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

A REVIEW ON ENHANCING DIABETIC WOUND HEALING WITH MULTI-FUNCTIONING SELF ADAPTIVE HYDROGELS

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ABSTRACT

Wounds associated with diabetes are more complex and difficult to treat, this is because they are generally difficult to heal, and if left untreated. they lead to a lot of severe complications not forgetting the fact that they generate more costs than any other wound in the health facilities . This paper aims at examining the synthesis of multifunctional self —healing hydrogels for improvement Of diabetic wound healing with the developed hydrogels releasing growth factors and antimicrobial agents to the affected area while at the same time having selfhealing properties that alter with the healing process .vivo and invitro tests portraying enhanced cell response, tissue generation rate as well as efficient anti-infection mechanisms superior to general dressings improved cellular responses. accelerated tissue regeneration and effective infection management compared to conventional dressings. The results presented point toward the potential of these innovative hydrogels as a true game-changer for diabetic wounds management as well as patients' treatment prognosis enhancement. Future studies of this hydrogel will concentrate on modulating the chemical makeup and evaluating the long-term performance. the ability of these hydrogels to maintain a moist wound environmental crucial for promoting cellular migration, collagen formation, angiogenesis-critical processes in wound healing. The self-healing and adaptive characteristics of these hydrogels can also reduce the need for frequent dressing

changes improving patient comfort and reducing healthcare costs. The integration of these multifunctional materials into wound care has the potential materials into wound care has the potential to revolutionize diabetic wound management, providing more effective, and patient-friendly solution multifunctional self-adaptive hydmgels offer an innovative and promising approach to address the challenges of diabetic wound healing, improving both the quality and speed of recovery for affected patients

Keywords:: Hydrogel, diabetic wound, chronic wound, wound miemenvironment, wound healing

Introduction

Diabetic wounds are difficult to manage in clinical practice, mainly because they take longer to heal and are prone to infection, which potentially cause complications like amputation. Diabetic wound healing is therefore slow because characteristic features such as poor blood circulation, nerve damage, and susceptibility to infections, often leading to severe complications such as amputations. The complexity of diabetic wound healing is attributed to factors like impaired blood flow, neuropathy, and immune responses. therefore, there is need for effective healing mechanism, new therapeutic approaches. New approaches in biomaterials have seen creation of multifunctional self-adaptive hydrogels which show great potential in improved diabetic wound healing These hydrogels have features including possession of highwater content biocompatibility ability to mimic the natural extracellular matrix Besides there adaptability in that they respond to changes in the microenvironment. such moisture, temperature, or PH. They can react quickly to changes in the wound microenvironment, such as shifts in temperature, moisture content, or PH, thanks to their adaptability. These bioactive components may improve hydrogels, which provide encouraging potential for improving diabetic wound healing. Among these hydrogels' special qualities are their high-water content, biocompatibility, and capacity to mimic extracellular and natural matrix. Additionally, because of their adaptability, they ean react quickly to changes in the wound microenvironment, including shifts in temperature, moisture contents or PH These bioactive substances may be added to hydrogels, which present encouraging options for improving diabetic wound healing. These hydrogels have special qualities, such as a high-water content, biocompatibility, and the capacity to replicate extracellular and natural matrix. Furthermore, their adaptive nature allows them to respond dynamically to changes in the wound environment, such as variations in pH, temperature, or moisture levels such moisture, temperature, or Ph. Because of their adaptable nature, they can react quickly to changes in the wound environment, including shifts in temperature, moisture content, or Ph. These bioactive substances may be added to hydrogels, which present encouraging options for improving diabetic wound healing. These hydrogels have special qualities, such as a high-water content, biocompatibility, and the capacity to replicate extracellular and natural matrix.

furthermore, their adaptive nature allows them to respond dynamically to changes in the wound environment, such as variations in pH, temperature, or moisture levels The integration of bioactive agents within these hydrogels can further promote wound healing by providing antibacterial properties, facilitating cell proliferation, and enhancing angiogenesis, these articleaims to explore the potential of multifunctional self-adaptive hydrogels in enhancing diabetic wound healing. We will discuss their design principles, mechanism of action, and latest research findings that highlight their effectiveness. By examining these advanced materials. we hope to provide insights into their transformative role in wound care, ultimately contributing to better outcomes for diabetic patients. Clinical studies indicate that these hydrogels not only promote faster epithelialization but also reduce the incidence of infections

The wound healing process is defined as a complex and well-orchestrated sequence of biological and molecular events of cellular migration, proliferation, extracellular deposition. healing process is interrupted by external factors, such as infection, continued trauma, or an intrinsic wound incapacity to heal. The variety of available wound dressing. including films, nano fibres, foams, topical formulation, wafers, transdermal patches, sponges, and bandages fail precisely in fulfilling several of these requirements

Phases of wound healing

The first stage, termed as haemostasis is the initial response towards an injured tissue. It is commenced by vasoconstriction which decreased blood flow to the damaged site. Pla via adhesion to the damaged tissue through the selection of surface receptors constructed the temporary thrombi and starting the process of inflammation. The second phase of healing is inflammation, within which neutrophils, macrophages, and lymphocytes migrate towards the wound site to clean the debris, bits of dead tissue and bacteria. During this phase there is inflammation which presents with signs such as redness, heat. swelling, and also production of pro-inflammatory cytokines and growth factors to help in the next phases of healing. The third phase involves the growth phase during which new tissues are formed as keratinocytes, fibroblast cells, and endothelial cells start to proliferate. This process results into the formation granulation tissue matrix that consist of collagen and several ECM proteins. This phase is characterized by re-epithelialization, migration of epithelial cell across the wound bed until the epidermal barrier is reformed. Essentially, the last form of weaving in wound healing phase called as the maturation [remodelling phase in which the extracellular matrix is reorganized and the wound contracts. This phase is marked by declining fibroblast, endothelial, and inflammatory cell numbers at the wound area combined with enhanced collagen fibbers' maturation. The rate of recovery increases day by day, the newly formed tissues become stronger mechanical load bearing and offers lesser tender point area.

In the four simultaneous processes of wound healing all the factors in the extracellular matrix, such as the growth factors, cytokines and chemokines act in harmony. Current health status of the individual including aspects like nutrition and diseases the person has, or medical conditions that he/she maybe suffering from can determine the rate and manner in which the wound will heal. That being said, in order for the wound to heal effectively, any medical conditions must be treated, balanced diet should be consumed and appropriate wound care must be ensured depending on medical advice formation. The inflammatory phase of wound healing is a crucial process, which involves the following events:

I. Vasoconstriction: After the initiål injury the blood vessels construct in order to minimize blood loss and achieve haemostasis.

2. Platelet aggregation: They are the first finger print of an injury. Platelets aggregate and adhere to the site of injury and the endothelium (inner layer of the vessel lining) and release several chemical mediators, leading to blood clot formation and eventually starting the inflammatory process.

3. Fibrin clot formation: Fibrin is then formed from plasma and is a stable clot that forms a seål over the wound and prevents further bleeding.

4. Release of chemical mediators: These chemicals released are Histamine, Bradykinin and prostaglandins originated from the platelets as well as the damaged cells. These mediators dilute the blood vessels around the injured area, makes the blood vessels walls more permeable, and stimulate the attraction of several immune cells, such as neutrophils and macrophages.

5. Neutrophil infiltration: The first responders are neutrophils which mobilize to the wound site where they engulf the bacteria in phagocytic bags and kill potentially damaging microorganisms using oxygen free radicals and enzymes.

6. Proliferative phase: The wound is said to be in the proliferative phase after the inflammatory phase, in which fibroblast growth, angiogenesis and the formation of granulation tissue take place. It is a phase in which vessel formation occurs, collagen biosynthesis is also carried out while offering strength to the wound.

7. Re-epithelialization: The wound edges begin to move over the granulation tissue and new epithelia cells actively begin to divide and migrate across the surface of the wound giving skin barrier again.

8. Remodelling: In the sear maturation, the collagen fibres reconstitute to become scar colour fades to pale pink, scar reduced in thickness and ceases to itch.

cell migration as well as tissue repair. , and fibroblast growth factor (FGF) which plays its role in the healing process. This process not only helps to treat on the bleeding but also starts compensating the damaged tissue. The platelet-rich fibrin (PRF) is a component of the above process and is derived from the fibrin mesh. PRF is a matrix containing various growth factors, cytokines and signalling molecules which create the optimal milieu for cell growth, differentiation and proliferation and hence, tissue healing and repair. The healing process involves several stages: such as haemostasis, inflammation, proliferation and remodelling. In the stage of haemostasis, the main objective in the

body is to prevent blood loss. In the inflammation stage the body retaliates with inflammation by trying to reduce damage and eliminate damaged tissues and cells. During the proliferation stage new blood vessels and connective tissue cells are formed, Lastly, in the remodelling stage, the fibre and matrix of the tissue are reconstituted, and the structure is rebuilt.

1.2. Platelet-rich fibrin plays a vital role in each of these stages:

I, Haemostasis: (PRF) platelet-rich fibrin as discussed earlier reduces blood loss as well as offer a short-term support on the processes of cell migration. In addition, it is essential for reinforcement and maturation of the clot in order to promote healing.

2. Inflammation: (PRF) platelet-rich fibrin consists of pro-inflammatory factors of cytokines and chemokines that can recruit various immune cells to the site of fibrinolysis. These immune cells come round to help clear the dead cell debris and to tidy up the scene for new tissue repair and construction.

