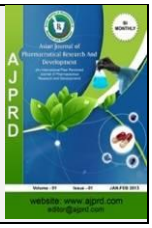
Available online on 15.06.2026 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research



Open Access

Review Article

Comprehensive Review on Hydrogel as Advanced Platform for Novel Drug Delivery Systems

Saurabh V Bodke *, Vikrant P. Wankhade, Abhishek D.Mankar, Ishika S. Bijore, Ajay Nemade

Department of Pharmaceutics, Vidyabharti College of Pharmacy, Amravati, Maharashtra, India

A B S T R A C T

Hydrogels have emerged as a transformative platform for advanced novel drug delivery systems (NDDS), address ing major limitations of conventional therapeutic administration such as poor localization, uncontrolled release, and systemic toxicity. Their three-dimensional, hydrophilic polymeric network enables exceptional biocompatibility, unable degradability, and controlled drug release kinetics. This review comprehensively explores the fundamental principles, fabrication techniques, and physicochemical properties that govern hydrogel performance in DDS. Special emphasis is placed on stimuli-responsive (smart) hydrogels, including pH-, temperature-, enzyme-, and redox-sensitive systems, which offer precise spatiotemporal control and responsiveness to pathological conditions. The article also highlights biomedicalapplications of hydrogels in oncology, ophthalmology, wound healing, and regenerative medicine, alongside challenges in large-scale manufacturing, regulatory classification, and product standardization. Finally, emerging trends such as hybrid nanocomposite systems and 3D printing are discussed as pivotal strategies for enhancing functionality and facilitating clinical translation. Hydrogels thus represent a cornerstone of next-generation precision drug delivery and personalized medicine.

Keywords: Hydrogels, Biocompatibility, Drug Delivery Systems (DDS), Novel Drug Delivery Systems (NDDS), Controlled Drug Release, Biodegradability,

A R T I C L E I N F O: Received 11 Dec.2025; Review Complete 23 Feb, 2026; Accepted 19 March. 2026; Available online 15 June. 2026

Cite this article as:

Saurabh BV, Wankhade VP, Mankar AD, Bijore IS, Nemade A, Comprehensive Review on Hydrogel as Advanced Platform for Novel Drug Delivery Systems, Asian Journal of Pharmaceutical Research and Development. 2026; 14(3):173-185
DOI: http://dx.doi.org/10.22270/ajprd.v14i3.1776

*Address for Correspondence:
Bodke V. Saurabh, Department of Pharmaceutics, Vidyabharti College of Pharmacy, Amravati, Maharashtra, India

INTRODUCTION

The Imperative for Controlled and Localized Drug Delivery

Conventional systemic drug administration routes frequently encounter significant limitations that compromise therapeutic efficacy and patient safety. Challenges include the rapid degradation of labile drugs, inadequate local drug availability at the target site, lack of spatiotemporal control over drug concentration, and high systemic toxicity resulting from broad distribution. For many critical therapeutics, such as proteins, peptides, and small molecules used in oncology or regenerative medicine, these drawbacks necessitate the development of localized and controlled release vehicles.

Hydrogels have emerged as a revolutionary platform addressing these pharmaceutical needs. They function as highly effective carriers that not only protect therapeutic agents from premature loss or degradation during transportation but also facilitate efficient, often on-demand, release to the desired locus. The capability to protect labile drugs, coupled with physicochemical tail or ability, positions hydrogels as essential components in the next generation of drug delivery systems".

Definition, Structure and Fundamental Advantages of Hydrogels.

Hydrogels are defined as highly hydrated, three-dimensional (3D) polymeric mesh networks**.** These networks are composed of hydrophilic polymers derived from natural, synthetic, or semi-synthetic sources, held together by chemical crosslinking (permanent covalent bonds) or physical crosslinking (temporary non-covalent interactions). The defining characteristic of hydrogels is their substantial water content often exceeding 90% of their total mass which endows them with high bio compatibility and mechanical properties similar to native soft tissues[2]. For drug delivery, hydrogels offer distinct

Advantages:

- Hydrogels are highly biocompatible and produce minimal foreign body response.
- They provide controlled and sustained release of

drugs over an extended period.

- Hydrogels protect encapsulated drugs from physical and chemical degradation.
- Their physical properties can be easily tuned as per formulation needs.
- They offer controllable degradability for predictable drug release.
- Hydrogels enhance the stability of sensitive therapeutic agents.
- Hydrogels improve patient compliance by reducing dosing frequency.
- They enable localized drug delivery with reduced systemic side effects.

The complexity of these systems, however, creates a fundamental challenge for regulatory and scientific consensus. While hydrogels are praised for their unique ability to be tuned in terms of properties, degradability, and release kinetics1, this heterogeneity across different designs and preparations means that comparing findings from various investigations is exceptionally difficult. The field currently suffers from a lack of standardized methodologies used to characterize and evaluate drug release. This absence of harmonized practices is a core scientifichurdle that impedes accurate comparison and slows clinical development, as regulatory compliance requires rigorously reproducible and comparable data[2].

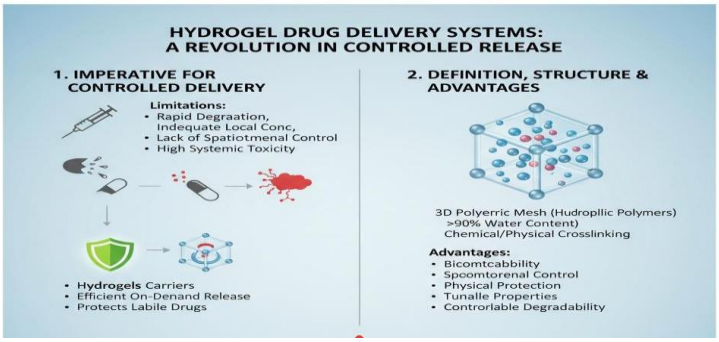


Figure 1: Introduction to the Hydrogel

Physicochemical Basis and Engineering of Hydrogel Networks:

Classification by Origin and Composition: Hydrogels can be broadly classified based on the polymeric source used in their fabrication, impacting their biological interaction, mechanical performance, and degradation profiles.

Natural Polymer

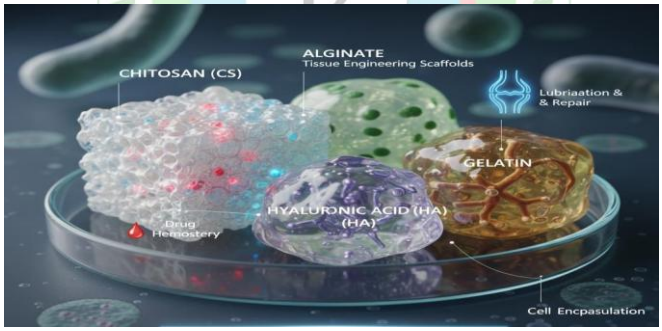


Figure 2: Natural Polymer

Hydrogels derived from natural biopolymers such as Chitosan (CS), Alginate, Hyaluronic Acid (HA), and Gelatin are prized for their inherent characteristics". They offer high biocompatibility and biodegradability, which are critical for safe in vivo use. Chitosan based hydrogels, in particular, demonstrate advantageous properties such as mucosal. adhesion and hemostatic activity, offering significant potential for localized tissue engineering and drug delivery applications".

