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Review Article

LIPOSOMAL HYDROGELS AS ADVANCED TOPICAL DRUG DELIVERY SYSTEMS FOR DERMATITIS: A COMPREHENSIVE REVIEW

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ABSTRACT

Dermatitis is a chronic inflammatory skin disorder characterized by erythema, pruritus, dryness, scaling, and impaired skin barrier function. The condition affects a significant proportion of the global population and is influenced by genetic predisposition, immune dysregulation, environmental factors, allergens, irritants, and psychological stress. Conventional therapeutic approaches, including corticosteroids and immunomodulators, often provide symptomatic relief but may be associated with adverse effects during prolonged use. Consequently, the development of advanced topical drug delivery systems has gained considerable attention for improving therapeutic efficacy and patient compliance. Liposomes are phospholipid-based vesicular carriers capable of encapsulating both hydrophilic and lipophilic drugs, thereby enhancing drug stability, skin penetration, and targeted delivery. Their biocompatibility, biodegradability, and ability to reduce systemic toxicity make them attractive candidates for dermatological applications. Hydrogels, on the other hand, are three-dimensional hydrophilic polymeric networks capable of retaining large amounts of water and providing controlled drug release, improved skin hydration, and prolonged residence time at the site of application. The combination of liposomes and hydrogels into a liposomal hydrogel system offers synergistic advantages, including enhanced drug permeation, sustained release, improved therapeutic efficacy, and better patient acceptability. This review highlights the pathophysiology and types of dermatitis, the structure and properties of liposomes, hydrogel classification and preparation methods, and the potential applications of liposomal hydrogels in topical drug delivery. The integration of liposomal carriers within hydrogel matrices represents a promising strategy for the effective management of dermatitis and other inflammatory skin disorders.

Keywords: Dermatitis, Eczema, Atopic Dermatitis, Contact Dermatitis, Liposomes, Hydrogel, Liposomal Hydrogel, Topical Drug Delivery, Skin Inflammation, Controlled Drug Release, Nanocarriers, Transdermal Delivery.

INTRODUCTION

Dermatitis, often referred to as eczema is a common condition of skin that affects millions of people worldwide. It is characterized by inflammation of the skin, leading to redness, itching, and discomfort. Dermatitis can manifest in different forms and degree of severity and its impact on quality f life can be significant. Dermatitis forms from a complex interplay of environmental, immune and genetic factors. Some of the other commonest factor that facilitates dermatitis is the family history of dermatitis which can increase the likelihood of an individual developing the condition. Certain genetic variations may predispose the skin to react excessively to environmental triggers (Marsella, 2021).

Allergens, such as pollen, pet dander, and certain foods, can trigger allergic reactions that manifest as dermatitis. Contact with these allergens can lead to skin inflammation and discomfort. Exposure to irritants like detergents, harsh soaps, cleaning products, and chemicals can disrupt the skin's protective barrier, causing inflammation and leading to dermatitis. Changes in temperature, humidity, and air quality can influence the onset and severity of dermatitis. Cold and dry climates, for instance, can contribute to skin dryness and irritation. Emotional stress can exacerbate dermatitis symptoms. Stress triggers the release of certain hormones that can compromise the skin's barrier function and trigger inflammation (Marsella *et al*., 2021).

Types of dermatitis

Dermatitis manifests in different forms, each with its own distinct characteristics and triggers. Some common types of dermatitis include:

Atopic Dermatitis

Also known as eczema, atopic dermatitis is often linked to a family history of allergies and asthma. It typically begins in infancy or childhood, presenting as red, itchy rashes on the face, scalp, and joints. Scratching the affected areas can lead to further inflammation and infection (Shiku, 2023)

Contact Dermatitis

This type of dermatitis results from direct contact with irritants or allergens. It can be classified into two subtypes: irritant contact dermatitis (caused by exposure to harsh substances) and allergic contact dermatitis (triggered by an immune response to allergens like nickel, fragrances, or latex) (Rozas *et al*., 2012).

Irritant contact dermatitis

This type of dermatitis developed when the skin is in contact with irritating substances such as solvents and detergents. These substances strip the skin surface of its natural oil. Therefore, this type of dermatitis developed when there is regular or prolonged contact with such kind of irritating substances. It was noted that the most important factors in causing irritant contact dermatitis are the amount and concentration of the irritating substances coming across the skin.

