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## “HYDROGEL- A REVIEW”

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### Keywords:

Natural Polymer Hydrogel,  
Synthetic Polymer Hydrogel,  
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### ABSTRACT:

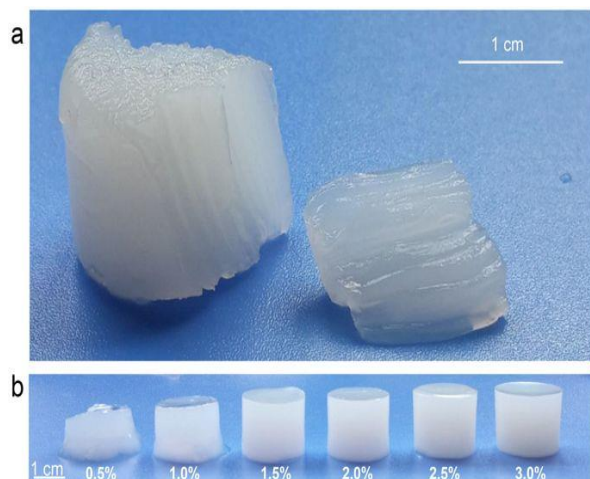
Hydrogel's may be defined as a network of polymer chains that are hydrophilic, water insoluble sometimes found as a colloidal gel in which water is a dispersion medium. Their ability to absorb water is because of its cross linking network structure which is formed by polymer bearing hydrophilic groups. Hydrogel's are insoluble due to the presence of chemical and physical cross-links Such as entanglements. It is also respond to the fluctuation of environmental stimuli (ionic strength, temperature. pH, presence of enzyme etc.) and swell or shrink accordingly in the swollen state they are soft and rubbery resembling the living tissue exhibiting excellent biocompatibility Hydrogel are commonly used in clinical practice and experimental medicine for a wide range of applications, including food additives, Tissue engineering, regenerative medicines, Pharmaceuticals drug delivery devices and membranes for biosensors etc.

### Introduction:

Hydrogels may be defined as a network of polymer chains that are hydrophilic, water insoluble sometimes found as a colloidal gel in which water is a dispersion medium. Their ability to absorb water is because of its cross linking network structure which is formed by polymer bearing hydrophilic groups such as -OH, -COOH, -CONH, -SO<sub>3</sub>H, and -NH<sub>2</sub>. [1,2,] hydrogel are commonly used in clinical practice and experimental medicine for a wide range of applications, including food additives [3], Tissue engineering, regenerative medicines, Pharmaceuticals [4], drug delivery devices and membranes for biosensors etc. Hydrogels are insoluble due to the presence of chemical and physical cross-links Such as

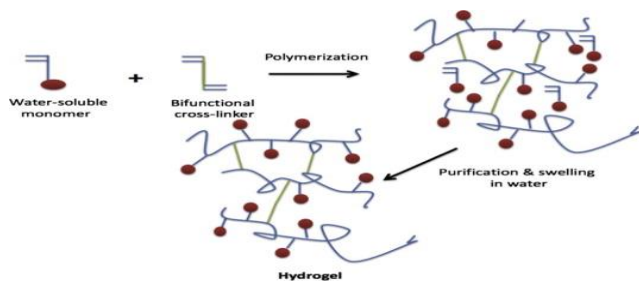
entanglements. Hydrogel's are also provides required mechanical strength and physical integrity to the Hydrogel's. [5]. It is also respond to the fluctuation of environmental stimuli (ionic strength, temperature. pH, presence of enzyme etc.) and swell or shrink accordingly in the swollen state they are soft and rubbery resembling the living tissue exhibiting excellent biocompatibility [6]. The history of hydrogel's can be divided in three main blocks. A hydrogel's first generation that comprises a wide range of cross-linking procedures. The general aim is to develop material with high swelling, good mechanical properties and relatively simple rationale. A second generation of materials capable of a response to specific stimuli, such as variations in temperature, pH

or concentration of specific molecules in solution. These specific stimuli can be exploited to trigger likewise specific events, for example the polymerization of the material, a drug delivery or an in situ pore formation.