SyntheticPolymers

Synthetic polymers, including Polyethylene Glycol (PEG) and Poly(vinyl alcohol) (PVA),are frequentlyutilizedduetothecontroltheyofferoverthere sultingmaterial's properties[6]. Synthetic materials allow for precise tuning of mechanical stability, degradation kinetics, and purity, often leading to reproducibility compared to their natural counterparts[8].

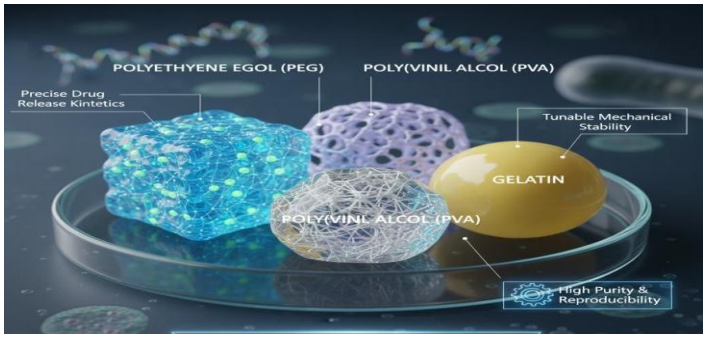


Figure 3: Synthetic Polymer

Hybrid and Nanocomposite Systems

Advanced systems are often synthesized by combining natural and synthetic polymers to create hybrid hydrogels, thereby merging the advantageous properties of both classes, such as the biocompatibility of a natural material with the mechanical robustness of a synthetic one". Examples include PEG-chitosan hydrogels, which have been explored for biosensing applications (e.g., glucose monitoring). Further sophistication is achieved in nanocomposite hydrogels, where functional nanoparticles (NPs) are embedded within the polymer matrix. For instance, magnetic nanoparticles (MNPs), often coated with, dextran, or PEG, can be integrated into PEG, PVA, chitosan, or gelatin matrices. These systems facilitate novel functionalities, such as magnetically triggered drug delivery, essential for targeted chemotherapy".

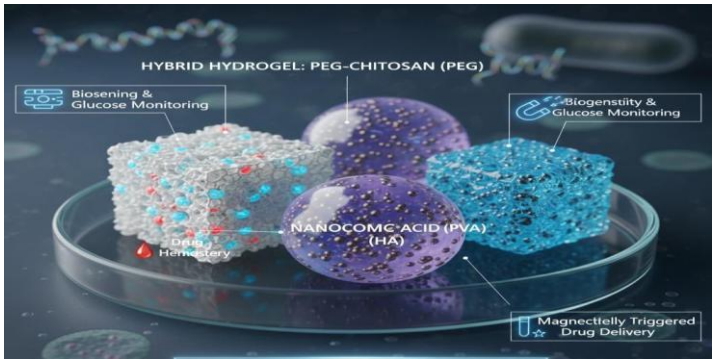


Figure 4: Hybride Hydrogel

Hydrogel Network Fabrication and Crosslinking Mechanisms

The method of crosslinking dictates the stability and performance of the hydrogel network. Crosslinking can be physical or chemical.

Physical Crosslinking

Physical crosslinking involves non-covalent interactions that form temporary junctions. Methods include ionic interaction, utilized when crosslinking alginate using divalent calcium ions at room temperature and physiological pH. Hydrogen bonding (Bonding). such as that occurring between the carboxylic group of polymethacrylic acid or polyacrylic acid and the oxygen of polyethylene glycol, is another key physical mechanism. Thermal methods, like heating and cooling polymer solutions, are also applied to induce gelation".

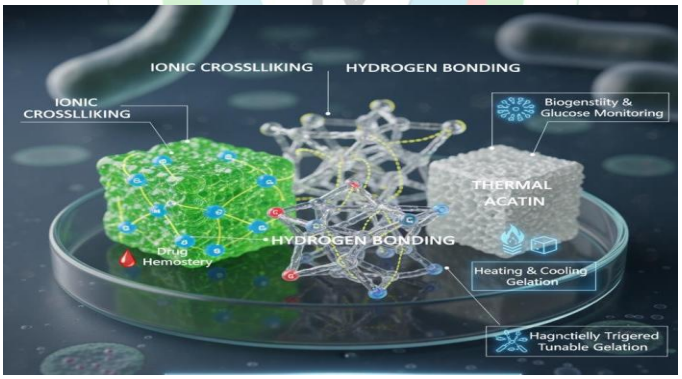


Figure 5: Physical Crosslinking In Hydroge

Chemical Crosslinking

Chemical crosslinking forms permanent junctions through covalent bonds. Techr often involve condensation reactions or photopolymerization processes". chemical crosslinking offers high control over network density and stability, preparation methods can be energy-intensive and may require specialized equip contributing to the high cost associated with scaling up production11.

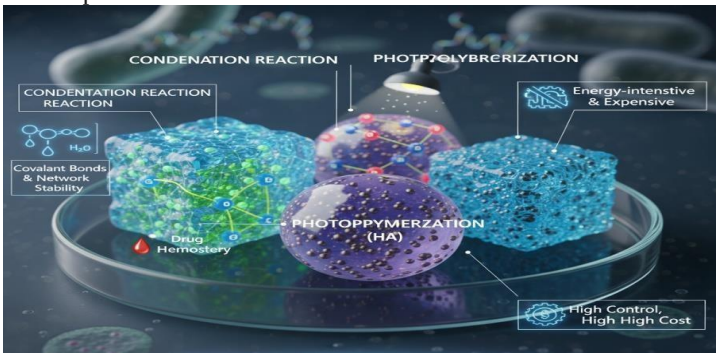


Figure 6: Chemical Crosslinking

Critical Physicochemical Properties Governing DDS Performance

The functionality of a hydrogel DDS is intrinsically linked to its physical and che characteristics particularly its swelling capacity and mechanical resilience.

Critical hysicochemical Properties Governing DDS Performance

The functionality of a hydrogel DDS isintrinsically linked to its physical and chemical characteristics, particularly its swelling capacity and mechanical resilience.

The **Swelling Ratio and Mesh Size** are fundamental determinants of drug transport. The hydrogel network acts as a barrier, and the rate of drug diffusion is critically influenced by the size and charge of the drug molecules relative to the hydrogel's internal meshsize**.** External stimuli, such as temperature, pH, or light, can affect both the mesh size and swelling properties, dynamically influencing the release profile[3].

