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# ADVANCES AND APPLICATIONS OF HYDROGELS IN BIOMEDICAL AND PHARMACEUTICAL SCIENCE

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**Abstract:**

*Hydrogels have emerged as one of the most promising materials for biological applications because of their unique qualities. With properties including flexibility, adaptability, responsiveness, and a soft structure, hydrogels are networks of polymers that can absorb huge amounts of water. These characteristics outperform those of other biomaterials because they closely resemble live tissue. The source, preparation, ionic charge, responsiveness, crosslinking, and physical characteristics of hydrogels can all be used to categorize them. They have shown great promise in tissue engineering, contact lenses, wound healing, and personal hygiene products. Hydrogels are still not widely used in commercial tissue engineering and drug delivery applications, despite these benefits. Only a small number of drug-delivery devices and scaffolds have made it to market, despite the fact that many have been created, evaluated, and even patented. This review focuses on hydrogel-based biomaterials and their applications in wound healing, tissue engineering, cosmetics, drug delivery, and contact lenses.*

***Keywords:*** *Hydrogel, Adaptability, Drug-delivery devices, Biomaterials etc.*

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## INTRODUCTION:

Since material synthesis technologies have advanced so much, biomaterials have emerged as the basis for a wide range of new pharmacological and medical applications. Particularly effective in absorbing fluids are three-dimensional, hydrophilic networks of polymers called hydrogels. Hydrogels are different from other types of synthetic biomaterials because of their soft consistency, high water content, and porosity, which allow them to closely resemble real living tissue. Wichterle and Lim provided a detailed description of "hydrogel" after van Bemmelen coined the name in 1894. The criteria states that a substance must contain at least 10% water in order to qualify as a hydrogel. In general, there are two primary forms of hydrogels: chemical and physical gels. Physical hydrogels, also known as reversible gels, are created by secondary forces such hydrophilic contacts, hydrogen bonds, or ionic bonds, or by molecular organization.

All of these processes are essential for the formation of their network-like structure. Hydrogels for different organs and tissues have been developed during the last 60 years to be implantable, injectable, and even spray able. Van der Waals forces, electrostatic interactions, hydrophobic contacts, and hydrogen bonding all affect how much a hydrogel swells at equilibrium. The equilibrium swelling characteristics of cross-linked polymer systems, in which the polymer chains interact in the solid state and have a Gaussian distribution, have been described by a number of theories. The most fascinating aspect of hydrogel swelling is how quickly it occurs, which is influenced by a number of physicochemical factors, including The most intriguing feature of hydrogel swelling is its speed, which is determined by various physicochemical parameters, such as porosity and pore structure. Based on their pore structure, hydrogels can be classified into four categories: super-porous, macroporous, microporous, and non-porous.

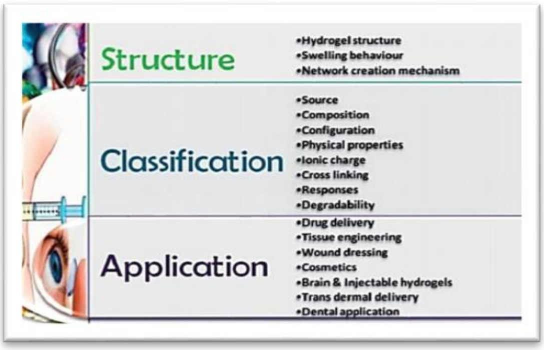


**Figure No. 01 Hydrogel**

### Structure of hydrogel:

A network of cross-linked polymeric chains makes up hydrogels in their solid state. Because of their three-dimensional (3D) network structure, hydrogels can have a molecular weight that is practically unlimited. The size of the mesh and the molecular weight of the polymer chains connecting the cross-links are two examples of the molecular parameters that affect the structure of hydrogels. Both chemical and physical crosslinking techniques are commonly used to create hydrogels. A stronger and more stable hydrogel network is formed by chemical crosslinking, which involves the production of covalent bonds, as opposed to physical crosslinking, which uses processes like hydrogen bonding.

