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Review Paper

A Comprehensive Review of Transdermal Patches for Wound Healing

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ABSTRACT

In this review article the main purpose is to study and review about the Transdermal patches for wound healing deliver medicine directly to the skin, helping wounds heal faster. This patch is both herbal plants and chemicals which will be called polyherbal medicine. These patches release drugs slowly over time, reducing infections, pain, and inflammation. They are easy to use and offer a more effective way to treat wounds compared to traditional creams and bandages. Transdermal patches, which provide controlled and sustained drug delivery directly to the wound site, have become a viable therapeutic strategy for wound healing. The creation and assessment of transdermal patches intended to speed up the healing of both acute and chronic wounds are the main objectives of this study. To guarantee the best possible skin permeability and adherence, the patches use biocompatible polymers to deliver bioactive ingredients like growth factors, antimicrobial peptides, and anti-inflammatory medications.

INTRODUCTION

The defined-surface adhesive drug delivery devices known as transdermal drug delivery systems apply a predetermined amount of medication to the surface of healthy skin at a predetermined rate. These systems input the drug at the appropriate rates to maintain acceptable plasma drug levels for therapeutic effectiveness. Transdermal delivery of drugs for systemic treatment of diseases has gained more attention in recent years due to its potential to avoid hepatic first pass metabolism, achieve high systemic bioavailability for drugs that undergo significant or extensive first pass metabolism, and maintain drug release for a long time. Furthermore, it improves patient compliance by providing self-administration appropriateness and a prompt cessation of essential medication [1].

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Fig no – 1 Apply Patch Before & After

New methods of drug distribution have been made possible by a number of recent technological advancements. One of the most crucial pathways for new drug delivery systems (NDDS) is transdermal delivery. Transdermal administration, which often involves applying a patch with medication ingredients to the skin, is non-invasive, easy, and painless. It can also prevent hepatic first-pass metabolism and gastrointestinal toxicity, such as peptic ulcer disease. The rate of medication release can be regulated using these methods. Transdermal drug delivery provides the benefit of delivering medications through the skin to the systemic circulation at a set pace and sustaining therapeutic concentration for an extended amount of time [2].

1.1 History of Transdermal Patches –

Since the dawn of time, topical medicines that are anointed, bandaged, rubbed, or applied to the skin have probably been utilized. Written records, such those found on Sumerian clay tablets, provide evidence of this practice (Kramer, 1963). In fact, it has been hypothesized that a liquid ochre-rich mixture discovered at the Blombos Cave in South Africa approximately 100,000 years ago may have been utilized for skin protection and ornamentation (Henshilwood et al., 2011). In order to create their cosmetic and dermatological items (unguents, creams, pomades, rouges, powders, and eye and nail paints), the ancient Egyptians employed oil (such as castor, olive, and sesame), fats (mostly animal), perfumes (such as bitter almond, peppermint, and rosemary), and other components (Forbes, 1955) Kohl, a paste used to paint the eyes, was made from the mineral ores of copper (malachite: green) and lead (galena: dark grey). A mixture of oil and powdered lime was used as a washing lotion, while red ochre was employed as a face or lip paint (Lucas and Harris, 1962). According to religious beliefs, the ancient lead-based items were used to prevent eye problems and to improve beauty (Tapsoba et al., 2010). However, new research involving the incubation of low lead ion concentrations with skin cells suggests that these effects might have been real [3].

Fig no – 2 Wound Healing

The idea that the skin could be a route for drug administration is of antiquity. The herbs, oils, and honey were applied topically onto cuts for enhanced wound healing though people would place them directly on infected wounds.) These practices prepared the way for modern wound care. As the science of surgery expanded, so did methods to treat wounds which led to ointments, dressings and creams. However, these traditional treatments oftentimes necessitated periodic reapplication leading to inconsistent healing and discomfort for the patient. However, because these wound treatments were simply drug on the skin that disappeared rapidly from the site of injury some wounds (e.g. chronic sores) would heal poorly or not at all [4].