**Fig.01. Hydrogel's in different sizes**

Finally, a third generation of hydrogels focusing on the investigation and development of stereo complexed materials (e.g. PEG-PLA interaction) hydrogels cross linked by other physical interactions (e.g. cyclodextrine)[7].



**Fig.02. Formation of Hydrogel**

### 1.1 Advantages of Hydrogel.

1. Hydrogels are biocompatible.
2. Hydrogels are easy to modify.
3. They are biodegradable.
4. Hydrogels have the ability to sense changes of pH, temperature or the concentration of metabolic and release their load as result of such change.
5. Hydrogel are medicines or nutrients timely.
6. Hydrogels can be injected.
7. It is also possess good transport properties.
8. Hydrogel is more elastic and stronger

9. Entrapment of microbial cells within polyurethane hydrogel beads bears the advantage of low toxicity.

10. Hydrogel-based micro valves shows a number of advantages over conventional micro valves, incorporating moderately simple fabrication, no outer power requirement, no integrated electronics, large displacement and large force generation<sup>[08-09]</sup>

### 1.2 DISADVANTAGES OF HYDROGELS

1. The main disadvantage of hydrogels are expensive.
2. Low mechanical strength of hydrogel.
3. Hydrogels are difficult to load with drugs or Nutrients.
4. They are non – adherent and may need to be secured by secondary dressing .
5. Disadvantages of hydrogel in contact lenses are lens deposition, hypoxia, dehydration and red eye reactions.
6. Hydrogel can be hard to handle.
7. Difficulty in loading.
8. Difficulty in sterilization.
9. Hydrogels causes thrombosis at Anastomosis sites<sup>[09-10]</sup>

### 2.0 TYPES OF HYDROGEL

Hydrogel's may be two types on the basis of origin :

1. Natural Polymer Hydrogel.
2. Synthetic Polymer Hydrogel.

#### 2.1. NATURAL POLYMER HYDROGEL :

Natural polymers prepared by using natural polymers. Example of natural polymers are - Dextran, Chitosan, Collagen, Dextran Sulfate, Gelatin etc.

#### Advantages of Natural Polymers :

1. Natural polymers generally have high biocompatibility.
2. Intrinsic cellular interactions.
3. Biodegradable.
4. Low toxicity by products.

#### Disadvantages of Natural polymers :

1. Does not possess sufficient mechanical strength.
2. Batch variation.
3. May contain pathogen<sup>[11]</sup>

#### 2.2. Synthetic Polymer Hydrogel's :

It may be prepared by using Chemical polymerization. Example of synthetic polymer hydrogels are – Polyvinyl pyrrolidone (PVP), Hydroxyethyl – Methacrylate (HEMA), Vinyl acetate (VAc),

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Polyethylene glycol (PEG), Polyethylene oxide (PEO) etc.

#### Advantages of Synthetic Polymer Hydrogel :

1. It has precise control and mass produced.
2. Low immunogenicity.
3. It can be tailored to give a wide range of properties.

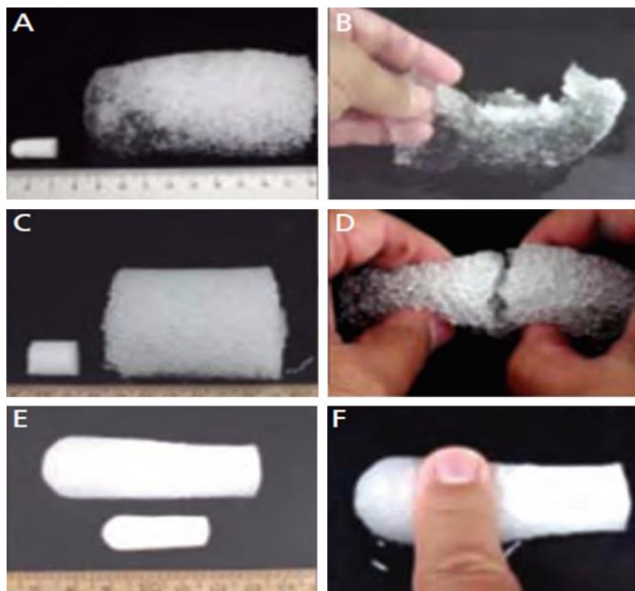
#### Disadvantages of Synthetic Polymer Hydrogels :