Mechanical Strength and Biocompatibility are crucial for *in vivo* performance and retention. For injectable systems, especially those utilized in dynamic anatomical sites like the vitreous humor of the eye or joints, sufficient mechanical strength is necessary to prevent premature collapse or clearance[12].

A critical design trade-off exists between mechanical stability and permeability. Experimental observations reveal that increasing the crosslinking intensity of ten leads to enhanced mechanical strength but conversely resultsin adecrease in the swelling ratio. For example, the ionic interaction of polyelectrolyteions with from chitosan increases crosslinking intensity, strengthening the gel but reducing its capacity to swell[14]. This inverse relationship presents a significant engineering challenge: optimizing the mechanical resiliencenecessaryforlocalretentioninherently constrains the rate of drug diffusion and release[3]. There fore, advanced DDS engineering must focus on strategies, such as hybrid materials or reversible crosslinking, that can effectively decouple these two vital parameters to maximize both stability and therapeutic efficacy.

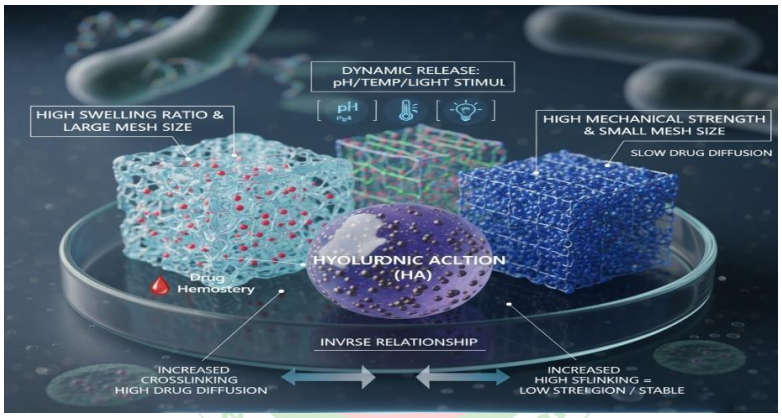


Figure 7: Critical Physicochemical Properties Governing DDS Performance

Mechanisms and Kinetics of Drug Release:

Fundamental Mechanisms of Drug Release

The release of therapeutic agents from the hydrogel matrixis classified in to four primary mechanisms[10]

Diffusion-Controlled Systems

In these systems, the hydrogel matrix acts as a physical barrier to the drug molecules. Release is governed by the concentration gradient across the matrix and the pore (mesh) size of the network.This mechanism allows for sustained drug release over an extended period, which is advantageous for long-term localized therapies[3]

Table 1: Classification and Engineering Parameters of Hydrogel Materials

Hydrogel Type	Example Materials	Key Advantages for DDDS	Tunable Properties/mechanism	Represantion
Natural Polymers	Chitosan. Alginate HA, Gelatin	High Biocompabality Biodegradable, Mucosal Adhesion	Ionic Interaction Potential, Degradation Rate, Swelling Rate	6
Synthetic Polymer	PEG,PVA PNIP Am	Excellent MechenicalProperties , Reproducibility, Stimuli Responsive	Phase transistiontemperature, Crosslinking density, Mesh size	8
Hybrid\Composite	PEG-chitosan NP-Loaded Hydrogel	Combined properties, Enhanced stability, Multifunctionality (eg. Magnetic triggering)		6

Swelling-Controlled Systems

This mechanism is typical of glassy hydrogel matrices containing dissolved or dispersed drugs**.** As water penetrates the glassypolymer, the polymer undergoes swelling, lowering its glasstransition temperature and transforming the material into a rubbery state. The dissolveddrug then diffuses through this swollen, rubbery region into the surrounding medium

16

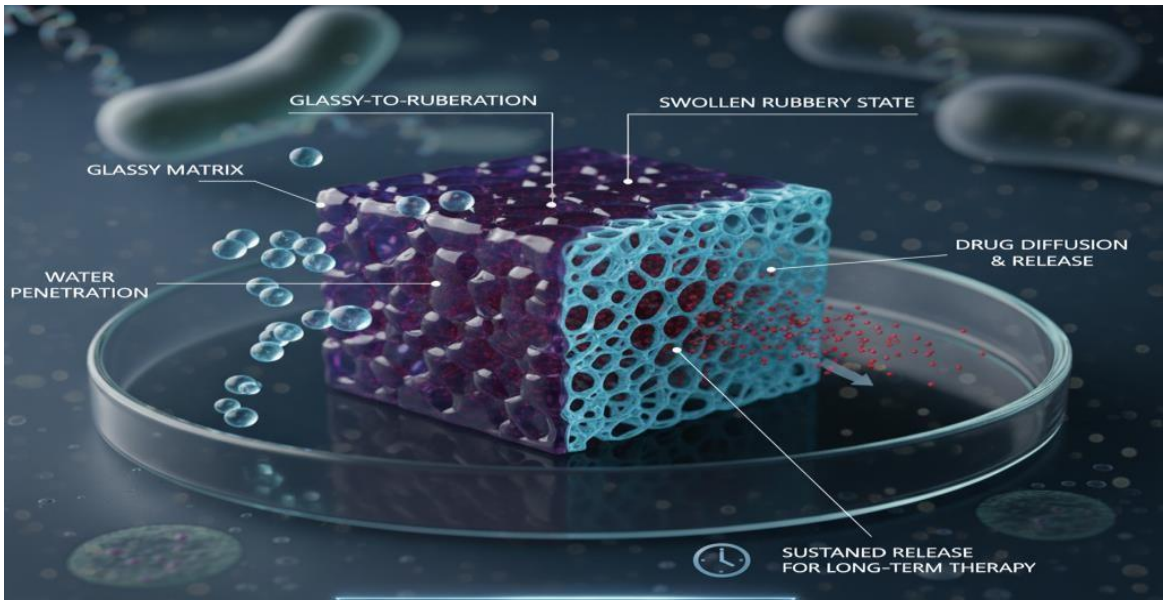


Figure 9: Swelling controlled system

Chemically-Controlled Systems

Drug release in these systems is dictated by chemical processes, such asthe hydrolysis or enzymatic degradation of the polymer backbone itself, or the cleavage of specific linkers connecting the drug to the hydrogel scaffold[10]. This mechanism is key to designing environmentally sensitive or smart delivery systems.