### Mechanism and different theories of hydrogel swelling

Over the past few decades, modelling of swelling in polymeric networks has been investigated at many sizes, from macroscopic to microscopic theories. For example, statistical theory explains the global swelling ratio of polyelectrolyte gels. According to this macroscopic theory, the equilibrium stage of swelling is reached when the Gibbs free energy (F) reaches its minimal value. Both chemically and thermally stimulated hydrogels can be used with this paradigm. Another illustration of a macroscopic or mesoscopic continuous theory is the idea of porous media. This theory, which explains the swelling behaviour of hydrogels, is based on the idea of mixes and has been expanded to include the idea of volume concentrations. Discrete element theory describes the micromechanical behaviour of hydrogels at the microscopic level. In this approach, the hydrogel network is considered to consist of dispersed particles that mechanically interact with one another. These interactions help define the overall structure and behaviours of the hydrogel as it swell.

### Network creation mechanism

The process of gelation creates increasingly larger branched, but soluble, polymers by joining macromolecular chains. The structure and conformation of the initial materials determine this process. When monomers at nearby locations form bonds with one another, the chemical reaction between them is described as a random process. As the reaction progresses, the extent of the reaction increases from zero to unity, representing the fraction of all potential networks produced at any given stage. A polymer is depicted in this model as a collection of monomers (sites) joined by bonds. When every potential bond has been created and the polymer network is fully grown, the gelation process is said to be finished. Chemical gelation, in contrast, involves the formation of covalent bonds, leading to the creation of a permanent, robust gel structure. The primary chemical gelation reactions include vulcanization, condensation, and addition polymerization.

**Properties of hydrogel**
Hydrogels are network polymers capable of absorbing and retaining water, which causes the hydrogel to swell.

**Swelling of hydrogel**
The equilibrium swelling of hydrogels is calculated using the following formula:[ \text{Swelling ratio} = \frac{W_t - W_d}{W_d} ]where ( W_t ) is the weight of the swollen hydrogel, and ( W_d ) is the weight of the dried hydrogel after freeze-drying.In typical hydrogel systems, drug release primarily occurs through the swelling or contraction of the hydrogel and the diffusion of the drug through the polymer network. When a hydrogel's properties, such as swelling behaviours, structure, mechanical strength, or permeability, change in response to various stimuli, it is referred to as a stimulus-responsive or biologically sensitive hydrogel. These hydrogels can be effectively utilized to modify the release of drug agents, allowing for controlled drug delivery.

**Mechanical properties**
When designing hydrogels for medicinal purposes, their mechanical characteristics are crucial. In tissue engineering, the mechanical characteristics of hydrogel scaffolds, both at the macroscopic and microscopic levels, play a significant role in influencing cell behaviours. These scaffolds' strength, elasticity, and stiffness are essential for supporting tissues and encouraging healthy cell division and growth.

**Biological properties**
Biocompatibility, non-toxicity, adequate mechanical strength, suitable viscosity, stability, and biodegradability are among the biological characteristics of injectable hydrogels used in medical applications. Hydrogels must have mechanical and biological characteristics that closely mimic the tissue they are meant to replace in order to be used in medicine. This facilitates effective tissue regeneration or repair and guarantees appropriate interaction with the surrounding biological environment.

**Classification of Hydrogel**
Classification of hydrogel base on the source, preparation, responsiveness, composition, ionic charge, crosslinking and physical characteristics and biodegradation are all used to classify hydrogel .The characterisation of hydrogel in figure 2.

**1. Based on source**
According to their origin, hydrogels can be divided into three groups: natural, synthetic, and hybrid or semi-synthetic (El-Sherbiny & Yacoub, 2013). Natural hydrogels are perfect for biological applications since they are very biocompatible. But they frequently have poor stability and mechanical qualities (Singh et al., 2016). Collagen, gelatin, alginate, and chitosan are a few types of natural polymers. Crustacean shells contain chitin, which is deacetylated to produce chitosan, a biopolymer made up of N-acetyl D-glucosamine and D-glucosamine units (Croisier & Jérôme, 2013). A promising biomaterial for abdominal tissue engineering, for example, is an in situ forming hydrogel made by Youming et al. using a Schiff base cross-linking reaction based on chitosan and hyaluronic acid. This hydrogel demonstrated enhanced cellular responsiveness (Deng et al., 2017). Because of their facile gelation mechanisms and biocompatibility, natural polymers are also frequently employed in bioinks. Because of their repeatable and adjustable mechanical or physicochemical characteristics, synthetic hydrogels are appealing for use in biomedical applications. Their main drawback, though, is occasionally their lack of biocompatibility.