1. It has low biodegradability.
2. Can include toxic substances<sup>[11,12]</sup>

**3. Properties of hydrogels :** Hydrogels are used in the field of pharmaceutical and biomedical engineering.<sup>[12]</sup>

**3.1. Swelling properties** A small change in environmental condition may trigger fast and reversible changes in hydrogel. The alteration in environmental parameters like electric signal, pH, temperature, and presence of enzyme or other ionic species may lead to a change in physical texture of the hydrogel. The swelling ratio of the hydrogels may also be influenced by the chemical structure of the polymer.

**3.2. Mechanical properties :** The desired mechanical property of the hydrogel could be achieved by changing the degree of crosslinking and by increasing the degree of crosslinking a stronger hydrogel could be achieved though the higher degree of crosslinking decreases the % elongation of the hydrogels creates a more brittle structure .



**fig.03 Swelling and Mechanical Properties of Hydrogel**

#### 4. Classification of Hydrogel's

##### 1. Based on the method of preparation, hydrogel's are classified into:

- A) Homopolymer hydrogels.
- B) Co-polymer hydrogels.
- C) Multi polymer hydrogels.

##### 2. Based on the ionic charges hydrogels can be classified into:

- A) Neutral hydrogels.
- B) Anionic hydrogels.
- C) Cationic hydrogels.
- D) Ampholytic hydrogels.

##### 3. Based on the structure hydrogels can be classified into :

- A) Amorphous hydrogels.
- B) Semi-crystalline hydrogels.
- C) Hydrogen bonded hydrogels.

##### 4. Based on the mechanism controlling the drug release they are classified into:

- A) Diffusion controlled release systems.
- B) Swelling controlled release systems.
- C) Chemically controlled release systems.
- D) Environment responsive systems<sup>[13]</sup>

**5. Materials or Polymers used in Hydrogel-** Different polymers can be used for the Development of hydrogel systems including Natural and synthetic polymers and other material such as Cross-linking agent<sup>[14]</sup>

##### A) Synthetic polymers :-<sup>[11]</sup>

01. Hydroxyethyl methacrylate (HEMA),
02. Hydroxyethoxyethyl methacrylate (HEEMA),
03. Hydroxydiethoxyethylmethacrylate (HDEEMA),
04. Methoxyethyl methacrylate (MEMA),
05. Methoxyethoxyethyl methacrylate (MEEMA),
06. Methoxydiethoxyethyl methacrylate (MDEEMA),
07. Ethylene glycol dimethacrylate (EGDMA),
08. N-vinyl-2-pyrrolidone (NVP),
09. N-isopropyl AAm (NIPAAm),
10. Vinyl acetate (VAc),
11. Acrylic acid (AA),
12. N-(2-hydroxypropyl) methacrylamide (HPMA).
13. Ethylene glycol (EG), PEG acrylate (PEGA).
14. PEG methacrylate (PEGMA).
15. PEG diacrylate (PEGDA).
16. PEG dimethacrylate (PEGDM).

##### B) Natural polymers:-<sup>[11, 14]</sup>

01. Alginate
02. Chitosan.
03. Carrageenan.
04. Hyalurona

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05. Dextran.

06. Guar Gum.

07. Xanthan.

08. Carboxymethyl cellulose (CMC)

**C) Cross-linking agent such as :-**

01. Epichlorohydrin (ECH) <sup>[14]</sup>,

02 N,N0-Methylene - bis-acrylamide (N,N0-MBAAm)(BIS) <sup>[13]</sup>

03 Divinyl sulfone (DVS) <sup>[15]</sup>

**6. The Method of Preparation of Hydrogel Polymers are :-<sup>[15,16]</sup>**

1) Homopolymer hydrogels.

2) Co-polymer hydrogels.

3) Multi polymer hydrogels.