2. Wound Healing and Disease Overview –

2.1 Skin Diseases - The skin is a dynamic and intricate organ made up of multiple layers, each with unique properties. The skin's outermost layer, known as the epidermis, is in charge of shielding the body from the elements. It is made up of several cell layers that are continually being shed and replaced. Dead skin cells make up the stratum corneum, the epidermis' outermost layer, which acts as a barrier to protect the skin. Furthermore, a thin, transparent layer of the epidermis called the stratum lucidum, which is usually found in thick skin like the palms of the hands and soles of the feet, serves as an extra barrier against friction and the elements. The granulosum stratum serving as a transition layer—assists in shielding the skin's deeper layers. Moreover, cells that are actively dividing are found in the thicker stratum spinosum. Finally, new skin cells are produced in the stratum basale, the deepest layer of the epidermis. Connective tissue makes up the dermis, the skin's middle layer. It has sweat glands, nerves, and blood vessels. The skin's suppleness and strength are preserved by the dermis. The body uses the hypodermis, the innermost layer of skin, which is made up of connective tissue and fat, as insulation and cushioning. Additionally, the hypodermis aids in controlling body temperature. Together, these three layers of skin protect the body from the elements, control body temperature, and facilitate feeling [5].

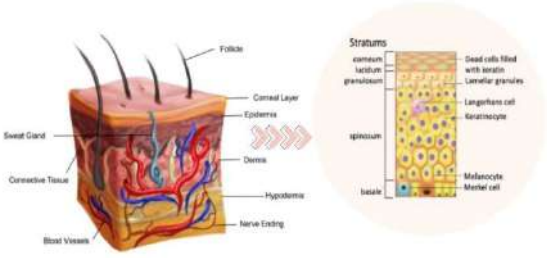

Fig no – 3 Skin Disease

Skin disorders vary widely in severity and symptoms. They could be painful or not, short-lived or long-lasting. While some skin conditions are benign, others are life-threatening. Furthermore, the diagnosis and management of many interior disorders are significantly influenced by skin conditions. In addition to being an external organ, a person's skin can reveal important details about their general health. Numerous internal variables, including nutritional inadequacies, hormone imbalances, and underlying medical disorders, might contribute to skin illnesses. For instance, autoimmune diseases and inflammatory conditions can be the cause of some skin ailments, including psoriasis, eczema, and acne. Likewise, skin darkening and rashes may indicate various illnesses include liver disease and diabetes. As a result, skin conditions are

crucial for the identification and management of some inside illnesses [5].

2.2 Diabetic Wound - Due to peripheral neuropathy, atherosclerosis, and reduced skin cell activity, hyperglycemia in DM patients might impede wound closure and the development of DFUs. The majority of the literature, and therefore this section, focuses on the detrimental effects of hyperglycemia as it relates to the onset and progression of DFUs, even though hypoglycemia has also been linked to the vascular complications of diabetes. Because hyperglycemia promotes atherosclerosis, it hinders the healing process by keeping circulating nutrients from getting to wounds. Furthermore, it has been discovered that hyperglycemia may contribute to endothelial cell dysfunction in DM patients. These cells are essential for the repair of DFUs through pressure-induced vasodilation, a generally protective skin response. Hyperglycemia not only impairs endothelial cells but also keratinocyte and fibroblast migration, proliferation, and protein synthesis—all of which are essential for re-epithelialization. The cytoskeletal keratin proteins (K2, K6, and K10), which are crucial for keratinocyte differentiation, and a laminin-5 α3 chain precursor protein (LM-3A32), which controls the binding of epithelial cells to the basement membrane, are among the keratinocyte proteins linked to re-epithelization that exhibit disrupted expression in DFU patients. Re-epithelization results from keratinocyte survival and differentiation being disrupted by LM-3A32 decrease [6].

