JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

BOTANICAL BANDAGES: A COMPREHENSIVE REVIEW ON HERBAL HYDROGEL FILM FOR WOUND HEALING

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Abstract: Wound healing remains a complex clinical problem so appropriate and effective wound care is essential. Much work is focused on wound care, emphasizing new therapies and technologies for the care of acute and chronic wounds. Hydrogel film has enormous potential as an ideal alternative to traditional wound dressings such as gauze. This is mainly due to its three-dimensional (3D) cross-linked polymer network, which has a high water content that promotes a moist environment that supports effective burn healing. In addition, the hydrogel facilitates the penetration of loaded therapeutic substances to the entire wound surface, fights against burn pathogens with its moisturizing effect, and thus improves the healing process. Herbal crude drugs often contain bioactive compounds with inherent healing properties, such as antimicrobial, anti-inflammatory, antioxidant, and wound-healing agents. Natural ingredients reduce the risk of allergic reactions, skin sensitization, or other adverse events commonly associated with synthetic compounds. This comprehensive review examines herbs used for wound healing, innovation in moist wound management, efficacy, fabrication methods, advantages, and applications of hydrogel film.
Keywords: Wound healing, Herbs, Hydrogel Film, Moist wound management, Transdermal drug delivery

I. INTRODUCTION

The human skin, being the largest organ, is essential for several bodily functions, including regulation of body temperature, commencement of vitamin D synthesis, protection against toxins and infections, and hydration [1]. An injury to the skin produced by an internal disease or an external injury is referred to as a wound. The Skin has an excellent self-recovery ability to restore its structure and function that involves four complex and partially overlapping phases of hemostasis, inflammation, proliferation, and remodeling. However, the healing process can be hindered by various biological, chemical, and physical factors. Prolonged wound exposure increases the possibility of skin exposure to external harmful factors [2]. The inherent physiological response to tissue damage is wound healing. It is a sophisticated, carefully regulated series of molecular and cellular events that include angiogenesis, inflammation, cell migration, synthesis of the provisional matrix, collagen deposition, and re-epithelialization [3]. Among the following are necessary for optimal wound healing in adult humans: 1. fast hemostasis; 2. suitable inflammation; 3. mesenchymal cell differentiation, proliferation, and migration to the wound site; 4. appropriate angiogenesis; 5. prompt re-epithelialization (regrowth of epithelial tissue over the wound surface); and 6. Proper collagen synthesis, cross-linking, and alignment provide strength to the healing tissue [4].

Conventional treatments for wound healing, as discussed in numerous medical journals, encompass a range of strategies aimed at protecting, cleansing, and promoting the natural healing process. These methods include surgical wound closure, which involves the use of sutures, staples, or adhesive skin closures to approximate wound edges and facilitate healing. Dressings and bandages, such as gauze, hydrocolloids, hydrogels, alginates, elastic, and cohesive bandages, are also crucial in maintaining a clean and moist wound environment conducive to healing. Antibiotics, either orally or topically administered, play a vital role in preventing or treating infections that may arise during the wound healing process. Compression therapy, using bandages or stockings, is particularly beneficial for patients with leg ulcers, as it helps improve blood circulation and promotes wound healing. Debridement, either manually, through saline irrigation, or with specialized dressings, is essential for removing non-viable tissue and foreign bodies, creating a suitable environment for wound healing and preventing infection. Wound irrigation with sterile saline or other wound irrigation solutions is another crucial aspect of conventional wound care, as it helps maintain wound cleanliness and reduces the risk of infection. Lastly, pain management through the use of analgesics like paracetamol or ibuprofen is vital, as pain can hinder the healing process and negatively impact the patient's overall well-being. As medical science progresses, researchers and clinicians continue to explore innovative and effective ways to accelerate wound healing and improve patient outcomes.