3. Proliferation: Several of the components in (PRF) — the growth factors and signalling molecules enhance growth, differentiation and proliferation which is important in angiogenesis — the formation of new blood vessels, connective tissue and cells. Also, it has been reported that PRF can induce angiogenesis, that is the generation of new blood vessels using the current blood vessels, which is better for the delivery of oxygen and nutrients to the healing tissue.

4. Remodelling: PRF involved in rearrangement of the extracellular matrix and reconstruction of the tissue architecture. TGFß, FGF and PDGF found in the PRF are responsible for the synthesis and degradation of proteins that build or rebuild the stroma within the tissue, making the tissue strong.therefOre, platelet-rich fibrin is an essential part Of clotting as it serves as more than a mere clot but facilitates the different healing phases that are involved in tissue repair and regeneration. Stem cell niche owing to the complexity of growth factors, cytokines, and signalling molecules fulfils all the requirements required for cell growth, differentiation, and proliferation to reconstruct the required damaged tissues with acute wounds, they do not get through all the stages of healing. Chronicity results from failure to re epithelialize, suboptimal inflammatory response, and limited angiogenesis, and granulation tissue development- This leads to a constant inflammation, an issue believed to be linked to inadequate blood flow, infection, diabetes, and aging. The key factors leading to chronic wound development are:

L Impaired microcirculation: Such wounds may exhibit poor circulation which restricts the transport of nutrients, oxygen and immune system components that are important for healing.

2. Infection: Such chronic wounds have increased potential for bacterial colonization and infection, the process that does not only slow down the healing process but also fuels chronic inflammation.

3. Diabetes: Diabetic individuals have changed immunity, impaired blood flow, diminished ability to create new blood vessels and impaired wound healing which can lead to formation of chronic wounds.

4. Advanced age: Chronic wounds occur with age due to a loss of cell vitality, decreased blood flow and the ability of the body to fight infection.

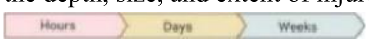
5. Excessive matrix metalloproteinases (MMPs): MMPs are often found at elevated concentrations in individuals with chronic wounds because the excessive amount of these enzymes may cause further destruction of the ECM that interferes with the healing process.

6. Imbalance of growth factors: Specifically; chronic wounds may possess an adverse environment where specific growth factors such as the transforming growth factor-beta TGF13, and the platelet-derived growth factor PDGF, are not at favourable levels of concentration for tissue healing and repair,

7. Cell death and senescence: Among the cellular pathophysiology observed in chronic wounds are altered cell viability including increased cell death and senescence, which result in limited availability of healthy cells for tissue repair.

8. Oxidative stress: Using improvements in this situation, Chronic wounds are frequently characterized by excessive amounts of ROS, which harms healing cells and therefore has a negative impact on physical health.

Conclusively, chronicity results in aberrant healing profiles owing to inadequate blood supply, infection, diabetes, ageing, excessive MMPs, altered growth factors, apoptosis, Cellular senescence and oxidant stress. All of these factors play part and part in sustaining the chronic inflammation and impede the wound to go to other phmses of physiological healing. Finally, to overcome these all factors and facilitate healing in chronic wounds certain advanced wound dressings, infection control measures and cellular and growth factors-based therapies may be adopted. such as prolonged inflammatory phase, non-response to repair stimulation, and persistent infection. Individuals with conditions such as diabetes mellitus, venous or arterial insufficiency, immunosuppression, or who experience prolonged pressure due to immobility are at risk of developing chronic diabetic wounds. Acute wounds are expected to heal usually within 8 to 12 weeks, depending on the depth, size, and extent of injured layers.



Hemostasis md

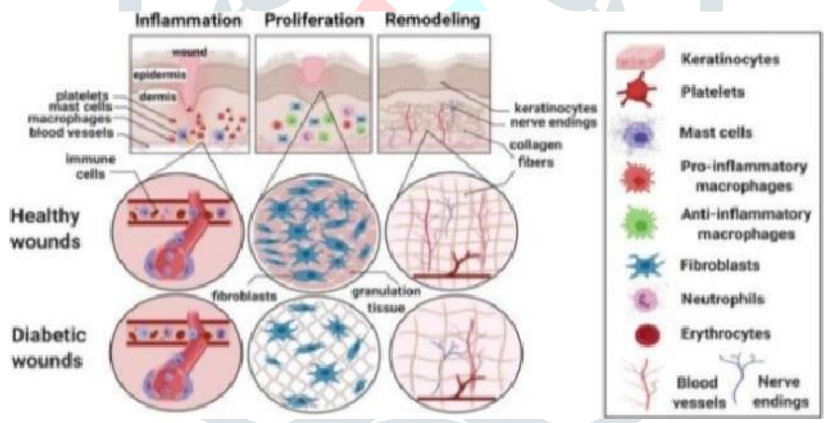


Figure I : comparing between healthy wounds v/s diabetic wound healing of pathophysiology and mechanism of wound healing involved keratinocytes, platelets, mast cells, fibroblast, neutrophils, erythrocytes.

Self- Adaptive Hydrogel properties

l.Biocompatibility: They are designed to be non-toxic and compatible with biological tissues, minimizing adverse reactions.

2.moisture Retention: these hydrogels maintain a hydrated environment, which is crucial for promoting cellular activities and preventing tissue desiccation,

3.MechanicaI flexibility: self-adaptive hydrogels can mimic the mechanical properties of natural tissues, providing support and reducing pain during movement.

4,Self-healing Ability; many self- adaptive hydrogels can autonomously repair themselves after damage, ensuring sustained functionality over time.

5.Responsive behaviour: They can change their properties in response to environmental stimuli, such as PH, temperature, or ionic strength, allowing for tailored drug release and enhanced healing.

6,AntimicrobiaI properties: incorporation of antimicrobial agents can help prevent infections, a critical factor in diabetic wound care.

7 .Bioactivity: These hydrogels can be functionalized with bioactive molecules, such as growth factors, to promote cell proliferation and tissue regeneration.

8.controIIed release: They can facilitate the sustained release of therapeutic agents, optimizing the treatment regimen for regimen for chronic wounds

1.3. Understanding diabetic wound Pathophysiology

Diabetic foot ulcer management requires the multifactorial concept and addresses the cause of the prolonged healing time. Some key elements of diabetic foot ulcer management include:

I. Glycaemic control: It becomes necessary to maintain proper blood sugar levels as a way of boosting the body's immunity to the diseases in order to promote healthy healing. This may include insulin injection. oral anti-diabetic drugs or other modalities for lowering the blood glucose level depending on the patient's needs.

2, Off-loading: Relieving the stress that is usually p aced on the affected foot is critical in the healing process. This can be done using shoes with additional cushioning or cast walkers that help push weight off the ulcer area.

3. Wound care: Wound care delegation includes cleaning the root lesion document by removing necrotic tissue at least twice a day while ensuring the wound is clean and moist. Hydrogels, alginates or hydrocolloids might be needed as an advanced wound dressing to aid in the healing process.

4. Infection control: Infection ought to be managed more aggressively. This may require antibiotic therapy, removal of the infected tissue, and other times surgical treatment.

5. Vascular assessment and intervention: Evaluating and intervene- t ion of peripherål vascular disease is important in enhancing circulation within the affected site. This may be done through changes in the lifestyle, drugs and or invasive techniques like angioplasty or bypass surgery.

6. Neuropathy management: In diabetic neuropathy patients, analgesia, proper footwear, and foot examination may be used to prevent subsequent levels of injury and ulceration.

7. Multidisciplinary team approach: Health care associated with diabetic foot ulcers should involve a team approach with physicians including endocrinologists' podiatrists, vascular surgeons, and infectious disease physicians,

8, Patient education: The patients need to be advised on the importance of foot care, monitoring their blood glucose level and the need to attend follow up appointments in case of complications or to notify their progress.

9, Nutrition: Healthy intake of calorie and protein is essential in order to help the wound heal properly, But there are situations in which a person needs extra intake of the nutrients mentioned above. In conclusion, good glycaemic control, appropriate management of the wound including de history should all be addressed by a team approach to ensure efficient treatment of diabetic foot ulcer in the management of diabetes. brisement. cessations of infection and other contributing factors in the elderly patient's history should all be addressed by a team approach to ensure efficient treatment of diabetic foot ulcer in the management of diabetes.