Allergic contact dermatitis

occurs when allergy develops to a specific chemical or substance that has been in contact with the skin. Examples of these substances include metals such as nickel, rubber, chemicals in hair dye and perfumes or preservatives in creams and cosmetics. It is not known why some people develop allergy to these substances while others do not. In some cases, some less common substances in vegetables and fruits can result to immediate allergic reaction when touched.

Seborrheic dermatitis

This type of dermatitis primarily affects areas that were rich in sebaceous glands such as face, chest and scalp. It is characterized by red, scaly patches that may be accompanied by itching. This condition is often associated with an overgrowth of yeast on the skin (Shiku *et al*., 2023).

Liposomes

"Liposome" was first discovered in the year 1965 by Bangham and the word was derived from Greek word "lipo" means "fatty constitution" and "soma" means "structure" (Dua *et al*., 2012). Liposomes are relatively small in size and it ranges from 50nm to several micrometers in diameter. These are spherical vesicles in which aqueous core is entirely enclosed by one or more phospholipid bilayers. It is having the unique ability to entrap both lipophilic and hydrophilic compounds.

These molecules are inserted into the bilayer membrane, whereas hydrophilic molecules can be entrapped in the aqueous center. Because of their biocompatibility, biodegradability, low toxicity, and aptitude to trap both hydrophilic and lipophilic drugs and simplify site-specific drug delivery to tumor tissues. Many studies have been performed on liposomes inorder to decrease the drug toxicity and cell specific targeting. Various nanocarriers like nanoparticles, microparticles, polysaccharides etc, can be used to a targeted drug delivery system.

Liposomes are very useful because they act as carriers for a variety of drugs, having a potential therapeutic action. These vesicles are formed when phospholipids are hydrated in aqueous medium or aqueous solution.

Components of liposomes

The major components of liposomes include:

- Phospholipids
- Cholesterol

Phospholipids

Phospholipids are the major constituents of liposomes.

Phospholipids are of 3 types:

- ➢ Phosphotidylcholine
- ➢ Phosphotidylethanolamines
- ➢ Phosphotidyl serine

Cholesterol

- Cholesterol itself does not form a bilayer.
- It acts as a fluid buffer.
- It provides rigidity to the bilayer.
- Due to cholesterol bilayer become more stable towards temperature change.
- Cholesterol generally incorporated in 1:1 or 1:2 molar ratio of PL.

Classification of liposomes

Classification based on structural features

- Small Unilamellar Vesicles: 20-100nm.
- Large Unilamellar Vesicles: >100nm.
- Giant Unilamellar Vesicles: >1000nm.
- Oligo lamellar Vesicles: 100-1000nm.

Multilamellar Large Vesicles: >500nm.

Classification based on preparation method

- Reverse phase evaporation method.
- Stable plurilamellar vesicles.
- Vesicles prepared by fusion.
- Vesicles by extrusion technique.
- Frozen-thawed MLV.

Properties of liposomes

Solubilization

- It solubilizes lipophilic drugs that would otherwise be difficult to administer intravenously.

Protection:

- Liposome encapsulated drugs are inaccessibleto metabolizing enzymes.

Amplification

- Liposome can be used as an adjuvant in vaccine formulations.

Internalisation

- Liposomes are endocytosed or phagocytosed by cells,opening up opportunities to use liposome-dependent drugs.

Duration of action:

- Liposomes can prolong the drug action by slowly releasing the drug in the body.

Classification based on targeting concepts of liposomes:

- PEG ethylated liposomes.
- Immuno liposomes.
- Cationic liposomes.

Mechanism of formation of liposomes

The mechanism involves the following steps:

a) Phospholipids together with hydrophobic compound are placed in an aqueous media containing hydrophilic compounds.

b) Phospholipids form aggregated complexes to shield their hydrophobic sections from the water molecules. Hydrophobic compounds dissolved in lipids are entrapped into the liposomal bilayers.

c) Providing a sufficient amount of energy to the aggregated phospholipids makes the bilayer sheet to arrange in the form of organized, closed bilayer vesicles. During this process, liposomes can entrap hydrophilic compounds present in the hydration media inside their aqueous core.

