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A COMPREHENSIVE REVIEW ON HYDROGEL AND NOVEL APPLICATIONS IN PHARMACEUTICS

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INTRODUCTION

Hydrogel is with chemicals or physically cross-linked, three-dimensional chemical compound network, extensively employed in varied medicine and pharmaceutical applications. It will swell and hold an outsized quantity of biological fluid and water whereas, maintaining its structure while not dissolution. By dominant the cross-linker density, precursor content and property, the porous structure of gel may be tuned. The mix of biocompatibility, biodegradability, porous structure, extraordinary capability of retentive water and biological fluid mimic the extracellular matrix. Therefore, it may be employed in numerous biological applications like membrane for biosensor drug delivery lining for implant material for covering, and tissue engineering [1]. Even though hydrogels are employed in numerous industries, additional researches are getting in the sphere of medical specialty applications due to its resembles to living tissue, biocompatibility, and biodegradability [2]. By chemical approaches, the polymers are certain along through valency bonds that endow environmental stability and intensive mechanical strength. Compared, physical hydrogels trust non-covalent interactions like H bonding, electricity interactions, and metal-ligand coordination [3]. The extremely porous structure of gel will simply be tuned by dominant the density of cross-links within the gel matrix and therefore, the affinity of the hydrogels for the liquid surroundings within which they're swollen. Their consistence additionally permits loading of medication into the gel matrix and resulting drug unharness at a rate keen about the diffusion constant of a tiny low molecule or a super molecule through the gel network [4].

Technical options of hydrogel

The highest permeability below load [5]:

- The highest absorption capability
- The highest sturdiness and stability within the swelling surroundings and through storage
- The highest biodegradability while not formation of deadly species
- pH scale neutrality once swelling in water.

Classification of hydrogel

- Based on sources
- Based on polymeric composition
- Based on configuration
- Based on network electrical charge
- Based on the mechanism of action [6] (Table 1).

HYDROGEL PREPARATION METHODS

A. General method: Bulk polymerization

Many vinyl monomers will probably be used for the assembly of hydrogels. Bulk hydrogels are often shaped with one or a lot of sorts of monomers. Usually, a little quantity of cross-linking agent is value-added to colloidal gel formulation. The chemical change reaction is often initiated with radiation, ultraviolet, or chemical catalysts. The selection of an appropriate leader depends upon the sort of monomers and solvents getting used. This polymerized colloidal gel is also made during a wide range of forms together with films and membranes, rods, particles, and emulsions. Bulk chemical change is the simplest technique that involves solely compound and compound soluble initiators. The consistency of reaction will increase markedly with the conversion that generates the warmth throughout chemical change. These issues are often avoided by dominant the reaction. The majority chemical change of monomers to form a homogenous colloidal gel produces a glassy, clear chemical compound matrix that is incredibly onerous. Once placed in water, the glassy matrix swells to become soft and flexible.

1. Solution polymerization/ cross–linking

In answer copolymerization/cross-linking reactions,

Table 1: Classification of hydrogel.

S. No	Classification	Examples
1.	Based on sources	Natural and synthetic
2.	Based on polymeric composition	Homo polymeric hydrogel, co polymeric hydrogel, Multi polymer interpenetrating polymeric hydrogel.
3.	Based on configuration	Crystalline, amorphous, semi crystalline
4.	Based on network electrical charge	Non- ionic, ionic, amphoteric, zwitter ionic
5.	Based on the mechanism of action	Diffusion controlled system, swelling controlled system, chemically controlled system, environment responsive system

Table 2: Gelating agents preparation (*in situ*).

S. No	Method of preparation	Materials / Polymers
1.	Thermo reversible *in situ* Gelling System	A) Pluronics: [Pluronic F68, Pluronic F127, Pluronic F128. B) Poloxamer C) Chitosan D) Gellan gum. E) Cellulose derivatives :HPMC, Ethyl (hydroxy ethyl) cellulose, Xyloglucan, Tetronic
2.	Ion Sensitive *in situ* Gelling System	Sodium Alginate, Hyaluronic Acid, Gelrite
3.	pH Sensitive *in situ* Gelling System	Carbopol, carbomer, diethylaminoacetate (AEA), polyethylene glycol(PEG), cellulose acetate phthalate latex(CAP), polymethacrilic acid (PMMA) and pseudolatexes

Table 3: Novel application of hydrogels.