Polyethylene glycol, polyacrylic acid, polyethylene oxide, and polyvinyl alcohol are examples of common synthetic polymers used in hydrogels. For instance, by encouraging nerve healing and preventing nerve fiber degeneration, polyethylene glycol is biodegradable, biocompatible, and appropriate for treating spinal cord injuries (Kong et al., 2017). Furthermore, because polyvinyl alcohol-polyacrylic acid hydrogels decrease platelet adherence, they are attractive materials for vascular access (Mannarino et al., 2020). Semi-synthetic or hybrid hydrogels, such as gelatin methacrylate and cellulose derivatives (Utech & Boccaccini, 2016), are favored for many applications because they combine the advantages of both natural and synthetic polymers.

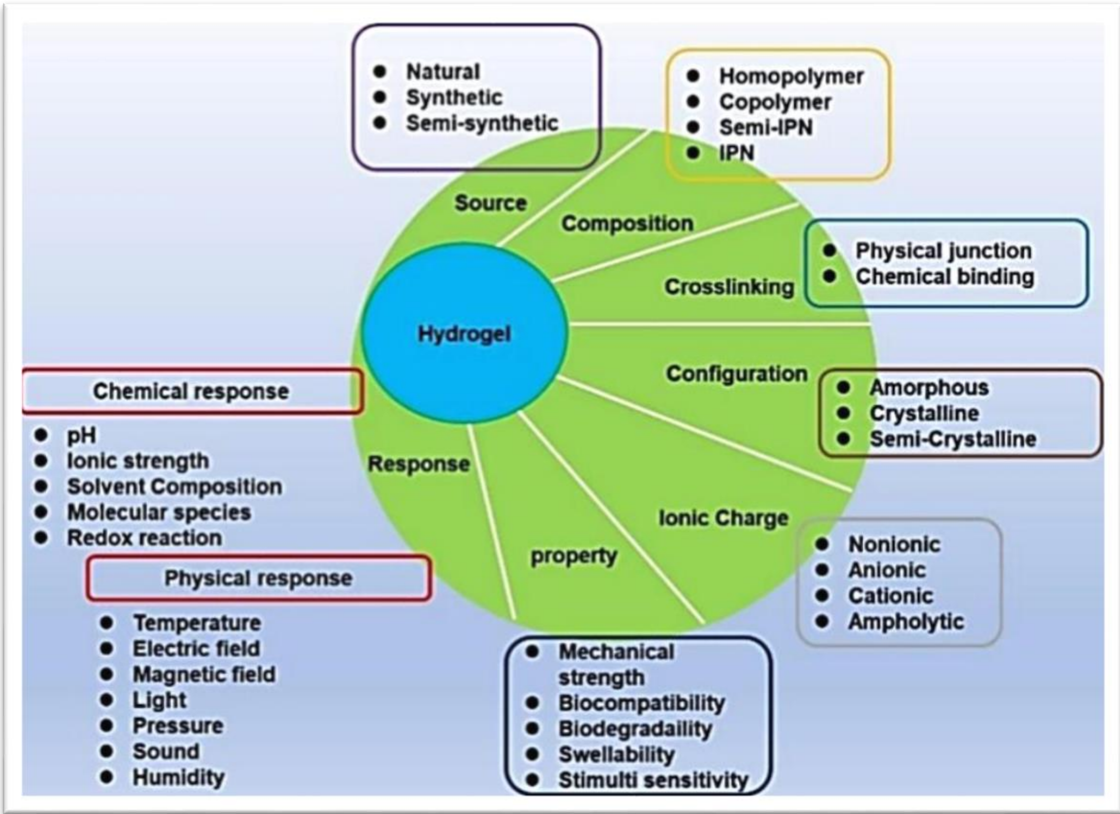


**Figure No. 02 Classification of Hydrogel**

**2. Based on the composition**

**i) Homopolymeric Hydrogels:**

These hydrogels consist of a polymer network derived from a single species of monomer, the fundamental structural unit of any polymer network (Takashi et al., 2007).

**ii) Homopolymer:**

The structure of homopolymeric hydrogels can vary depending on the monomer type and the polymerization method used, with some having a cross-linked skeletal structure.