Advantages

Some of the advantages of liposome are as follows:

- Provides selective passive targeting to tumour tissues (Liposomal doxorubicin).
- Increased efficacy and therapeutic index.
- Increased stability via encapsulation.
- Reduction in toxicity of the encapsulated agents.
- Site avoidance effect.
- Improved pharmacokinetic effects (reduced elimination, increased circulation life times).
- Flexibility to couple with site specific ligands to achieve active targeting.

Liposome action of drug delivery

The steps involved in the liposome action of drug delivery include:

1. Adsorption
2. Endocytosis
3. Fusion
4. Lipid exchange

1. Adsorption: Liposome adsorption to cell membrane is one of the important mechanism that is involved in the intracellular drug delivery. The adsorbed liposomes, in the presence of cell surface proteins, become leaky and release those contents that are required into the cell membrane. Thus, results in a higher concentration of drug close to cell membrane and facilitates cellular uptake of drug by passive diffusion or transport (Allen *et al*., 1981).

2. Endocytosis: Adsorption of liposomes on the surface of cell membrane is followed by engulfment and internalization into endosomes. Endosomes transport liposomes to lysosomes. Subsequently, lysosomal enzymes degrade the lipids and release the entrapped drug into the cytoplasm (Lipowsky, 1995).

3. Fusion: Fusion of lipid bilayer of liposomes with lipoidal cell membrane by intermixing and lateral diffusion of lipids results in direct delivery of liposomal contents into the cytoplasm (Wojewodzka *et al*., 2005).

4. Lipid exchange: Due to similarity of liposomal membrane lipids with the cell membrane phospholipids, lipid transfer proteins in the cell membrane recognize liposomes and consequently cause lipid (Knoll *et al*., 1988). This results in the destabilization of liposomal membranes and intracellular release of drug molecules.

An understanding of the mechanisms of the intracellular drug delivery by liposomes provides the basis for bringing about manipulations in the characteristics of liposomes to enhance their favourable interaction with cell membranes and hence the drug delivery.

Applications of liposomes

1. Cationic liposomes for delivery of nucleic acid

Cationic lipids, which are the core components of nanoparticles, have a structure of positively charged head group and one or two hydrophobic tail region made of hydrocarbon chains or steroid structures. Lipoplexes of cationic liposomes and nucleic acids still suffer from several limitations. One is their low stability in the bloodstream, which is caused by characteristics of cationic lipids. Until they reach their target cells, cationic lipid components can interact with serum proteins, potentially disrupting the integrity of liposomal structure or forming aggregates that are too large to be taken up by cells. Ti increase the in-vivo stability of lipoplexes in the blood, researchers often include PEG-conjugated lipids and cholesterol as components of the cationic liposomes. Another limitation is the relatively weak delivery of nucleic acids into target cells. For anti-cancer therapy, enhanced retention and permeability may serve as an initial driving force for delivery of lipoplexes to tumour tissues.

Once in the tumour tissues, the effective recognition off tumour cells and intracellular delivery should proceed (Fan and Zhang, 2013). Cisplatin is another widely used anticancer drug, which induces DNA lesions and mitochondrial apoptosis. This sometimes, may lead to toxicities including nephrotoxicity, neurotoxicity, and ototoxicity which demand new formulations to be developed to reduce toxicity and potentiate efficacy such as Cisplatin liposomes (Bonde and Nair, 2017).

2. Liposomes used in Cancer

A significant treatment in the treatment of cancer involving chemotherapy is the efficient delivery of cytotoxic agents to tumour tissues while at the same time minimizes the undesired negative side effects with these drugs. The use of DDS such as liposomes can modify drug pharmacokinetic and distribution in a manner that improves the overall pharmacological properties of generally used chemotherapeutics. Liposomes are particularly attractive to DDS in part due to the ease with which they can be generated and modified such that they can be used to treat a wide variety of cancers. Breast cancer, in particular, has been the focus of many studies concerning liposome based chemotherapeutics in part due to the clinical success of various drugs such as Doxil, which is a liposomal formulation currently employed to treat recurrent breast cancer (Nekkanti and Kalepu, 2015).