S. No	Application	Research study	Result
1.	Skin wounds	***In vivo* study:** [photo thermal antibacterial activity] The potency of photothermal therapy was developed using N-carboxyethyl chitosan (CEC), benzaldehyde-terminated Pluronic F127/carbon nanotubes (PF127/CNT) and the moxifloxacin hydrochloride was loaded	Provides effective photo thermal for the treatment of infected wounds [9]
2.	Transparent interpenetrating network (IPN) Hydrogel	Hydrogel was developed by fabrication with sericin and polyacrylamide.	IPN shows real time monitoring of wounds [10]
3.	Water shutoff treatment	***In situ* method:** [Thermo-elastic and self-healing polymer composite hydrogels was obtained by the preparation of polyacrylamide (PAM) and 2D fillers] with the utilization of cross linkers like: Hydroquinone (HQ) and hexamethylenediamine (HMT).	The added 2D fillers increased the swelling properties and self-healing properties which is applicable for water shut off treatment. [11]
4.	Antioxidant activity	**Solvent casting technique:** Collagen- and chitosan combination hydrogel and caffeic acid (CA) 5–30 wt.% was loaded. Antioxidant activities were investigated through DPPH·	Thus the prepared hydrogel using chitosan and collagen was used in pharmaceutical and cosmetic research. [12]
5.	Wastewater treatment	Two-dimensional layered materials was used [graphene, black phosphorus] graphene oxide (rGO) hydrogel was obtained from reduction with L- ascorbic acid then the black phosphorus nano sheets (BPNS) was added	The current research provides new ideas for the preparation of functionalized composite hydrogel and BP nanomaterials. [13]
6.	Rapid tissue repair of bacterial infected wounds	Free radical polymerization:[Ammonium and double-bond modified chitosan and metal–organic framework (MOF) particles (Prussian blue nanoparticles [PBNPs]]	The antibacterial ratio of the hydrogels could reach up to 99.97% and 99.93% against **Staphylococcus aureus** and **Escherichia coli**. Thus, the synthesized hydrogels have great potential as a safe and efficient wound dressing. [14]

7.	Controlled therapeutics delivery	Glycan-based alginate hydrogels. Anthracene into these gels leads to reversible control on crosslinking and transition between gel/sol states.	The research would be useful for systems where multiple controls is required with high precision. [15]
8.	Medical application	**Injectable hydrogel:** [polylysine (ε-PL) and carboxymethyl chitosan (CMCS)] was prepared.	Results shown that rapid gelation, low toxicity and low irritation. [16]
9.	Treatment of glaucoma	Topical ocular drug delivery system: formulation includes chitosan was achieved by mixing sodium hydrogen carbonate with β-glycerophosphate as a gelling agent.	Timolol maleate as an anti-glaucoma model drug. [17]
10.	Treatment of breast cancer after surgical resection	Paclitaxel-nanoparticles-loaded double network (PTX-NPs-DN) hydrogel: preparation includes collagen and self-crosslinking of Polyvinyl alcohol (PVA).	In result showed that feasibility, tolerability and efficiency of PTX-NPs-DN hydrogel for the local treatment of breast cancer. [18]
11.	Periodontal infections	Photo polymerization	Antigen nanoparticles can be used as microbial growth inhibitors for treating periodontal disease. [19]
12	Bacterial Conjunctivitis	*In-vitro* diffusion study	Result proved that *in situ* gelling formulation used for long acting ocular delivery. [20]
13	Oral thrush	Korsmeyer - Peppas exponential model, Diffusion across the chicken cheek mucosa	Buccal drug delivery systems are better suitable for antifungal drugs particularly for oral thrush. [21]
14	Diabetes Treatment	*In-vitro* and *in-vivo* study	Hydrogel have effect in reducing the blood glucose levels in rats. [22]
15	Myocardial Repair	*In-vitro* and *in-vivo* study	ECM hydrogels enhanced stem cell therapy by the scaffold. Combination of ECM hydrogel and the cardio myogenic cells may represent a promising strategy for cardiac tissue engineering. [23]

Table 4: Wide application of hydrogels.

