Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

# Nanosponge Application in Burn Wound Models for Enhanced Wound Healing: A Review

**Ankit Kumar[1], Manish Pathak*[1]**

[1]*Faculty of Pharmacy, Swami Vivekanand Subharti University, Meerut (U.P) INDIA-250005*

***(Received: 07 January 2024 Revised: 12 February 2024 Accepted: 06 March 2024)***

**KEYWORDS**

Physiology of wound healing, local delivery systems.

**ABSTRACT:**

Specialized institutions focus on stabilization, infection control, and functional rehabilitation for burn patients, making them a major critical care concern. Burns research has resulted to better patient stabilization and lower fatality rates, especially for younger patients and those with moderate burns. However, patients in the intensive care unit encounter unique difficulties that make assistance and stabilization more difficult. Wounds from fires are difficult to treat, and sometimes even late intervention or lifetime rehabilitation is needed. Recent studies have led to improvements in burn wound treatment that will lead to enhanced functional recovery. Curcumin, a naturally occurring polyphenolic compound, has been employed in Ayurvedic medicine for thousands of years due to its anti-inflammatory and wound-healing effects. Curcumin's ability to eliminate ROS, boost collagen deposition, granulation tissue production, and wound contraction has been shown in several scientific studies. However, curcumin's potential in wound healing has been limited by its poor solubility, quick metabolism, and shorter plasma half-life. By encouraging the right kind of mobility throughout the different stages of wound healing, nanotechnology has shown to be an efficient method for hastening recovery time. Nano-carriers loaded with curcumin are utilized to specifically target wounds for drug delivery. Curcumin and its nano-formulations have been discussed in this review for its potential in promoting wound healing.

## Introduction

Sskin is the biggest organ in the human body [1]. It shields the interior structures from environmental stressors that are mechanical, chemical, biological, and physical in any form. In addition, it has a role in sensing, immune-regulatory monitoring, thermoregulation, preventing water loss, and agglutination of vitamin D3 [2-4]. A wound is any impairment or abnormality to the skin's normal structure. According to their location, depth, cause, kind of harm, and appearance, wounds may be categorized [5]. Wounds are categorized as either acute or chronic in clinical terms. Acute wounds heal on their own in 8 to 12 weeks, while chronic wounds take longer to heal because of ongoing inflammation (sometimes even months). Chronic wounds are caused by a number of reasons, including age, obesity, accidents, and long-term illnesses including diabetes and cancer [6, 7].

The physiological process of wound healing is complex and involves the synchronized overlapping stages of proliferation, inflammation, hemostasis, and tissue remodeling [8]. The most important response in the first minutes after an injury is hemostasis. Fibrin is activated at the site of damage by platelets and inflammatory cells, in the initial phase of wound healing; a mesh-like structure acts as a binding agent, effectively holding platelets together. When combined with vasoconstriction, this mesh formation creates a clot that plays a crucial role in halting additional bleeding [9]. The subsequent stage in the wound healing process is known as inflammation, which follows the hemostasis phase. Neutrophils are recruited to clear and prepare the wound for healing once a fibrin clot forms, a process facilitated by the complement cascade. The phagocytic cell's secretion of transforming growth factor (TGF-) is an important signal for starting the healing process. These factors work together to draw fibroblasts, keratinocytes, and endothelial cells to repair the injured blood vessels. The third phase is called proliferation, and it is at this time that the wound contracts and dermal and subcutaneous tissues are replaced.

Fibroblast cells induce the creation of collagen, epithelialization, and angiogenesis. Fibroblasts are stimulated to produce collagen by TGF-β platelets and

Journal of Chemical Health Risks

www.jchr.org

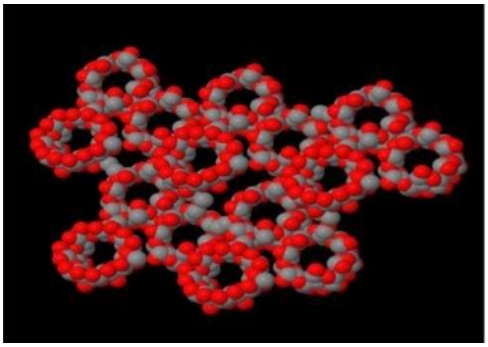
JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

macrophages. The last stage of this process is remodeling, which is the healing phase; it consists of the skin's fibroblast cells forming wound surface renewal and collagen type I at the site of injury, The next step involves the cross-linking and reorientation of this structure along tension lines [9, 10]. Various environmental and genetic factors, such as diabetes, hinder the body's innate wound healing capacity. Wounds associated with diabetes exhibit multiple irregularities, including heightened inflammation, anomalous cellular infiltration, disrupted cytokine production, neuritis, and impaired neo-angiogenesis. The increasing expenses of healthcare, a growing elderly population, and the prevalence of biofilms in medical contexts have also become significant factors, and the persistent worldwide threat of diabetes and obesity all contribute to the enormous clinical, social, and economic burden that chronic wounds pose. According to the retrospective study, more than 8.2 million Medicare recipients had wounds in 2018. There is expected to be a $15-22 billion annual demand for wound care products by 2024. An estimated 5.7 million people in the US alone have chronic wounds, and their yearly medical expenses come to around USD 20 billion [11]. All of these points to the need and breadth of research that needs to be done on wound healing. Because they encourage natural mending processes, plants have traditionally been an integrated and most extensively researched field in this respect [12]. Scientific progress has caused a change in focus from entire plants to their active chemical components. The leader in the field of wound healing is curcumin. Curcuma longa and Curcuma aromatica rhizomes naturally contain curcumin, a low-molecular-weight polyphenolic component [13].

