ISSN: 2457-0400

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

www.wjahr.com

Impact Factor: 7.675

Volume: 10, Issue: 3

Page N. 144-147

Year: 2026

Original Article | **Coden USA: WJAMA3**

HYDROGELS: A SMART STIMULI –RESPONSIVE SYSTEMS: STRUCTURE, MECHANISM, AND BIOMEDICAL APPLICATIONS

***Vaishnavi Samadhan Suradkar**

India.

Article Received: 05 February 2026 | **Article Revised:** 25 February 2026 | **Article Published:** 05 March 2026

***Corresponding Author: Vaishnavi Samadhan Suradkar**

India.

DOI: https://doi.org/10.5281/zenodo.18872038

How to cite this Article: Vaishnavi Samadhan Suradkar (2026). Hydrogels: A Smart Stimuli–Responsive Systems: Structure, Mechanism, and Biomedical Applications. World Journal of Advance Healthcare Research, 10(3), 144–147.

ABSTRACT

Hydrogels are made up of crosslinked polymer chains that form a three-dimensional (3D) network, allowing them to absorb and retain substantial amounts of fluid. Their soft texture, high water content, and porous architecture make them closely mimic the characteristics of natural biological tissues. In recent years, they have found wide-ranging applications across various sectors, including agriculture, biomaterials, the food industry, drug delivery, tissue engineering, and regenerative medicine. This review begins with an overview of the fundamental aspects of hydrogels, including their structure, classification, and synthesis methods. It then explores recent developments in their use for 3D cell cultures, drug delivery systems, wound dressings, and tissue engineering.

INTRODUCTION

Hydrogels are composed of a three-dimensional (3D) network capable of absorbing large amounts of water and swelling, primarily due to the presence of hydrophilic functional groups such as $–NH_2$, –COOH, –OH, –$CONH_2$, –CONH, and –SO_3H.[1.9] This network is typically formed through the crosslinking of polymer chains, although in some cases, it can also be established via crosslinked colloidal clusters.[10,17] Their ability to absorb water contributes to their flexibility and soft texture.[2]

Hydrogels can be fabricated using chemical or physical crosslinking methods, employing either natural or synthetic polymers.[18,22] Due to their high water content, soft consistency, and porous structure, they effectively replicate the physical properties of living tissues. Over the last six decades, hydrogels have been extensively developed for a wide range of biomedical applications, including implantable, injectable, and sprayable systems, each customized for targeted organs and tissues.[23,24]

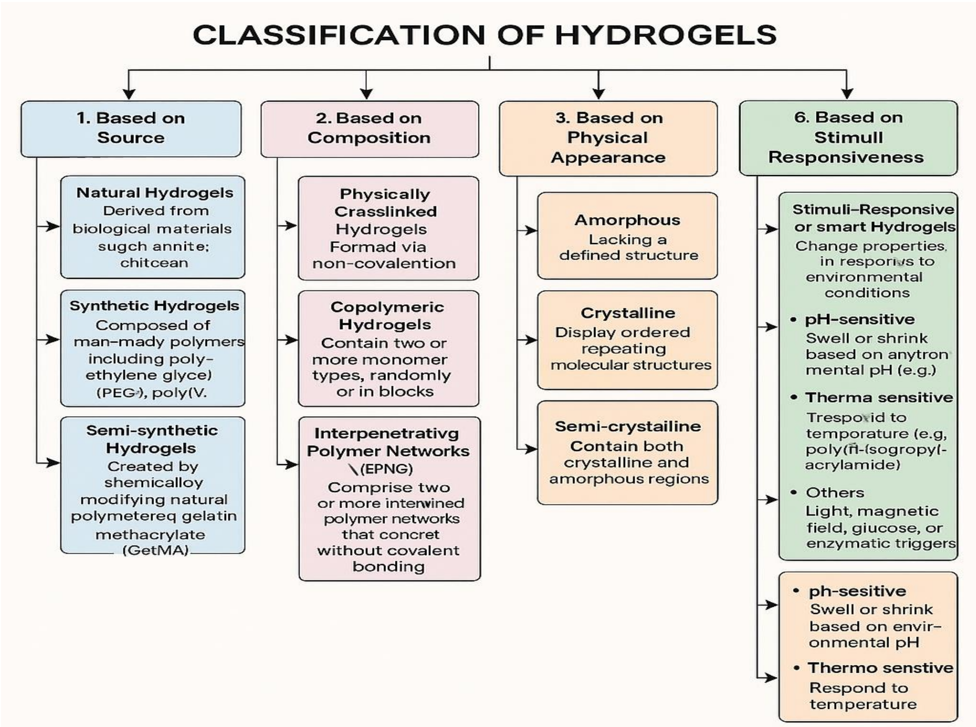
This review begins by exploring the fundamental aspects of hydrogels, focusing on their structure, classification, and synthesis techniques.We then focus on their most recent biomedical applications, with particular emphasis on their utilization in 3D cell culture, targeted drug delivery, wound repair,