**6.1 Homopolymer Hydrogel Method:**

Homopolymers can be prepared by using polyethylene glycol dimethacrylate as cross-linking agent, poly (2-hydroxyethyl methacrylate) (poly HEMA) as a monomer and benzoin isobutyl ether as the UV-sensitive initiator. They are a basic structural unit. The film was prepared in de-ionised water and treated with UV radiation ( $\lambda = 253.7$  nm, 11 mm distance from the source for 20 minutes). The film was then immersed for 24 h in water until it is fully saturated in order to remove toxic or unreacted substances that could damage a living tissue. It can be applied in contact lenses, artificial skin manufacturing and burn dressing. It is also used in bone marrow and spinal cord cell regeneration, scaffolds for promoting cell adhesion and in artificial cartilage production.

**6.2 Co-Polymer Hydrogel :** It is synthesized by polymerization of BLG N-Carboxyanhydride initiated by diamine groups located at the ends of poly (ethylene oxide) chains of the poloxamer a thermoplastic co-polymeric hydrogel based on  $\gamma$ -benzyl L-glutamate (BLG) and poloxamer was formed. These hydrogels were pH and temperature sensitive and characterized for drug delivery application.

**6.3 Multi Polymer Hydrogel :** It is an important class of hydrogels, having a network system which is made of two independent cross-linked synthetic and/or natural polymer components. This method can overcome thermodynamic incompatibility which occurs due to the permanent interlocking of network segments and limited phase separation can be obtained.

**Table 1 : Example Of Hydrogel Prepared By Different Methods<sup>[6]</sup>**

Sr no.	Preparation Methods	Type	Polymer System
01.	Solution polymerization/crosslinking by redox initiator.	pH	Poly(methacrylic acid-co methylmethacrylate).
02.	Solution polymerization/crosslinking by redox initiator.	Thermo	Poly(N-t butyl acrylamide-co acrylamide).
03.	By physical cross-linking.	pH	Chitosanalginate, chitosan CMC sodium and chitosan carbopol.
04.	Solution polymerization/crosslinking by redox initiator	Thermo	Poly(N-isopropylacrylamide) (PNIPAAm)-poly(ethylene glycol) diacrylate.
05.	Polymerization by radiation	pH	Agarose and carbomer 974P macromers
06.	Solution polymerization/crosslinking by redox initiator	pH	Poly (acrylamide-co-acrylic acid)
07.	Solution polymerization/crosslinking by redox initiator.	Thermo	N-allyl maleamic acid (AMA) with acrylamide and acrylic acid.
08.	Solution polymerization/crosslinking by redox initiator.	Thermo	N-allyl maleamic acid (AMA) with acrylamide and acrylic acid.
09.	Solution polymerization/crosslinking by redox initiator.	pH	Poly(ethylene glycol) methacrylate graftpoly(glutamic acid)
10.	Gamma radiation.	Ion	Acrylamide/2-hydroxyethyl methacrylate

**7. Technologies Adopted in Hydrogel Preparation<sup>[17,18]</sup>**

In general, hydrogels can be prepared from either synthetic polymers or natural polymers. A hydrogel is simply a hydrophilic polymeric network cross-linked in some fashion to produce an elastic

structure. Origin is cross-linked to form hydrogels in a number of ways:

01. Linking polymer chains via chemical reaction.
02. Using ionizing radiation to generate main-chain free radicals which can recombine as cross-link junctions.
03. Physical interactions such as entanglements, electrostatics, and crystallite formation.

The various polymerization techniques can be used to form gels, Such as :-

- A) Bulk Polymerization.
- B) Solution Polymerization / Cross- Linking.
- C) Dispersion Polymerization.
- D) Grafting to a support.
- E) Polymerization by irradiation.

**Bulk polymerization:** - Bulk hydrogels can be formed with one or more types of monomers. Bulk polymerization is the simplest technique which involves only monomer and monomer-soluble initiators<sup>[17]</sup>. **Solution Polymerization / Cross-Linking:-** In solution copolymerization/cross-linking reactions, the ionic or neutral monomers are mixed with the multifunctional cross linking agent. the major advantage of the solution polymerization over the bulk polymerization.<sup>[17,18]</sup>

