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Recent advances in hydrogel fabrication approaches and pharmaceutical applications

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Abstract

Hydrogels represent a unique class of three-dimensional crosslinked polymer networks that demonstrate exceptional capacity to absorb and retain water while maintaining structural integrity. Their water-laden composition closely resembles the physicochemical environment of living tissues, making them particularly attractive for biomedical and pharmaceutical research. Over recent decades, a progressive transition has been observed from naturally derived hydrogels toward engineered synthetic variants, owing to improvements in mechanical stability, tunable water retention, and designer functional properties. Synthetic hydrogels can be engineered with precisely controlled architectures, enabling programmable degradation rates and responsive behaviors under physiological conditions. Structurally, hydrogels are classified as two- or multi-component systems, where polymer chain networks form a scaffold with water filling the interstitial voids — a balance governed by the nature and cross link density of the polymer matrix. This review explores the structural basis, physicochemical attributes, classification frameworks, synthesis routes, characterization methods, and emerging biomedical utilities of hydrogels, with emphasis on recent technological breakthroughs.

Keywords: Hydrogel; Polymer Network; Crosslinking; Drug Delivery; Tissue Engineering; Biomedical Applications

1. Introduction

Among the many functional polymeric materials developed over the past century, hydrogels occupy a distinctive characterized by their extraordinary affinity for water. These materials consist of crosslinked macromolecular networks bearing hydrophilic moieties that facilitate extensive water uptake without structural disintegration. Unlike simple water-soluble polymers, the crosslinked architecture of hydrogels enables them to swell to many times their original volume while retaining a cohesive gel form. Their physical properties — notably their softness, deformability, and moisture content — bear a striking resemblance to biological tissues, positioning them as preferred materials in biomedical engineering.[1]

Hydrogels are broadly categorized as either 'physical' or 'chemical' gels based on the nature of their network junctions. Physical gels rely on non-covalent interactions such as hydrogen bonding, ionic associations, and hydrophobic clustering to maintain their network structure, making them reversible and often thermosensitive. Chemical gels, by contrast, are stabilized through covalent cross links, conferring greater mechanical robustness and long-term stability. Over the past two decades, synthetic hydrogels have increasingly natural ones in research and clinical contexts. This shift is attributable to the superior mechanical performance, greater batch-to-batch consistency, and virtually unlimited scope for chemical modification that synthetic systems offer. Synthetic hydrogels can withstand abrupt changes in temperature and environmental conditions without losing their gel architecture, a critical advantage for applications requiring material durability.[1]

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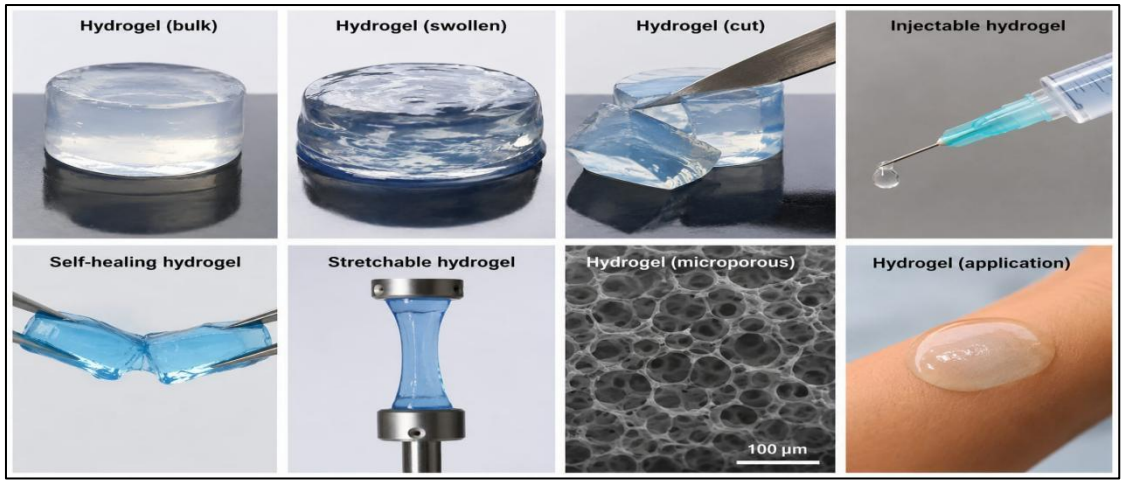