HISTORY

The development of hydrogels spans over a century, beginning with simple polymer networks and evolving into sophisticated, smart stimuli-responsive systems tailored for advanced biomedical applications.[17]

CLASSIFICATION OF HYDROGELS

Hydrogels are three-dimensional, hydrophilic polymer networks that can absorb and retain substantial amounts of water without compromising their structural integrity.[2]



STRUCTURE OF HYDROGELS

Hydrogels comprise a 3D network of hydrophilic polymer chains designed to hold and retain water within their structure.[1]

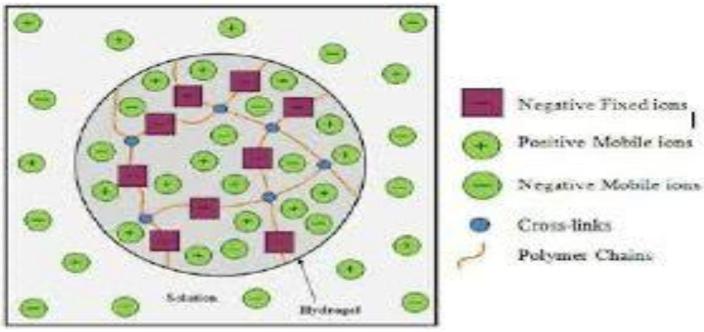
1. Crosslinked Polymeric Network[22]

2. Water Content[2]

3. Mesh Size and Porosity[3]

4. Crosslinking Types[22]

5. Biomimetic Structure[7]



APPLICATIONS OF SMART STIMULI-RESPONSIVE HYDROGELS IN DENTISTRY AND BIOMEDICAL FIELDS

Smart hydrogels, capable of responding to external stimuli such as pH, temperature, enzymes, magnetic fields, and light, are gaining significant attention in both dentistry and biomedicine. Their tunable responsiveness, biocompatibility, and ability to mimic biological tissues make them ideal for numerous therapeutic and diagnostic applications.

1. Dental Applications of Smart Hydrogels

a. Periodontal Regeneration

Smart hydrogels have been developed to deliver growth factors or antimicrobials in response to periodontal pocket pH changes. In inflamed tissues, the acidic pH triggers hydrogel swelling or degradation, enabling site-specific drug release.

Example: pH-sensitive hydrogels loaded with chlorhexidine or doxycycline have been used to suppress Porphyromonas gingivalis and promote periodontal healing.[21]

Furthermore, enzyme-responsive hydrogels designed to degrade in the presence of matrix metalloproteinases (MMPs) are also used to enhance guided tissue regeneration (GTR) in periodontitis.[16]

b. Pulp Regeneration and Endodontics

In regenerative endodontics, injectable hydrogels responsive to temperature or enzymes are used to deliver stem cells and growth factors into root canals.[15] These hydrogels gel at body temperature, filling irregular canal geometries and creating a favorable environment for pulp tissue regeneration.

Example: A thermosensitive hydrogel based on chitosan/β-glycerophosphate has shown success in pulp tissue engineering.

c. Antimicrobial and Biofilm-Resistant Coatings
Smart hydrogels embedded with antimicrobial agents or nanoparticles release their contents upon changes in pH or temperature, helping to reduce biofilm formation on implants or orthodontic devices.