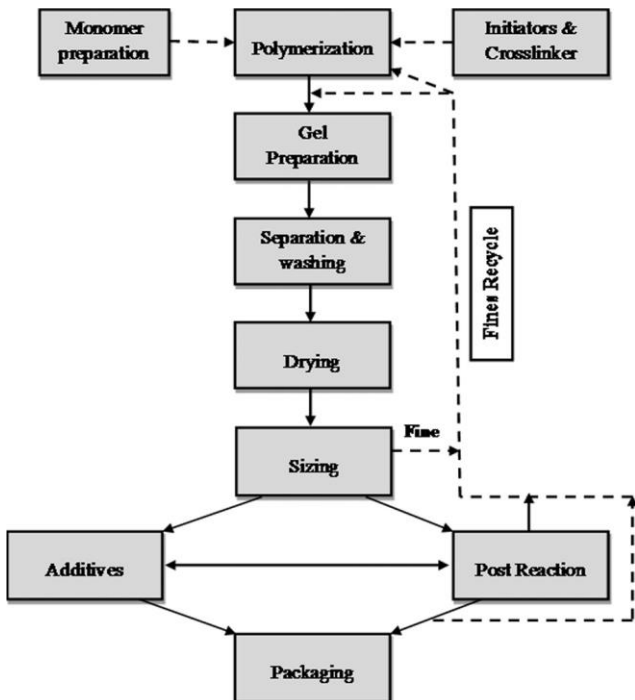


Fig. 04 Hydrogel preparation (solution polymerization).<sup>[17]</sup>

**Dispersion Polymerization:** - Dispersion polymerization is an advantageous method since the products are obtained as powder or microspheres

(beads). In this technique, the monomers and initiator are dispersed in the hydrocarbon phase as a homogenous mixture. Since water-in-oil (W/O) process is chosen instead of the more common oil-in-water (O/W), the polymerization is referred to as “inverse suspension”.

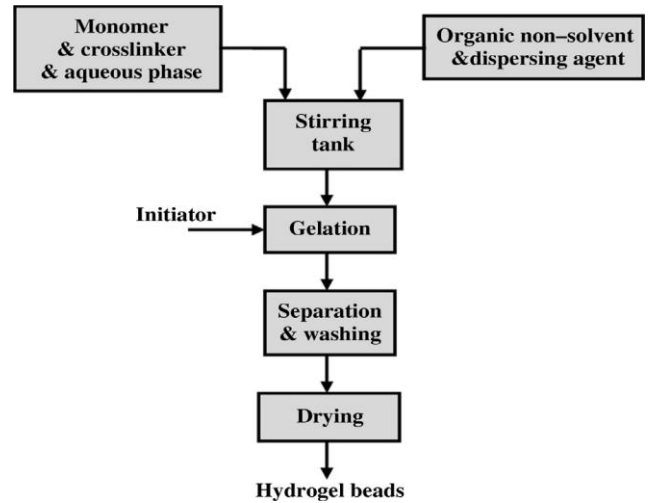


Fig.05 Block diagram of suspension polymerization process.

**Grafting to a support:** - This techniques is improve the mechanical properties of a hydrogel, it can be grafted on surface coated onto a stronger support.polymeric supports have been used for the synthesis of hydrogel by grafting techniques<sup>[17]</sup>.

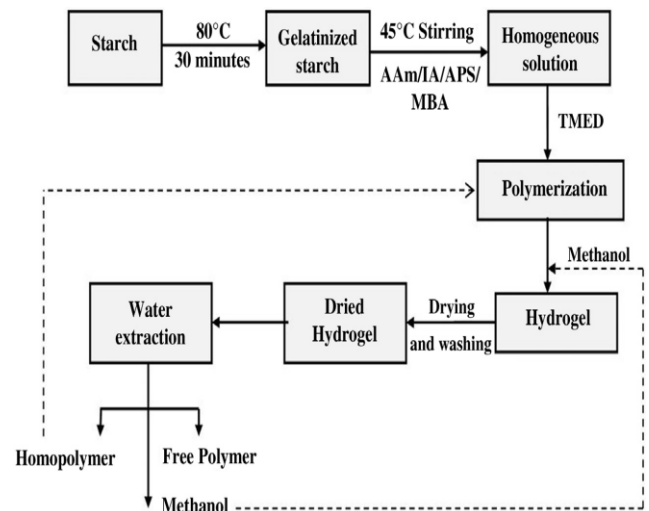


Fig.06 Preparative flowchart for grafted starch and P(AM-co-IA) hydrogel

**Polymerization by irradiation :-** In this techniques the Ionizing high energy radiation, like gamma rays and electron beams has been used as an initiator to prepare the hydrogels of unsaturated compounds. The

major advantage of the radiation initiation over the chemical initiation is the production of relatively pure and initiator-free hydrogels.