Figure 1 Structure of Hydrogel

2. Advantages of hydrogels

- Excellent elasticity and mechanical resistance compared to rigid polymeric materials.
- High optical clarity and adaptable physical form, allowing versatile processing.
- High moisture content confers tissue, enabling comfortable patient use.
- Inherently bio compatible and biodegradable, with capacity for minimally invasive delivery via injection.
- Stimuli-responsive release of encapsulated therapeutic agents triggered by pH, temperature, or metabolic signals.
- Controlled and predictable release kinetics enhance therapeutic efficacy.[3]

3. Disadvantages of hydrogels

- Manufacturing and raw material costs remain relatively high.
- Non-adhesive surface characteristics may provide secondary fixation dressings in wound care.
- Sterilization presents technical challenges due to material sensitivity.
- Ophthalmic hydrogel devices may contribute to hypoxia, dehydration, and ocular irritation if not properly designed.[2]

4. Characterization of hydrogel

4.1. Stimuli-Responsive Behavior

A defining feature of hydrogels is their dynamic responsiveness to environmental stimuli Minor fluctuations in external variables — including temperature, pH, ionic strength, electrical stimulation, and enzymatic activity — can trigger rapid and reversible structural transitions. These changes in the polymer network manifest as visible alterations in texture, volume, or permeability, enabling smart drug delivery and bio-sensing applications.[2]

4.2. Mechanical Properties

The rheological and mechanical behavior of hydrogels is governed by cross link density, polymer concentration, and network architecture. Stiffness can be modulated by adjusting crosslinking conditions or thermal treatment, generating materials ranging from soft, tissue-like gels to firm, load-bearing scaffolds. Comprehensive mechanical characterization — including tensile testing, compression analysis, and rheological profiling — is essential to match material properties with specific end-use requirements.[2]

4.3. Constituent Polymers

Hydrogels may be formulated using naturally derived or synthetic macro molecules. Natural-origin polymers include polysaccharides and proteins. Synthetic alternatives encompass acrylic acid derivatives, vinyl acetate, methacrylates, and vinyl pyrrolidone copolymers, each contributing distinct mechanical and chemical attributes.

4.4. Biocompatibility

Biocompatibility encompasses two principal dimensions: bio-functionality (the capacity of the material to fulfill its designated role) and bio-safety (the absence of cytotoxicity, mutagenicity, or adverse local and systemic host responses). Hydrogels intended for clinical applications must demonstrate satisfactory performance across both dimensions prior to regulatory approval.

5. Classification of hydrogels

5.1. Based on Origin

Natural Hydrogels: Derived from biological polymers including polysaccharides (chitosan, alginate, hyaluronic acid) and proteins (collagen, gelatin, lysozyme). These materials exhibit inherent biocompatibility, biodegradability, and favorable cell-adhesion properties.

Synthetic Hydrogels: Engineered polymers such as polyethylene glycol (PEG)-based systems offer far greater control over mechanical performance and chemical functionality than their natural counterparts. Their low immunogenicity and non-toxicity make them particularly suited to implantable biomedical devices.

Hybrid Hydrogels: Composite systems combining synthetic and natural polymers — such as poly(N-isopropylacrylamide) with dextran or chitosan — are engineered to capture the complementary strengths of both classes.