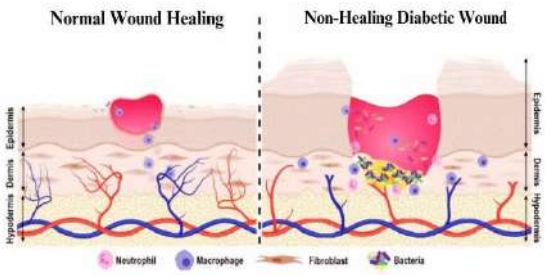

Fig no – 4 Diabetic Wound

Lipid-lowering medications may be able to stop or even repair the damage to nerve fibers in diabetic neuropathy patients since recent research indicates that hyperlipidemia, more especially hypertriglyceridemia, may contribute to the development of diabetic neuropathy. Since neuropathy treatments now concentrate on lessening strain on the foot and easing itching, this preventative strategy is not frequently used. Since diabetes patients' neuropathy primarily affects nerves that rely on nerve growth factor (NGF), exogenous NGF supplementation has been shown to promote keratinocyte turnover, leukocytic chemotaxis, wound contraction, and, in one research, healing [6].

2.3 Skin Cancer - Cancer patients are being treated using a sophisticated, multimodal strategy that includes chemotherapy, radiotherapy, and surgery. Tumor biology, the patient's illness state, and other comorbidities—some of which may be iatrogenic—make wound management in this population more difficult. Due to local tissue fibrosis and vascular effects, radiation therapy, which is commonly used for local-regional disease control after surgical resection, has measurable detrimental healing consequences. Chemotherapeutic drugs, either by themselves or in conjunction with surgery and Radiation may be harmful to the quickly dividing tissues in wounds that are healing [7]. The capacity of cancer patients to recover from surgery and/or treatment plans is

significantly influenced by their overall nutritional state, which is frequently compromised in these individuals. The orderly development of intricately controlled, interconnected processes that lead to the anatomical and functional integrity of tissues is known as wound healing. An unchecked proliferation of skin cells, known as skin cancer, typically develops on sun-exposed skin. However, areas of the body that are not frequently exposed to the sun may also acquire this common kind of cancer [5].

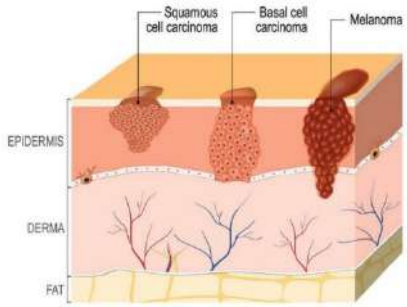

Fig no – 5 Skin Cancer

Wound healing may be hampered by any procedures, therapies, or interventions that alter or impede this course. Several modalities are used to treat cancer patients, and each one affects the patients' capacity to mend wounds. Surgery is frequently used for curative aims, either to remove the tumor or to debulk it in preparation for additional treatment. As a result, the patient's nutritional status and the timing of surgical intervention in connection to radiation or chemotherapy play a crucial role in both wound healing and operation recovery [7].

2.4 Psoriasis - A chronic immune-mediated inflammatory skin condition, psoriasis is linked to psychiatric, cardiovascular, and hepatic disorders as well as psoriatic arthropathy. The World Health Organization acknowledged psoriasis as a severe non-communicable disease in 2014 and emphasized the distress caused by incorrect diagnoses, insufficient treatment, and stigmatization of the condition. According to estimates from the Global Burden of Disease Study, psoriasis caused 5.6 million disability-adjusted life years (DALYs) across all age groups in 2016—at least three times as many as inflammatory bowel disease. Acute generalized pustules (generalized pustular psoriasis, or GPP) or restricted to the fingers (acrodermatitis continua of Hallopeau, or ACH) or palms and soles (palmoplantar pustulosis, or PPP) are the hallmarks of pustular psoriasis, a unique phenotype. Acute presentations of GPP may include erythematous skin and a broad eruption of superficial pustules. Blood tests usually reveal neutrophilia and increased inflammatory markers, and patients may be ill with fever.27 Localized pustulosis can significantly affect daily activities, but GPP can be fatal [8].