3. Sustained release liposomes

Anticancer drugs can be delivered to systemic circulation in a sustained release mode by encapsulating in the liposomes. DepoFoam, a sustained release injectable technology of Skye Pharma, is applied in DepoCyt that is used in the treatment of lymphoma, i.e., lymphomatous meningitis. In comparison to unentrapped Cytarabine, DepoCyt administered through intrathecal route maximized the therapeutic potential of cytotoxic agents that are specific to the S-phase of cell cycle. Furthermore, the dosing frequency reduced due to the prolonged CSF t1/2 of Cytaribine (Fan and Zhang, 2013).

4. Liposome Vaccine

Typically, either a purified antigen or an attenuated pathogen is used as an immunogen in a known vaccine. However, a long-term immune response may not be induced by purified antigens and even sometimes does not induce a response at all. On the other hand, attenuated vaccines can produce a reaction in the patient under immunization (Bonde and Nair, 2017).

5. Liposomes used for Fungal Treatment

A polyene antibiotic, AmpicillineB, is used for the treatment of fungal infections. It binds to sterols in fungal membrane as well as mammalian membranes which reslt in the formation of transmembrane, pores where leakage of vital intracellular components takesplace leads to cel death. Binding to the cholesterol-containing mammalian membranes results in toxicity. Nephrotoxicity was reported in the systemic use of AmpB and often resulted in central nervous system side effects on chronic use. Studies revealed the effectiveness of liposomal AmpB in experimental fungi and parasitic diseases (Nekkanti and Kalepu, 2015).

6. Immuno liposomes

Among the various types of liposomes, immune liposomes have gained wide attention due to their targeting capabilities. Due to the presence of antibodies attached on to their surface, these liposomes exhibit immunologic response. The preparation of immune liposomes, i.e., conjugation of antibodies to liposomes, is not that straight forward and even can pose a challenge during their formulation. Protein molecules and monoclonal antibodies can be conjugated directly in to the liposome, PEGylated liposome, or PEG chain of the PEGylated liposomes. Similar to other liposomes, the RES can scavenge and clear the immunoliposome from systemic circulation. Increase circulation half-life, targeting specificity, and minimized drug loss and degradation are the major advantages of immune liposomes. Apart from the promising applications, immunoliposomes suffer from a major drawback, i.e., immunogenicity and increase rate of clearance from circulation can be observes due to repeated injections (Lamichhane *et al*., 2018).

7. Liposomes used for gene delivery

Liposomes have been extensively studied in areas such as gene therapy and drug delivery due to their observed stability and favourable toxicity profile over traditional treatments. Liposomes can encapsulate biomolecules or drugs that are hydrophilic and increase their internalization and solubility through the lipid bilayer of the cell. Various discoveries related to human genomes and their use in disease treatment have become more approachable with the advances in science and technology. In spite of these developments, choosing a right carrier for the delivery of the gene to the target is of paramount importance.

One such important carrier is liposomes, which can deliver DNA, antisense oligonucleotides, RNA, and other potential agents into the nucleus. Especially, engineered liposomes such as cationic liposomes, pH-sensitive liposomes, fusogenic liposomes, and genomes are explored for gene delivery.

8. Liposomes used for Protein and Peptide Delivery

Proteins and peptides are potent therapeutic agents used in the treatment of various diseases. However, due to their unstable nature and degradation at physiological conditions, the delivery of these drugs at the targets site is extremely complicated. Most of the protein and peptide drugs produce their mechanism of action extra cellular by interacting with the receptors, Encapsulation of proteins and peptides into lipid vesicles for improving the therapeutic properties has been extensively investigated (Kerry *et al*., 2019).

9. Liposomes used in Inhales

The pulmonary route is a promising drug delivery route. The carriers used for this purpose are target selective and can control drug release. The advantages of the carrier system include decrease drug toxicity, increased the stability of drug, and the local irritation which is prevented. Nebulizers are used in the actual liposome formulation for inhalation. The nebulizers used include ultrasonic, air-jet, and passively vibrating mesh nebulizers (Yang *et al*., 2015).