The most abundant bioactive component found in turmeric rhizomes is curcumin (77%) which is followed by demethoxycurcumin (17%), bisdemethoxycurcumin (3%), and cyclocurcumin (3%). It has long been used in traditional medicine to alleviate inflammation and promote the healing of damaged wounds. It is well-established that topical use of curcumin contributes significantly to wound healing processes. Curcumin promotes wound healing overall by acting at many stages, including the inflammation, maturation, and proliferative phases. Curcumin's medicinal effectiveness is, however, limited by a few characteristics, including poor bioavailability, low water solubility, and quick metabolism. Another drawback of curcumin is that it might be toxic at high quantities when used topically [13–15]. In order to fully realize curcumin's potential in wound healing, it would be worthwhile to explore the utilizing various nano delivery systems to regulate its constraining elements. This review focuses on the role and relevance of curcumin and its nano-formulations in the healing process. The literature also covers a variety of related pharmacological actions.

Nanosponge is a novel material with a few-nanometer hollow that may encapsulate numerous molecules [61]. These particles may convey lipophilic and hydrophilic compounds and make water-insoluble molecules soluble [62]. A virus-sized, biodegradable scaffold, nanosponge. To cross-link long polymer strands, tiny molecules having affinity for polymer components are combined in solution [63]. They have transformed disease therapy, and early studies demonstrate that this technique targets breast cancer cells five times better than standard methods [64].

Fig: 1- Structure of Nanosponge



Polymer: Polymers alter nanosponge development and performance. For complexation, the nanosponge cavity size should accommodate drug molecules of a certain size. Functional and reactive groups must be replaced for polymer crosslinking. Choice of polymer depends on desired release and drug encapsulation [65].Examples include highly crosslinked polystyrenes, cyclodextrin, and its derivatives, such as Alkyloxy carbonyl, Methyl β-Cyclodextrin, and 2-Hydroxy Propyl β-Cyclodextrin.Ethylcellulose, polyvinyl alcohol.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

Crosslinkers: The polymer structure and medication formulation determine the crosslinking agent. Carboxylic acid dianhydrides, Diphenyl Carbonate, Diarylcarbonates, Diisocyanates, Pyromellitic anhydride, Epichloridrine, Glutaraldehyde, 2, 2-bis (acrylamido) Acetic acid, dichloromethane.

Preparation of Nanosponges:

Solvent Method: the polymer is combined with an appropriate solvent, particularly an aprotic solvent that is inpolar, such as dimethylformamide or dimethyl sulfoxide. After that, this combination is added to an excessive amount of cross-linkers, ideally with a crosslinker-to-polymer molar ratio of 1:4. The reaction is carried out at temperatures ranging from 100 degrees Celsius to the temperature at which the solvent is in a state of reflux, and the duration of the reaction ranges from one to forty-eight hours. Dimethyl carbonate and carbonyl diimidazole are two examples of carbonyl compounds that are considered to be the most effective cross-linking agents. Following the completion of the reaction, the solution should be allowed to cool at room temperature. After that, the product should be added to a significant quantity of extra double-distilled water, a vacuum filter should be used to collect the product, and the Soxhlet purification process should be extended.

Emulsion Solvent Diffusion Method: Nano-sponges may be made from ethyl cellulose and polyvinyl alcohol in various quantities. Improved drug loading and customized release are achieved by changing drug-polymer ratios. The medication and polymer dissolved in 20 ml of dichloromethane are slowly added to a particular quantity of polyvinyl alcohol in 100 ml of aqueous external phase using a magnetic or mechanical stirrer at 1000-1500 rpm for 3-5 h. Filter and dry nanosponges in a 40 °C oven for 24 h before packaging.

Ultrasound-assisted Synthesis: Under ultrasonic and solvent-free conditions, the polymer reacts with the cross-linking agent. Polymer and cross-linking agents are combined in the flask. In a water-filled ultrasonic bath, heat the flask to 90 ºC and sonicate for 5 hours. Cool and wash to remove unreacted polymer. Purification included extended Soxhlet extraction with ethanol. Store the product at 25 ºC after vacuum drying [66].

The quasi-emulsion solvent diffusion approach may also be used to make nanosponges with varying polymer quantities. The internal phase is prepared by dissolving eudragit RS100 in a solvent. Add the medicine and dissolve it under ultrasound at 35 °C. Pour the inner phase into the PVAaqueoussolution (outerphase), stir for 1 h, and filter to separate nanosponges. Dry the nanosponge in a 40 ºC air oven for 12 hours [67].

Hypercross-Linked B-Cyclodextrin: Here, β-cyclodextrin serves as a drug delivery carrier. Reacting cyclodextrin with a crosslinker produces nanosponges.Due to its 3D network, it may be a protein-sized spherical structure with channels and pores. Cyclodextrin interacts with diisocyanate, dicarbonate, etc. For molecular connection, sponge size is determined by porosity and surface charge density. Neutral or acidic nanosponges may be made. Nano sponges typically have a diameter of less than 1µm, however fractions less than 500 nm may be used. They improve water solubility of weakly water-soluble medicines. They are solid particles crystallized.[68]

Polymerization: The monomer makes a non-polar drug solution and adds an aqueous phase with a surfactant and dispersion agent to suspend it.Once catalyzed or heated, the monomer forms a suspension of distinct droplets of the required size. Polymerization creates a porous reservoir-type structure.