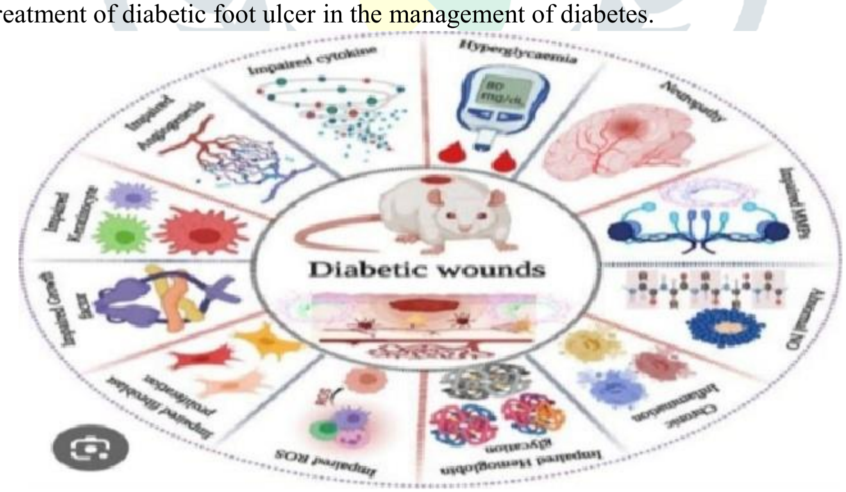


Figure 1.2: Diabetes mellitus is a prevalent cause of mortality worldwide and can lead to several secondary issues, including which are caused by hyperglycaemia, diabetic neuropathy, impaired ROS, impaired keratinocytes, impaired angiogenesis, impaired cytokine, chronic inflammation

2.1 Types, drug delivery mechanism, self-healing properties, patient-centric approaches, impact of nutrition, environmental consideration, future trends of multifunctional hydrogels in wound care management

Definition and structure

Hydrogels are crosslinked, water-swellable polymer systems capable of embedding a tremendous amount of water without losing their integrity. They are made from natural or synthetic polymers and can increase massively when soaked in water and assume the state of gel.

Hydrogels have certain characteristics that would allow them a special place in the appropriate applications, especially in Biomedical applications. Hydrogel consists of:

I) Cross-linking agents: These form the network structure through which the hydrogel absorbs water-

2) Water: A chief constituent making hydrogels possess their characteristic features. In conclusion, it is possible to specify that the main constituents of hydrogels are polymers, cross-linking agents and water. This leads to a creation of a versatile material that can be used in a myriad of ways with a focus being made to biomedical engineering. Mechanism of action of hydrogels in Diabetic wound healing Primary mechanism of action:

In summary, hydrogels offer several advantages for wound healing:

I .Hydration: They create moisture which is necessary for wound healing and do not allow scab formation on the skin surface.
2.Autolytic debridement: Thus, hydrogels help in the physiologic process of removing of the nonviable tissue and subsequent formation of new and healthy tissue.
3.Controlled drug release: Hydrogels can encapsulate a range of therapeutic agents and deliver them consistently, thus reducing the unwanted systemic effects of the drug- This is appropriate when administering antimicrobial agents, growth factors and antiinflammatory drugs at the site of the wound-
4.Moisture Retention: However, hydrogels contain a significant amount of water-swellable polynu content which has a role in wound healing. They crute a moist environment at the site of the wound, to avoid the wound cracking and to minimize the formation of a scar.
5.CeIIuIar Response: In its natural form hydrogels are biocompatible, md may also elicit a cellular response in the area of the wound allowing for tissue growth and the formation of new tissue.
6.Pain Reduction: Hydr»gels incluLse the humidity of the wound and IV lieve pain; in dlis case, the wound remains protected from the action of micmorganisnrs and detrimental effects of exposure to atmospheric air,

7-wound Contraction: It may assist in wound contraction that is the natural way by which the skin shortens to heal the wound. It reduces the period of treatment and helps to fonn healthy tissue of the skin.

8, Oxygen and Nutrient Delivery: Hydmgels nut)' also act as a vehicle for delivering nuuients and oxygen to the affected area, and also, suppæss the synthesis of hard, scar-like tissue.

9. Anti-inflammatory B•operties: Some hydrogels have anti-inflammatory effects and, as a result, promote better inflammation or healing reaction within the wound site.

10. Convenience: With hydrogel dressings, the process of application and removal is less painful for the patient and may be done as often as leg ulcers require, or as often as solution requires.
11,Cost-effective: As for other wound care product, hydrogel dressings are relative cost-effective approach to wound management, which could be beneficial to both, patients and caregivers.

12.Versatility: It can be applied to a partial thickness wounds including ulcets and burns. ms well ms an adjunct to other wound care devices. Due to their non-specific nature, they can be very useful in an overall management of a wound

mechanism of drug delivery for diabetic wound healing depends on the type of drug delivery system and the method used to release the drug:
Microneedle: use dissolution-based release, where the drug is released when the material dissolves. The duration of the dissolution determines the drug release time.
lipid nanoparticles (LNPs): use a diffusion-controlled mechanism, where the drug gradually diffuses through the lipid matrix. The release rate can be adjusted by changing the LNP's formulation parameters.

Dissolution -based release: Microneedles release drugs by dissolving the materials that contain the molecules. The duration of the dissolution determines the release time

Exosomes: can be used to deliver drugs and treat diseases. Exosomes are secretory products Of bone marrow mesenchymal stem cells that can promote wound healing.

PH-responsive hydrogels: use a PH-responsive backbone to convert glucose to gluconic acid, which changes the PH and triggers the release of the drug,
Diffusion-controlled mechanism: Angiogenic agents gradually diffuse through the lipid matrix of lipid nanoparticle (LNPs) release rate can be adjusted by changing the LNPs composition, size, and surface properties.
Topical nitric oxide (NO)deIivery: NO is an important scavengers of reactive oxygen species (ROS), which can inhibit wound healing. Topical NO delivery can help with healing.
Anti-sense oligonucleotides (ASOs): These nucleic acids regulate gene expression to improve wound healing. For example, ASOs can be used to target the gap junction protein cx43, which is increased in diabetic wounds.

Other factors that can help diabetic wound heal include:

- Keeping blood sugar levels stable

- Eating a healthy diet rich in protein, vitamins, and minerals
- Cleaning and dressing the wound regularly

2.2. Types of multifunctional hydrogels:

In recent (Rules, intelligent multifunctional hydrogels have been studied and leported to overcome the limitations of traditional hydrogels, such as poor nechanical propelties, restricted compatibility. and limited lifetime. By regulating their physicochemical structure and chemical composition, intelligent hydrogels with stimuli- responsive, injectable, self- healing, shape- memory, conductive, and real time [M)nitoring properties can be designed and fabricated. "Ihis self-healing property endows hydrogels with an extended life time. Preventing damage during unavoidable movements. Moreover, the injectable hydmgels based on self -healing property.

The smart hydrogels are created to be sensitive to more subtle cues like pH, light, temperature and electric fields thus affecting their swelling pattern or degradation rates mechanical properties and conductivity respectively, These features place them in a number of uses such as; drug delivery, tissue engineering and wound healing, New properties such as nanomaterials and bioactive molecules can also be incorporated into the hydrogels enhancing its performance to treat wounds.

In the treatment of diabetic wounds, the use of intelligent hydrogels has shown promising results due to their ability to enhance the healing process through:

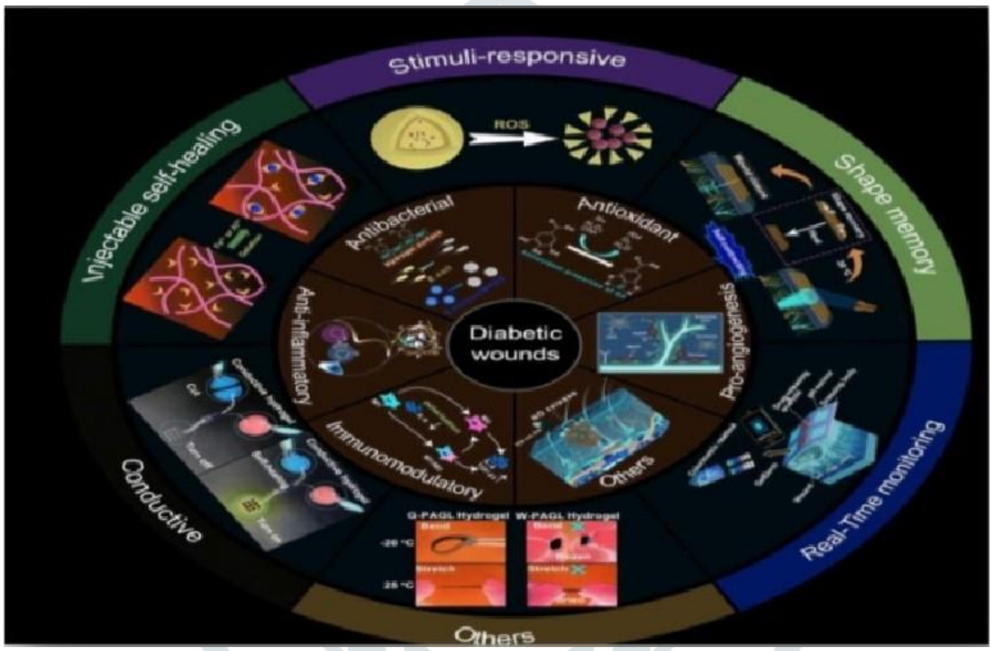


Figure 1.3: Illustration of the stimuli-responsive€ injectable self- healings shape-memory, conductive. and real-time monitoring hydrogels in accelerating diabetic wound healing possessing antibacterial, pro-angiogenic, anti-inflammatory, and antioxidant properties. Some applications of multifunctional hydrogels are shown. Beneficial for irregular and deep wound coverage, with prolonged service life. The shape-memory property also endows hydrogels with the capacity for shape transition, which water and also to provide shield against pathogenic organisms. Skin injuries may be caused by an injury, infection, or a health condition like diabetes. This paper will seek to look at this aspect of skin repair to understand how wounds heal from the time of injury up to when the skin regenerates itself wholly, The skin might also take very long to heal just as diabetic ulcers demonstrate, therefore can become persistent for a while. Hydrogels are emerging as important soft materials in the management of chronic and difficult to heal wounds because of their high-water contents biocompatibility and adjustability of mechanical characteristics. Smart hydrogels have been found to be potential in wound healing management due to their inherent property of sensitivity to external signals and support created to cells and tissues.

l. Controlled drug delivery: Smart hydrogels may load and deliver growth factors, antibiotics, or any other bioactive molecules, thus delivering therapeutic substances at the localized site at the right concentration.