5.2. Based on Polymeric Composition

- Homopolymeric Hydrogels: Networks assembled from a single monomer type; network topology is influenced by the polymerization method and monomer chemistry.
- Copolymeric Hydrogels: Formed from two or more monomers, at least one of which is hydrophilic, arranged in alternating, random, or block sequences along the polymer backbone.
- Interpenetrating Network (IPN) Hydrogels: Two independently crosslinked polymer networks interpenetrate without covalent bonding. Semi-IPN variants incorporate one crosslinked and one linear polymer component.

5.3. Based on Biodegradability

1.Biodegradable Hydrogels: Include naturally derived polymers such as chitosan and fibrin, as well as synthetic analogs like poly(N-isopropylacrylamide) and polyanhydrides.

2.Non-Biodegradable Hydrogels: Prepared from vinyl-based monomers such as 2-hydroxyethyl methacrylate, methoxy-poly(ethylene glycol), and acrylamide, these materials offer long-term structural permanence.

6. Methods of preparation

Hydrogels can be fabricated from either synthetic or naturally derived polymer precursors. Synthetic polymers generally exhibit greater chemical stability and hydrophobicity, while natural polymers offer inherent bioactivity. Several polymerization strategies are employed:

6.1. Bulk Polymerization

In this approach, predominantly vinyl monomers are polymerized in the absence of solvent, with small quantities of crosslinking agents incorporated into the formulation. The reaction is initiated via chemical catalysts, ultraviolet irradiation, or high-energy radiation. The resulting hydrogel can be fashioned into diverse product forms including films, rods, particles, and emulsions.

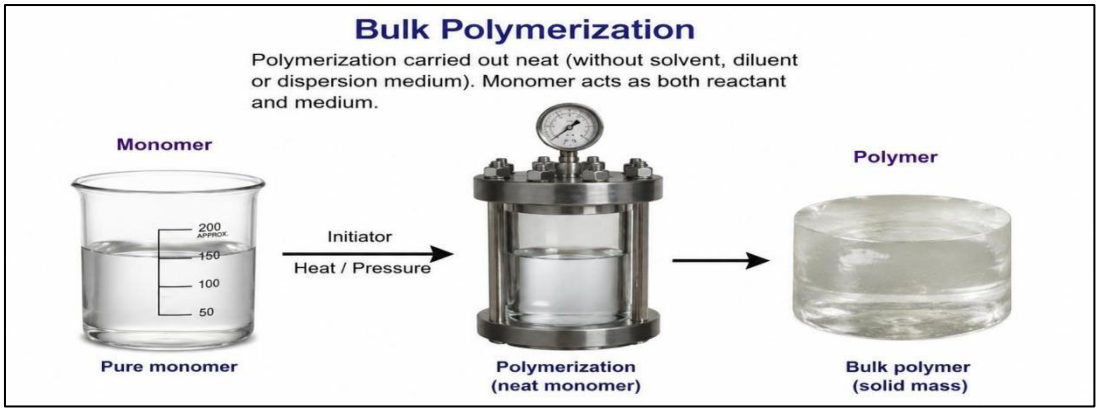

Figure 2 Bulk polymerization

6.2. Free-Radical Polymerization

This widely adopted method employs monomers bearing reactive vinyl groups — such as acrylates, vinyl lactams, and acrylamides. The mechanism proceeds through initiation, propagation, chain transfer, and termination stages. A spectrum of initiators is available, including thermal decomposition agents, photoinitiators (UV and visible), and redox pairs, providing flexibility in processing conditions.

6.3. Solution Polymerization

Monomers — whether ionic or neutral — are dissolved along with crosslinking agents and polymerized in the presence of a solvent medium. The solvent functions as a thermal buffer, absorbing the heat of reaction and reducing the risk of runaway exotherms. Post-synthesis purification with distilled water eliminates unreacted monomers, initiators, and extractable oligomers.

