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Development of Hydrogel Delivery Systems for Anti-Inflammatory Action

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Abstract

Hydrogels' biocompatibility, adjustable characteristics, and capacity for controlled drug release have made them attractive delivery systems for anti-inflammatory drugs. These technologies lessen the drawbacks of traditional medication delivery techniques, namely their low bioavailability and systemic side effects. The development, workings, and developments of hydrogel-based delivery methods specifically designed to reduce inflammation are examined in this paper. It explores the various kinds of hydrogels, their potential for therapeutic use, and the present difficulties in bringing these systems from the lab to the clinic.

Keywords: Hydrogel, Anti-Inflammatory, Delivery System, Transdermal, Gels

Introduction

As one of the most important organs of the human body, which protects us from harsh external environments, the skin is often damaged by traumas, severe burns, ulcers and various other injuries, thus disrupting its protective barrier functions and vital role in sensory perception. In addition, such injuries affect a patient's mental health and constitute an enormous societal economic burden [1]. Therefore, identifying effective therapeutic strategies to promote wound healing is an extremely urgent requirement. A vital biological reaction to damage or illness, inflammation is necessary to start the healing process.

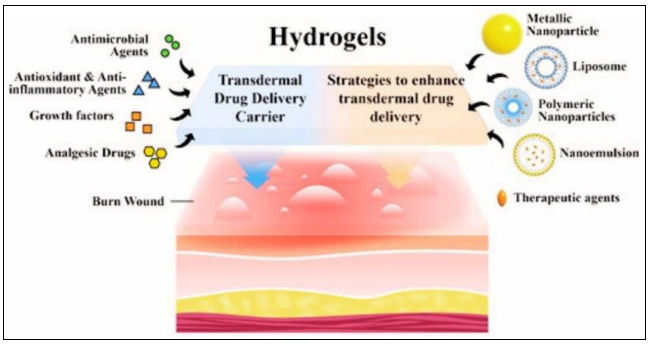

Fig 1

On the other hand, severe illnesses including arthritis, cardiovascular disease, and neurological disorders can result from persistent or excessive inflammation. Such disorders are frequently treated with anti-inflammatory medicines, such as corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs). Even though these treatments work, when administered through traditional means, they frequently have systemic side effects, low absorption, and low patient compliance. Because they are hydrophilic and three-dimensional polymers, hydrogels provide a unique way to get around these problems. These substances can encapsulate bioactive substances, guarantee targeted administration, regulated release, and enhanced stability of

the medicinal compounds. With an emphasis on their design, use, and potential for the future, this paper explores the development of hydrogel systems in the delivery of anti-inflammatory drugs [2].

History

According to Lee, Kwon, and Park, the term "hydrogel" originated in an article that was published in 1894. In any case, the substance described was not a hydrogel in the modern sense; rather, it was an Inorganic salt used to create a colloidal gel. It is noteworthy, however, that the name itself has a consistently lengthy history. Hydrogels are the first materials to be used in permanent contact applications with human tissues. In any case, the first crosslinked network material to appear in literature and be described by its typical hydrogel properties, one of which is its high water affinity, was a polyhydroxyethylmethacrylate (pHEMA) hydrogel created much later, in 1960 [3]. Since poly(2-hydroxyethyl methacrylate) (pHEMA) was first used in soft contact lenses in the 1960s, hydrogel delivery systems have been developed. This sparked interest in hydrogels' potential uses in biomedicine by revealing their special qualities, including their high water content, flexibility, and biocompatibility. Initially, regulated drug delivery and wound healing were the main areas of investigation. By the 1980s, hydrogels were showing promise as vehicles for encapsulating and delivering corticosteroids and NSAIDs to specific inflammatory areas. Early systems used hydrogels' ability to swell to control drug release, which was a big help in lowering systemic adverse effects and enhancing the anti-inflammatory drugs' therapeutic efficacy [4].

The creation of stimuli-responsive "smart" hydrogels transformed medication delivery methods in the 1990s. These hydrogels are especially useful for targeting inflammatory tissues because they may react to stimuli like pH or temperature changes. The use of nanotechnology in the 2000s resulted in hybrid systems that combined natural and synthetic polymers for improved mechanical strength and medication delivery effectiveness. Bioengineered and multifunctional hydrogels are examples of contemporary advances that emphasize tissue regeneration, precise on-demand medication release, and personalized therapy. This development emphasizes how hydrogels have the potential to revolutionize anti-inflammatory treatments [5].