2. Wound dressing: Hydrogels can help make an optimal environment that will support the migration, growth and proliferation of cells which are major in healing processes. They also assist in balancing between the amount of fluid intake together with avoiding a possibility of contacting diseases.

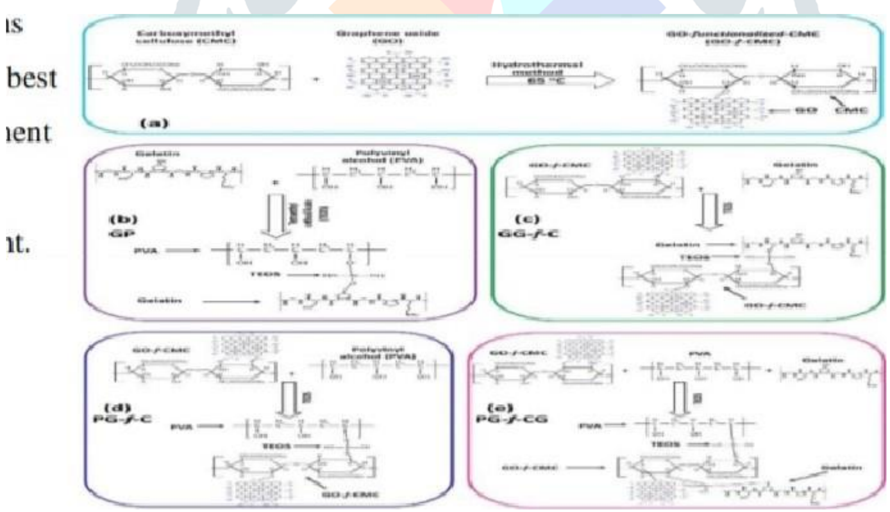
3. Mechanical properties: Smart hydrogels devised for tissue engineering applications, contain mechanical characteristics, for example, elasticity and compression strength in order to resemble ECM native morphology and support for the wound tissue throughout the healing process.

4. Electrical stimulation: The conductivity of intelligent hydrogels can support increased electricål signalling aiding the process of wound healing as the functional activity of cells including migration, proliferation and tissue formation is known to be positively influenced by electricål stimulation,

5. Biocompatibility: This means that the natural and synthetic polymers used for the making of the hydrogels used in the fabrication layers naturally allow the hydrogels to make long term contact with the wound tissue.

Thus, the approach to design the intelligent hydrogels can be considered as a perspective direction in the management of diabetic ulcers as it combines various features that are crucial for efficient and effective wound healing. However, more experimental studies are needed to develop and improve fabrication and methods to apply intelligent hydrogels for Wound healing in clinical practice is a process of regaining skin tissue's morphological and physiological integrity disrupted due to injury. It can be affected by a number of factors for instance fluids, infection as well as diet, Skin is also considered as one of the main sensory organs of the human body which is involved in the process of thermoregulation, as well as acting as a shield to the human body against bacteria and viruses. Some investigations reveal that skin masses constitute over 10% of total body mass Additionally, nursing students observed from practice experience that skin thickness increases in cold climates because skin acts as an insulator. The skin is made up of three complex layers: which include the epidermis, dermis, and hypodermis. Wound can be categorized according to the degree of skin injury, and the two major divisions are the partial thickness and the full thickness. He points out that partial-thickness wounds only affect the epidermis and dermis like, scratches, cuts and burns while full thickness wounds involve destruction of the epidermis, dermis, and the hypodermis third-degree burns. Wound healing process can be classified in to acute and chronic wound. Acute wounds are usually associated with trauma or surgery, and progress through the predefined stages of wound healing: the chronic wounds are generated by pathological processes that are unable to heal within a certain period of time. Chronic wounds can be classified into vascularity ulcers and they possess several features resembling usual characteristics such as elevated concentration of pro-inflammatory cytokines, reactive oxygen species (ROS), and senescent cells. These wounds also sustain chronic inflammation and infections and dermal/epidermal cells fail to respond to repair stimulatory signals.

Basically, Chronic wounds do not exhibit typical skin healing, where the healing process is altered and the wound remains inflamed for longer duration than the normal skin, Hydrogel dressings involve properties make them ideal for the particular management of specific types of wounds, as explained earlier in this paper. As there is the availability of a plethora of medical technologies that require specific kinds of dressings, it is imperative that dressings that include perfect mechanical characteristics, moisture absorption, permeability to oxygen as well as comfort, be developed. For different types of wound hydrogel dressings can be developed with provisions that ensure healing environment and leading to positiveoutcome for the patient.



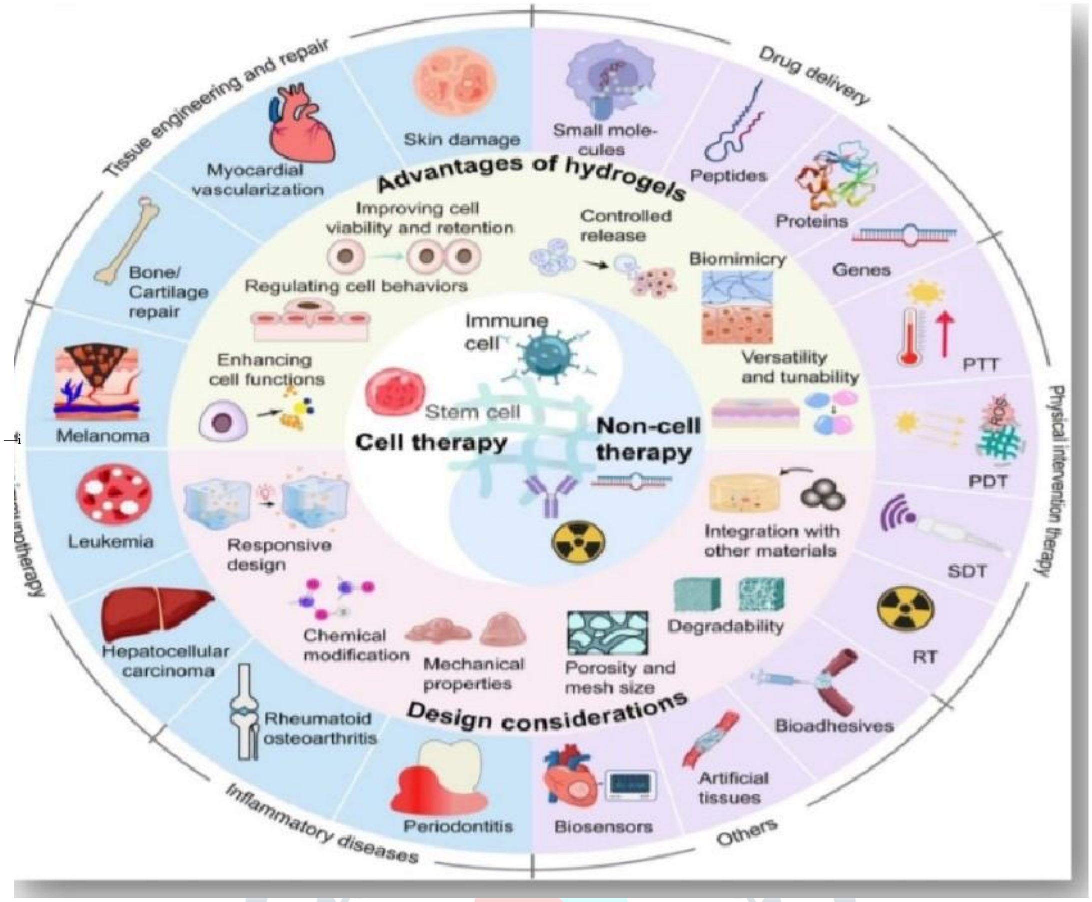


Figure I .4: The proposed chemical reaction during the fabrication of hydrogels. (a)graphene oxide- functionalized-carboxymethyl cellulose by hydrothermal method. (b) gelatine and polyvinyl alcOhoI and crosslinked with tetraethyl orthosilicate by a simple blending method. (c) GO-F-CMC gelatine crosslinked with TEOS by a simple blending method. (e) Gelatine, GO-f-CMC, and PVA are crosslinked with TOES by a simple blending method.

Figure 2.1: advantages and disadvantages of hydrogels and therapy, design considerations of cell therapy and noncell therapy and others

Advantages of hydrogels:

➢ Biocompatible, ➢ It is to modify.
Biodegradability.
Transparency.
➢ Flexibility.
➢ Good transport of nutrients to cells and products from cells.
➢ Enhancing cell functions.
➢ Regulating cell behaviour.