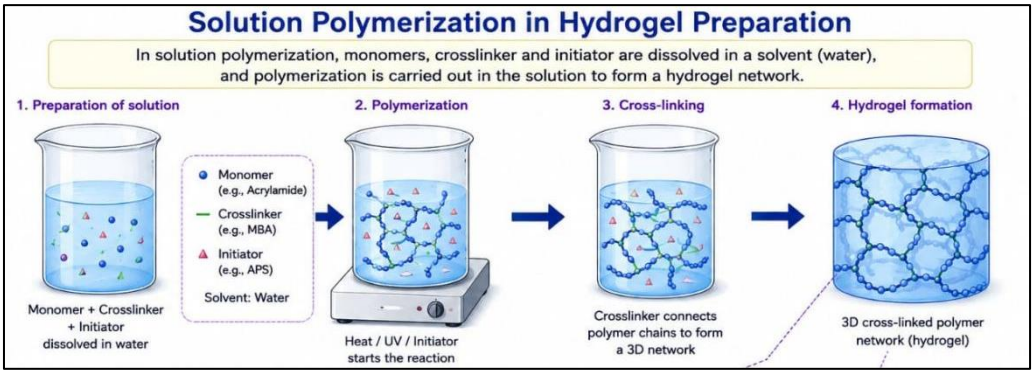

Figure 3 Solution polymerization

6.4. Suspension Polymerization

This technique produces spherical hydrogel microparticles with diameters ranging from 1 μm to 1 mm. Monomer droplets are dispersed and stabilized within a non-solvent phase using appropriate stabilizers, and free-radical decomposition initiates polymerization. Thorough washing removes residual reactants from the resulting microparticles.[3]

7. Drug release mechanisms

7.1. Diffusion-Controlled Release

The most prevalent drug release mechanism in hydrogel systems, governed by Fick's law of diffusion with either fixed or concentration-dependent diffusion coefficients. Drug diffusivity values are typically derived from free-volume theory, hydrodynamic models, or obstruction-based frameworks.[16]

7.2. Chemically Controlled Release

Drug liberation in this mode is governed by chemical events within the delivery matrix, including enzymatic or hydrolytic polymer chain scission, and reversible or irreversible drug-polymer binding interactions. In certain formulations, erosion of the hydrogel surface or bulk controls the release rate, while in others, binding of drug availability.

7.3. Swelling-Controlled Release

This mechanism operates when drug diffusion occurs at a rate exceeding the rate of hydrogel matrix swelling. The moving boundary between glassy and rubbery polymer phases acts as a dynamic drug reservoir, and mathematical modeling requires accommodation of shifting boundary conditions.[1]