Disease

Chronic rhinosinusitis

5–15% of people worldwide suffer from rhinosinusitis, an inflammatory condition of the sinus mucosa. The symptoms include mucopurulent discharge, nasal obstruction, thick nasal discharge, loss of smell, facial pain, sinus and nasal cavity obstruction, and oedema. When symptoms of rhinosinusitis last more than 12 weeks, it is deemed chronic [6].

Cystitis-interstitial (IC)

The chronic condition known as interstitial cystitis (IC), or painful bladder syndrome, has no recognized cause and is typified by frequent, urgent urination, suprapubic pain, and pressure on the pelvic region without any infections. There are two varieties of IC: Glomerulations, which are bleeding spots on the bladder lining, and Hunner's ulcers, which are characteristic lesions of inflammation on the bladder wall.

Inflammation of Stomach

Crohn's disease (CD) and ulcerative colitis (UC) are two types of inflammatory bowel disease (IBD), which is a set of intestinal illnesses caused by an abnormal inflammatory response to intestinal bacteria in genetically sensitive individuals. Due to the intestinal microbiota being exposed to the compromised intestinal barrier, IBD is characterized by immune cells infiltrating the lamina propria and an excess of proinflammatory cytokines [6].

Post Surgical Inflammation

Patients who undergo open surgery sustain serious damage and experience changes in their immunological, metabolic, and neuroendocrine systems. Pharmacotherapy is an essential component of postoperative care since pain, inflammation, and infection are frequent side effects of surgery [319,320]. Corticosteroids and NSAIDs are used to treat inflammation following surgery. Systemic medication, however, may hinder bone regeneration, disrupt metabolism, and postpone wound healing [6].

Classification for Hydrogel

Hydrogels can be categorized according to several factors, such as their composition, physical characteristics, responsiveness, crosslinking process, and place of origin.

1. Natural Hydrogels as the Basis

These hydrogels are biocompatible and biodegradable because they are made from natural polymers. Examples include collagen, hyaluronic acid, gelatin, chitosan, and alginate. Applications include medication administration, tissue engineering, and wound healing. Examples include polyvinyl alcohol (PVA), polyacrylamide, and poly(ethylene glycol) (PEG). Applications include biosensors, contact lenses, and controlled medication delivery.

Hydrogels that are hybrid a blend of synthetic and natural polymers, utilizing their respective benefits. Collagen-polyacrylamide and alginate-PEG are two examples. Applications include regenerative medicine and multipurpose drug delivery systems.

2. Predicated on the Crosslinking Process

Hydrogels that are physically crosslinked are created by physical interactions such as ionic, hydrophobic, or hydrogen bonds. Reversible and sensitive to changes in the environment are its properties. Examples include ionic gels and thermoresponsive hydrogels. Hydrogels that are chemically crosslinked are created when polymer chains form covalent bonds.

3. Non-Responsive

Hydrogels based on Stimulus Responsiveness Drugs are released quietly, unaffected by environmental factors. **Uses**: Basic medication administration methods. Smart hydrogels, also known as stimulus-responsive hydrogels, alter their characteristics in reaction to external inputs.

pH-responsive: At particular pH values, they swell or contract. Hydrogels for gastrointestinal drug delivery, for instance. Temperature-responsive: Changes in temperature cause them to expand or contract.

4. Degradability-Based

Hydrogels That Are Not Degradable maintain their organization over time. Long-term biomedical devices are among the applications. Hydrogels that degrade naturally naturally break down in biological settings. Applications include medication delivery and temporary implants.

5. Ionic Charge-Based

There is no ionic charge in neutral hydrogels. Negatively

charged groups are present in ianionic hydrogels. Positively charged groups are present in cationic hydrogels [7].

Dosage form for Hydrogel

Because of their exceptional biocompatibility, high water content, and adjustable qualities, hydrogels are adaptable materials that can be utilized in a variety of dosage forms to deliver medications. These are the typical hydrogel dosage forms, arranged according to how they are applied and administered:

1. Forms of Topical Dosage

Because of their high water content, cooling and relaxing properties, and skin adherence, hydrogels are widely employed in topical treatments. Gels are semi-solid substances that are applied directly to the skin or mucous membranes. Common uses include wound care, antibiotic delivery, and the administration of NSAIDs (such as diclofenac gel). Patches and Films: Drugs are delivered locally using thin hydrogel layers. Common applications include pain relief, burn therapy, and transdermal medication administration [11].