Disadvantages of hydrogels:

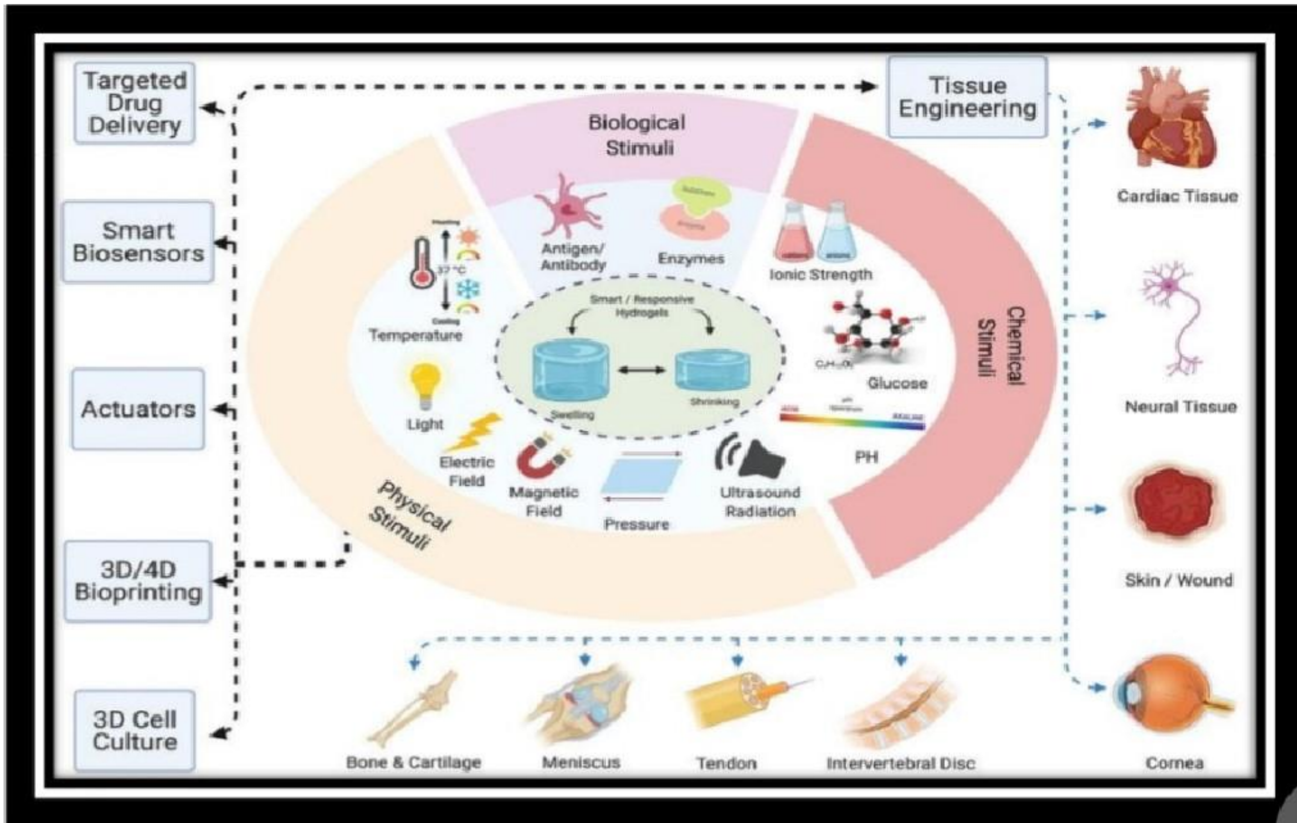
Hydrogels are expensive.

Can ➢ be hard to handle, Usually mechanically weak.
➢ Difficult to be sterilized.

2.3 ➢ stimuli-Responsive Hydrogels

Stimuli- Responsive Hydrogels with stimuli-Responsive units in the backbone allow for triggered and reversible transitions that induce the formation or breaking of chemical bonds, and adjustable interactions of responsive groups. The volume, stiffness, and sol-gel transition of hydrogels can then be controlled to achieve injectability, self-healing, shape memory effect, and actuation. In the microenvironment Of diabetic wound, internal stimuli including PH, enzyme, glucose, ROS, MMP-9, and external stimuli including temperature, light, magnetic field, and microwave, have been used to reversibly trigger the transformation Of hydrogels.

Because the PH value changes with the different states of skin wounds when bacterial infection occurs or diabetic wounds form, PH-responsive hydrogels can be used to realize the controlled release of drugs. For example, Schiff base bonds have been widely studied because of their biocompatibility and rapid formation, which can be used to enhance the mechanical strength and self- healing properties. By varying the PH value, the controlled release of drugs or antibacterial peptides, PH-tHggered shape memory processes, in situ phase transitions, and controlled dissolution at the wound site, can be realized the PH-responsiveness of Schiff base bond-crosslinked oxidized DEX-dopamine (ODEX-DA) / carboxymethyl chitosan (HTCC) hydrogels can realize the controlled release of Ag NPs and DFC) for improved bacterial killing and angiogenesis, respectively. Benzene boric acid and its derivatives with pika of 7.8-8.6 can quickly bond with polymers containing 0-diol structure to form dynamical covalent bonds of boronic ester. These dynamic bonds exhibited strong PH. Glucose, and ROSresponsive effects. In our previous study, the dynamical hydrogel of 3-carboxyl-4fluorophenylboronic acid grafted quaternate ehitosan (QCS)/PVA was crosslinked by boronic ester-based reaction, which responded to hydrogen peroxide and glucose to release DFO loaded gelatine microspheres, In addition, the dynamic bonds of the Schiff base and boronic ester could be combined to broaden the responsiveness of the hydrogel. Biochemicål stimuli. such as enzymes and glutathione make hydrogels dynamically respond to the microenvironment. Owning to the overexpression of MMP 9, the gelatine microspheres release the loaded drug under the effect of MMP-9 to regulate the microenvironment. The silk protein hydrogel loaded with a metal-chelating dipeptide accelerates infected diabetic wounds by inactivating MMP-9 through its potent chelating effects from MMP-9active centre. Mechano-æsponsive poly (PSBMA)hydrogels enable the release of drugs precisely controlled by the extent and cycles of mechanical loading and unloading, as shown in figure. The host-guest complex also showed mechano-responsive properties under mechanical stress. External stimuli such as temperature and light, are used to endow hydrogels with injectability and controlled drug delivery. For example, the UV light dissociates the host-guest linkage of azobenzene s, and the loaded EGF can be controlled released. Moreover, in recent years, light-responsive hydrogels with photothermal or photodynamic propenies have been designed with improved functionality. Photo thermal substances such as Ag NPs, GO, CNTs, and Fe- containing materials, are introduced into hydrogels to endow them with photothermal properties under near-infrared (NIR) irradiation, which improves their antibacterial property. Compared to traditional antibiotic therapy, photothermal therapy is not restricted by bacterial resistance. In addition, the heat treatment at about 40-41 c has been proved to induce the ring formation of endothelial cells and increase neovascularization. Therefore, the stimuli-responsive properties of hydrogels are mainly obtained by regulating dynamic bonds or other physical interactions, which not only endow hydrogels with controlled release of drugs, cells, and other therapeutic substances to accelerate wound effects (SME), and photothermal effects, which will be discussed in the following sections.



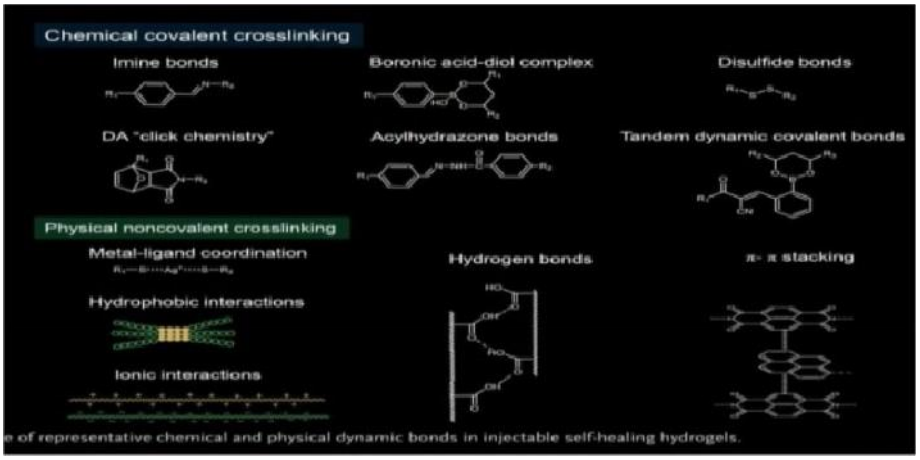
property are always formed by dynamical crosslinks and exhibit shear-thinning dependence and reversible transformation. Dynamically crosslinked hydrogels always exhibit self-healing properties, which prolong their service life.

Figure 2.2: stimuli-responsive hydrogels types based on biological stimuli. chemical stimuli. physical stimuli and new technologies development of smart biosensors, actuators, 3D/4D Bioprinting, 3D cell culture

2.4.Injectable self-Healing Hydrogel:

Injectable hydrogels are a class of hydrogels that can be extruded through a syringe to form an in situ solid gel. Injectable hydrogels have traditional clinical practice less invasive and more effective, The injectable property endows the hydrogel with the precise delivery of drugs or cells in a minimally invasive manner, which is beneficial for its application in the fields of tissue engineering drug delivery, others. The injectable property ensures that the hydrogel can be directly injected and filled irregular or deep wounds without wrinkling or fluting, Researchers have developed a series of injectable hydrogels based in in situ gelation, microgels, and shear-thinning. Among the injectable hydrogels, hydrogels based on the shear-thinning

figure 2.3: The figure represents the difference between chemical covalent crosslinking v/s noncovalent crosslinking in injectable self-healing hydrogels. In chemical covalent crosslinking involved imine bonds, boronic acid-diol complex, disulfide bonds, and in physical noncovalent crosslinking involved metal-ligand coordination, hydrogen bonds, ionic interactions.



e of representative chemical and physical dynamic bonds in injectable self-healing hydrogels.