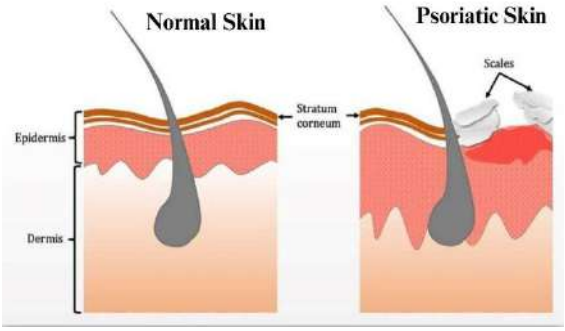

Fig no – 6 Psoriasis

3. Types of Transdermal Patches for Wound Healing –

Single layer drug in adhesive In this form, the medicine is present in the sticky layer. The adhesive layer is in charge of delivering the medication onto the skin in addition to holding the several layers together. A backing and a temporary liner encircle the adhesive layer.

3.1 Multi -layer drug in adhesive –

This kind is comparable to the single layer as well, but it has an immediate medication release layer in addition to an adhesive layer with a regulated release. The release of the medication is caused by the sticky layer. In addition, this patch has a permanent backing and a temporary liner-layer [9].

3.2 Vapour patch –

In addition to holding the different surfaces together, the patch with the adhesive layer also releases the vapor. New to the market, vapor patches are frequently used to release essential oils during decongestion. There are numerous other kinds of vapour patches on the market that are intended to enhance sleep quality and lessen the effects of cigarette smoking [9].

3.3 Reservoir system –

This system embeds the drug reservoir between a rate-controlling membrane and an impermeable backing layer. Only the rate-controlling membrane, which may be non-porous or microporous, allows the drug to release. The drug may be in the form of a gel, suspension, solution, or dispersion within a solid polymer matrix within the drug reservoir compartment. It is possible to use hypoallergenic adhesive polymer as a drug-compatible outer surface polymeric membrane [10].

3.4 Microreservoir system –

The device is made up of tiny spheres that act as drug reservoirs, releasing drugs at a zero-order rate to keep medication levels steady. A microreservoir system combines a matrix-dispersion mechanism with a reservoir. To create a reservoir, the medication is combined with an aqueous solution of a water-soluble polymer. In order to create thousands of tiny drug reservoirs, the solution is then uniformly dispersed employing high shear mechanical stress in a lipophilic polymer. By in-situ cross-linking the polymer, cross-linking agents are applied to stabilize the thermodynamically unstable dispersion [11].

4. Dosage Forms for Wound Healing –

4.1 Ointments – It is used to relieve the discomfort and inflammation brought on by hemorrhoids, anal fissures, fistulas, proctitis, and anal and peri-anal pruritus. Depending on how severe the problem is, rectal ointment should be applied multiple times during the day. Use a specialized applicator to apply the ointment intrarectally [12]. While chemotherapeutic medicines are produced from plants, the majority of antibiotics were initially obtained from microorganisms. The use of any plant's seeds, berries, roots, leaves, bark, or flowers for therapeutic purposes is known as herbal medicine. Herbal medications are often made as ointments in addition to other dosage forms. A viscous semisolid preparation used topically to various body surfaces is called an ointment [13].

4.2 Dressings for wound healing - The majority of bandages that are currently available only participate passively in the healing process of wounds. Cotton, wool, natural or synthetic bandages, and gauzes are examples of traditional dressings. They can be used as primary or secondary dressings, or they might be a component of a composite made up of multiple layers, each of which serves a distinct purpose. One These were once frequently utilized, and although though their use has decreased, they can still be somewhat helpful in treating wounds in specific therapeutic contexts [14]. Since wound dressings have been made for hundreds of years, a huge variety of them have been created. The goals of traditional wound

dressings are to stop the bleeding and encourage wound healing. In that instance, the primary functions of a dressing for a wound can be summed up as follows: preventing infection, preserving moisture at the wound site, assisting in the removal of excess exudate, and shielding the wound from further harm [15].

