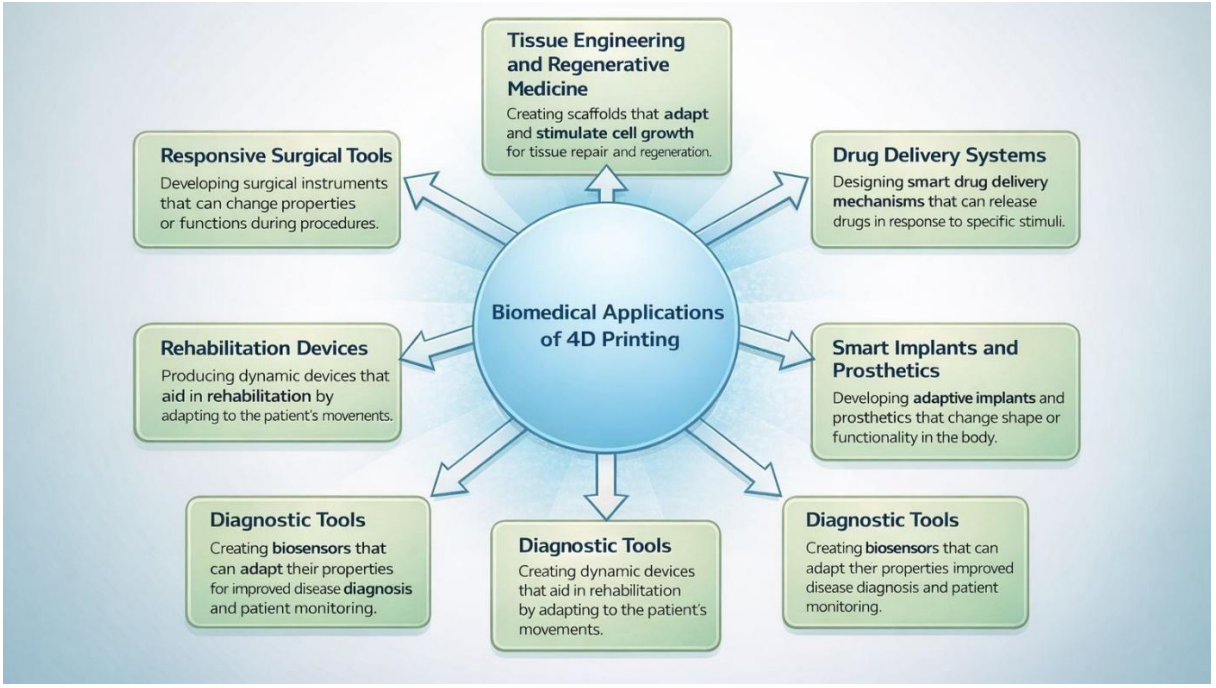

FIGURE NO 08: BIOMEDICAL APPLICATION OF 4D PRINTING TECHNOLOGY

4D printing for developing unfolding/expandable dosage forms

Thermoplastic, flexible, and elastic polyurethanes are widely used in the field of medical and pharmaceutical research as implants, dosage forms, or components of medical devices. Various shaped and foldable objects can be obtained using the 3D printing technique from polyurethane filaments, to be applied in expanding (unfolding) dosage forms.

Exploitation of the shape memory behavior was performed to fold and package the designed dosage forms in hydrophilic hard gelatin capsules. [21] Time for unfolding as well as dimensional recovery of prepared objects was considered as critical factors that were correlated with the material properties and shape. This could be useful for designing flexible dosage forms

which can acquire an unfolded size fitting for gastroretentive purposes. However, careful consideration should be taken into account regarding the stability of the designed shapes after storage regarding dimensional recovery and expansion time. The proposed perception of the hybrid shape memory effect could be convertible to develop innovative medical devices or sustained release dosage forms which require to possess flexible and elastic behavior. [22]

Expandable gastroretentive system was designed based on the shape memory behavior of poly vinyl alcohol. The designed device would be administered in a collapsed form suitable for swallowing, then get into a larger size in situ, allowing longer residence time in the stomach, hindering escape from the pylorus. Prototypes containing allopurinol, with various original shapes, were successfully fabricated by 4D fused-deposition modeling printing or manually by processing of extruded rods. The attained size was fitted within commercial hard gelatin capsules. [24] Shape modifications of the extruded samples were evaluated by a quantitative method over time in a static acidic environment at body temperature. Results revealed the ability of the prototypes to regain the original shape, attaining the required spatial encumbrance in short time. Release of the drug had no correlation with the shape of the systems, yet it was decelerated by coating with Eudragit® RS/RL.

4D printing also was exploited to develop coated expandable drug delivery systems with extended retention and controlled drug release into hollow muscular organ, as the bladder. The shape memory behavior of polyvinyl alcohol was used to attain prototypes able to be programmed in a temporary configuration suitable for administration, which recover into the original intended shape and retain at the targeted site. [25] Coating of the 4D-printed prototypes was carried out using the insoluble, yet, permeable Eudragit® NE despite their shapes (elongated or folded). The coating process turned out to be reproducible, yielded samples with good physical and technological features, regarding the reproducible thickness, release performance and capability to effectively restore the required original shape from the temporary one, upon contacting the aqueous fluids at the physiological temperature.