The self- healing properties of hydrogels are achieved through reversible chemical covalent bonds and physical non covalent interactions. The reversible chemical covalent bonds such as boronic acid-diol complex, imine bonds, Diel-Alder (DA), acyl hydrazone bonds, disulfide bonds, provide hydrogel self-healing property. similarly, physical noncovalent interactions include metal ligand coordination, hydrogen bonding, hydrophobic interaction, host-guest interactions, ionic bonds, are also effective to make hydrogen heal. The chemical structures of the dynamic interactions, the polymeric network Of hydrogels can be destroyed under shear stress and spontaneously reconnected after the removal of the stress, Hydrogels may become less viscous after being squeezed through a syringe, and the viscosity may increase again to facilitate gel formation. many hydrogels can also realize reversible (gel-sol) transformation by changing the environment, such as temperature, PH, and light. However, we focused on developing injectable self-healing hydrogels based on thixotropic or shear-shinning mechanisms,

Generally. the self-healing properties of hydrogels weaken their mechanical strength. Good mechanical strength depends on the crosslinks in the structures, which negatively affect the dynamic interactions. In addition. the design of tough hydrogels is mainly based on mechanical energy dissipation to reduce crack propagation, which is absent in swollen hydrogels. Several methods have been used to improve the mechanical properties of selfhealing hydrogels. Introducing nanomaterials such as carbon-based CNTs or GO, mineral nanosheets, and magnetic nanomaterials to form nanocomposite hydrogels is an effective method to improve the mechanical properties. Other methods, including interpenetrating polymer network structures and hybrid crosslinking have also been adopted. wan et al. designed a tough and self-healing hydrogel in which mechanical strength was improved by introducing of tannic acid (TA)- coated cellulose nanocrystals. Wii et al. fabricated injectable self-healing hydrogels using Schiff-based crosslinked CMCS and poly (dextran-g-4-formylbenzoic acid) (DEX-CHO), Hydrogels, in which antimicrobial peptide -modified polyacrylonitrile (PAN) nanofibers were homogeneously dispersed in injectable hydrogels reinforced their mechanical properties and improve the antibacterial properties. The injectable hydrogel also exhibited the self-adapting properties and was used for diabetic wound healing. After being cut in half, the hydrogels immediately healed into a single piece after being brought together for 2 min.
injectable self- healing CMCS hydrogels can also be formed via metal coordination bond.

2.5. Shape-memory Hydrogels

SME is defined as a property in which materials have capacity to fix one or more programmed temporary shapes and recover the permanent shape under appropriate stimuli. Hydrogels possessing SME, namely shape-memory hydrogels (SMHs), have been widely investigated in the past decades. owing to their wet nature, shape transition properties, adaptability and enriched biocompatibility, SMHS have the potential to be used in biomedical fields, such as soft robots, actuators, surgical sealants, and tissue engineering scaffolds. However, owing to the high-water content in SMHS and the physiological application environment, the design of suitable chemical structures and stimuli-responsive shape transmission is limited,

The design of SMHS should focus on two types of structure.one structure is the hard segment which is constructed by net-points composed of physical or chemical crosslinking links, and responsive for remaining the permanent shape and driving the shape transformation.environment, such as temperature, PH, and light. However, we fOcused on developing injectable self-healing hydrogels based on thixotropic or shear-shinning mechanisms.
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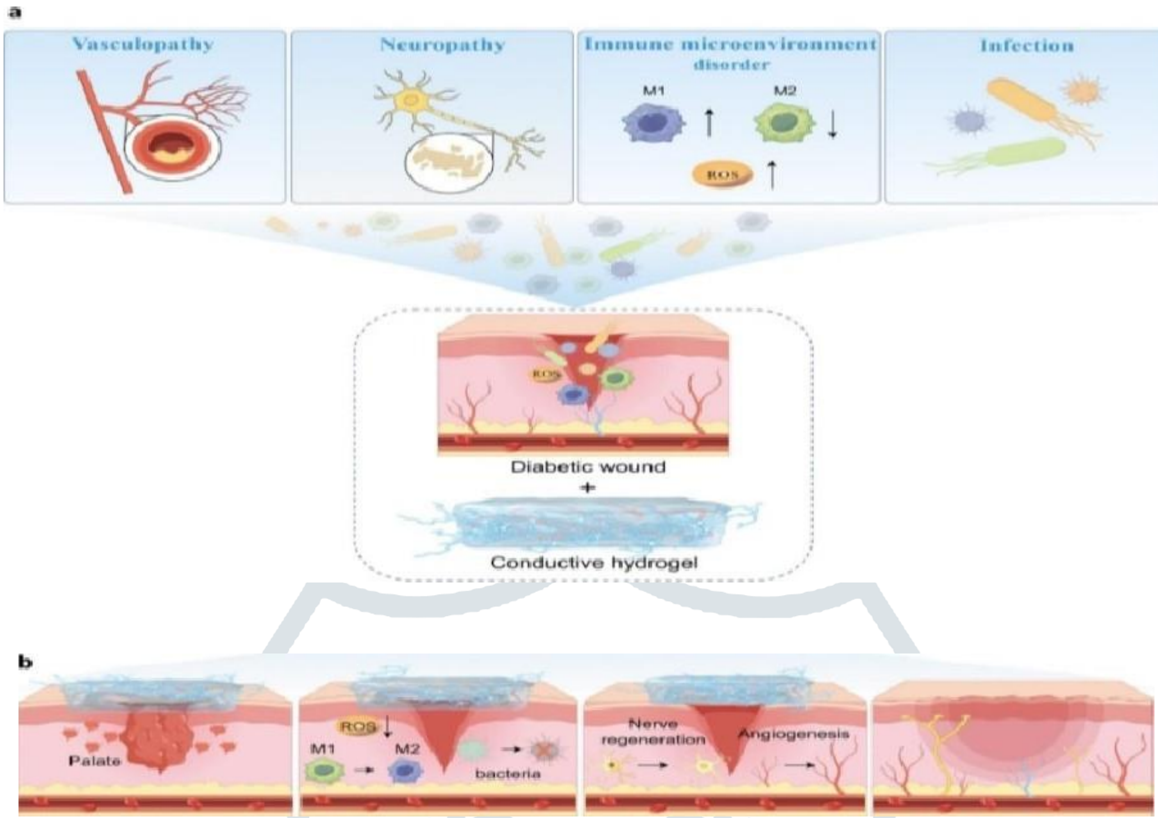
The design of SMHS should focus on two types of structure.one structure is the hard segment which is constructed by net-points composed of physical or chemical crosslinking links, and responsive for remaining the permanent shape and driving the shape transformation from temporary shape to the original shape. Another structure is switching segment, which serves as a stimuli-response switch to fix and recover the temporary shapes. Stimuli such as PH, temperature, light, water or salt solution, metal ions, and sugar, have been used to realize the shape transformation of SMHs in biomedical fields. In our previous studies, polyampholyte hydrogels were fabricated by free radical copolymerization, in which strong hydrogen bonds acted as the hard segment and ionic bonds coexisted in the hydrogels, which could respond to different salt concentrations to realize a triple SME. Body temperature and water-induced shape-memory hydrogels were fabricated using tetra-PEG. Water-induced shape memory hydrogels were fabricated using tetra-PEG. water or elevated temperatures could destroy the crystalline region in the PEG chains to realize shape recovery. The gentle stimuli of water, salt solution, and temperature are practical for biomedical applications.

SMHs exhibit unique advantages in deep. non-compressible and irregularly shaped wound healing, including haemostasis and wound closure. Because of the shape transition under mild stimuli, SMHs can fill deep and irregular wounds, GUO et al, applied injectable cryogens in wound healing, with shape recovery triggered by water and blood, which are used as haemostatic agents in deep wound haemostasis on the other hand, a recovery force is existed, which can be used for non-invasive wound closure. Xie et al. fabricated self-adhesive SMHs using oxidized starch]gelatine. The hydrogels exhibit shape transition when heating to 38 cand display sufficient recovery force of 4 Kpa to realize successful non-invasive wound closure The hydrogel treatment also resulted in thicker epidermis and dermal layers. Zhao et al. applied strain-programmed patches based on the shape-memory mechanism to treat diabetic wounds, which could mechanically contact the wounds in a programmable manner.

2.6. Conductive Hydrogels

By encouraging fibroblast migration and proliferation and keratinocyte ECM production, electrical stimulations (ES) can hasten wound healing. For whole-wound treatments, however, it is inappropriate to implant electrodes close to wounds in order to administer low-intensity currents. Effective wound healing may be facilitated by the combination of conductive materials with ES. Conductive polymers. nanoparticles, or other conductive components have been incorporated into conductive hydrogels utilising a variety of techniques to create conductive hydrogels with electrical or ionic conductivity. Conductive hydrogels have been extensively researched and used to support wound healing, tissue regeneration, drug administration, and biosensors because of their adaptable physical and biochemical properties that satisfy the demands of the biomedical industry.