Drug loading into Nanosponges:Pre-treat drug delivery nanosponges to produce particles below 500 nm. Sonicating and centrifuging the nanosponge in water removes aggregates and creates a colloidal component. The supernatant is removed and freeze-dried. Make an aqueous nanosponge suspension, scatter the surplus drug, and stir continuously for a specified duration. Centrifugation separates the undissolved and complexed drugs after compounding. After solvent evaporation or freeze-drying, nanosponges form solid crystals.

**2. Underlying mechanisms of burn injuries**

Dry thermal burns (resulting from fire or flame exposure) and wet thermal burns (caused by scalding water) constitute approximately 80% of all reported burn cases [16]. The severity of these burns can be classified in various ways. When a significant area of

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

skin, typically 20% or more of the total body surface area (TBSA), is affected, it can trigger systemic responses extending beyond the localized burn site damage [17]. Burn shock is characterized by increased hydrostatic pressure in the microvasculature, elevated capillary permeability, and fluid and protein redistribution from intravascular to interstitial spaces, heightened systemic vascular resistance, reduced cardiac output, and hypovolemia requiring fluid resuscitation [18]. Interstitial edema occurs rapidly within the first eight hours post-burn and gradually over the subsequent eighteen hours [19]. The necessary resuscitation volume is determined based on the patient's weight (or body surface area) and the burn severity, with additional considerations including the extent of full-thickness burns, time elapsed since the incident, and the presence or absence of inhalation injuries. The actual infusion rate is then adjusted hourly, taking into account physiological responses like urine output to ensure adequate resuscitation.

Hyper-metabolism, chronic inflammation, and loss of lean body mass following successful resuscitation remain longer in patients with more body surface area burned [20].

The increased vulnerability to infection that results from an impaired immune system may also lead to sepsis. Wound healing is slowed by chronic inflammation and increased metabolic demand. There is a positive correlation between the size of the burn and the number of circulating cytokines [21] and the size of the hyper-metabolic response. Similarly, the severity of the burn is an excellent predictor of the likelihood of dying in the hospital and the length of time spent there.

Based on variables such as blood flow and tissue damage, one model classifies the burn site into three distinct zones [22]. The wound's core, or the zone of coagulation, takes the brunt of the heat and wear and tear. Extreme protein denaturation, disintegration, and coagulation at the site of injury lead to tissue necrosis because Proteins undergo denaturation when exposed to temperatures exceeding 41°C (106°F). The region surrounding the core coagulation zone is known as the stasis zone, or ischemic zone, characterized by diminished perfusion and the potential for salvaging tissue. If not addressed, hypoxia and ischemia in this area may result in tissue necrosis within 48 hours after the injury [23]. Although the exact processes causing necrosis and apoptosis in the ischemia zone are still unknown, they seem to include delayed-onset apoptosis that occurs 24 to 48 hours after burn and acute autophagy that occurs during the first 24 hours of damage [24]. Depending on the severity of the burn damage, further research has shown that apoptosis may begin as early as 30 minutes after the burn. Preclinical research has shown encouraging decreases in necrosis with systemic antioxidant treatment, suggesting that oxidative stress may contribute to the formation of necrosis [25]. The zone of hyperemia in the outermost parts of the burn site gets enhanced blood flow by inflammatory vasodilation and is expected to heal, barring infection or other harm.While there are some differences between burns and other types of wounds, all wounds go through Wound healing is a dynamic and multifaceted process with phases that overlap [26]. Various factors, including systemic inflammation, can influence this process (see Table 1). In the initial inflammatory phase, neutrophils and monocytes are mobilized to the injury site through localized vasodilation and fluid extravasation to initiate an immune response, which is further sustained by the recruitment of macrophages via chemokines [27]. The inflammatory phase of wound healing not only protects the site from infection but also removes damaged tissue and sets out signals that promote healing. The activation of keratinocytes and fibroblasts by cytokines and growth factors characterizes the proliferative phase, which occurs after and overlaps with the inflammatory response. During this stage of the wound healing process, keratinocytes move across the site to help with closure and vascular network repair [28]. Closure and revascularization are two processes in the healing process that are determined by this interconnected system include immunological, stromal, and endothelial cells.

Table 1: Stages in the wound healing process [29]

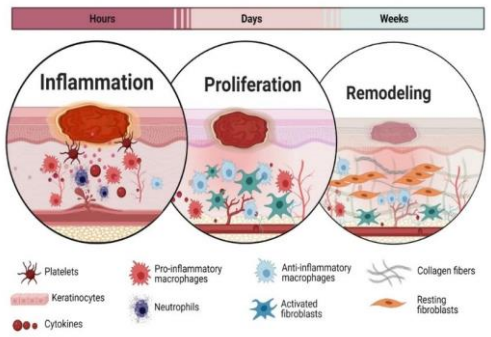
| Phase | Characteristics | Key players |
|---|---|---|
| Inflammatory | Vasodilation | Neutrophils |
| | Fluid extravasation | Monocytes |
| | Edema | Macrophages |
| Proliferative | Wound closure | Keratinocytes |

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

| | | |
|---|---|---|
| | Revascularization | Fibroblasts |
| Remodeling | Wound maturation | Collagen |
| | Scarring | Elastin |
| | | Fibroblasts/myo-fibroblasts |

The last stage of healing entails reconstructing the wound and overlaps with the proliferative phase. The wound scar grows throughout the remodeling phase as collagen and elastin are deposited and are constantly rebuilt when fibroblasts develop into myofibroblasts [30]. Myofibroblasts are important in wound contracture because they take on a contractile nature. Transforming fibroblasts into myofibroblasts controls the pliability of the healed wound by balancing contraction and re-epithelialization.