Hydrogel

Hydrogels are hydrophilic, three dimensional network that hold the large quantity fluid water is the large constituents of human body which applied for the biomedical purposes and first proposed by Witchterle and Lim in the 1960s (Kim *et al*., 2018). Hydrogels are generally cross-linked by physical or chemical methods which have been widely used for drug release, cell culture, tissue engineering and adhesion. Polymers used in hydrogel can be divided into natural polymer hydrogels and synthetic polymer hydrogels. Synthetic polymers are formed by chemical reactions of small organic monomers. Synthetic polymers possess strong water absorption and excellent mechanical properties, a certain extent of biodegradability and potential toxicity have limit the application of polymer hydrogel. As a natural ingredient, protein has different genetic coding structures and functions with biocompatibility and degradability (Yadav and Jitender, 2020).

Hydrogels formulation applied on the skin surfaces which categories into two groups such as topical and transdermal route. Topical formulations provide the drug at the particular site of the skin surfaces without systemic exhibition while transdermal formulations applied to the local area of the skin surfaces which maintain and deliver the effective concentration of drug in the systemic circulations (Yuanhan and Xin, 2022).

Classification of Hydrogel

Hydrogels can be classified into two groups based on their natural or synthetic origins. Classification according to polymeric composition, the method of preparation leads to formations of some important classes of hydrogels:

(a) Homopolymeric hydrogels are referred to polymer networks derived from a single species of monomer, which is a basic structural unit comprising of any polymer network. Homopolymers may have crosslinked skeletal structure depending on the nature of the monomer and polymerization technique.

(b) Copolymeric hydrogels are comprised of two or more different monomer species with at least one hydrophilic component, arranged in a random, block or alternating configuration along the chain of the polymer network.

(c) Multipolymer interpenetrating polymeric hydrogel (IPN) an important class of hydrogels, is made of two independent cross-linked synthetic and/or natural polymer component, contained in a network form. In semiIPN hydrogel, one component is a cross-linked polymer and other component is a non-cross-linked polymer (Wang *et al*., 2020).

Prepared techniques of hydrogels

Hydrogels are three-dimensional polymer networks capable of absorbing and retaining large amounts of water, making them invaluable in various biomedical applications. Their synthesis and fabrication involve diverse techniques that tailor their properties for specific uses. This section explores the primary methods of hydrogel synthesis and fabrication, highlighting their advantages and applications;

a) Chemical Crosslinking

Chemical crosslinking forms covalent bonds between polymer chains, offering high mechanical stability. Common crosslinking agents include N,N'- methylenebisacrylamide (MBAAm) and glutaraldehyde.

This method is widely used for synthetic polymers like polyacrylamide (PAAm) and polyethylene glycol (PEG), creating durable hydrogels for drug delivery and tissue engineering (Acciaretti *et al*., 2022; Siqueira *et al*., 2023).

b) Physical Crosslinking

Physical crosslinking relies on non-covalent interactions such as hydrogen bonds or ionic interactions. Techniques include freeze-thaw cycles for polyvinyl alcohol (PVA) hydrogels and stereocomplex formation for biodegradable polymers. This method is biocompatible and suitable for natural polymers like alginate and chitosan, used in wound dressings and drug delivery.

c) Irradiation-Based Crosslinking

Irradiation with UV or gamma rays initiates polymerization without catalysts, offering rapid hydrogel formation. This method is efficient but may lack uniform crosslinking, making it less common in biomedical applications due to potential cytotoxicity concerns

d) Additive Manufacturing

3D printing techniques like extrusion and inkjet printing enable precise fabrication of complex hydrogel structures. These are used in tissue engineering and drug delivery, allowing customization for specific anatomical needs (Hameed *et al*., 2024).

e) Self-Assembly of Peptide Hydrogels

Peptide hydrogels form nanostructures through stimuli like pH changes or temperature, offering biocompatibility and biodegradability. They are ideal for drug delivery and tissue engineering due to their porous structure and ease of functionalization (Siddheshwar *et al*., 2025).

f) Hybrid Hydrogels

Combining natural and synthetic polymers, hybrid hydrogels balance biocompatibility with mechanical strength. They are used in drug delivery and tissue engineering, leveraging the strengths of both polymer types (Zhou *et al*., 2020).