Conductive hydrogels have been proven that they can regulate cellular, including cell adhesion, proliferation, migration, and isolation of electrically hyperexcitable cells. Conductive hydrogels can also be used as detectors to descry biomolecule or stir. colourful accoutrements have been incorporated into hydrogels to endow them with electronic conductivity. conductive polymers similar as (Papy), polyaniline, poly thiophane's were hydrogels with good conductivity and flexible mechanical parcels have been considerably studied. still, conventional conductive hydrogels have been studied, and conductive rudiments are tone mending structures have been introduced into hydrogels. the tone mending medium is analogous to that of injectable tone- mending hydrogels, relations, including Schiff base bonds, ionic relations, essence ion collaboration, host- guest relations, and hydrogen cling. have been used to combine tone mending parcels with conductive hydrogels. The Papy- functionalized boronic ester group were stoutly crosslinked with the CS and PVA hydrogels. After breaking piecemeal, the hydrogels were reformed without applying any external stimulants, and their mechanical parcels and conductivity were recovered. also, PVA- grounded hydrogels parade mechanical tone- mending parcels, as measured by strain dependent oscillatory shear rheology. conductivity was restored. Conductive hydrogels represent a burgeoning class of intelligent crack dressings, furnishing innovative strategies for habitual crack form and monitoring promoting cell migration and proliferation, parade important antibacterial and antiinflammatory parcels, and enhance collagen deposit and angiogenesis. These capabilities, combined with real- time monitoring functions, play a vital part in accelerating collagen conflation, angiogenesis, and nonstop crack surveillance



Homosiasisinflammation Proiifora ikon Tissue remodoiing

Figure 2.4 : diabetic wound with conductive hydrogel show the action of vasculopathy, neuropathy,infection involved patho of hemostasis, inflamation, proliferatio, tissue remodeling in the different stages involved the mechanism og inflammation Ml and M2 ROS in th proliferation phase nerve regeneration turns again tissue remodeling.

5.ReaI-Time monitoring Hydrogels

It is important to monitor the wound healing process in real time and assess the efficacy of treatment. The microenvironment of wounds changes dynamically during the healing process, including the PH value, infection status, ROS level, glucose level, and temperature, which affect wound healing. The state of the hydrogel on the wound was also remarkable. In addition, the real time monitoring of wound pressure is important for pressure ulcers and can be realized using flexible sensors. Thus, the design of hydrogels with real-time monitoring properties is important for monitoring and optimizing treatments. The detection of wound infection is critical for effective clinical interventions to improve wound treatment. current detection methods rely on time-consuming culture-based laboratory tests or clinical assessments, leading to delays in timely administration. With the recent development of flexible electronics, the advanced sensors based on functional hydrogels have enabled the detection of parameters such as PH. temperature. pressure and humidity. The direct and rapid

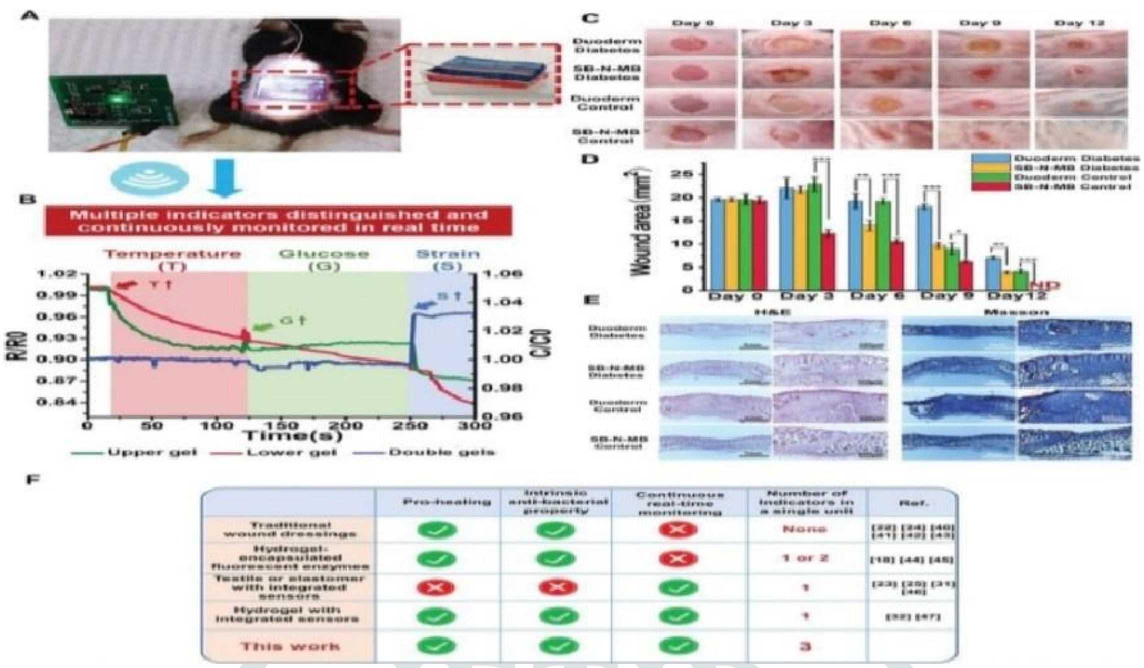


Figure 3. I : In vivo wound healing test and continuous real-time monitoring on diabetic wounds

A) schematic photograph of real-time monitoring on diabetic wounds B) Resistance and capacitive response curves to temperature (T), glucose concentration(G), and strain(s) continuously monitored and distinguished in real-time C) photographs of the wound healing process and D) wound area measurement in healthy and diabetic using zwitterionic skin sensors and dressings from Day I to Day 12. F) Comparison chart of currently reported wound dressings.

detection of wound infection is important for clinical interventions. The PH value changes with different states of the skin wounds. The PH of acute wounds is approximately 4-6, accompanying the activity of neutrophils in preventing bacterial colonization, Therefore, monitoring the PH value is an effective way to identify different healing phases and provide a warning of infection risks. Diabetic wounds are always alkaline at PH 7-9, which are vulnerable to bacterial infections. Conversely, the PH value increase to above 7 after bacterial infection occurs at the wound site, where bacteria and enzymes exists, PH indicator dye, such as phenol red and bromothymol blue, can be used to monitor the PH values in wound sites. the hydrogel was incubated with staphylococcus aureus for different stages, the colour changed from greyish-blue to light yellowish-green. which was consistent with the colour change can be used to monitor bacterial infections to diabetic wounds.

2.7. Anti-Innammatory and Immunomodulatory Hydrogels:

The inflammatory response in diabetic wounds is always excessive because of constant cytokine stimulation and the recruitment of immune cells to the wound. Dysfunctional immune cells such as MI macrophages and neutrophils secrete pro inflammatory chemokines, leading to chronic inflammation, To promote diabetic wound healing, anti-inflammatory hydrogels have been studied and used to promote diabetic wound healing. Anti-inflammatory hydrogels are fabricated by loading cells, cytokines, anti-inflammatory drugs or components in the networks, Anti-inflammatory materials can also be used to fabricate hydrogels that regulate macrophage polarization and promote wound healing through immunomodulation.

Anti-inflammatory drugs, such as naproxen, diclofenac, Nimes Lide, ibuprofen, have been used to promote wound healing. Insulin a drug used to maintain blood glucose levels within a normal range, shortens the inflammatory phase. Artemisia Argy extract has good antiinflammatory and anti-bacterial properties. Chinese traditional Tibetan medicine is also used in to treat diabetic wounds. As a type of nonsteroidal anti-inflammatory drug, diclofenac exerts an anti-inflammatory effect by inhibiting the aggregation if immune and platelet

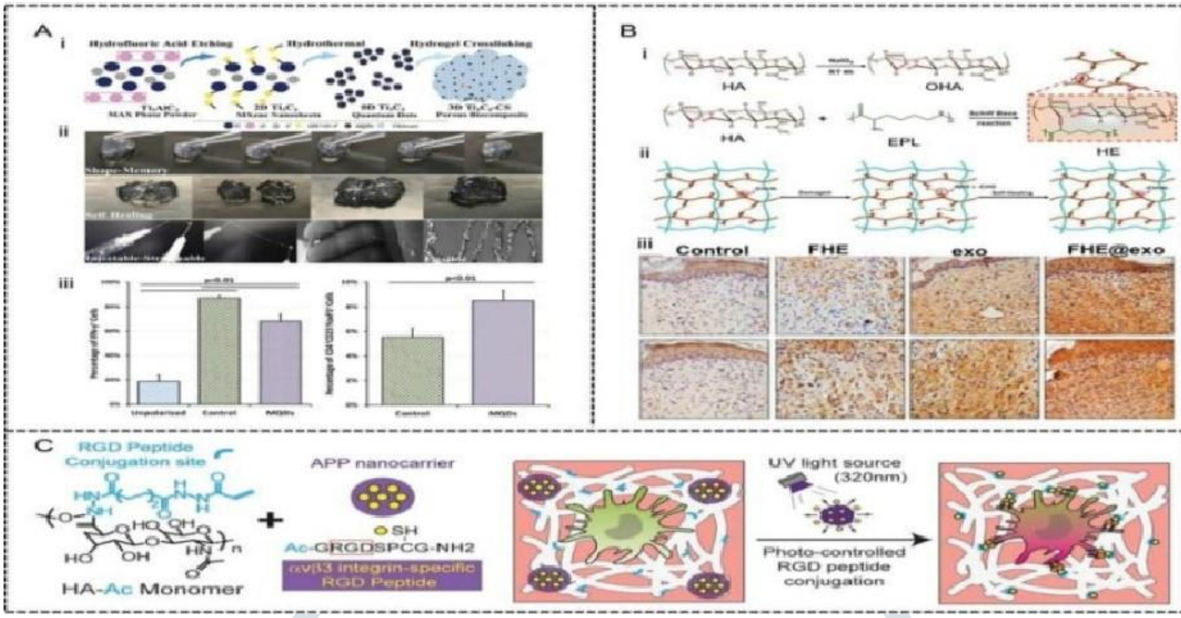


Figure A)lmmunomodulatory MQDs-CS hydrogels with shape-memory and injectable selfhealing properties
Scheme illustration of the synthesis process of MQDs-CS by thermal treatment and MQDs decorated hydrogeIs.(B)hydrogeIs with adipose-derived MSC exosomes (e) photo-responsive composite hydrogel with controlled adhesion sites for dynamic macrophage immunomodulation.