Fig 2: Stages in wound healing




**3. Enhancing the healing of burn wounds**

Inflammation: Inflammation (caused by cytokines, kinins, lipids, and other chemicals) is necessary for the proliferative phase of wound healing, during which leukocytes and macrophages are recruited and activated to begin the repair process [31]. In the proliferative phase, cytokines recruited during the inflammatory phase Stimulation of keratinocyte and fibroblast activation or migration from transformed hair follicles and similar epidermal structures to support wound re-epithelialization and eventual closure. Although this suggests that inflammation plays a crucial role in wound healing, hypertrophic scarring has also been associated with abnormal inflammatory pathways, and anti-inflammatory medications may worsen symptoms and postpone wound healing [32]. Inflammation is often accompanied by significant edema that is brought on by a number of variables, such as vasodilation, extravascular osmotic activity, and enhanced micro-vascular permeability. Prolonged or excessive inflammation and edema worsen pain and delay the healing of wounds [33]. Remarkably, research indicates that tissue regeneration may occur without the need for inflammation when there is no infection. Since inflammation may affect burn wound healing in both positive and negative ways, managing inflammation and only using therapeutic intervention when edema and inflammation reach unacceptable levels is the clinical issue. Large burns are difficult to treat for inflammation, as has been recently covered in depth elsewhere. Wound healing is hampered by conventional anti-inflammatory therapies that aim to suppress prostaglandin production, such as glucocorticoids and non-steroidal anti-inflammatory medications [34]. Nonetheless, a number of modest trials have shown that the use of steroids may shorten the hospital stay, lessen pain, and decrease inflammation in burn patients. As a result of its efficacy in preventing infection and scarring, early excision has become the standard of care for treating both full- and deep-skin burns [35].

Opioids and other non-traditional anti-inflammatory medications have drawn a lot of interest, but they haven't yet been able to convert encouraging preclinical findings into clinical use for wound healing. Clinical trials have revealed little to no impact on inflammation, despite the bulk of animal research showing Opioids consistently inhibit inflammation in peripheral neurons [36]. Additionally, topical morphine sped up the proliferative phase and delayed the first inflammatory

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

phase. This is corroborated by in vitro research that demonstrates the promotion of keratinocyte migration by opioids. There are currently no extensive clinical studies assessing the effectiveness of opioids on wound healing.

Infection: The skin is essential for the maintenance of fluid balance and body temperature, as well as for the provision of sensory input, metabolic and immunological support, The skin serves both as a protective barrier against the external environment and as an integral component of the innate immune system. Injury to this barrier following a burn weakens the body's natural defenses and elevates the risk of bacterial infection [37]. Using Pseudomonas aeruginosa in a rat model, criteria for identifying burn wound infections were established. These criteria encompassed wound colonization, tissue invasion within a span of 5 days, loss of granulation tissue, hematogenous lesions, leukopenia, hypothermia, and ultimately mortality, representing progressive stages in the development of burn wound infections. In patients with burns, particularly those with drug-resistant infections, the consequences of such infections can be far-reaching, including extended hospital stays, delayed wound healing, increased healthcare costs, and even higher mortality rates [38]. Furthermore, severe immune responses to infections, such as septic shock, may result in low blood pressure and impaired perfusion to the skin and other vital organs, all of which can slow the healing of wounds. Additionally, sepsis and multi-organ failure are the main causes of mortality after severe burns, thus treating burn patients with an emphasis on infection control and prevention is crucial [39]. It's challenging to diagnose an illness early and accurately: Since procalcitonin ability to diagnose burns is debatable; the most often employed tests are C-reactive protein and the white blood cell count. Recently, consensus criteria of infection and sepsis have been put out that are more pertinent to the burn patient and are often used in clinical settings, but they still need to be validated. There have been several reviews of the treatment of burn wound infections elsewhere. Systemic infections and mortality have continuously declined since the 1970s and later with the introduction of topical antibiotics, such as silver sulfadiazine in the 1970s and mafenide in the 1960s, as well as early excision and grafting [40]. But even after burn injuries, bacterial infections, both Gram-positive and Gram-negative, continue to rank among the leading causes of death. The use of bacterial cultures may help in the selection of a suitable antibiotic, particularly when there is bacterial drug resistance. However, in order to optimize the effectiveness of antibiotics, it is important to take into account the changed pharmacokinetic characteristics in burn patients and modify the dosage appropriately [41]. Significantly, fungal wound infections are linked to higher death rates in major burns (>30% TBSA) because there are no effective topical antibiotics for invasive fungal infections [80]. Due to the high mortality, any indication of an invasive burn wound infection must be investigated quickly, usually by histology, and the wound must be excised or re-executed [42].