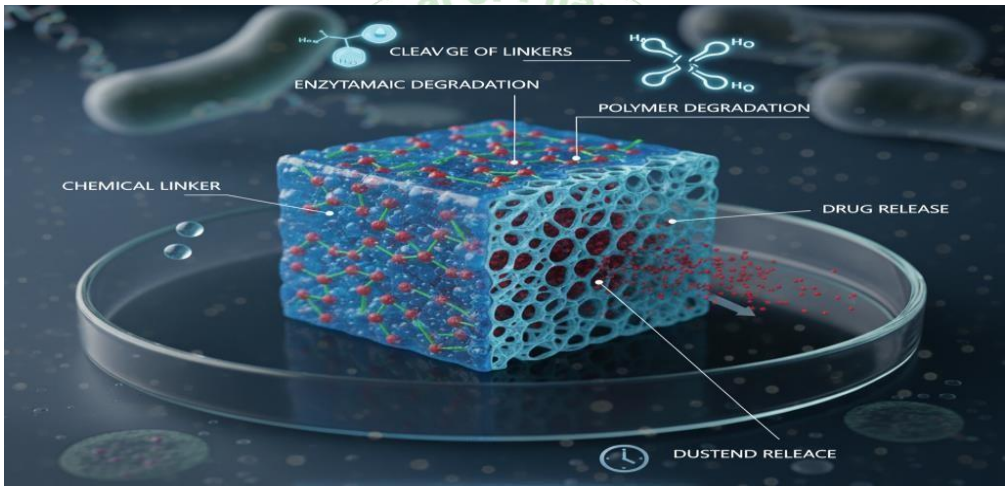


Figure 10: Chemically-Controlled Systems

Mathematical Modeling of Drug Release Kinetics

1. Understanding and accurately predicting drug release requires rigorous mathematical modeling. Transport mechanisms are fundamentally categorized as Fickian or Non- Fickian.
2. True **Fickian diffusion** occurs when the rate of drug transport is solely dependent on the concentration gradient, typically observed when the diffusion exponent (DEB) is less than
3. However, drug release from swelling glassy hydrogel matrices rarely follows a simple Fickian mechanism[16].
4. Many hydrogel carriers exhibit **Non-Fickian (Anomalous) transport** .This occurs when the polymer relaxation and swelling process significantly contributes to the observed release kinetics along side diffusion .When the diffusion exponentis equal to 1, CaseII transportis anticipated, depending on the relative importance of Fickian diffusion and the polymer relaxation process[16].
5. The goal of DDS design is often to achieve constant-rate (zero-order) drug delivery[5]. Achieving this predictability is made substantially more difficult by the nature of Non- Fickian behavior. The dynamic factors in herent in anomalous transport,such as the local drug concentration and the velocity of polymer relaxation/swelling, mean that *in vivo* performance prediction is complicated[16]. In biological environments, physiological fluids and mechanical stresses will alter swelling and relaxation rates, potentially resulting in undesirable initial burst releases or premature depletion of the drug reservoir. This highlights the critical need for developing improved theoretical models that can accurately predict therapeutic outcomes, akey endeavor required to bridge the gap between laboratory success and widespread clinical applicability[4].

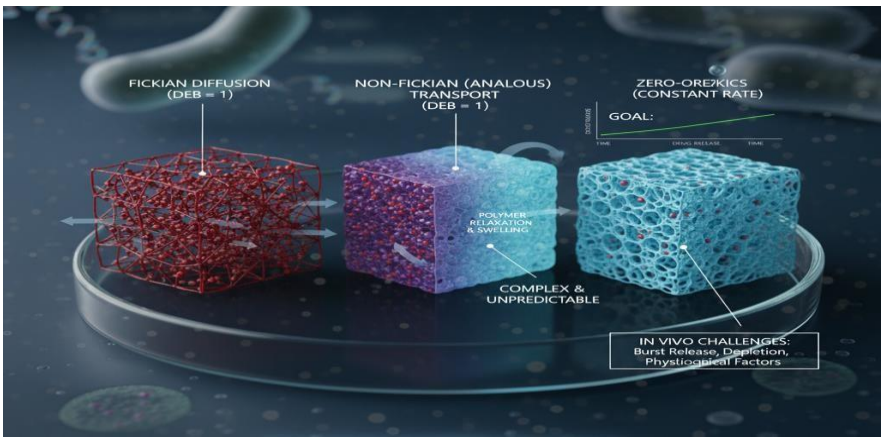


Figure 11: Mathematical Modeling of Drug Release

Advanced Stimuli- Responsive Hydrogel Systems: The Novelty Factor:

A major advancement in hydrogel technology involves the design of stimuli - responsive systems, also known as "smart hydrogels," which actively modulate drug release in response to specific triggers[7]

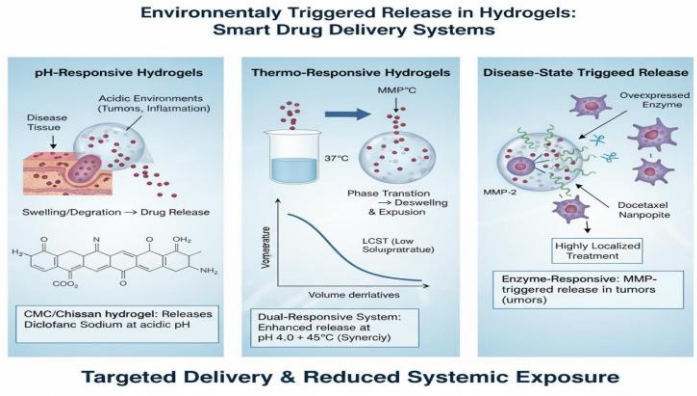


Figure 12: Advanced Stimuli-Responsive Hydrogel Systems

Environmentally Triggered Release

Environmentally responsive hydrogels release the therapeutic payload only upon sensing an external stimulus or changes in the local physiological environment, ensuring targeted delivery and reduced systemic exposure[7].

pH-Responsive Hydrogels

These systems utilize changes in often capitalizing on the acidic environments found in tumor tissues, sites of inflammation, or within intracellular compartments (endosomes/lysosomes) to trigger swelling or degradation. For instance, modified carboxymethyl cellulose/chitosan (-CMC/-CS) hydrogels have been designed to enable the controlled release of model drugs, such as diclofenac sodium, specifically under target physiological conditions, thereby improving therapeutic efficacy[18].

Thermo-Responsive Hydrogels

Thermo-responsive materials, such as derivatives of Poly(N-isopropylacrylamide) (pNIPAm), exhibit a Low Critical Solution Temperature. Above the, the polymer undergoes a rapidphase transition, leading to deswelling and subsequent drug expulsion. Highly engineered systems often integrate dual responsiveness. For example, a hydrogel system demonstrated significantly enhanced drug delivery when exposed to the combination of 4.0 and 45°C due to synergistic triggered protonation and temperature-induced phase transition[15].

Disease-State Triggered Release

The most sophisticated systems exploit specific biochemical cues associated with pathological states, offering highly localized treatment.

Enzyme-Responsive Hydrogels

Enzyme-responsive hydrogels achieve targeted release by exploiting altered enzyme expression levels in diseased tissues[17].This approach represents a significant step toward precision medicine.

There are several methods for achieving enzyme dependant release:

1. **Matrix Degradation:** The most common method involves the enzymatic destruction of the scaffold itself, releasingen capsulated therapeutics.
2. **Cleavage of Covalent Linkages:** Therapeutics can be covalent lyaflached to the hydrogel scaffold via enzy matically sensitive cross-linkages.Cleavage of these links releases the drug.
3. **Specific Therapeutic Linkers:** Labile linkers with known molecular structures canbe used to connect the therapeutic agent to the scaffold, tailored for cleavage byenzymes elevated in specific disease states[17].