Example: Smart hydrogel coatings for titanium dental implants that release silver nanoparticles in response to infection-related stimuli are under development.[13]

2. Biomedical Applications of Smart Hydrogels
a. Smart Drug Delivery Systems
Smart hydrogels are extensively used for on-demand and site-specific drug delivery. They react to internal stimuli such as pH or glucose levels, as well as external triggers like light or magnetic fields. Example: Glucose-responsive hydrogels containing glucose oxidase release insulin in diabetic patients when blood glucose levels rise, providing a self-regulated delivery system.[8]

b. Cancer Therapy
In tumor environments, where pH is slightly acidic and enzymes are overexpressed, smart hydrogels can selectively release chemotherapeutic drugs, minimizing systemic toxicity.

Example: Dual-responsive hydrogels (pH and redox-sensitive) have been used to release doxorubicin specifically at the tumor site.[3]

c. Tissue Engineering and Regenerative Medicine
Smart hydrogels provide dynamic, ECM-mimicking scaffolds that adapt to cellular microenvironments. For instance, thermo-sensitive injectable hydrogels can form gels at body temperature and support bone, cartilage, or cardiac tissue regeneration.

Example: A thermosensitive Pluronic F127-based hydrogel has been applied in cartilage regeneration and myocardial repair.[7]

d. Wound Healing
Smart hydrogels loaded with growth factors or antimicrobials release their payloads in response to wound conditions, such as temperature, enzymes, or pH changes, promoting faster healing and infection control.

Example: Enzyme-responsive hydrogels degrade upon exposure to proteases found in chronic wounds, releasing VEGF or epidermal growth factor (EGF).[13]

e. Biosensing and Diagnostics
Smart hydrogels integrated into biosensors respond to biomolecular changes and convert them into measurable signals. These are used for detecting glucose, lactate, or pathogens in real time.

Example: Hydrogel-based glucose sensors using phenylboronic acid-functionalized polymers enable continuous glucose monitoring in diabetic patients.[9]

CHALLENGES AND ROADBLOCKS IN HYDROGELS AND SMART STIMULI-RESPONSIVE HYDROGELS

Hydrogels and smart stimuli-responsive hydrogels hold immense potential in biomedicine and dentistry due to their biocompatibility, tunable properties, and responsiveness to environmental cues.

1. Mechanical Fragility and Structural Instability.[10]
2. Incomplete or Non-Specific Responsiveness.[16]
3. Poor Control over Degradation and Drug Release.[8]
4. Limited Long-Term Biocompatibility and Safety.[2]
5. Manufacturing, Scalability, and Regulatory Hurdles.[22]
6. Sterilization and Storage Instability.[24]

FUTURE PERSPECTIVES

The integration of smart hydrogels with wearable devices, neural interfaces, and robotics is promising. Personalized medicine, where hydrogels are tailored to a patient's genetic and physiological profile, is on the horizon. AI-driven hydrogel design, bioresponsive logic gates, and bioprintable organ-on-chip models are emerging fields.[7,17]

CONCLUSION

Smart stimuli-responsive hydrogels represent a transformative class of biomaterials with a wide spectrum of applications. Despite current limitations, advancements in polymer chemistry, bioengineering, and nanotechnology are rapidly addressing these challenges. As the field matures, these intelligent hydrogels will play a vital role in next-generation therapies, diagnostics, and regenerative medicine.

REFERENCES

1. Peppas NA, Hilt JZ, Khademhosseini A, Langer R. Hydrogels in biology and medicine: From molecular principles to bionanotechnology. Adv Mater., 2006; 18(11): 1345-60. doi:10.1002/adma.200501612.
2. Caló E, Khutoryanskiy VV. Biomedical applications of hydrogels: A review of patents and commercial products. Eur Polym J. 2015; 65: 252-67. doi:10.1016/j.eurpolymj.2014.11.024.
3. Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. J Adv Res. 2015; 6(2): 105-21. doi:10.1016/j.jare.2013.07.006.
4. Hoffman AS. Hydrogels for biomedical applications. Adv Drug Deliv Rev., 2012; 64: 18-23. doi:10.1016/j.addr.2012.09.010.
5. Drury JL, Mooney DJ. Hydrogels for tissue engineering: Scaffold design variables and applications. Biomaterials., 2003; 24(24): 4337-51. doi:10.1016/S0142-9612(03)00340-5.