**8. Characteristics of hydrogels:** Hydrogels are characterized by following methods/tests<sup>[16,19]</sup>

1. Rheology.- Hydrogels are evaluated for viscosity under constant temperature (4°C) by using Cone Plate viscometer.
2. Temperature responsive hydrogels.- : It can be hydrogel containing polymers such as chitosan PEG-poly, Nisopropylacrylamide hydrogel (PNIPAA), methyl cellulose and tetronics. They can be used in sustained drugs, gene delivery and tissue engineering<sup>[18]</sup>
3. PH responsive hydrogels.- pH of hydrogels is measured by using digital pH meter. pH meter must be calibrated before its use..
4. Atomic Force Microscopy (AFM).- The surface morphology of the hydrogels is studied by a Multimode Atomic Force Microscope
5. Network pore size- Network pore size is measured by a number of techniques like Quasi-elastic laser light scattering, electron microscopy, mercury porosimetry, rubber elasticity measurements, and equilibrium swelling experiments<sup>[20]</sup>.
6. Cross-linking and mechanical strength – It is measured by Ultimate compressive strength, change in polymer solubility with time<sup>[3,21]</sup>.
7. X-ray Diffraction- X-ray diffraction is used to understand whether the polymers Retain their crystalline nature or they get deformed during the pressurization process<sup>[21]</sup>.
8. Analyte- it should be function under physiologically relevant temperature, pH and ionic strength. Mono and disaccharides, enzymes, antigens and various ions are among the stimulus for analytic responsive hydrogels<sup>[17]</sup>
9. Swelling Behavior- Hydrogels are allowed to immerse in aqueous medium or medium of specific pH to know their swellability. These polymers show increase in dimensions related to swelling<sup>[22]</sup>.
10. Fourier Transform Infrared Spectroscopy- Formation of coilor helix which is indicative of cross linking is evident by appearance of bands near 16 cm-1 FTIR. Any change in the

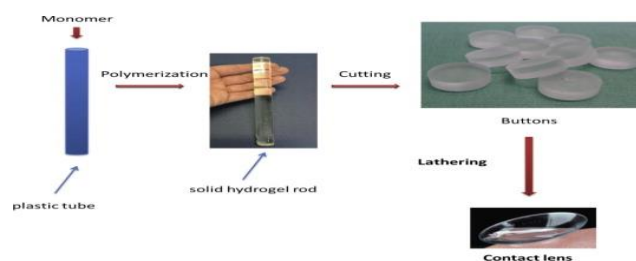
morphology of hydrogels changes their IR absorptionspectra<sup>[14]</sup>

## 9. APPLICATIONS OF HYDROGELS

**01. Wound Healing:** A modified polysaccharide that occurs in cartilage has been used in formation of hydrogels to treat cartilage defects has been developed. Polyethylene glycol fumarate hydrogels is formulated for wound healing. Wound healing is particularly useful for the determination and elucidation of the structure of hydrogel that is the estimation of the particular structure of hydrogel. Hydrogel is a crosslinked polymer matrix which has the ability to absorb and hold water in its network structure. Hydrogels act as a moist wound dressing arterial and have the ability to absorb and retain the wound exudates along with the foreign bodies, such as bacteria, within its network structure<sup>[22]</sup>.

**02. Industrial Applicability:** Hydrogels have been used as absorbents for industrial effluents like methylene blue dye. Methylene blue dye is particularly useful as absorbant for the industrial applicability of hydrogel that is used as absorbent for the industrial effluent for a large number of compounds that are particularly useful for a large variety of hydrogels. Hydrogels are used as absorbant for industrial effluents like methylene blue dye. Another example is adsorption of dioxins by hydrogel beads<sup>[23]</sup>.