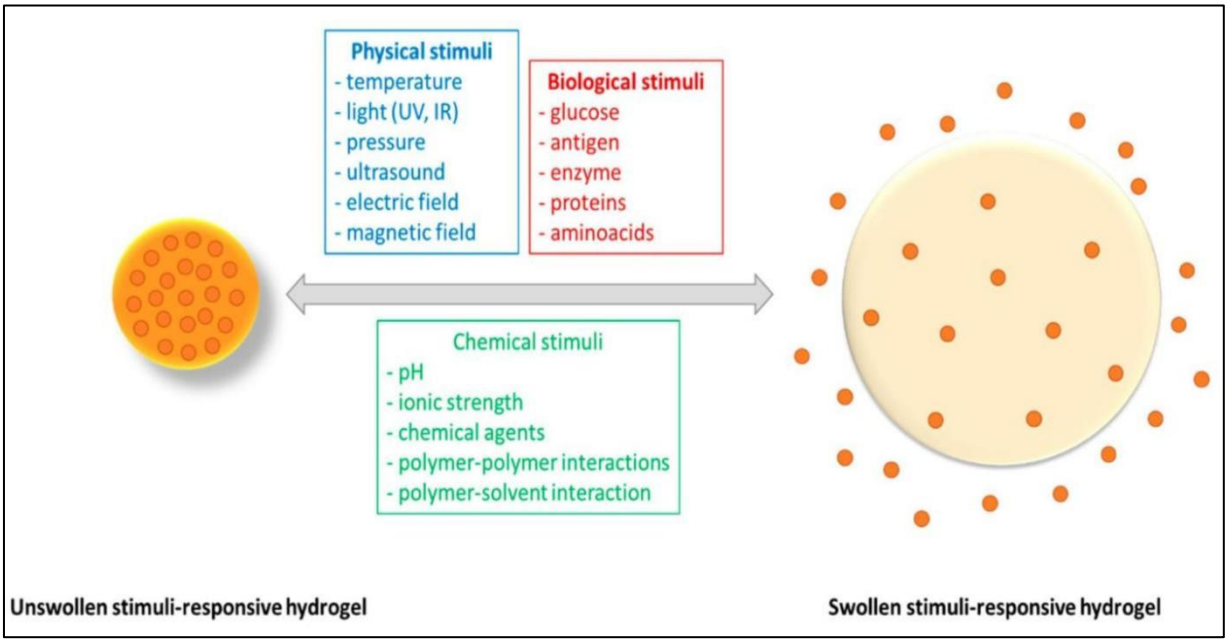

Figure 4 Drug Release Mechanisms of Hydrogel

8. Evaluation of hydrogel

pH Measurement: Digital pH meters are used to assess the acidity or alkalinity of swollen hydrogel formulations.

Scanning Electron Microscopy (SEM): Enables high-resolution visualization of surface morphology, porosity, and elemental composition of the hydrogel scaffold.

X-Ray Diffraction (XRD): Quantifies the degree of crystallinity or amorphous character in hydrogel networks and assesses structural changes induced by processing conditions.

Skin Irritancy Testing: Conducted in rabbit models to evaluate potential for erythema and edema; irritation scores are derived by averaging erythema and edema ratings over specified time intervals.

Fourier Transform Infrared Spectroscopy (FTIR): Identifies chemical bonding environments and detects interactions between drug and polymer matrix through peak shifts and broadening patterns.

Swelling Studies: Dry hydrogel specimens are immersed in deionized water for 48 hours; swelling ratio is calculated as (Ws - Wd) / Wd, where Ws and Wd denote the swollen and dry weights, respectively.

Rheological Analysis: Viscosity measurements at defined rotational speeds using a Brookfield viscometer characterize the flow and deformation behavior of gel formulations.

Spreadability Assessment: A standardized apparatus measures the time required for two glass slides — bearing the gel under a fixed load — to separate, providing a quantitative index of spreadability.[1]

9. Pharmaceutical applications

9.1. Wound Dressings

Wound management remains one of the most clinically significant applications of hydrogels. Their capacity to absorb wound exudate, maintain a moist healing interface, and provide a protective physical barrier makes them ideal dressing materials. Hydrogel dressings facilitate tissue regeneration through their inherent biocompatibility and flexible, conformal properties. Crucially, their inherent lubricity minimizes wound adhesion, reducing trauma upon dressing changes and supporting pain-free wound care.[2]

9.2. Drug Delivery Systems

The utility of hydrogels as drug carriers stems from their ability to encapsulate diverse pharmacological agents, regulate formulation consistency and strength, promote controlled degradation, govern release kinetics, and mask unpleasant pharmaceutical odors. These capabilities collectively enhance therapeutic precision and patient acceptability in drug delivery applications.

9.3. Dental Pulp Regeneration

Injectable hydrogel formulations offer a compelling solution for endodontic tissue engineering. In liquid form prior to gelation, the material can be injected to fill the entire pulp chamber and root canal system. After sol-gel transition, the hydrogel adheres firmly to surrounding tissue and provides a uniform three-dimensional scaffold for encapsulated cells — addressing the challenge of achieving homogeneous cell distribution within the confined geometry of the root canal.

9.4. Cardiac Tissue Engineering

Myocardial infarction leads to irreversible cardiomyocyte loss and progressive fibrosis, culminating in heart failure. Conventional organ transplantation is constrained by donor scarcity and immune rejection. Injectable hydrogels have emerged as a promising platform for cardiac cell therapy, supporting transplanted cardiomyocyte survival by replicating the extracellular matrix microenvironment. These materials can be delivered via catheter for minimally invasive myocardial injection, combining biocompatibility, low immunogenicity, and mechanical tunability in a single platform.