2. Forms of Injectable Dosage

The purpose of injectable hydrogels is to administer drugs inside the body in a controlled and targeted manner. In-situ gelling systems are solutions that, when injected, solidify into gels in response to changes in pH, temperature, or ionic strength. Delivery of growth factors, peptides, and anti-inflammatory medications are common uses. Drug-encapsulated injectable particle systems are known as hydrogel microspheres or nanogels. Common Applications: Inflammation, tissue regeneration, and the controlled release of medicinal chemicals in cancer treatment.

3. Forms of Oral Dosage

Drugs' controlled release and bioavailability in the gastrointestinal (GI) tract are enhanced by the use of hydrogels. Hydrogel tablets and capsules are hydrophilic matrices that expand in the gastrointestinal tract to release drugs under controlled conditions. NSAID, antibiotics, and hormone delivery are common uses. Hydrogel beads are isolated, tiny hydrogel units that deliver drugs over time. Common Applications: Protein, peptide, and probiotic encapsulation [8].

4. Forms of Ocular Dosage

Because hydrogels can extend the duration of a drug's contact with the ocular surface, they are frequently employed in eye care. Eye Drops: Formulations based on hydrogel that gel when they come into contact with the eye. Common Applications: Antibiotic, lubricant, and anti-inflammatory drug delivery. Contact lenses: Hydrogel lenses loaded with drugs for long-term drug administration. Common Uses: Post-operative care, dry eye, and glaucoma treatment [8].

New Drug and Drug Profile

01. Carbopol-940: A synthetic polymer derived from acrylic acid, carbopol 940 finds extensive application in industrial, cosmetic, and medicinal formulations. It is prized for its ability to thicken, gel, and emulsify, which makes it a flexible component of many different products [9].

Fig 2

02. Propylene glycol: A synthetic, multipurpose substance, propylene glycol (PG) is frequently utilized in industrial, cosmetic, and pharmaceutical compositions. Propylene glycol has certain qualities that can make anti-inflammatory compositions more effective, even though it is not an anti-inflammatory substance in and of itself [9].

Fig 3

03. Ashwagandha extract: A popular herb in Ayurvedic medicine, ashwagandha (Withania somnifera) is well known for its medicinal and adaptogenic qualities, which include strong anti-inflammatory actions. Ashwagandha's anti-inflammatory properties are mostly due to its bioactive components, especially withanolides [11].

Fig 4

04. Aloe vera gel: A well-known medicinal plant with calming, anti-inflammatory, and restorative qualities is aloe vera (Aloe barbadensis miller). Many bioactive substances found in the gel made from its leaves support its anti-inflammatory properties.

Fig 5

05. Methyl paraben: Because of its antibacterial qualities, methyl paraben is frequently employed as a preservative in food, cosmetic, and pharmaceutical goods. Some evidence indicates that it may play secondary functions in controlling inflammation, even though its anti-inflammatory actions are not its primary function. Its main use in formulations, however, is as a preservative to guarantee product stability and stop microbiological growth [10].

Fig 6

06. Triethanolamin: A chemical substance called triethanolamine (TEA) is frequently found in industrial, cosmetic, and medicinal compositions. Its main functions are stabilizing, emulsifying, and adjusting pH. TEA is essential to the development of anti-inflammatory medications because it helps with the distribution and stability of active components, even though it is not an anti-inflammatory agent by nature [10].

Patents

In keeping with developments in controlled drug delivery technology, several patents have been filed for hydrogel delivery systems intended for anti-inflammatory uses. Here are some noteworthy patent

Examples:

1. **Thermosensitive Injectable Hydrogel:** A hydrogel composed of a polyethene oxide-propylene oxide copolymer and hyaluronic acid (HA) is described in US Patent US9364545B2. The gel can develop at body temperature thanks to the thermosensitive reaction provided by this injection delivery technology. It reduces systemic medication exposure and increases therapeutic efficacy.
2. **Composite Hydrogel Systems:** The development of composite hydrogels, which blend different polymers for targeted drug administration, is described in US9254267B2. These are intended to deliver NSAIDs and other anti-inflammatory pharmaceuticals, providing controlled release and enhancing the bioavailability of medications to inflammatory areas.
3. **pH-Responsive Hydrogels:** Several developments centre on hydrogels that modify medication release in response to pH variations. Because inflammation changes the pH environment, these are especially good at getting anti-inflammatory medications to places like the gastrointestinal system.
4. **Smart Hydrogels:** According to advanced patents, these hydrogels react to environmental stimuli like pH or temperature changes to release anti-inflammatory medications exactly when they're needed. This method guarantees long-lasting therapeutic benefits while reducing adverse effects.