Nutrition: The degree and duration of sustained hyper-metabolism, hormone increases, and muscle atrophy that accompany severe burn injuries are specific to burns and all influence the clinical outcome. As such, it has been reviewed elsewhere that minimizing the effects of a hyper-metabolic state and ensuring sufficient nutrition are important elements that influence the healing and recovery process after a burn injury [43]. It is challenging to strike a balance between

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

the extra calories required to fulfill hyper-metabolism's demands and the negative effects of overindulging in certain nutrients. The topic of nutritional assistance after burn damage is complicated. For instance, vigorous feeding and early excision in children do not reduce energy expenditure, but they are linked to a reduced incidence of burn sepsis, a reduction in muscle protein catabolism, and a considerable drop in the number of bacteria found in excised tissue [44]. Adults who get early nutritional assistance had shorter hospital stays, faster wound healing, and lower infection risk. A number of dietary considerations need to be made. Consuming too many carbohydrates, for instance, might cause hyperglycemia, the effects of which include exacerbating systemic inflammation and wasting of muscle [45]. Increased susceptibility to sepsis and infection may also result from a diet high in fat, which may have a similar effect as severe burn injuries on immunosuppression. As a result, a burn patient's intake of fat and carbs must be strictly monitored.

Resuscitation: Stabilization of severe thermal burns involving a significant skin area (>20% TBSA) need fluid resuscitation. Maintaining organ perfusion with the least amount of fluid required is the aim of fluid resuscitation, despite the fact that volume recommendations and fluid compositions vary greatly throughout centers [46]. Typical classical resuscitation formulae, such the Parkland and modified Brooke formulas use lactated Ringer's crystalloids, which are sodium, chloride, calcium, potassium, and lactate-containing. The use of colloids as adjuncts, such as albumin or fresh frozen plasma, has shown effective in lowering the overall volume during large-volume resuscitations. Little is known about how resuscitation affects wound healing, despite a great deal of study on the compositions and quantities of resuscitation fluid [47]. A recent meta-analysis revealed a significant correlation between hypernatremia and the frequency of grafting operations, indicating that elevated blood sodium levels might prevent graft take. We have recently shown that patients who got less fluid resuscitation in a 24-hour period healed much faster.

Covering and Grafting of Wounds: There are many distinct skin replacements and dermal analogs (Table 2), which may be roughly categorized into two groups: those that replace the dermis and those that replace the epidermis. Normal dermal components are absent from epidermal replacements, which are typically just a few cell layers thick. Acellular matrices often derived from human sources (e.g., Integra; Integra LifeSciences, Plainsboro, NJ, USA) or other sources (e.g., Alloderm or GraftJacket), are commercially available dermal replacements [48]. The semisynthetic, bilaminar material Bio-brane (Smith & Nephew, London, UK) is made up of an epidermal analogue of silicone and a dermal analog of nylon mesh combined with pig collagen. For the temporary closure of donor sites and superficial burns, bio-brane is employed. Currently under development are dermal scaffolds that promote revascularization by creating a favorable cellular environment with the help of stem cells and growth factors.

Table 2: Alternatives for Skin Coverage and Substitution [49]

| Product Name | Classification | Characteristics | Availability |
|---|---|---|---|
| EpiDex | Autologous | Keratinocyte-based | No |
| Alloderm | Acellular | Human origin | Yes |
| GraftJacket | Acellular | Human origin | Yes |
| Integra | Acellular | Bovine/shark origin | Yes |

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

| | | | |
|---|---|---|---|
| Biobrane | Acellular | Bio-composite bandage consisting of collagen and nylon fibers in silicone | Yes |
| Dermagraft | Cellular | Scaffold made of human fibroblasts (of neonatal origin) cultured on a biodegradable poly-glactin mesh. | Yes |
| Epicel | Cellular | Autologous cultured epidermal transplant | Yes |
| Recell | Cellular | Keratinocyte, fibroblast, Langerhans cell, and melanocyte autologous cell suspension | Yes |

**Tracking and anticipating wound recovery:**

The burn team's careful monitoring of the wound healing process—or lack thereof—cannot be replicated by any new skin-based device. Wound Flow, an electronic version of the traditional Lund-Browder diagram, was developed to facilitate the measurement and monitoring of burn injuries over time [50]. Wound Flow is a digital mapping program used to assess burn severity and track recovery. Future studies comparing healing rates and outcomes after different treatments will benefit from accurate tracking of the duration it takes for burn wounds to recover. Notably, this investigation showed that a notably greater risk of death was linked to delay wound healing [51].

Predicting whether or not a burn wound will heal on its own would be a huge help to patient care [52]. Moreover, the capacity to customize therapy for every patient will enhance patient outcomes; shorten the time it takes for a functional recovery, and save total healthcare costs. Biomarkers have the potential to facilitate customized treatment plans and provide light on the processes involved in wound healing.

Guidelines

- Proper burn size estimation using a Lund–Browder chart [53]
- Thoroughly adjusted fluid resuscitation, taking into account the dangers of both persistent hypo-perfusion and edema development. [54]
- Starting topical antimicrobial treatment (using creams or dressings containing silver or mafenide acetate) early on and effectively [55]
- A trained surgeon or wound care specialist inspects the wounds every day. [56]
- All full thickness and deep partial thickness burns are excised and grafted as soon as possible. [57]
- Severe treatment of infected wounds (resuscitation, excision or re-excision, broad-spectrum topical and systemic antibiotics) [58]
- Rehabilitation in the intensive care unit to reduce the functional effects of extended immobility and the development of contractures [59]

Table 4: Various examples of Nanosponges

| Drug | Nanosponge Vehicle | Category of drug | Study |
|---|---|---|---|
| Itraconazole | Betacyclodextrinand copolyvidonum | Antifungal | Solubility |