A prominent example involves Matrix Metalloproteinases (MMPs), which are often

overexpressed in the tumor microenvironment to facilitate invasion and metastasis[19]. Researchers have synthesized poly(acrylicacid) hydrogels conjugated with-2 sensitive peptides (e.g., Gly-Pro-Leu-Gly-Val-Arg-Gly-Lys). *Invitro* studies demonstrated that peptide fragments were released specifically and proportionally to the concentration of- 2 present[19]. The effectiveness of thisactive, targeted delivery mechanism is evidenced by preclinical datas howing that-responsive microplates loaded with docetaxel-containing nanoparticles result edina 20-fold decrease in the effective concentration compared to a non-degradable control in-2/9 over expressing brain cancer celllines (-MG)[20].

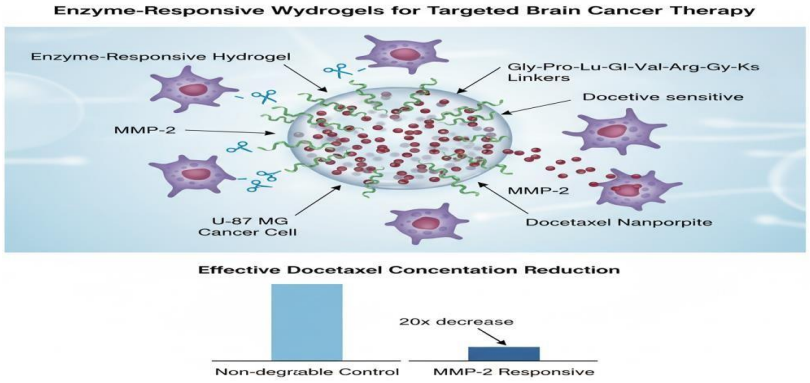


Figure 13: Enzyme-Responsive Hydrogels System

Glucoseand Redox-Responsive Systems

Other systems are designed to monitor or respond to metabolic indicators. For instance, chitosan hydrogels loaded with glucose oxidase facilitatereal-time glucose monitoring through enzymatic reactions, showing potential in diabetic care[6].

The transition from passive diffusion systemsto enzyme-responsive systemsis pivotal in drug delivery advancement.

The high specificity inherent in enzyme-responsive systems significantly reduces off-target toxicity compared to systemic or passive local delivery, while dramatically increasing efficacy, as demonstrated by the large improvements achieved in cancer models.[20] This capability is fundamental for implementing precision medicine strategies, where thetherapeutic agent is activated or released only when the localized pathological environment dictates drug exposure.

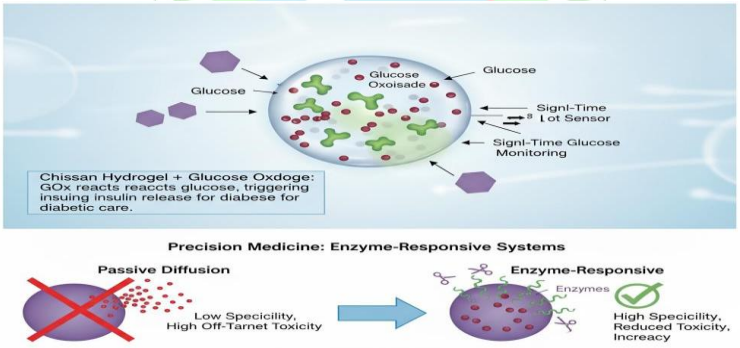


Figure 14: Glucose Responsive Hydrogel For Diabetes Management

Table 2: Overview of Stimuli-Responsive Hydrogels for Targeted Drug Delivery

Stimulus Category	Mechanismof Response	Material Example	Targeted Disease /Condition	Release Outcome Significance
Change	Protonation/de protonation causing electrostatic repulsion and subsequent swelling/deswe lling	-CMC/-CS, Poly (acrylic acid)	Tumor microenvironm ent, Gastrointestin al delivery, Inflammation	Controlled release, improving therapeutic efficacy at target site[18]
Temperature	Phase	derivatives	Localized	Significantly
Change	transition()		hyperthermia,	enhanceddrug
	causingrapid		Injectable	delivery
	volumechange		systems	efficiency,
	(coil-to-globul			especially
	etransition)			when
				combinedwith
				15
Enzyme	Cleavageof	sensitive	Cancer (-2/9)	Highlyspecific,
Activity	specific	conjugates	Over expression	proportional,
	peptidelinkers			andrapid
	integratedinto			release,

	the			yieldinghigh
	scaffold/crossli			local
	nks			concentration
				andefficacy[19]

Biomedical Applications and Therapeutic Efficacy:

Injectable Hydrogels: Minimally Invasive Localized Therapy

Injectable hydrogels represent a highly valued format in clinical practice, offering minimally invasive administration through a needle, which significantly reduces patient discomfort[10]. These systems capital ize on *in situ* gelation,where a liquid precursor solution is [12].

administered and quickly forms a solid hydrogel network at the target site. This process ensures prolonged drug retention and allows the material to conform precisely to irregulartissuedefectsoranatomical structures[13]. Injectable hydrogel shold promise in diverse fields, including cardiac regeneration, treatment of joint diseases, and postoperative analgesia[13]. They are also extensively investigated for treating ocular disorders, capitalizing on the need for controlled, localized drug delivery within the sensitive structures of the eye

Figure 15: Injectable Hydrogels

Specialized Applicationc Focus: Oncology and Ophthalmic Delivery Oncology

Hydrogels serve a crucial role in cancer therapy by enabling the local delivery of chemotherapeutics, such as Doxorubicin, directly to solid tumors or resection voids. This localization maximizes the therapeutic effect while minimizing systemic toxicity. Advanced hybrid hydrogels, particularly those formulated to release loaded nanoparticles, have demonstrated an ability to greatly extend the release period and significantly enhance drug retention and permeation within the tumorsite**.** degradable hydrogels, which exploit the acidic tumor micro environment, are showing significant potential for the local therapy of solid tumors, including those treated post-resection, such as glioblastoma[7].