The rate of wound infection is reduced by newer occlusive dressings that accelerate re-epithelialization, stimulate collagen synthesis, produce a hypoxic environment at the wound bed to encourage angiogenesis, and lower the pH at the wound surface. By doing so, they create an environment that is unfavorable to bacterial growth and lowers the rate of wound infection. Most of today's dressing products are interactive dressings, meaning they interact with your wound bed to create the optimal environment at the site of wound dressing. Technology has evolved with the understanding that a moist environment promotes healing, so it's now possible to create dressing products that have the characteristics of an optimal dressing [5]

Herbal medicine, also known as complementary and alternative medicine, has been used for decades to treat disease and promote health through its biological components. Over time, people discovered which types of plants worked best to treat certain ailments. The use of medicinal herbs is a standard practice in traditional Chinese medicine, Ayurveda, Unani, Russian herbalism, and other medical systems, which use plants topically to treat wounds and other ailments. Dermatological problems. In addition, the biological activities of plant secondary metabolites produce medicinal effects. There are a surprising number of wound-healing botanicals that have been broadly utilized within the Northern Half of the globe, counting *Matricaria chamomilla*, *Achiella millefolium*, *Althaea officinalis*, *Boerhavia diffusa*, *Calendula officinalis*, Aloe vera, *Curcuma longa*, Eucalyptus, Jojoba, plantain, pine, green tea, pomegranate, and Inula [6]

II. PHASES OF WOUND HEALING

The wound-healing phase begins with hemostasis and inflammation. This step involves the removal of platelets and immune cells to control bleeding and eliminate pathogens. Immune cells initially play an important role in secreting chemokines and growth factors, which attract cells and guide the healing process to the next stage. The proliferative phase involves several events, such as the development of granulation tissue (provisional formation of ECM), angiogenesis (formation of blood vessels), and re-epithelialization (formation of the epidermal layer), which results in wound reduction. This specific step is determined by communication between different types of cells, including macrophages, fibroblasts, endothelial cells, and keratinocytes. The final phase is the repair session, where the previously formed matrix gradually transforms into the formation of functional skin or small/non-functional scars [7].

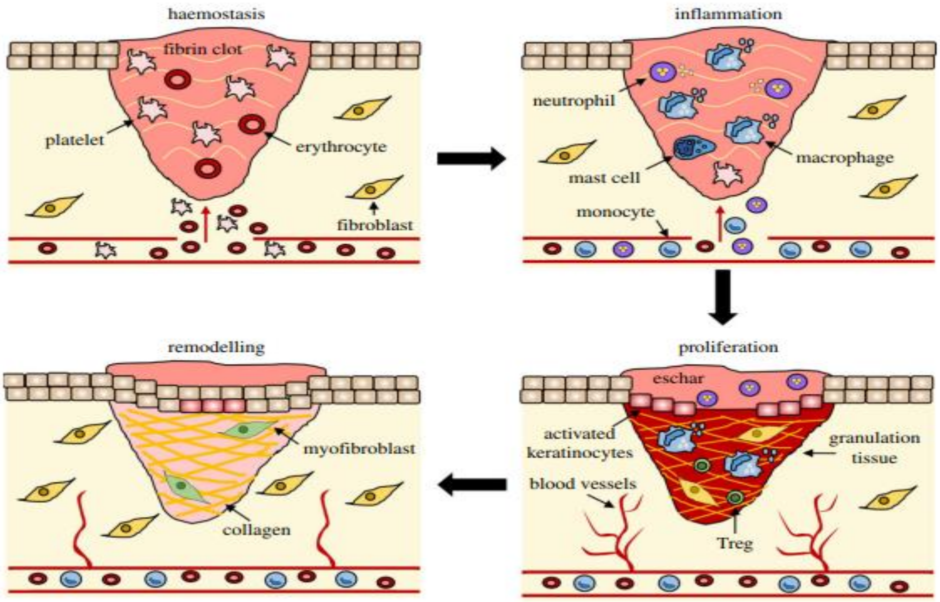

Figure 1: The phases of wound repair and major cellular composition

III. NATURE'S REMEDIES: HERBS WITH WOUND-HEALING PROPERTIES

In the realm of natural remedies and traditional medicine, herbs have long been revered for their therapeutic properties. Among their many applications, herbs are frequently utilized in wound healing, a practice that spans cultures and civilizations throughout history. From ancient civilizations to modern times, the use of herbs for wound care has endured, with a rich tapestry of botanical knowledge informing their efficacy. Herbs used in wound healing possess a myriad of beneficial properties, including antimicrobial, anti-inflammatory, and tissue-regenerating qualities. These botanical agents offer a holistic approach to wound care, addressing not only the physical injury but also supporting the body's natural healing processes. In this exploration of herbs used for wound healing, we delve into the diverse array of botanicals renowned for their therapeutic effects. From the soothing properties of Aloe vera to the antimicrobial actions of *Calendula officinalis*, each herb offers a unique contribution to the healing process. Additionally, we'll examine the scientific evidence supporting their use, as well as practical considerations for incorporating herbs into wound care protocols [8]

Table 1: Medicinal plants, part used and their metabolites used for treating different types of wounds.