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

| | | | |
|---|---|---|---|
| Voriconazole | Ethyl cellulose, Poly methyl methacrylate 68. | Antifungal | Drug release |
| Miconazole Nitrate | Betacyclodextrin,Di-phenylcarbonate | Antifungal | Drug release |
| Celecoxib | Betacyclodextrin,N,N methylene diacylamine | NSAID | Solubility |
| Erlotinib | Betacyclodextrin | Tyrosinekinaseinhibitor (Anticancer) | Solubility |
| EconazoleNitrate | Ethylcellulose,PVA | Antifungal | Irritationstudy |
| Isoniazid | Ethylcellulose,PVA | Anti-tubercular | Drug release |
| Cephalexin | Ethylcellulose,PVA | Antibiotic | Drug release |
| Norfloxacin | BetacyclodextrinandDiphenyl carbonate | Antibiotic | Bioavailability |
| L-Dopa | Betacyclodextrin | Parkinson'sDisease | Drug release |
| Fenofibrate | Maizestarch,SDS | Fibrate | Solubility, Bioavailability |
| Nifedipine | Betacyclodextrin | Calcium-channelblocker | Solubility |
| Glipizide | Betacyclodextrin | Sulfonylurea | Drug release |
| Ibuprofen | EthylcelluloseandPVA | NSAID | Drug release |
| Resveratrol | Cyclodextrin | Antioxidant | Stability, cytotoxicity |
| Paclitaxel | Betacyclodextrin | Antineoplastic | Bioavailability |
| Camptothecin | Betacyclodextrin | Antineoplastic | Stability |
| Tamoxifen | Betacyclodextrin | Antiestrogen | Solubility |

## Conclusion

The numerous variables that impact wound healing must be balanced in order to minimize the duration of stay (and related treatment costs), the danger of infection, the time it takes to close the wound, and the total amount of time it takes to recover functionally from acute thermal injuries [60]. Several decades have passed since the first studies, both preclinical and clinical, addressed burn wounds. Considerable progress has been achieved in the treatment of patients, including monitoring the healing of wounds, creating innovative choices for grafts and coverings, managing inflammation, maximizing nutritional requirements, and experimenting with new pharmaceutical therapies [60]. Due to these efforts, there has been an improvement in patient survival and a corresponding reduction in the duration of stay, which lowers the expenses for both the patient and the healthcare providers. To assist the intensivist, a summary of specific clinical recommendations is given in Table 3. However, it is crucial to keep in mind that treatment decisions for burn patients must be customized to their individual needs because there are several factors (including age, TBSA, and comorbidities) that make caring for burn victims difficult. In order to further enhance burn wound care, current and future research will persist in identifying new targets and treatment paradigms.

## References

1. Gibran NS, Wiechman S, Meyer W, Edelman L, Fauerbach J, Gibbons L, et al. American Burn Association consensus statements. J Burn Care Res. 2013;34:361–5.
2. Mann R, Heimbach D. Prognosis and treatment of burns. West J Med. 1996;165:215–20.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

3. American Burn Association. Burn incidence and treatment in the United States: 2013 fact sheet. 2013. http://www.ameriburn.org/resources_ factsheet.php. Accessed 12 May 2015.
4. Sen S, Palmieri T, Greenhalgh D. Review of burn research for the year 2013. J Burn Care Res. 2014;35:362–8.
5. Wolf SE, Arnoldo BD. The year in burns 2011. Burns. 2012;38:1096–108.
6. Burd A. Research in burns – present and future. Indian J Plast Surg. 2010;43:S11–4.
7. Thomas SJ, Kramer GC, Herndon DN. Burns: military options and tactical solutions. J Trauma. 2003;54:S207–18.
8. American Burn Association. National Burn Repository 2014. 2014. http://www.ameriburn.org/2014NBRAnnualReport.pdf. Accessed 12 May 2015.
9. Kagan RJ, Peck MD, Ahrenholz DH, Hickerson WL, Holmes J, Korentager R, et al. Surgical management of the burn wound and use of skin substitutes: an expert panel white paper. J Burn Care Res. 2013;34:e60–79.
10. Nisanci M, Eski M, Sahin I, Ilgan S, Isik S. Saving the zone of stasis in burns with activated protein C: an experimental study in rats. Burns. 2010;36:397–402.
11. Robins EV. Burn shock. Crit Care Nurs Clin North Am. 1990;2:299–307.
12. Pham TN, Cancio LC, Gibran NS, American Burn Association. American Burn Association practice guidelines burn shock resuscitation. J Burn Care Res. 2008;29:257–66.
13. Shirani KZ, Vaughan GM, Mason Jr AD, Pruitt Jr BA. Update on current therapeutic approaches in burns. Shock. 1996;5:4–16.
14. Dries DJ. Management of burn injuries – recent developments in resuscitation, infection control and outcomes research. Scand J Trauma Resusc Emerg Med. 2009;17:14.
15. Porter C, Hurren NM, Herndon DN, Borsheim E. Whole body and skeletal muscle protein turnover in recovery from burns. Int J Burns Trauma. 2013;3:9–17.
16. Farina Jr JA, Rosique MJ, Rosique RG. Curbing inflammation in burn patients. Int J Inflamm. 2013;2013:715645.
17. Edgar DW, Fish JS, Gomez M, Wood FM. Local and systemic treatments for acute edema after burn injury: a systematic review of the literature. J Burn Care Res. 2011;32:334–47.
18. Sommer K, Sander AL, Albig M, Weber R, Henrich D, Frank J, et al. Delayed wound repair in sepsis is associated with reduced local pro-inflammatory cytokine expression. PLoS One. 2013;8, e73992.
19. Wilmore DW, Long JM, Mason Jr AD, Skreen RW, Pruitt Jr BA. Catecholamines: mediator of the hypermetabolic response to thermal injury. Ann Surg. 1974;180:653–69.
20. Sakallioglu AE, Basaran O, Karakayali H, Ozdemir BH, Yucel M, Arat Z, et al. Interactions of systemic immune response and local wound healing in different burn depths: an experimental study on rats. J Burn Care Res. 2006;27:357–66.
21. Pereira CT, Herndon DN. The pharmacologic modulation of the hypermetabolic response to burns. Adv Surg. 2005;39:245–61.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