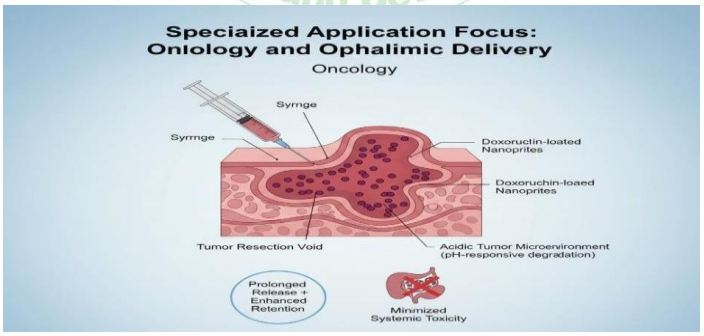


Figure 16: Oncology and Ophthalmic Delivery of Hydrogel

Ophthalmology

The human eye is a complex, multi-segmented structure, and ophthalmic diseases, suchas age-related macular degeneration, glaucoma, and diabetic retinopathy, affect hundreds of millions globally. The demand for effective eye therapies drives the development of specialized hydrogels for controlled intraocular delivery. Hydrogels are investigated as novel medical devices, serving as vitreous humor substitutes and delivery vehicles for drugs, factors, nanoparticles, and stem cells. Although many ophthalmology applications remain in preclinical investigation or clinical trials, injectable hydrogels are

already being approved by the for use a ssurgical sealants and tissue adhesives[12].

Hydrogelsin Wound Healingand Regenerative Medicine

Hydrogels are widely applied in wound management due to their ability to provide a moist healing environment, facilitate controlled release of therapeutic agents, and of fermechanical protection. Systems based on Chitosan and other materials exhibit useful properties such as hemostatic activity and mucosal adhesion, aiding accelerated wound closure.[7] Future research focuses on integrating

hydrogels with advanced wound care technologies, such as Negative Pressure Wound Therapy and bioactive dressings.The creation of hydrogels capable of releasing multiple therapeutic agents in a controlled manner, tailored specifically to the sequential stages of the wound healing cascade, represents a promising direction for more effective skin injury treatments[21].

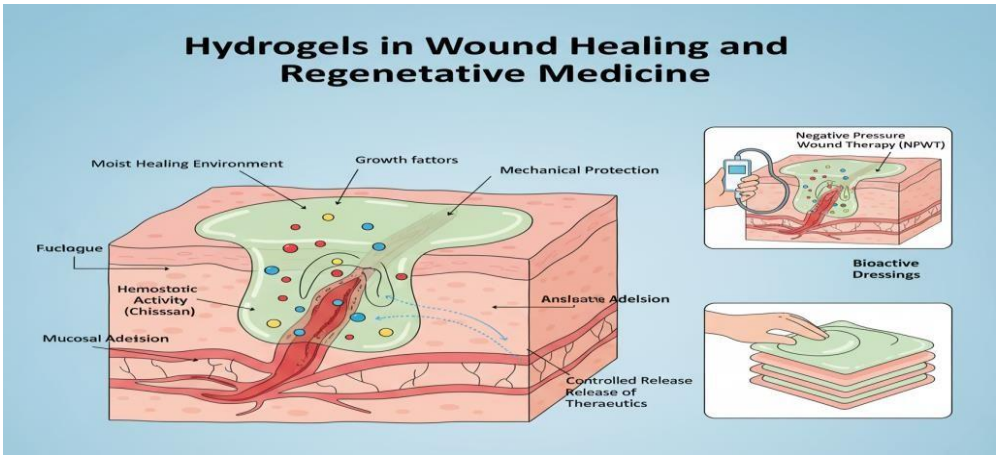


Figure 17: Hydrogels in Wound Healing and Regenerative Medicine

Alternative Administration Routes

Hydrogels offer a versatile and advanced platform for alternative drug administration routes. Their adaptability, controlled release capability, and compatibility with biological systems make them highly valuable in modern drug delivery, especially for targeted and sustained therapeutic effects.

Beyondinjection andtopical use, hydrogels are utilized across various administration routes. They are commonly incorporated in to transdermal patches and creams, where they effectively enhance drug permeation by promoting skin hydration. Hydrogels are also investigated for oral, buccal, vaginal, and ocular delivery, serving as stabilizing matrices for other drugdelivery systems like liposomes and nanoparticles [10].

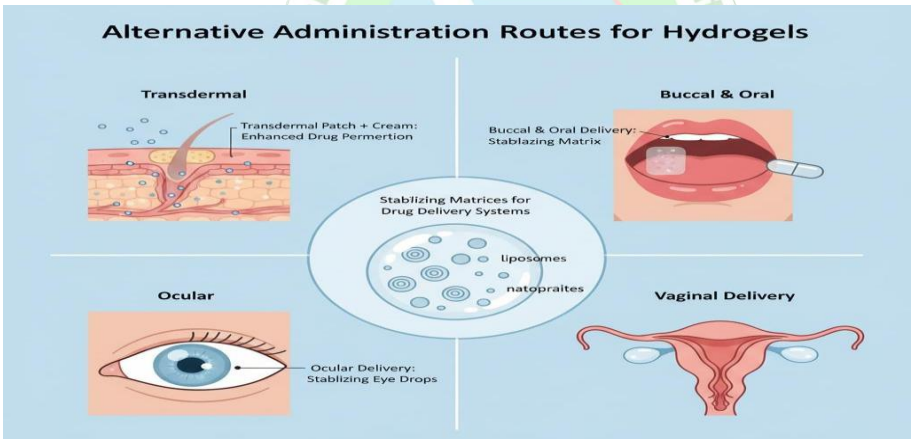


Figure 18: AlternativeH ydrogels Administration Routes

Translational Challenges and Commercial Landscape:

Despite the promising a tributes of hydrogel DDS, the transition from laboratory research to clinical adoption is complex, fraught with significant regulatory, manufacturing, and biological challenges[4].

Manufacturing and Scale-UpHurdles

Scaling up hydrogel production from laboratory synthesis to industrial manufacturing presents considerable economic andtechnical barriers. The production costs are often high, driven by the expense of specialized polymers or biopolymers and the energy- intensive nature of certain preparation methods, such as chemical crosslinking or advanced techniques like microfluidics and 3D printing[11].

A major hurdle is managing **atch-to-batchvariability**. Even minor deviations in raw material quality, synthesis parameters (e.g., polymerization time, crosslinking efficiency), or environmental condition (temperature) can result in inconsistencies in the final physicochemical properties. These inconsistencies such as slight differences in polymer chain length or crosslinking density significantly affect drug release profiles, stability, and ultimately, patient outcomes. Such variability poses a serious constraint on the quality assurance required for clinical applications and regulatory approval[11].