The shape memory effect was independent on the coatings. The promising results, obtained for the reservoir-like expandable prototypes intended for intravesical applications, encouraged the industrial scaling up. The potentiality of the suggested technique was verified by inspecting the coated prototypes regarding their physical–technological characteristics, shape memory restoring, and release performance in urine simulated fluids. The obtained results were promising encouraging taking out the challenge of processing and scaling up for more advanced prototypes. [26]

4D printing for developing drug-loaded stents

As another advanced application for 4D printing, soft robotics and medical devices could be manufactured, in high resolution and with tailorable functionalities, coupling novel shape memory photopolymer and digital light processing The major challenge being faced during the preparation of 4D objects is the type of materials used; nondegradable ones have limited clinical applications. Alternatively, using biodegradable elastomers is challenging, specifically if the transition points are in good match with the physiological temperature. [27]

Thus, shape fixation under ambient conditions is attained. Paunovic et al. reported the 4D printing processing of biodegradable shape memory elastomers using poly(D,L-lactide-co-trimethylene carbonate) methacrylate at different feed ratios of monomer. High-resolution digital light processing printed stents conserved their folded shape at room temperature, while restored their shapes effectively at body temperature. The materials were degradable under physiological conditions and cytocompatible. Tunable release kinetics when the devices were loaded with levofloxacin or nintedanib. This study shed the light for the potentiality of 4D printing in developing a new generation of medical devices. [28]

4D-printed tablets loaded with anticancer drugs

Drug-loaded binder jet printed tablets could be prepared adopting the drop-on-demand technique, where drugs are dissolved in either ethanol or water. The porosity in the tablets would arise from solvent evaporation and can be manipulated by controlling the percentage of ethanol and water. Rhodamine 6G was chosen as an example of a hydrophilic drug to be loaded in the designed tablet, as it could be assayed easily being fluorescent and the potential therapeutic anticancer effects. [29]

The ink solutions were printed on blank 3D-printed tablets, containing calcium sulfate hemihydrate utilizing the drop-on-demand technique. Then, tablets were characterized, after drying at room temperature. Results showed that increasing the water ratio in the ink solutions resulted in greater interaction with the bulk material, resulting in thicker tablets with heavier weights, while higher ethanol ratios showed faster tablet penetration. Investigation by SEM–EDX and fluorescent microscope revealed uniform drug distribution. In vitro drug release study indicated the reverse relation between water content and release rate. The performed study emphasized the impact of drop-on-demand technology in distributing drugs uniformly on the surface of tablet, and the significant influence of the ratio of water to ethanol on drug release from the fabricated tablets. [30]

Bone tissue engineering

4D printing has been utilized to create biodegradable scaffolds that can adapt to bone defects, promoting regeneration. Materials like polylactic acid (PLA) and polyglycolic acid (PGA) are commonly used due to their biocompatibility and ability to degrade into non-toxic by products. These scaffolds can be designed to change shape in response to physiological conditions, ensuring a better and integration with the host tissue. Porous shape memory cryogel Microspheres (CMS) made from GelMA have been fabricated using an emulsion technique combined with gradient cooling. These CMS can be loaded with human bone marrow-derived mesenchymal stem cells (hBMSCs) and human umbilical vein endothelial cells (HUVECs), promoting vascularized bone tissue regeneration upon subcutaneous injection in animal models. Blending PLA with PCL results in composites with improved shape memory behavior and mechanical properties suitable for bone applications. These composites can restore their original shape upon heating, mimicking the structure of cancellous bone. [31]

CONCLUSION:

In conclusion, the emergence of 4D drug delivery systems represents a significant breakthrough in the field of pharmaceuticals, offering unprecedented opportunities for personalized and targeted therapy. These systems, which leverage advanced technologies such as 3D printing and smart materials, enable the creation of devices that can change shape or release drugs in response to specific stimuli, like pH or temperature changes. By providing controlled release, personalized dosing, and targeted delivery, 4D drug delivery systems have the potential to revolutionize the way medications are administered, improving treatment outcomes, reducing side effects, and enhancing patient compliance.

The applications of 4D drug delivery systems are vast, ranging from cancer treatment and tissue engineering to pain management and beyond. As research in this field continues to advance, we can expect to see the development of increasingly sophisticated 4D printed devices that can adapt to the complex needs of individual patients. With the ability to tailor treatment regimens to specific patient populations, 4D drug delivery systems hold great promise for improving health outcomes and transforming the future of medicine.

The integration of 4D printing technology with pharmaceuticals has opened up new avenues for the development of smart drug delivery systems that can respond to the dynamic environment of the body. These systems have the potential to overcome the limitations of traditional drug delivery methods, providing more precise and effective treatment options for patients. As the field of 4D drug delivery systems continues to evolve, it is likely that we will

see the emergence of new and innovative applications that will further transform the way we approach healthcare.

The future of medicine is being shaped by the convergence of advanced technologies, and 4D drug delivery systems are at the forefront of this revolution. With their ability to provide personalized and targeted therapy, these systems are poised to make a significant impact on the treatment of various diseases, improving patient outcomes and enhancing quality of life. The development of 4D drug delivery systems represents a major breakthrough in the field of pharmaceuticals, offering new hope for patients and healthcare providers alike.

As we move forward in this exciting era of personalized medicine, it is clear that 4D drug delivery systems will play a critical role in shaping the future of healthcare. With their potential to improve treatment outcomes, reduce side effects, and enhance patient compliance, these systems are an important step towards creating a more patient-centric and effective healthcare system.

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