S. No	Types of ophthalmic drugs	Action
1.	Conventional approach	Increase the corneal contact time of an ophthalmic drug and to provide a better controlled action [24]
	Solutions and Suspensions	
	Eye drops	An important place in the dosage regimen from decades and they are used only for a lubricating and tear replacement purpose. [25]
	Ointments	On the surface of eye and after instillation into the eye, ointments break into small droplets and remain in the cul-de-sac for appropriate duration showing its effect. [26]
	Viscous Solutions	Enhance the viscosity of ophthalmic preparations so that the residence time could be increased in the pre-corneal area and with a hope of increasing bioavailability of drugs. [27]
2.	Novel approach	These are solid dosage forms and are helpful in maintaining a higher concentration of drug at the site for a longer period also. Ocular inserts are also efficient in decreasing the frequency of administration, thus resulting into a better patient compliance. [28]
	Ocular Inserts	
	Artificial Tear Inserts	Responsible for giving a sustained effect for higher duration. Mainly for e patients suffering from dry eyes. [29]
	Nanoparticles and Microspheres	The drug gets bind to these carrier molecules and they provide a much higher absorption and penetration rate in the eye as compared to the conventional ones. Then the bioavailability is also enhanced.[30]
	Implants	Increasing the trans-corneal penetration, enhancing the patient compliance, absorbing the drug within the anterior or posterior segments in a better and prolonged way, thus enhancing bioavailability. [31]

the ionic or neutral monomers are mixed with the multifunctional cross-linking agent. The chemical change is initiated thermally by UV irradiation or by an oxidation-reduction leader system. The ready hydrogels have to be compelled to be washed with H_2O to get rid of the monomers, oligomers, cross-linking agent, the leader, the soluble and removable compound, and different impurities. Part separation happens and also the heterogeneous gel is made once the number of water throughout chemical change is over the water content adores the equilibrium swelling. Typical solvents used for answer chemical change of hydrogels embrace water, ethanol, water–ethanol mixtures, and benzyl radical alcohol.

2. Suspension polymerization or inverse-suspension polymerization

Dispersion chemical process is an associate advantageous methodology since the merchandise are obtained as powder or microspheres (beads), and thus, grinding isn't needed. Since water-in oil (W/O) method is chosen rather than the additional common oil-in-water (O/W), the chemical process is spoken as "inverse-suspension" technique. During this technique, the monomers and initiators are spread within the organic compound part as an even mixture. The consistence of the chemical compound resolution, agitation speed, rotor style, and dispersant sort principally governs the rosin particle size and form. The dispersion is thermodynamically unstable and needs each continuous agitation and addition of an occasional hydrophilic-lipophilic balance (HLB) agent [7-9].

3. Polymerization by irradiation

Ionizing high energy radiations like gamma rays Associate in nursing negatron beams are used as leader to arrange the hydrogels of unsaturated compounds. The irradiation of binary compound chemical compound resolution ends up in the formation of radicals on the chemical compound chains. Also, lysis of water molecules ends up in the formation of radical radicals that conjointly attack the chemical compound chains, leading to the formation of macro-radicals.

4. Grafting to a support

Hydrogels ready by bulk chemical change have inherent weak structure to enhance the mechanical properties of a gel, it will be grafted on surface coated onto a stronger support. This method involves the generation of free radicals onto a stronger support surface and so polymerizing monomers directly onto it, as a result, a sequence of monomers square measure covalently warranted to the support.

B. In situ gelating agents' preparation

This is explained in detail in Table 2 [10-20].

APPLICATION OF HYDROGELS

Novel applications of Hydrogels (Table 3). Wide applications of hydrogel in ophthalmic drug delivery system (Table 4) [20-30].

CONCLUSION

The present review focusses on the biomedical application of hydrogel in a pharmaceutical field.

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