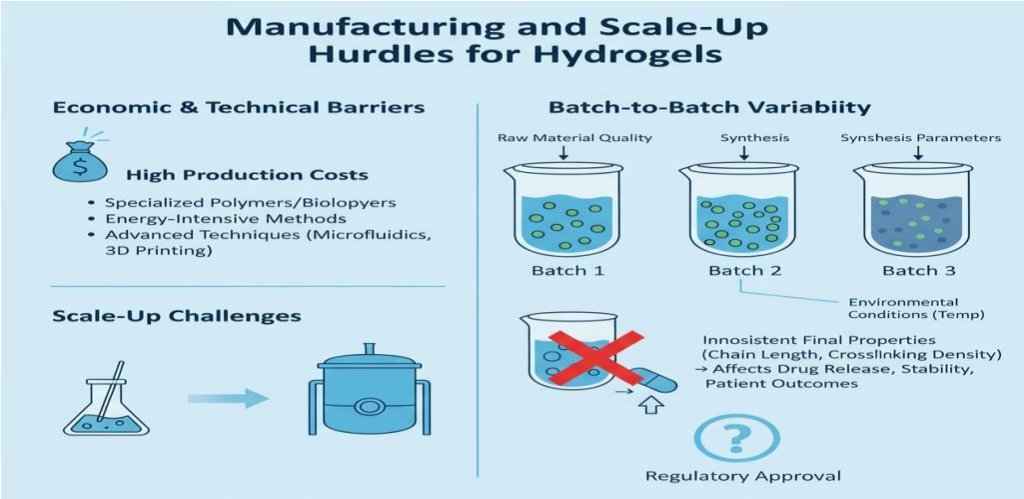


Figure 19: Manufacturing and Scale-Up Hurdles

Regulatory Pathways: TheCombination Product Dilemma

Hydrogels designed to deliver drugs or biologicals are often regulated by theas **Combination Products**. The classification and resulting regulatory pathway are determined by the Primary Mode of Action.

If the primary therapeutic benefit is led by the drug or biologic component (e.g., controlled release of an anti-cancer agent), the product is regulated through a New Drug Application or Biologic License Application. Conversely, if the hydrogel primarilyacts as a mechanical device (e.g.,atissue spacer orsealant),it maybe approved orcleared asa medical device via the Class I, Class II, or Class III pathways[23].

Navigating this regulatory environment is complicated, requiring specialized guidance from the 's Office of Combination Products[24]. Developers must adhere to complex requirements, including Current Good Manufacturing Practice for combination products[24]. Moreover, the lack of standardized methodologies for characterizing and evaluating drug release profiles across different labs poses significant difficulty in generating the rigorous, comparable data required for regulatory filings and assessment of efficacy[2].

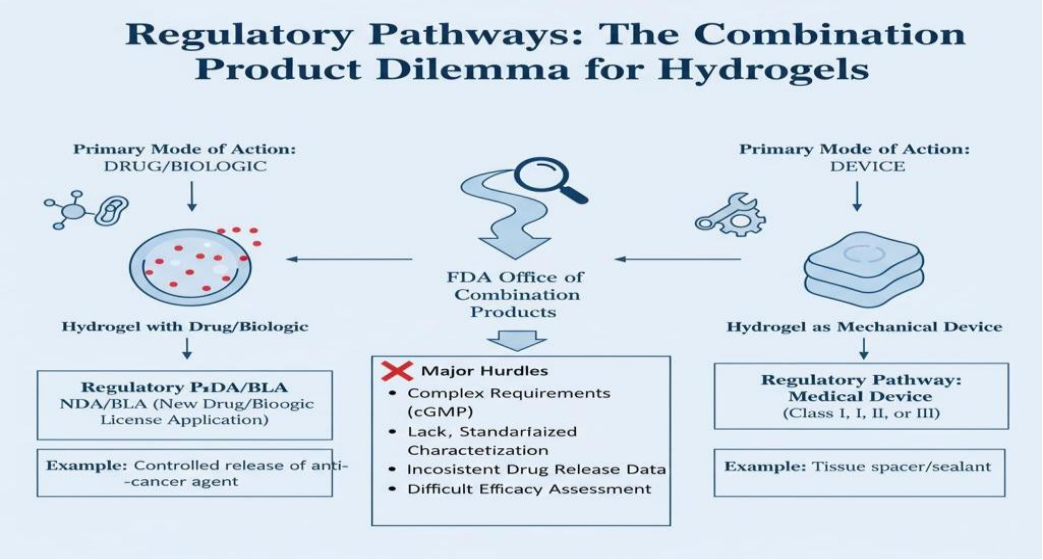


Figure 20: Regulatory Pathways the Combination Product Dilemma

Overview of Commercialized Hydrogel Productsand Clinical Status

Despitethetechnicalandregulatoryhurdles,thehydrogel marketisrobust,projectedto reach 31.4 billion by 2027. While much research remains at the preclinical or early clinical trial stage, several hydrogel-basedproductshaveachieved commercial success, utilized via injectable, topical, and transdermal administration routes[10].

Successful commercial products often include dermal fillers, such as Teosyal RHA, Beloterobalance®,and Restylane® products, which are primarily based on Hyaluronic Acid and regulated as injectable devices[5]. Other notable examples include the -based surgical spacer SpaceOAR®[5].Commercial s is also seen in transdermal patches and topical creams that utilize hydrogels for enhanced drug permeation[10].

A review of the commercialized landscape highlights a critical observation regarding regulatory complexity: the successful hydrogel products that have reached the market, particularly the based fillers, tend to be systems where the Primary Mode ofAction is mechanical functioning as tissue augmentations or spacers[23]. In contrast, the highly complex, enzyme-triggered, or multi-agent release systems that offer true pharmacological novelty are often stalled in development due to high manufacturing costs, batch variability, and the demanding regulatory pathway associated with combination products[10]. This suggests that prioritizing design simplicity and material reproducibility is a pragmatic, critical strategy to meet regulatory standards and accelerate the progression of hydrogel technology toward wide spread clinical adoption[4]. Table 3 provides examples of commercially successful hydrogel formulations.

.

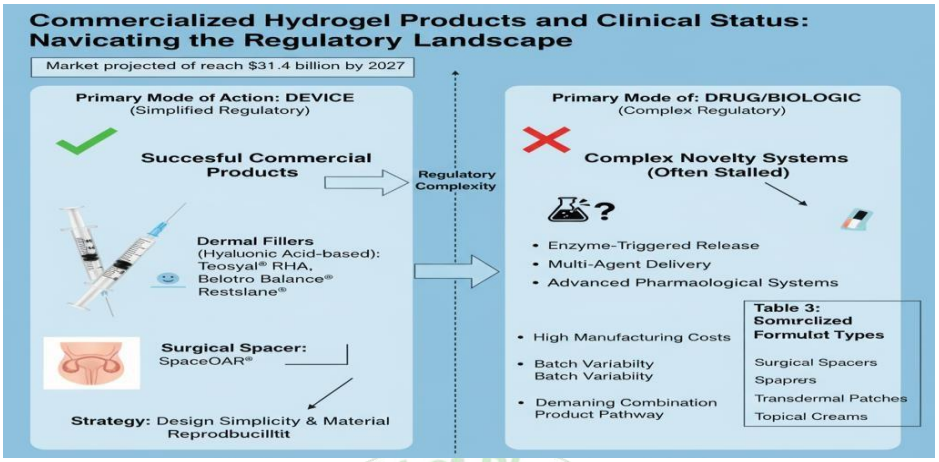


Figure 21: Overview of Commercialized Hydrogel Products and Clinical Status

Table 3: Select Commercialized Hydrogel Products and Regulatory Status

Product Name Company)	Hydrogel Material	Primary Application	Administration Route	FDA Regulatory Status/Type
Teosyal RHA (Teoxane SA)	Hyaluronic acid	DermalFiller	Injectable (Dermis)	Commercialized/Device [25]
Belotero balance (Merz)	Hyaluronic acid	DermalFiller	Injectable (Dermis)	Commercialized/Device [25]
SpaceOAR	Polyethylene Glycol	Prostate Protection/Spa cer	Injectable (In situ gelation)	Commercialized/Device [5]
Transdermal Patches (Various)	Varied Polymers(e.g., PVA, HEC)	Transdermal DrugDelivery	Topical/Transd ermal	Commercialize d/Combination Product[10]