**iii) Copolymeric Hydrogels:**

Copolymeric hydrogels are composed of two or more distinct monomer species, with at least one hydrophilic component. These monomers can be arranged in random, block, or alternating configurations along the polymer chain (Yang et al., 2002).

**iv) Multipolymer or Interpenetrating Polymeric Network (IPN) Hydrogels:**

IPN hydrogels consist of two independent cross-linked polymer networks, which may be synthetic, natural, or a combination of both. In the case of semi-IPN hydrogels, one component is a cross-linked polymer, while the other is a non-cross-linked polymer.

**3. Based on the configuration**

Configuration plays a critical role in determining the properties of hydrogels. Based on their configuration, hydrogels can be categorized into three types

**i) Amorphous (Non-crystalline):**

These hydrogels lack an ordered structure and do not exhibit any crystalline phases.

**ii) Semi-crystalline:**

Semi-crystalline hydrogels consist of a complex mixture of amorphous and crystalline phases. This structure provides a balance between flexibility and strength.

**iii) Crystalline:**

Polymers crystallize in crystalline hydrogels as lamellae, which are layers of chain folds. Spherulites are spherical structures made up of clusters of these lamellae. The polymers display crystalline phases when the lamellar chains are organized in systematic ways. On the other hand, the polymers display amorphous phases when the lamellae are organized irregularly.

Usually, polymers crystallize from the melt into spherulitic structures; the cooling rate, crystal mass, and nucleation sites all affect the spherulites' size. The order of molecular arrangement in polymers is measured by the degree of crystallinity, which is given as a percentage. The degree of crystallinity varies from almost 0% (totally amorphous) to 95%

(very crystalline), depending on the cooling rate and the structure of the polymer.

**4. Based on the crosslinking**

Hydrogels are categorized into two types based on their crosslinking methods:

i) Physical gels (reversible gels) and
ii) Chemical gels (permanent gels).

Because physical gels are reversible, they are commonly used. Molecular entanglements or other interactions like hydrogen bonding, ionic bonds, or hydrophobic interactions hold these gels together. Under specific circumstances, the gel may be able to switch between gel and sol states thanks to these physical interactions, which also give the network stability.

Chemical gels, on the other hand, have a more stable and long-lasting structure because they use permanent crosslinks, usually created by covalent bonds.

**Application of hydrogel in biomedical field**

- **Hydrogen for wound dressing**

Because of their special qualities, hydrogels are in fact well known as superior materials for wound treatment. They are particularly helpful for treating wounds with high exudate levels because of their cross-linked polymer structure, which allows them to hold huge volumes of water and medications. Hydrogels' ability to retain moisture contributes to the creation of the ideal environment for wound healing, encouraging tissue regeneration and lowering the risk of infection. Their capacity to retain moisture while absorbing exudates promotes tissue remodelling and cell proliferation, which speeds up the healing process. Hydrogels are adaptable and efficient in a range of wound care applications, from treating burns to chronic ulcers, thanks to this mix of qualities.

- **Tissue engineering**

Hydrogels are perfect for tissue engineering and regenerative medicine applications because of their highly hydrated polymer networks, which closely resemble extracellular matrices (ECMs). Damaged osteocortical joints and articular cartilage tissue have been repaired using a variety of hydrogels made from natural and synthetic polymers. The capacity of alginate, a naturally occurring polysaccharide polymer that is frequently isolated from brown seaweed and certain bacteria, to physically cross-link with divalent cations such as calcium ($Ca^{2+}$) at room temperature has drawn attention. Because of this characteristic, alginate is especially helpful in a variety of biotechnological processes, including molding and spraying.

- **Hydrogel ocular drug delivery**

The use of hydrogels, specifically in drug delivery systems and micro-optical arrays, in the treatment of eye diseases is covered in the text. The biocompatibility, transparency, and long-term medication retention of hydrogels make them extremely valuable. They improve the bioavailability and efficacy of drugs in a variety of ways, including soft and hard contact lenses. Only 1–5% of the medication in traditional ocular treatments, like ointments and eye drops, reaches the intended area, causing sluggish and occasionally ineffective treatment. Hydrogel-based solutions, on the other hand, provide longer-lasting and more regulated drug release, which makes them a viable option for enhancing eye therapy. The paper also notes that cutting-edge methods like photolithography and polymer particle assembly can be used to economically make hydrogels.