9.5. Peripheral Nerve Repair

Peripheral nerve injuries disrupt axonal continuity, triggering distal fiber degeneration and loss of motor and sensory function. Conventional autologous nerve grafts are limited by donor availability and anatomical size mismatches. Hydrogel-based nerve conduts offer an attractive alternative: their properties approximate those of native neural tissue, their three-dimensional swollen architecture supports axonal growth, and their capacity to incorporate neuroactive compounds enables sustained pharmacological support for nerve regeneration.

10. Advancement in hydrogel formulation

10.1. Solar-Driven Water Purification

Researchers have developed hydrogel-based solar vapor generators capable of producing clean drinking water from contaminated or saline sources using only ambient sunlight. These hybrid gel systems exploit the dual hydrophilic and semiconducting properties of specially engineered polymer networks to drive evaporation efficiently. Trials using water from the Dead Sea — among the world's most saline bodies of water — demonstrated substantial salinity reduction, confirming the technology's potential as a cost-effective, infrastructure-light desalination alternative to energy-intensive conventional methods.

10.2. Extended-Release Oral Capsules

Innovative hydrogel capsule systems have been developed that reside within the gastrointestinal tract for up to nine days, enabling weekly, monthly, or continuous dosing regimens. Overcoming the mechanical demands of the gastric environment — which requires materials resilient enough to resist peristaltic forces without causing mucosal injury —

was a key engineering challenge. Patients can swallow the hydrogel capsule in its moistened state, after which it expands and anchors in the stomach.

10.3. Ophthalmic Hydrogel Innovations

A novel injectable elastic gel has been developed as a vitreous humor substitute in ophthalmic surgery. Administered as a liquid, the material undergoes rapid in-situ gelation within the ocular cavity, providing optical clarity and biomechanical support comparable to the native vitreous gel. Preliminary studies in animal models have demonstrated promising outcomes, opening new avenues for the management of retinal detachment and other vitreoretinal conditions.

10.4. Hydrogels in Melanoma Therapy

Hydrogel-based platforms have gained traction as localized delivery vehicles for melanoma treatment. Polymeric formulations — both natural and synthetic — loaded with cytotoxic or immunomodulatory are being evaluated for transdermal drug delivery against skin cancer. Additionally, magnetically responsive hydrogel composites are being explored for combined photothermal and thermomagnetic tumor strategies, representing a convergence of materials science and oncology.[17]

11. Conclusion

Hydrogels occupy an increasingly central position in both pharmaceutical science and biomedical engineering, underpinned by their unique combination of water-rich composition, tunable mechanical behavior, biocompatibility, and stimuli-responsive functionality. Their structural adaptability enables application across a broad therapeutic spectrum — from wound management and controlled drug release to regenerative medicine and organ repair. While challenges related to cost, sterilization, and mechanical limitations remain, ongoing advances in polymer chemistry, materials processing, and nanotechnology continue to expand the functional envelope of hydrogel systems. The convergence of hydrogel platforms with emerging technologies such as solar-driven purification, extended-release pharmaceuticals, and localized cancer therapy underscores their transformative potential across both healthcare and environmental domains.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed

References

[1] Malpure PS, Patil SS, More YM, Nikam PP. A review on hydrogel. Am J PharmTech Res. 2018;8(3):2249-3387.

[2] Ahmed EM. Hydrogel: preparation, characterization and application: a review. J Adv Res. 2015;6(2):105-121. doi:10.1016/j.jare.2013.07.006.

[3] Akhtar MF, Hanif M, Ranjha NM. Methods of synthesis of hydrogels: a review. Saudi Pharm J. 2016;24:554-559.

[4] Reddy VRK, Nagabhushanam MV, Naik ER. Swellable hydrogels and cross-linking agents—their role in drug delivery systems. Res J Pharm Technol. 2017;10(3):0974-3618.