Applications

Wound Healing

Super absorbent hydrogels, also called super porous hydrogels, can absorb up to 90% of their weight in water without breaking down, making them ideal for wound healing dressings, such as alginate-based hydrogels. They offer bioadhesive and sealant mechanisms, providing alternatives to staples or sutures. Wound healing has four phases: homeostasis, inflammation, proliferation, and remodeling (Fan *et al*., 2021). Delays in healing, especially beyond three months, can lead to chronic wounds, often due to prolonged inflammation. Hydrogel dressings are effective for chronic wounds because they can be customized with growth factors, biomolecules, and drugs. Adding anti-inflammatory agents like phenolic compounds from honey or plant extracts can enhance hydrogels, speeding up healing by reducing inflammation. Xin *et al*. developed a hydrogel for diabetic wound healing by combining oxidized Gastrodia elata polysaccharide (OGEP) with a gastrodin-chitosan compound (GAS/CS) through a Schiff base reaction. The hydrogel, loaded with EGCG microspheres, was tested for therapeutic effects on diabetic wounds, as well as its biosafety, rheology, and hemostasis properties (Cheng *et al*., 2024).

Contact Lenses

Contact lenses are mainly used as an alternative to spectacles for vision correction. They are also being developed for drug delivery, corneal defect treatment, post-surgical wound repair, and cosmetic purposes. Traditional methods like eye drops and ointments have drawbacks, such as limited permeability and frequent dosing. Thus, contact lenses are being explored as a promising option for ophthalmic drug delivery. Ideal contact lens materials should be durable, stable, clear, and allow adequate oxygen to the cornea. Lens characteristics include mechanical, optical, and chemical aspects. Wettability maintains a stable tear film, while mechanical testing impacts comfort, fit, and durability. Optical properties ensure good vision. Hydrogels are recommended due to their high compatibility with corneal cells. Hydrogels have advanced clinical ophthalmology through their use in SCL, IOL, and drug-eluting hydrogels, focusing on the eye's anterior segments. Polymeric hydrogels, like pHEMA, are popular for SCL and drug delivery (Moreddu *et al*., 2019; Narayanaswamy and Torchilin, 2019).

Tissue Engineering

Hydrogels are notable for their versatility in drug delivery and tissue engineering. Tissue engineering regenerates tissue by integrating cells with a scaffold under physiological conditions. The essential elements, or "triad," are cells, scaffolds, and growth factors. Hydrogels, used as scaffolds, support cell attachment, growth, and tissue regeneration (Kesharwani *et al*., 2021). Their 3D polymer networks retain significant water, making them ideal for this purpose. Hydrogels can be customized to mimic the extracellular matrix (ECM) of native tissues through various crosslinking methods. Most ECMs are porous networks, similar to hydrogels, with fibrous proteins in a matrix of glycosaminoglycans (GAGs) and proteoglycans. Hydrogels are key in tissue engineering for repairing dermal tissue, cartilage, blood vessels, bone, cornea, and other soft tissues (L'opez *et al*., 2021). They effectively mimic the ECM, making them ideal for replacing damaged tissues. Cartilage, which lacks lymphatics, blood vessels, and nerves, relies on ECM for maintaining cell microenvironment homeostasis. Cartilage scaffolds need excellent biocompatibility, porosity, and mechanical strength, resembling Type II collagen. Elastic hydrogels with smooth surfaces and high-water content are ideal for cartilage regeneration as they closely mimic the ECM (Reakasame and Boccaccini, 2018).

3D Bioprinting

Bioprinting with hybrid hydrogels integrates the benefits of both technologies, supporting layer-by-layer printing with solid filament structure and physical gelation during extrusion. These hydrogels enhance cell functions crucial for tissue engineering, including proliferation, migration, and differentiation. Extrusion-based bioprinting is favoured for its compatibility with low-viscosity hydrogel precursors. Hydrogel bioinks, composed of cells and precursor solutions, are essential for replicating tissues and organs in bioprinting, requiring optimal rheological and biochemical properties (Deo *et al*., 2020). Various crosslinking methods and bio ink formulations have been developed to mimic specific tissue architectures, demonstrating effective printing with materials like HA-based bioink crosslinked with calcium solutions. Boons *et al*. created a 3D bioprinting platform to produce hydrogels with live dialgae, used as biological indicators for water quality (Abdollahiyan *et al*., 2020).