Conclusion and future perspectives:

Hydrogels represent a highly versatile and potent platform for novel drug delivery, offering solutions to key challenges faced by conventional therapeutics, particularly concerning localization, controlled release, and protection of labile drugs.The irability tobe engineered into highly specific, stimuli-responsives ystems such as those triggered by, temperature, or disease-associated enzymes positions them centrally in the future of precision medicine.

The path toward wide spread clinical adoption, however, is contingent upon overcoming manufacturing and regulatory of necks. Future endeavors must focus on simplifying hydrogel designs to streamline regulatory compliance and reduce batch-to-batch variability. Further more, the complexity of release kinetics, particularly Non-Fickian behavior in swelling systems, necessitates the development of improved theoretical modelsto ensure predictable therapeutic out comes *invivo*.

Advancements in inter disciplinary collaboration among material scientists, clinicians, and regulatory experts are essential to harmonize practices for characterization and evaluation.

Addressing scalability and resolution limitations associated with advanced manufacturing techniques like 3D printing is also vital. By embracing these strategies, the field can effectively bridge the gap between sophisticated laboratory research and clinical integration, solidifying the role of hydrogels as central components in next- generation drug delivery systems[4]

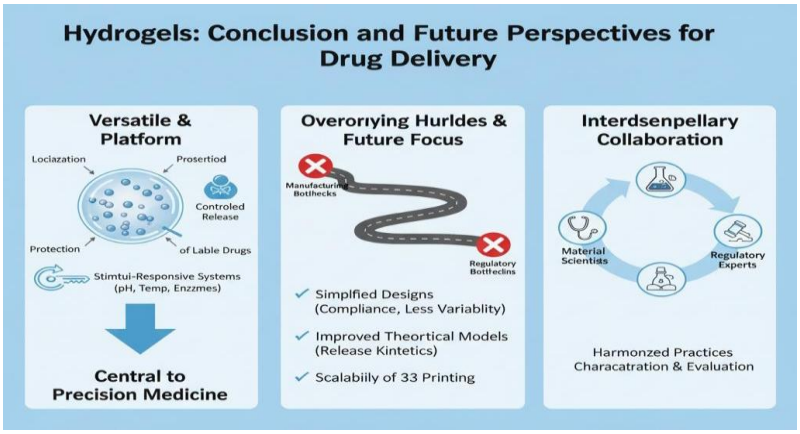


Figure 22: Hydrogels Conclusion and Future Perspectives

REFERENCES:

1. **Peppaskkk NA, Hilt JZ, Khademhosseini A, Langer R.** Designing hydrogels for controlled drug delivery. *Proc Natl Acad Sci U S A.* 2000;
2. **Makwana SB, Patel VA, Parmar SJ.** Hydrogels as drug delivery systems: a review of current characterization and evaluation techniques. *J Control Release.* 2020;
3. **Wojciechowski K, et al.** Diffusion-limited processes in hydrogels with chosen applications from drug delivery to electronic components. *Molecules.* 2023;28(15):5931.
4. **Zhang L, Wang Y, LiQ, etal.** Advancesin hydrogel-based drug delivery systems. *Front Pharmacol.*2024;
5. **Hoare TR, Kohane DS.** Hydrogel-based products that are FD Aapproved or in clinical development. *Research Gate.*
6. **Thakur VK, Thakur MK.** Advancements in hydrogels: a comprehensive review of natural and synthetic innovations for biomedical applications. *Polymers (Basel).* 2023;17(15):2026.
7. **Jain E,etal.** Stimuli-responsive injectable chitosan-based hydrogels for controlled d rug delivery systems**.** *Front Bioeng Biotechnol.* 2022;
8. **Kumari A, et al.** Hydrogel encapsulation techniques and its clinical applications in drug delivery and regenerative medicine: a systematic review. *ACS Omega.* 2024;
9. **Zhao X, et al.** Emerging fabrication strategies of hydrogels and its applications. *J Control Release.* 2022;
10. **Patel G,etal.** Commercial hydrogel product for drug delivery based on route of administration. *Front Chem.*2024;
11. **Caló E, Khutoryanskiy VV.** Injectable hydrogels for ophthalmic applications. *Mater Sci Eng C.* 2017;
12. **Ahmed EM.** Advancements and applications of injectable hydrogel composites in biomedical research and therapy. *Gels.* 2023;9 (7):533.
13. **LiJ, Mooney DJ.** Fundamental concepts of hydrogels:synthesis, properties, andtheir applications. *Adv Drug DelivRev.* 2020;
14. **Rathore M, et al.** pNIPAm-based pH and thermoresponsive copolymer hydrogel for hydrophobic and hydrophilic drug delivery. *Gels.* 2024;10(3):184.
15. **Siepmann J, Peppas NA.** Kinetics of drug release from hydrogel matrices. *Research Gate.*
16. **WangL, etal.** Controlled release of therapeutics from enzyme-responsive biomaterials. *Front Biomater Sci.* 2022;
17. **Chowdhury P, et al.** Site-specific drug delivery using injectable pH-responsive biopolymeric hydrogel: instant crosslinking and shear thinning. *ACS Appl Polym Mater*. 2024;
18. **Wylie RG,etal. m**Im proving matrix metallo proteinase-2 specific response of a hydrogel system using electrophoresis.*Biomaterials* 2012;
19. **Chakraborty S, et al.** Matrix metalloproteinase responsive hydrogel microplates for programmed killing of invasive tumour cells. *Lab Chip.* 2023;
20. **Wang S, etal.** Areview ofadvanced hydrogel applications fortissue engineering and drug delivery systems as biomaterials. *Gels.* 2024;10(11):693.
21. **TiwariS,etal.**3D-Printedhydrogelfordiverseapplications:areview.*Gels.* 2023;9(12):960. **Zhu J, et al.** The FDA regulatory pathways of different types of hydrogel products. *ResearchGate.*
22. **U.S. Food and Drug Administration.** Combination products guidance documents. *FDA.*
23. **Appel EA, et al.** Hydrogels in the clinic. *Nat Rev Mater*. 2020;


Asian Journal of Pharmaceutical
Research and Development
Rx