22. Hussain A, Dunn KW. Predicting length of stay in thermal burns: a systematic review of prognostic factors. Burns. 2013;39:1331–40.
23. Colohan SM. Predicting prognosis in thermal burns with associated inhalational injury: a systematic review of prognostic factors in adult burn victims. J Burn Care Res. 2010;31:529–39.
24. Jackson DM. The diagnosis of the depth of burning. Br J Surg. 1953;40:588–96.
25. Hettiaratchy S, Dziewulski P. ABC of burns: pathophysiology and types of burns. BMJ. 2004;328:1427–9.
26. Kowalske KJ. Burn wound care. Phys Med Rehab Clin North Am. 2011;22:213–27.
27. Tan JQ, Zhang HH, Lei ZJ, Ren P, Deng C, Li XY, et al. The roles of autophagy and apoptosis in burn wound progression in rats. Burns. 2013;39:1551–6.
28. Singer AJ, McClain SA, Taira BR, Guerriero JL, Zong W. Apoptosis and necrosis in the ischemic zone adjacent to third degree burns. Acad Emerg Med. 2008;15:549–54.
29. Matylevitch NP, Schuschereba ST, Mata JR, Gilligan GR, Lawlor DF, Goodwin CW, et al. Apoptosis and accidental cell death in cultured human keratinocytes after thermal injury. Am J Pathol. 1998;153:567–77.
30. Deniz M, Borman H, Seyhan T, Haberal M. An effective antioxidant drug on prevention of the necrosis of zone of stasis: N-acetylcysteine. Burns. 2013;39:320–5.
31. Tiwari VK. Burn wound: how it differs from other wounds? Indian J Plast Surg. 2012;45:364–73.
32. Gurtner GC, Werner S, Barrandon Y, Longaker MT. Wound repair and regeneration. Nature. 2008;453:314–21.
33. Reinke JM, Sorg H. Wound repair and regeneration. Eur Surg Res. 2012;49:35–43. 34. Werner S, Krieg T, Smola H. Keratinocyte–fibroblast interactions in wound healing. J Invest Dermatol. 2007;127:998–1008.
34. Pastar I, Stojadinovic O, Yin NC, Ramirez H, Nusbaum AG, Sawaya A, et al. Epithelialization in wound healing: a comprehensive review. Adv Wound Care. 2014;3:445–64.
35. Widgerow AD. Cellular/extracellular matrix cross-talk in scar evolution and control. Wound Repair Regen. 2011;19:117–33.
36. Singer AJ, Clark RA. Cutaneous wound healing. N Engl J Med. 1999;341:738–46.
37. Hinz B. Formation and function of the myofibroblast during tissue repair. J Invest Dermatol. 2007;127:526–37.
38. Snowden JM. Wound closure: an analysis of the relative contributions of contraction and epithelialization. J Surg Res. 1984;37:453–63.
39. Shih B, Garside E, McGrouther DA, Bayat A. Molecular dissection of abnormal wound healing processes resulting in keloid disease. Wound Repair Regen. 2010;18:139–53.
40. Brack A, Rittner HL, Stein C. Immunosuppressive effects of opioids – clinical relevance. J Neuroimmune Pharmacol. 2011;6:490–502.
41. Rook JM, Hasan W, McCarson KE. Morphine-induced early delays in wound closure: involvement of sensory neuropeptides and modification of neurokinin receptor

expression. Biochem Pharmacol. 2009;77:1747–55.