Future Prospects

Although there is still considerable room for improvement, hydrogel-based drug delivery technologies for anti-inflammatory therapy have advanced significantly in recent years. With an emphasis on boosting specificity, reducing side effects, and increasing therapeutic outcomes, these systems have a bright future. Future advances are anticipated in the following important areas:

Hydrogels that Respond to Stimuli

One key area for future research is the creation of smart hydrogels, which can react to external stimuli including light, magnetic fields, pH, and temperature. By enabling controlled medication release, these hydrogels minimize systemic exposure and minimize side effects by guaranteeing that anti-inflammatory medicines are exclusively administered at the intended location. Since inflammation frequently changes the local pH, pH-responsive hydrogels, for instance, could be used to deliver medications straight to inflammatory tissues. As this technology develops, it may make it possible to treat chronic inflammatory conditions like Crohn's disease, rheumatoid arthritis, and even inflammation brought on by cancer more effectively.

Materials That Are Biocompatible and Biodegradable

The use of completely biodegradable and biocompatible materials, such as synthetic polymers (like PEG-based systems) and natural polymers (like chitosan, alginate, and hyaluronic acid), is anticipated to change in hydrogel delivery systems in the future. By breaking down naturally, these materials lessen the need for surgery to remove them and avoid long-term issues. Long-term usage of these systems will be safer thanks to improved biocompatibility, which will lessen unpleasant effects.

Systems of Combination and Multi-Drug Therapy

Hydrogels may be created in the future to administer several anti-inflammatory medications or even to combine anti-inflammatory medications with other therapeutic medications (such as biologics, painkillers, or antioxidants). Combination medications can target intricate inflammatory pathways and potentially result in more successful treatment plans, particularly for conditions like psoriasis or rheumatoid arthritis that have multiple underlying causes. By limiting the dosage of individual medications and minimizing side effects, this approach may maximize therapeutic benefits through synergistic effects.

Enhanced Penetration and Targeted Delivery

More focused hydrogel systems that are made especially to identify and attach to inflammatory markers—like certain proteins or cell receptors expressed in inflammatory tissues—are anticipated. By adding ligands or antibodies to

the hydrogel network, this might be accomplished. Anti-inflammatory medications will be supplied straight to the site of action thanks to targeted drug delivery, increasing therapeutic effectiveness and lowering adverse effects. Furthermore, improving these hydrogels' skin penetration for topical treatments would allow for the deeper and more efficient administration of anti-inflammatory agents.

Precision And Personalized Medicine

The creation of patient-specific hydrogel delivery systems has the potential to revolutionize anti-inflammatory therapies as personalized medicine gains traction. Hydrogels customized to the patient's particular disease profile, including the details of their inflammation indicators and response to treatment, will be made possible by cutting-edge technology like 3D printing. This degree of customization might help patients receive the best anti-inflammatory medication possible by optimizing drug distribution.

Conclusion

The pharmaceutical and biomedical industries have shown a great deal of interest in the development of hydrogel delivery systems for anti-inflammatory applications because of their potential to provide targeted, localized, and controlled drug release. By guaranteeing the sustained and accurate delivery of active pharmaceutical ingredients (APIs) to inflammatory tissues, these systems are intended to increase patient compliance, decrease systemic adverse effects, and improve the efficacy of anti-inflammatory therapy. Hydrogels' special qualities, such as their high water retention, biocompatibility, and responsiveness to external stimuli, have made them an effective drug delivery platform.

One significant benefit of hydrogels is their capacity to contain physiologically active anti-inflammatory medicines, including biologics, corticosteroids, and nonsteroidal anti-inflammatory medications (NSAIDs) while regulating their release over time. This prolonged-release technique keeps the drug's therapeutic level at the site of inflammation constant, minimizes the chance of adverse effects, and lowers the frequency of doses. Furthermore, some hydrogels' pH-responsive and temperature-sensitive qualities are helpful in the treatment of localized diseases, where the inflammatory site frequently displays changed pH or temperature profiles. The ability of these responsive systems to release medications precisely where they are needed boosts treatment effectiveness and lowers systemic exposure.

In conclusion, hydrogels present a promising and innovative solution for the controlled delivery of anti-inflammatory drugs. With ongoing advancements in materials science, nanotechnology, and drug formulation strategies, the future of hydrogel-based therapies for inflammation management looks extremely promising. The potential to create more efficient, safer, and personalized therapies will undoubtedly transform the treatment landscape for chronic and acute inflammatory diseases, offering patients more effective and convenient treatment options shortly.

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