S. no.	Medicinal plants	Part used	Metabolites	Uses	Reference
1	Turmeric (*Curcuma longa*)	Rhizomes	Curcumin, vitamin A, proteins	Chronic wound healing	[9]
2	Theaceae (*Camellia pubipetala*)	Leaves	Flavonoids, theanine & caffeine	Excision wound healing	[10]
3	Neem (*Azadirachta indica*)	All portions	Azadirachtin, azadirone, Nimbin, nimbidin, nimbinin	Open wound healing	[11]
4	Aloe (*Aloe bardedensis*)	Leaves	Anthraquinone, C and E vitamins, amino acids	Open wound healing	[12]
5	Papaya (*Carica papaya*)	Latex, fruit	Papain	Diabetic, burn, soft tissue wounds	[13]

6	Betle Piper (*Piper betle L*)	Leaves	Phenolic complex, betal-phenol, chavicol	Excision wound healing	[14]
7	Drumstick tree (*Moringa oleifera*)	Leaves	Vitamins vicenin-2, beta-carotene, phenolics, amino acid	Excision, incision, Wound healing	[15]
8	Indian olive (*Olea europaea*)	Leaves, oil	Biophenolics, Oleuropein secoiridoid Luteolin	Incision wound healing	[16]
9	Bay (*Sphagneticola trilobata*)	Leaves	Flavonoids, terpenoids, alkaloid, and saponin	Incision wound healing	[17]
10	Punarnava (*Boerhavia diffusa*)	Leaves	Alkaloid, Flavanoid Tannin, phenolics	Excision wound healing	[18]

IV. TREATMENT ADVANCEMENTS IN WOUND HEALING

In recent years, the field of wound healing has witnessed a remarkable surge in research, innovation, and clinical application, leading to the development of advanced treatment modalities that have revolutionized the management of acute and chronic wounds. These advancements encompass a wide spectrum of approaches, ranging from novel biomaterials and sophisticated dressings to cutting-edge regenerative therapies and minimally invasive interventions. In acute wounds (eg, surgical wounds and traumatic wounds), bandages control bleeding, absorb exudate, and close the wound to facilitate healing. Therefore, recent developments in acute wound dressings focus on wound closure for hemostasis, absorption of wound exudate, and infection control. For example, strong adhesive dressings made of alginate and poly(N-isopropyl acrylamide) are effective in wound healing due to their healing properties, high stiffness, and rapid wound healing [19]. Recent efforts to combine adhesive hydrogels with surgical meshes have demonstrated the strong adhesion and flexibility of poly(N-isopropyl acrylamide)/chitosan hydrogels and polyethylene terephthalate surgical meshes in wounds subjected to mechanical stress [20].

Table 2: various types of wound dressings for the delivery of herbal constituents [8]

S. no.	Types of dressings	Formulations
1	Ointment	- Herbal ointment with extract of *Jatropha curcas* leaf - Hypericum perforatum oil-based ointment
2	Scaffolds	- Tissue scaffolds for skin wound healing - Gelatin nanofibers scaffolds - Dextrin hydrogel scaffolds - Peptide nanofiber scaffolds - Fibrin-based scaffolds
3	Fibers	- Mathematical model for collagen fiber - Micro-nanofibers for wound healing application - PVA blended nanofiber matrix for wound healing - Titanium fiber mesh - Curcumin-loaded alginate-gelatin composite fibers - Biopolymeric, nanopatterned fibrous carriers for wound healing
4	Hydrogels	- Alginate-based hydrogels - Glycosaminoglycan hydrogel - Ag/graphene hydrogel - Dextran hydrogel
5	Films	- Chitosan films containing basic fibroblast growth factor on wound healing - Gelatin film dressings - Carrageenan and polyox-based composite film dressings containing anti-microbial and anti-inflammatory drugs -Biocomposite films of carrageenan/locust bean gum for transdermal delivery of curcumin.