[5] Mohite PB, Adhav SS. A hydrogel: method of preparation and applications. Int J Adv Pharm. 2017;6(3):79-85.

[6] Pande PP, Anamica. Polymer hydrogels and their applications. Int J Mater Sci. 2017;12(1):0973-4589.

[7] Das N. Preparation methods and properties: a review. Int J Pharm Pharm Sci. 2013;5(3):0975-1491.

[8] Chirani N, Yahia LH, Gritsch L, Motta FL, Chirani S, Fare S. History and applications of hydrogels. J Biomed Sci. 2016;4:2.

[9] Garg S, Garg A. Hydrogel: classification, properties, preparation and technical features. Asian J Biomater Res. 2016;2(6):163-170.

[10] Devi A, Nautiyal U, Kaur S, Komal. Hydrogel: a smart drug delivery device. Asian Pac J Health Sci. 2014;1(4 Suppl):92-105.

[11] Shetye SP, Godbole A, Bhilegaokar S, Gajare P. Hydrogels: introduction, preparation, characterization and applications. Int J Res Methodol. 2015;1(1).

[12] Meshram PS, Kale SD, Labale PS, Mate KS. Hydrogel polymer: a unique material for bio-separation, bio-sensing and drug delivery. Int Adv Res J Sci Eng Technol. 2017;4(3).

[13] Singh A, Sharma PK, Garg VK, Garg G. Hydrogels: a review. Int J Pharm Sci Rev Res. 2010;4(2).

[14] Saini K. Preparation method, properties and crosslinking of hydrogel: a review. PharmaTutor. 2016;5(1):27-36.

[15] Singh SK, Dhyani A, Juyal D. Hydrogels: preparation, characterization and applications. Pharma Innov J. 2017;6(6):25-32.

[16] El-Sherbiny IM, Yacoub MH. Hydrogel scaffolds for tissue engineering: progress and challenges. Glob Cardiol Sci Pract. 2013;2013(4):38.

[17] Thakur VK, Thakur MK, Kessler MR. Handbook of composites from renewable materials. Vol. 6, Polymeric composites. Beverly (MA): Scrivener Publishing; 2017.

[18] Dwivedi S, Khatri P, Mehra GR, Kumar V. Hydrogel—a conceptual overview. Int J Pharm Biol Arch. 2011;2(6):1588-1597.

[19] Bhosale RR, Osummani RA, Ghodake PP, et al. Thermosensitive hydrogel: an inventive carrier for drug delivery. Int J Pharm Med Res. 2013;1(2):60-69.

[20] Pourjavadi A, Harzandi AM, Hosseinzadeh H. Modified carrageenan. 3. Synthesis of a novel polysaccharide-based super absorbent hydrogel via graft Copolymerization of acrylic acid onto kappa-carrageenan. Eur Polym J. 2004;40(7):1363-1370.

[21] Peppas NA, Mikos AG. Hydrogels in medicine and pharmacy—fundamentals. In: Peppas NA, editor. Hydrogels in medicine and pharmacy. Vol. 1. Boca Raton (FL): CRC Press; 1986. p. 1-25.

[22] Park MR, Chun CJ, Ahn SW, Ki MH, Cho CS, Song SC. Sustained delivery of human growth hormone using a Polyelectrolyte complex-loaded thermosensitive polyphosphazene hydrogel. J Control Release. 2010;147(3):359-367.

[23] Tabata Y. Biomaterial technology for tissue engineering applications. J R Soc Interface. 2009;6(Suppl 3):S311-S324.

[24] Gulrez SKH, Assaf S, Phillips GO. Hydrogels: methods of preparation, characterization and applications. Wrexham (UK): Glyn O Phillips Hydrocolloids Research Centre, Glyndwr University.

[25] Monica AS, Gautami J. Design and evaluation of topical hydrogel formulation of Diclofenac sodium for improved therapy. Int J Pharm Sci Res. 2014;5(5):1973-1980.