42. Rook JM, McCarson KE. Delay of cutaneous wound closure by morphine via local blockade of peripheral tachykinin release. Biochem Pharmacol. 2007;74:752–7.
43. Bigliardi PL, Buchner S, Rufli T, Bigliardi-Qi M. Specific stimulation of migration of human keratinocytes by mu-opiate receptor agonists. J Recept Signal Transduct Res. 2002;22:191–9.
44. Stein C, Kuchler S. Targeting inflammation and wound healing by opioids. Trends Pharmacol Sci. 2013;34:303–12.
45. Church D, Elsayed S, Reid O, Winston B, Lindsay R. Burn wound infections. Clin Microbiol Rev. 2006;19:403–34
46. Ehterami, A.; Salehi, M.; Farzamfar, S.; Samadian, H.; Vaez, A.; Sahrapeyma, H.; Ghorbani, S. A Promising Wound Dressing Based on Alginate Hydrogels Containing Vitamin D3 Cross-Linked by Calcium Carbonate/d-Glucono-δ-Lactone. Biomed. Eng. Lett. 2020, 10, 309–319. https://doi.org/10.1007/s13534-020-00155-8.
47. Simões, D.; Miguel, S.P.; Ribeiro, M.P.; Coutinho, P. European Journal of Pharmaceutics and Biopharmaceutics Recent Advances on Antimicrobial Wound Dressing: A Review. Eur. J. Pharm. Biopharm. 2018, 127, 130–141. https://doi.org/10.1016/j.ejpb.2018.02.022.
48. Victor, P.; Sarada, D.; Ramkumar, K.M. Pharmacological Activation of Nrf2 Promotes Wound Healing. Eur. J. Pharmacol. 2020, 886, 173395. https://doi.org/10.1016/j.ejphar.2020.173395.
49. Augustine, R.; Rehman, S.R.U.; Ahmed, R.; Zahid, A.A.; Sharifi, M.; Falahati, M.; Hasan, A. Electrospun Chitosan Membranes Containing Bioactive and Therapeutic Agents for Enhanced Wound Healing. Int. J. Biol. Macromol. 2020, 156, 153–170. https://doi.org/10.1016/j.ijbiomac.2020.03.207.
50. Dreifke, M.B.; Jayasuriya, A.A.; Jayasuriya, A.C. Current Wound Healing Procedures and Potential Care. Mater. Sci. Eng. C 2015, 48, 651–662. https://doi.org/10.1016/j.msec.2014.12.068.
51. Aderibigbe, B.A.; Buyana, B. Alginate in Wound Dressings. Pharmaceutics 2018, 10, 42. https://doi.org/10.3390/pharmaceutics10020042.
52. Milne, K.E.; Penn-Barwell, J.G. Classification and Management of Acute Wounds and Open Fractures. Surgery (United Kingd.) 2020, 38, 143–149. https://doi.org/10.1016/j.mpsur.2020.01.010.
53. Zainuddin, N.; Ahmad, I.; Zulfakar, M.H.; Kargarzadeh, H.; Ramli, S. Cetyltrimethylammonium Bromide-Nanocrystalline Cellulose (CTAB-NCC) Based Microemulsions for Enhancement of Topical Delivery of Curcumin. Carbohydr. Polym. 2021, 254. https://doi.org/10.1016/j.carbpol.2020.117401.
54. Zhang, M.; Zhao, X. International Journal of Biological Macromolecules Alginate Hydrogel Dressings for Advanced Wound Management.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(2), 828-840 | ISSN:2251-6727

Int. J. Biol. Macromol. 2020, 162, 1414–1428. https://doi.org/10.1016/j.ijbiomac.2020.07.311.

55. Mohanty, C.; Sahoo, S.K. Curcumin and Its Topical Formulations for Wound Healing Applications. Drug Discov. Today 2017, 22, 1582–1592. https://doi.org/10.1016/j.drudis.2017.07.001.
56. Sen, C.K. Human Wounds and Its Burden: An Updated Compendium of Estimates. Adv. Wound Care 2019, 8, 39–48. https://doi.org/10.1089/wound.2019.0946.
57. Majumdar, A. Alternative Approaches to Wound Healing; Alexandrescu, P.S.E.-V.A., Ed.; IntechOpen: Rijeka, Croatia, 2016; p. 21. ISBN 978-953-51-2679-9.
58. Rafiee, Z.; Nejatian, M.; Daeihamed, M.; Jafari, S.M. Application of Curcumin-Loaded Nanocarriers for Food, Drug and Cosmetic Purposes. Trends Food Sci. Technol. 2019, 88, 445–458. https://doi.org/10.1016/j.tifs.2019.04.017.
59. Salehi, B.; Stojanović-Radić, Z.; Matejić, J.; Sharifi-Rad, M.; Anil Kumar, N.V.; Martins, N.; Sharifi-Rad, J. The Therapeutic Potential of Curcumin: A Review of Clinical Trials. Eur. J. Med. Chem. 2019, 163, 527–545. https://doi.org/10.1016/j.ejmech.2018.12.016.
60. Jiang, T.; Liao, W.; Charcosset, C. Recent Advances in Encapsulation of Curcumin in Nanoemulsions: A Review of Encapsulation Technologies, Bioaccessibility and Applications. Food Res. Int. 2020, 132, 109035. https://doi.org/10.1016/j.foodres.2020.109035.
61. Bano N: Multifunctional nanosponges for the treatment of various diseases: A review. Asian J Pharm Pharmacol 2019; 5.
62. Panda S, Vijayalakshmi S, Pattnaik Sand Swain RP: Nanosponges: A novel carrier for targeted drug delivery. Int J Pharm Tech Res 2015; 8.
63. Kapileshwari GR: Novel drug delivery system of luliconazole - Formulation and characterisation. J Drug Deliv Sci Technol 2020; 55.
64. Dasht Bozorg B: Transdermal and dermatological formulations for delivery of pharma- and cosmeceuticals intohealthyanddiseasedskin.ProQuest Dissertations and Theses 2020.
65. Krabicová I: History of cyclodextrin nanosponges. Polymers 2020; 12.
66. Jyoti P, Tulsi B, Popin K and Chetna B: An innovative advancement for targeted drug delivery: nanosponges.Indo Glob J Pharm Sci 2016; 06:59-64.
67. Darandale SS and Vavia PR: Cyclodextrin-based nanosponges of curcumin: Formulation and physicochemical characterization. In Journal of Inclusion Phenomena andMacrocyclicChemistryKluwer Academic Publishers 2013; 75: 315-22.
68. Allahyari S, Trotta F, Valizadeh H, Jelvehgari M and Zakeri-Milani P: Cyclodextrin-based nanosponges as promising carriers for active agents. Expert Opinion on Drug Delivery 2019; 16.