- **Hydrogels for subcutaneous delivery and transdermal delivery**

The essay emphasizes how hydrogels' beneficial biodegradable qualities make them appropriate for creating implanted hydrogels that are utilized to deliver anticancer medications like cytarabine subcutaneously. Poly (2-hydroxyethyl methacrylate) (PHEMA) and other cross-linked polymers are used to create these hydrogels. Hydrogels can regulate the release of pharmaceuticals through a variety of drug delivery methods, including transdermal approaches. Swollen hydrogels are used as controlled release devices in wound healing to administer active chemicals, such as the anti-inflammatory medication desonide, over an extended period of time. Furthermore, the use of hydrogels in transdermal iontophoresis is being investigated to improve the penetration of goods such as nicotine and hormones, hence increasing therapy efficacy and patient compliance.

- **Hydrogel for cosmetics application**

Protecting the body from external factors like bacteria and UV rays is the main function of skin. It also aids in maintaining hydration and controlling body temperature. Lotions, moisturizers, and cleansers are examples of cosmetic products that are frequently used to improve the texture and appearance of the skin. Because of their high water content, flexibility, and biocompatibility, hydrogel-based cosmetics have become more and more popular recently. Hydrogels are especially helpful for treating skin problems like moisture, wrinkles, pigmentation, and aging. Caffeine, for instance, can be progressively released into the skin through bio-adhesive hydrogels, enhancing its texture. Collagen hydrogels are utilized to restore the suppleness and moisture of the skin, whereas liposome-hydrogel complexes are used to prevent photo aging.

- **Application of Hydrogel in drug delivery**

medicinal compounds' absorption and retention, increasing their bioavailability. Because hydrogels can offer continuous, controlled release at the intended spot, they are perfect for a variety of drug delivery methods. Hydrogels' three-dimensional network structure enables them to encapsulate and shield medications until they get to the intended site, where they can react to particular stimuli, such pH, temperature, or enzymes, to release the active ingredients. Because of their versatility and flexibility, hydrogels can also be tailored to satisfy a range of delivery requirements, including variable release rates and environmental trigger response. Because of their versatility, hydrogels can be used in a wide range of novel drug delivery systems. By providing precise control over dosage and release time, these systems could significantly advance customized medicine.

- **Injectable Hydrogel**

By providing minimally invasive therapies that shorten recovery times for patients and lower procedure risks, injectable hydrogels present intriguing substitutes for conventional surgical and intravenous techniques. Their excellent penetrability, ease of handling, and capacity to fill uneven defect areas make them perfect for a variety of biomedical applications, such as localized drug administration and tissue engineering. Injectable hydrogels, in particular, are beneficial for improving urethral tissue function because they allow for precise, regulated distribution with less discomfort and at a lower cost. Their efficacy has been confirmed by clinical and animal research, indicating that these hydrogels can be used as bulking agents to strengthen tissue, restore function, or directly provide medicinal chemicals where they are required. The promising results from these studies underscore the potential of injectable hydrogels in enhancing treatment options and reducing the invasiveness and complications associated with traditional therapies.

- **Hydrogel for dental application**

In the realm of dental tissue regeneration, injectable hydrogel-based scaffolds hold great promise as an efficient means of restoring missing or damaged craniofacial elements, including the pulp, dentin, and alveolar bone, temporomandibular joint and periodontal ligament. These injectable scaffolds in dentistry help overcome the drawbacks of conventional treatments, especially in pulp regeneration, which is essential for the creation of reparative dentin. For irreparably injured pulp, endodontic treatment is currently frequently the only viable choice; however, hydrogels present a novel strategy that may be able to rebuild and retain pulp tissue, enhancing long-term results.

## CONCLUSION:

Because of their special architectures, hydrogels—which can come from synthetic or natural sources—are able to absorb and hold onto large volumes of water. They are ideal for biological applications because of their qualities, which include biocompatibility and biodegradability. Their commercial applications are still somewhat limited, despite their potential. They are frequently found in goods like tissue engineering, contact lenses, wound dressings, and personal hygiene products. Though promising and often patented, sophisticated hydrogel-based medication delivery and scaffolding systems have not yet made a significant effect on the market. The necessity of continuous research to improve the biodegradability, durability, and adaptability of hydrogels for novel applications is emphasized throughout the book. Future research should concentrate on streamlining formulations and matching them to particular medical requirements in order to optimize their usefulness.

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