V. HYDROGEL FILM: INNOVATION IN MOIST WOUND MANAGEMENT

Hydrogels have emerged as a versatile and promising class of biomaterials with wide-ranging applications in various fields, including wound healing, drug delivery, tissue engineering, and regenerative medicine. These three-dimensional networks of hydrophilic polymers possess remarkable properties that make them ideal candidates for diverse biomedical applications. In the context of wound healing, hydrogels have garnered significant attention due to their unique ability to create a moist environment conducive to the natural healing process. By maintaining hydration and providing a scaffold for cell migration and proliferation, hydrogels offer an innovative approach to promoting wound closure and tissue regeneration [21]. Acting as a physical barrier, the hydrogel effectively protects the wound area from external contamination while creating a comfortable moist environment that promotes wound healing. This hydrogel is said to be sterile. In addition, the high water content of the hydrogel provides warmth and comfort, making it ideal for healing burn wounds [22].

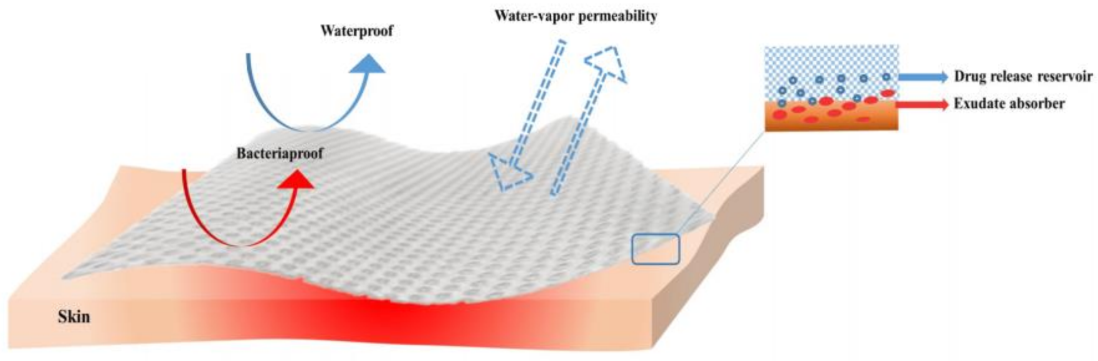

Figure 2: Properties of the hydrogel as an ideal wound dressing

The enhancement of wound healing in moist and humidified environments has been attributed to several mechanisms. These include easier migration of epidermal cells on moist surfaces6, faster epithelialization, and longer residence of proteins and growth factors [23]. Clinical studies have shown that wound healing fluid in moist conditions stimulates the growth of keratinocytes and the growth of fibroblasts, which ensures further growth. Property retrieval element [24]. Dyson et al compared the effects of wet and dry conditions on skin healing in a porcine model. An adhesive polyurethane dressing was used as a wet dressing, and a textile dressing exposed to air protected the healing process. They showed shorter inflammatory phases and faster skin repair of wounds under moist conditions compared to those healing under dry conditions [25]. Four years later, the same group conducted another comparative study between wet and dry environments to investigate the process of angiogenesis during skin repair. They concluded that wounds that survived in a moist environment had faster blood regeneration than wounds in a dry environment. Moist wounds also exhibited a more organized angiogenesis [26]. The development of hydrogel films for wound healing has been driven by a growing understanding of the importance of maintaining a moist environment at the wound site, which facilitates the natural healing process. Hydrogel films excel in this regard, as they can conform to irregular wound surfaces, maintain hydration, and provide a protective barrier against external contaminants.