**03 Soft Contact Lenses:** The first commercially available silicon hydrogels adopted two different approaches. A first approach by Bausch and Lomb was a logical extension of its development of silicon monomers with enhanced compatibility in hydrogel forming monomers. The second of ciba vision was the development of siloxy monomers containing hydrophilic polyethylene oxide segment and oxygen permeable polysiloxane units<sup>[24]</sup>



**Fig. 07. Hydrogel used in contact lenses.**

**04 Modified Dosage Forms:** An interesting research in the field of drug delivery is of bio-

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macromolecules like insulin delivered to the site of absorption with hydrogels of poly (methacrylamide co - it conic acid) .

**05. Drug Delivery in GI Tract:** Hydrogels deliver drug to specific sites in the GIT. Drugs loaded with colon specific hydrogels show tissue specificity and change in the pH or enzymatic actions cause liberation of drugs. They are designed to be highly swollen or degraded in the presence of microflora <sup>[25]</sup>.

**06. Tissue Engineering:** Micronized hydrogels are used to deliver macromolecules (phagosomes) into cytoplasm of antigen presenting cells. This property is also utilized in cartilage repairing. Natural hydrogel materials used for tissue engineering include agarose, methyl cellulose and other naturally derived products <sup>[25]</sup>

**07. Cosmetology:** For aesthetic purpose, hydrogels have been implanted into breast to accentuate them. These hydrogels swell in vivo in aqueous environment and retain water. These breast implants have silicone elastomer shell and are filled with hydroxyl propyl cellulose polysaccharide gel. Pharmaceutical companies are focussing on advanced drug delivery formulations to provide stable and economical drug delivery systems polymers that is backbone in designing the modified release dosage forms due to various properties that hydrogels have attained.<sup>[25]</sup>

**08. Transdermal delivery** – hydrogels can be used as controlled release devices in the filed of wound dressing due to it swelling properties. Hydrogel based formulations are being explored for transdermal iontophoresis to obtain enhanced permeation of products<sup>[26]</sup>

**09. Ocular Drug Delivery:** For ocular drug delivery of pilocarpine and timolol, the polymer which form gel such as xyloglucan have been used for sustained drug delivery. A number of anticholinergic drugs are available like timolol, atenolol, which is particularly useful as the polymer for the formulation as well as preparation of hydrogel. Ocular drug delivery device like that of anticholinergic drugs like Atenolol is particularly important for the drug delivery devices <sup>[27]</sup>

**Table 02: Marketed Formulations of Hydrogels<sup>[11]</sup>**

Sr. No	Name of The Hydrogel Drug	The Application
01.	Aquatrix II (Skin adhesive hydrogel).	Wound, Burn, Adhesive

*Review Article*

02.	Medicell	Medicated foam for burns
03.	Hydromer	Antithrombic DNA immobilization
04.	Aquamere(Coating hydrogel)	Cosmetics
05.	Dermaseal	Allergen blocker
06.	Aquatix	Super absorbent
07.	Mesocol Tablet	Oral controlled drug delivery system
08.	Galentic	Wound dressing
09.	Entofoam	Oral controlled drug delivery system
10.	Buscopam	Oral controlled drug delivery system
11.	Tegaderm Hydroge	Wound dressing
12.	Hydrogel Wound dressing	Wound dressing
13.	Protective Plasters	Burn

**CONCLUSION:-**

The Hydrogels are very popular because of their distinctive Properties such as flexibility, High water content, elasticity and biocompatibility etc. The hydrogels are used in many Application such as the fabrication of contact lenses ,tissue engineering scaffolds, drug delivery systems, wound dressings and various hydrogienic products.For the treatment of many diseases large molecular weight protiens are required. These can be availablewith the availability of hydrogels. Hydrogels are hydrophilic, three-dimensional networks,which ares able to imbibe large amounts of water or biological fluids, and thus

resemble, to a large extent, a biological tissue. They are insoluble due to the presence of chemical (tie-points, junctions) and /or physical crosslinks such as entanglements and crystallites. These materials can be synthesized to respond to a number of physiological stimuli present in the body, such as pH, ionic strength and temperature. The main aim behind this review project is to present the All information about the hydrogels like their properties, types, methods of preparation, Characteristics and their applications.

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