6. Kopeček J. Hydrogel biomaterials: A smart future? Biomaterials., 2007; 28(34): 5185-92. doi:10.1016/j.biomaterials.2007.07.044.
7. Annabi N, Tamayol A, Uquillas JA, Akbari M, Bertassoni LE, Cha C, et al. 25th anniversary article: Rational design and applications of hydrogels in regenerative medicine. Adv Mater., 2014; 26(1): 85-124. doi:10.1002/adma.201303233.
8. Li J, Mooney DJ. Designing hydrogels for controlled drug delivery. Nat Rev Mater., 2016; 1(12): 16071. doi:10.1038/natrevmats.2016.71.
9. Calvert P. Hydrogels for soft machines. Adv Mater., 2009; 21(7): 743-56. doi:10.1002/adma.200800534.
10. Gong JP. Why are double network hydrogels so tough? Soft Matter., 2010; 6: 2583-90. doi:10.1039/B924290B.
11. Haraguchi K. Nanocomposite hydrogels. Curr Opin Solid State Mater Sci., 2007; 11(3-4): 47-54. doi:10.1016/j.cossms.2008.01.002.
12. Wei Z, Yang JH, Du XJ, Xu F, Zrinyi M, Osada Y, et al. Dextran-based self-healing hydrogels formed by reversible Diels–Alder reaction under physiological conditions. Macromol Rapid Commun., 2013; 34(18): 1464-70. doi:10.1002/marc.201300262.
13. Liang Y, Zhao X, Hu T, Chen B, Yin Z, Ma PX, et al. Adhesive hemostatic conducting injectable composite hydrogels with sustained drug release for hemorrhage control and wound healing. Biomaterials., 2019; 192: 567-79. doi:10.1016/j.biomaterials.2018.11.030.
14. Reddy N, Yang Y. Citric acid crosslinking of starch films. Food Chem., 2010; 118(3): 702-11. doi:10.1016/j.foodchem.2009.05.050.
15. Li Z, Ramay HR, Hauch KD, Xiao D, Zhang M. Chitosan–alginate hybrid scaffolds for bone tissue engineering. Biomaterials., 2005; 26(18): 3919-28. doi:10.1016/j.biomaterials.2004.09.062.
16. Qiu Y, Park K. Environment-sensitive hydrogels for drug delivery. Adv Drug Deliv Rev., 2012; 64: 49-60. doi:10.1016/j.addr.2012.09.021.
17. Buwalda SJ, Boere KW, Dijkstra PJ, Feijen J, Vermonden T, Hennink WE. Hydrogels in a historical perspective: From simple networks to smart materials. J Control Release. 2014; 190: 254-73. doi:10.1016/j.jconrel.2014.03.052.
18. Park H, Park K, Shalaby WS. Biodegradable Hydrogels for Drug Delivery. CRC Press; 2011.
19. Peppas NA, Merrill EW. Crosslinked poly(vinyl alcohol) hydrogels as swollen elastic networks. J Appl Polym Sci., 1977; 21(7): 1763-70. doi:10.1002/app.1977.070210705.
20. Omidian H, Park K. Introduction to hydrogels. In: Encyclopedia of Polymer Science and Technology. Wiley; 2011; 1-27.
21. Gupta P, Vermani K, Garg S. Hydrogels: From controlled release to pH-responsive drug delivery. Drug Discov Today, 2002; 7(10): 569-79. doi:10.1016/S1359-6446(02)02255-9.
22. Hennink WE, van Nostrum CF. Novel crosslinking methods to design hydrogels. Adv Drug Deliv Rev., 2012; 64: 223-36. doi:10.1016/j.addr.2012.09.009.
23. Tiwari AP, Joshi MK, Lee J, Maharjan B, Ko SW, Kim CS. Electrospun polycaprolactone/cellulose nanocrystal composite nanofibers as an effective scaffold for tissue engineering. RSC Adv., 2016; 6: 73100-10. doi:10.1039/C6RA13821G.
24. Slaughter BV, Khurshid SS, Fisher OZ, Khademhosseini A, Peppas NA. Hydrogels in regenerative medicine. Adv Mater, 2009; 21(32-33): 3307-29. doi:10.1002/adma.200802106.