These hydrogels, exposed to different concentrations of salt, herbicides, and antibacterial agents, allowed visual assessment of diatom proliferation to detect water contaminants. The diatoms stayed metabolically active in the hydrogels, enabling pollutant sensitivity testing. Additionally, engineered bacteria such as Deinococcusradiodurans and *E. coli* have been used for infrared detection, but they need appropriate substrates for environmental adaptation (Antich *et al*., 2020).

Bio Sensors

Hydrogels, used in electronic skin and wearable biosensors, offer numerous advantages. They are flexible, elastic, and adhere well to human skin, providing enhanced comfort. Their water absorption helps keep the skin moisturized and stable, and their conductivity ensures reliable signal transmission. Traditional methods for designing advanced hydrogels are challenging, as they require adding many components to improve various properties. AI technology helps by efficiently screening and optimizing hydrogel components. High-throughput screening has led to the development of polysulfobetaine hydrogels with excellent mechanical and self-healing properties, expanding their use in flexible electronics and enhancing intelligent functions like real-time health monitoring and wireless communication. AI-integrated hydrogels can accurately recognize handwriting movements, making them ideal for smart human-device interfaces. Further research is needed to ensure the stability, safety, and privacy of these applications. Diaconu *et al*. immobilized laccase from Trametes versicolor into a nanocomposite film using a MWCNT-CS solution with 25 U/mL laccase (Diacon *et al*., 2010).

Catalysis

Hydrogels are widely used in biological and chemical catalytic reactions due to their unique structure and porosity. They prevent nanoparticle aggregation, increasing the surface area available for catalysis, which in turn boosts reaction efficiency. The porosity of hydrogels can be adjusted by environmental conditions, allowing precise control over reaction rates. Additionally, functional groups within the hydrogel matrix stabilize metal nanoparticles, protecting them from oxidation (Yang *et al*., 2021). Hydrogel-embedded metal nanocatalysts are commonly used to enhance hydrogen gas production through metal hydride-catalyzed hydrolysis. These nanoparticles can either be pre-formed and embedded in the gel or generated in situ within the gel.

For example, nickel nanoparticles can be produced directly within hydrogels during the reduction of nitrophenols and other nitro compounds. Nanoparticles can also form in hydrogels by soaking them in metal salt solutions and adding a reducing agent, like sodium borohydride or hydrogen gas, to convert the salts into metallic nanoparticles. However, not all catalytic reactions require this reduction step; for instance, 4-vinylpyridine hydrogels can directly form complexes with chromate ions to catalytically oxidize alcohols (Sahiner *et al*., 2011).

CONCLUSION

In conclusion, hydrogels are essential materials in regenerative medicine and smart device applications, showcasing significant potential across various organ systems. Their remarkable properties, such as high-water absorption, biocompatibility, and the ability to mimic native tissue, support cell proliferation and differentiation. Light-sensitive hydrogels are particularly promising, offering applications in drug delivery, microlenses, and biosensors due to their remote and non-invasive activation capabilities. Ongoing research aims to explore diverse hydrogel derivatives and their functionalities, paving the way for the development of novel materials with enhanced properties. Furthermore, tailored modifications and functionalizations can improve hydrogel performance, thereby extending their therapeutic applications and efficacy in tissue regeneration.

However, several challenges must be addressed to fully realize the potential of hydrogels in biomedical and supercapacitor applications. Biocompatibility remains a primary concern, necessitating the development of hydrogels from natural polymers or the modification of synthetic materials to minimize immune responses. Additionally, enhancing mechanical strength is crucial for durable applications, which can be achieved by incorporating reinforcing agents or creating hybrid hydrogels. Stability in biological conditions is vital for effective drug delivery and employing cross-linking or controlled degradation techniques can improve performance. Furthermore, optimizing the release of therapeutic agents requires precise tuning of hydrogel structures. The integration of AI technology in hydrogel-based biosensors can enhance screening and optimization processes. As research advances, hydrogels will continue to play a critical role in both biomedical and energy storage innovations.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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