VI. MERITS OF HYDROGEL FILM

1. **Maintaining Moist Environment**: Hydrogel films excel in creating and maintaining a moist wound environment, which is crucial for promoting optimal wound healing. This moisture helps facilitate cell migration, proliferation, and the natural wound healing process.
2. **Conformability**: Hydrogel films are thin and flexible, allowing them to conform closely to the contours of the wound bed. This conformability ensures intimate contact with the wound surface, maximizing their therapeutic efficacy.
3. **Ease of Application**: Hydrogel films are typically easy to apply and handle, making them suitable for various wound types and locations. Their simplicity of use facilitates healthcare providers' ability to manage wounds effectively.
4. **Enhanced Comfort**: The soft and pliable nature of hydrogel films provides comfort to patients during wear. Unlike traditional wound dressings, hydrogel films can adhere gently to the skin without causing discomfort or trauma upon removal.
5. **Transparency**: Many hydrogel films are transparent, allowing for easy visualization of the wound site without the need for frequent dressing changes. This transparency enables healthcare providers to monitor wound progress and assess healing status more efficiently.
6. **Protection and Barrier Function**: Hydrogel films serve as a protective barrier against external contaminants, minimizing the risk of infection and promoting a sterile wound environment conducive to healing.
7. **Sustained Moisture Release**: Some hydrogel films are designed to release moisture gradually over time, ensuring continuous hydration of the wound bed and prolonging their therapeutic effects.
8. **Biocompatibility**: Hydrogel films are generally biocompatible and well-tolerated by the body, reducing the risk of adverse reactions or allergic responses.
9. **Versatility**: Hydrogel films can be customized with various additives, such as antimicrobial agents, growth factors, or bioactive compounds, to further enhance their therapeutic properties and tailor treatment to specific wound characteristics.
10. **Minimizing Trauma**: Hydrogel films adhere gently to the wound surface, minimizing trauma during dressing changes and reducing the risk of disrupting the delicate healing process.

VII. FABRICATION METHOD OF HYDROGEL FILM

Various methods have been studied to form hydrogel films with thickness control. In general, hydrogel film formation starts with the formation of a film using a solution (non-cross-linked monomer or polymer) and then goes through the sol-gel transition of the solution to form a network structure.

Gelation based on polymerization of monomers: The first widely studied strategy for the preparation of gel films is gelation by free radical polymerization. In a typical formulation, a reaction mixture containing monomers, cross linkers, and initiators is confined between two planar substrates separated by thin spacers and then polymerized in situ. During the polymerization, the copolymerization of monomers and cross-linkers develops until the formation of a continuous polymer network. The thickness of the gel films can be easily adjusted with spacers. At the same time, the properties of the gel films can be regulated by the compositions of the previous solutions and thus the network structure on a molecular scale.

Gelation based on post-cross-linking of polymers: In this method, gelation is achieved by polymerizing a previous solution containing monomers and crosslinking agents, so only synthetic polymers are suitable for the production of hydrogel membranes for this method. More versatile methods need to be developed for fabricating hydrogel films based on various polymers. Hydrogel membranes can also be produced after cross-linking polymers. The main steps of this method are the formation of pre-gel films using polymer solutions and then the crosslinking of these pre-gel films. The former can be achieved by conventional film formation methods such as spin coating, dipping, solution casting, spray coating, and molecular self-assembly [27]. Physical or chemical crosslinking of pre-gel films is done wet or dry. status After rehydration of the cross-linked films, hydrogel films with a thickness of up to nanometers can be obtained. To achieve post-crosslinking, polymers must have reactive groups that allow chemical or physical crosslinks to form under certain conditions. For example, the crosslinking of copolymer-containing photocrosslinking agents (eg, benzophenone) has been widely used to produce sensitively responsive hydrogel membranes [28]. These reactions achieve efficient cross-linking of several different copolymers even in the air and provide high spatial resolution. lack of diffusion of small molecules. In addition, it is compatible with photolithography and thus suitable for the production of high-resolution planar-structured films. Recently, strong biopolymer-based hydrogel films with a thickness of 40–60 μm were prepared by mixing aqueous solutions of negatively charged κ-carrageenan and positively charged chitosan, evaporating the solvent, and then expanding the cast film to reach equilibrium. This gel membrane has biocompatibility and anti-adhesion properties, which makes it promising as an artificial sclera and membrane material in surgery [29].

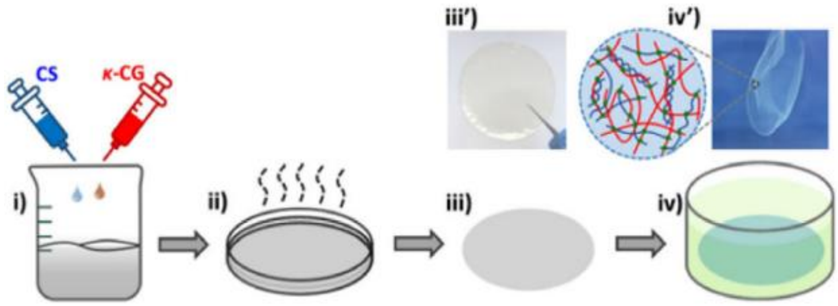

Figure 3: Solvent casting + polyelectrolyte complex - Hydrogel films prepared by casting the mixture solution of oppositely charged κ-carrageenan and chitosan and then rehydrating the dry film in water [29]