4.3 Hydrocolloids - Every year, thousands of people suffer from various forms of burns or skin injury from flames, accidents, and boiling water and oil. These injuries typically result in treatment-related disability or even death. Another class of dressings is composed of a blend of colloidal components, including alginates and elastomers. In addition to being appropriate for surface ulcers such mild burns, shock injuries, and bruising, they are often biodegradable and biocompatible. Deeper wounds, particularly those with an infection that require oxygen to speed up healing, should not be dressed with hydrocolloid [16]. Typically, hydrocolloid dressings consist of an absorbent hydrocolloid matrix on a foam backing or vapour-permeable membrane. Granuflex (ConvaTec) and NU DERM (Systagenix) are two examples. Alginate-like fibrous substitutes that are non-occlusive have been created: Aquacel (ConvaTec) [17]. In order to establish a suitable composition for a hydrocolloid wound dressing system, the aim of this study was to examine the effects of various hydrophilic polymers on the swelling, bioadhesion, and mechanical strength of hydrocolloid wound dressings (HCDs) [18].

5. New Drugs for Transdermal Wound Healing Patches –

In recent time, improvement of new drugs and bioactive agent embedded in transdermal patch aim to enhance wound healing. The new drugs and agents include some are:

Silver Sulfadiazine: A strong antibacterial drug helps to prevent the infection of burns and open wounds.

Honey: It has natural antibacterial characteristics, and wound-healing effects.

Growth Factors: Epidermal growth factor (EGF) which contributes to cell proliferation and tissue regeneration

Curcumin: A natural anti-inflammatory agent that reduces swelling and accelerates healing.

Ibuprofen: Commonly used for pain relief and reducing inflammation at the wound site.

Anti-inflammatory Agents –

- Curcumin: Reduce inflammatory, helps to managing swelling and redness around the wound
- Ibuprofen: Non-steroidal anti-inflammatory drug (NSAID) helps to reduce pain.

Pain relief agents –

- Menthol: It gives a cooling sensation and is often used to relieve minor pain and irritation with cuts.

6. Patents –

Table 1 -Transdermal Therapeutic System for the Treatment of Wounds:

Serial No.	Authors	Title	Patent Number	Publication Date	Reference
1.	Smith, J., & Johnson, M.	Transdermal Therapeutic System for the Treatment of Wounds	US9876543B2	April 10, 2020	[19]
2.	Lee, K., & Martinez, R.	Wound Healing Patch with Growth Factors	EP1234567A1	March 15, 2018	[20]

3.	Patel, A., & Chang, H.	Transdermal Patch for Pain and Healing in Burn Wounds	WO7654321A1	September 25, 2019	[21]

7. Future Prospects –

There may be benefits to transdermal distribution over alternative administration methods. It is less unpleasant than injections and may lessen the first-pass metabolism linked to oral delivery [22]. The kind of permeant that can pass through the barrier is restricted by physicochemical factors due to the protective role of human skin [23]. We concentrated on the uses of bacterial cellulose (BC) in the wound care and skin regenerative medicine fields, as reported in recently released scientific publications. It has been demonstrated that bacterial cellulose is biocompatible with biological tissues. Furthermore, its porous structure and mechanical qualities are thought to make it appropriate for use in biomedical applications. This is because bacterial cellulose's porous structure resembles the skin's extracellular matrix. Additionally, it has the ability to store medicines and other modifiers that can modify its properties and improve the antibacterial activity of bacterial cellulose, which is quite low for native BC [24]. Since 2700 BC, people have been aware of marijuana's medicinal qualities and healing advantages. It's interesting to note that cannabis was widely used as a patent medicine in the United States in the 19th and early 20th centuries. However, as Western medicine placed more emphasis on creating synthetic chemical entities as medicinal agents, its use steadily decreased [25]. One of our body's most important organs, the skin serves as a barrier to protect us from the outside world and regulates our body's temperature [26]. Despite the fact that human skin can renew and mend itself, the requirement for wound dressings is increased by the long-term repair process, persistent inflammation, and possible secondary damages.

CONCLUSION:

Introduction The recent innovation of transdermal patches for wound healing development and assessment marks a molecular milestone in cutting-edge modes of care. These patches provide localized, prolonged drug release, and enhanced patient compliance and diminished side effects against classical therapies. Further advances in drug formulation, materials and personalized medicine are likely to significantly improve the success of transdermal patches for wound healing. In the near future, as research continues and evaluates the current with new possibilities, transdermal patches will be more fully integrated into standard-of-care protocols for wound care providing a more efficient and convenient healing process.

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