VIII. APPLICATIONS OF HYDROGEL FILM

1. **Smart Wound Dressings:** Hydrogel films are being developed with embedded sensors or responsive materials to create smart wound dressings. These dressings can monitor wound healing progress, detect infection, and deliver targeted therapy based on real-time feedback, enhancing patient care and treatment outcomes.
2. **3D Bio-printing:** Hydrogel films are utilized as bioink materials in 3D bioprinting technologies for tissue engineering and regenerative medicine applications. They provide a printable matrix for creating complex tissue structures with precise control over cell distribution and organization, facilitating the fabrication of functional tissues and organs.
3. **Surgical Adhesives:** Hydrogel films are explored as bioadhesive materials for surgical applications, replacing traditional sutures or staples. These adhesive films can seal surgical incisions, promote tissue adhesion, and provide a barrier against fluid leakage, reducing surgical complications and improving wound closure.
4. **Bioactive Implants:** Hydrogel films are incorporated into bioactive implants for controlled drug delivery and tissue regeneration. These implants can release therapeutic agents locally to promote bone regeneration, cartilage repair, or dental tissue engineering, offering potential solutions for orthopedic and dental surgeries.
5. **Flexible Electronics:** Hydrogel films are integrated into flexible electronics as stretchable substrates or encapsulation materials. These flexible electronics can be worn on the skin or implanted in the body for biosensing, drug delivery, or neuromodulation applications, enabling personalized healthcare monitoring and therapeutic interventions.
6. **Sustainable Packaging:** Hydrogel films are explored as eco-friendly alternatives for sustainable packaging materials. These biodegradable films can be derived from renewable sources and exhibit excellent barrier properties against moisture, oxygen, and microbial contamination, reducing environmental impact and enhancing food preservation.
7. **Bioartificial Organs:** Hydrogel films are utilized in the fabrication of bioartificial organs for regenerative medicine and transplantation purposes. These organ scaffolds can be seeded with patient-derived cells and cultured in vitro to develop functional tissues or organs, offering potential solutions for organ transplantation shortages and personalized medicine.
8. **Personalized Medicine:** Hydrogel films are employed in personalized medicine approaches for drug screening and patient-specific therapy. These films can be functionalized with patient-derived cells or disease models to evaluate drug efficacy, toxicity, and personalized treatment responses, advancing precision medicine and therapeutic development.
9. **Cosmetic Applications:** Hydrogel films are incorporated into cosmetic formulations for skincare and beauty applications. These films can deliver active ingredients, such as antioxidants, moisturizers, or anti-aging compounds, to the skin, promoting hydration, rejuvenation, and overall skin health.
10. **Environmental Remediation:** Hydrogel films are utilized in environmental remediation strategies for water purification and pollutant removal. These films can absorb and encapsulate contaminants, such as heavy metals or organic pollutants, from water sources, contributing to environmental sustainability and resource conservation [30]

IX. CONCLUSION

In conclusion, botanical bandages represent a promising frontier in the realm of wound healing, offering a natural and effective alternative to conventional wound dressings. Through this comprehensive review, we have explored the potential of herbal hydrogel films in harnessing the therapeutic properties of botanical extracts for enhanced wound care. From ancient herbal remedies to modern hydrogel technology, the integration of botanicals into hydrogel films holds immense promise for promoting the healing of acute and chronic wounds. These botanical ingredients, rich in bioactive compounds such as antioxidants, antimicrobials, and anti-inflammatory agents, exhibit synergistic effects that contribute to accelerated wound closure, reduced inflammation, and improved tissue regeneration. The unique properties of hydrogel films, including moisture retention, conformability, and biocompatibility, complement the therapeutic benefits of botanical extracts, creating an ideal environment for optimal wound healing. Furthermore, the biodegradable nature of these films aligns with the growing demand for sustainable and eco-friendly wound care solutions. In summary, by harnessing the healing potential of botanicals within the framework of hydrogel films, we have the opportunity to revolutionize wound management and promote the well-being of patients through a holistic and sustainable approach.

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