3.1. Impact of nutrition on wound healing

focus on nutrition supplementation with mixed results regarding effectiveness to support wound healing. Nutrition plays a critical role in wound healing, as it provides the necessary nutrients with wounds. Poor nutrition before or during the healing process may delay healing and impair wound strength, making the wound more prone to breakdown.

A nutritious diet should include proteins and amino acids (20%), carbohydrates (40%), and fruit and vegetables (40%) to ensure optimal consumption of vitamins, iron, zinc and fats calcium, vitamins k, and E, proteins and amino acids, polyunsaturated fats, and zinc important for haemostasis and the inflammatory phase. Weight loss plans may not be appropriate during wound healing. A wide range of nutrients can improve healing, yet malnutrition in everyday diet Impact diet can have on the capability of a wound to heal itself. Wound healing is a complex process that can be enhanced by optimising nutrition. There appears to be a strong link between Determine how healthcare professionals perceive their role in nutrition assessment and management, and explore barriers and enablers to assessment and management of nutrition in individuals with mixed methods including a cross-sectional online survey derived from current international guidelines and theoretical domains framework, and semi-structured interviews with conventional content analysis was performed- Many health professionals are not confident in their ability in this area of practice, are uncertain their nutrition advice or management will be effective in assisting wound healing outcomes and are uncertain their intervention would result in adequate behaviour change by the individual with major barriers to implementation of nutrition assessment and management were: inadequate time, lack of knowledge and lack of clinical guidance and enablers were as follows. Nutrition is recognised as essential for timely wound healing, with inadequacy of energy, protein, zinc, vitamin c and vitamin D prolonging tissue repair. Protein and zinc are imperative for white blood cell formation, function in immune response, and are important for collagen synthesis and immunomodul ation involved in the proliferative and remodelling phases of wound healing. Adequate vitamin D intake has demonstrated anti-inflammatory affects and supports structural integrity in wound healing. numerous studied have explored nutrition interventions the majority poor nutrition and factors including delayed wound healing and the risk of complications such as infections, During healing, different stages of wound-healing process progress at different rates and a poor nutritional status can cause delays. Wounds place increased metabolic and hence nutritional demands on especially in older patients in the community.This article reviews the phases of wound healing and the associated nutritional requirements required for optimal healing.Ageing and impaired nutrition can affect wound healing many factors such as smoking, diabetes, anemia, steriods and malnutrition, often impede the wound healing process. Several studies have indicated that nutritional deficiences are more prevalent with chronic wounds.malnutrition may alter the inflammatory response, collagen synthesis, and wound tensile strength, all of which are crucial for wound healing.AIthough the specific role of nutrition and supplementation in wound care remains uncertain.

Figure 3.3: nutrition food in diabetic wound healing the food to eure and maintain healthy diabetic wound healing patient care.

3.2. Future trends in wound care technology:

1. Smart sensors and wound dressings: Artificial intelligence supported chronic skin monitoring Integration of intelligent and efficient wearable sensors with well-optimized wound dressing bandages holds a technological transformative era in contactless chronic skin monitoring can be established. HOWEVER, this approach is at an early stage and needs systematic research to connect components such as sensing, machine-skin interfacing, rapid data analytics. Introduction of artificial intelligence algorithms harness the predict and optimize tissue regeneration trajectories.

2. Recent advances on 3D-bioprinted gelatine methacrylate hydrogels for tissue engineering in wound healing

Advancements in tissue engineering, particularly the revolutionary technology of 3D bioprinting, have in a new era regenerative medicine including scalability of 3D bioprinting techniques overcoming these challenges through multidisciplinary collaboration, advancing manufacturing techniques and embracing personalized medicine paradigms.

3.Recent developments and future perspectives of microfluidics and smart technologies in wearable devices

Wearable devices are gaining popularity in the fields of health monitoring, diagnosis, and drug delivery. Recent advances in wearable technology have enabled real-time analysis of biofluids such as sweat, interstitial fluid, tears, saliva, wound fluid, and urine. The integration of microfluidics and emerging smart technologies, such as artlficial intelligence (Al), machine learning (ML) wearable devices offers great potentiål for accurate and non-invasive monitoring and diagnosis

4. A MG Battery-integrated Bioelectronic patch provides Efficient Electrochemical stimulations for wound healing

Bioelectronic patches hold promise for patient comfort wound healing prov iding simplified clinical operation. They face paramount challenges in establishing long-term effective electronic interfaces with targeted cells and tissues due to inconsistent energy output and high bio interface impedance. A new electrochemical stimulation technology is reported, using a simple wound patch, which integrated the effective generation and delivery of stimulation. The Mg battery enhances fibroblast functions (proliferation, migration, and growth factor secretion) and regulates macrophage phenotype (promoting regenerative polarization and downregulating pro-inflammatory cytokines.

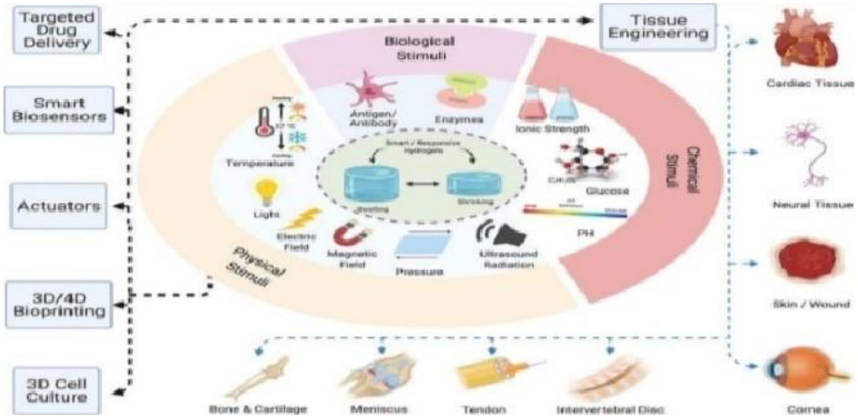


Figure 3.4: future technology development in diabetic wound care and recent advance treatment for patient care advance drug delivery and monitoring and diagnosis based on types of hydrogel s.

4.1. ConclusionIn conclusion, diabetic wound healing presents significant challenges due to the physiological complications associated with diabetes€ suCh as poor circulation, impaired immune function, and high blood glucose levels. These factors can delay the healing process and increase the risk of infection. leading to chronic wounds. However. with appropriate management strategies—ranging from blood sugar control and effective wound care to the use of advanced therapies like negative pressure wound therapy, bioengineered skin substitutes, and growth factors—healing outcomes can be significantly improved. The key to successful management lies in early intervention, personalized care, and a multidisciplinary approach that involves healthcare professionals from various specialties. By addressing the root causes of delayed healing and tailoring treatments to individual needs, it is possible to enhance wound recovery, prevent complications, and improve the quality of life for individuals with diabetes.

4.2. Reference:

1) Sezen S, Bilici C, Zarepour A, Khosravi A, Zarrabi A, Mostafavi E. Mechanical Properties of Multifunctional Hydrogels-lnMu1tifunctiona1 Hydrogels 2024 Apr 19 (pp. 214-233). CRC Press.

2) Wang X, Li R, Zhao H. Enhancing angiogenesis: innovative drug delivery systems to facilitate diabetic wound healing. Biomedicine & Pharmacotherapy, 2024 Jan 1;17():116035.

3) Yang Y, Zhong S, Meng F, Cui X. Multi-Functional hydrogels to promote diabetic wound Healing: A review. Chemical Engineering Journal. 2024 Aug 14:154855.

4) Duarte J, Mascarenhas-MeIo F, Pires PC, Veiga F, Paiva-Santos AC. Multifunctional hydrogels-based therapies for chronic diabetic wound healing. European Polymer Journal. 2024 Apr 8: 113026.

5) Xiang T, Guo Q, Jia L, Yin T, Huang W, Zhang X, Zhou S. Multifunctional hydrogels for the healing of diabetic wounds. Advanced Healthcare Materials. 2024):2301885. 6) Yang Y, Zhong S, Meng F, Cui X. Multi-Functional hydrogels to promote diabetic wound Healing: A review. Chemical Engineering Journal. 2024 Aug 14:154855.

7) Hanson D, Langemo D, Thomson P, Anderson J, Hunter S. Understanding wound fluid and the phases of healing. Advances in Skin & Wound Care. 2005 Sep1;18(7):3

8) Guo SA, DiPietro LA. Factors affecting wound healing. Journal of dental research. 2010 Mar;89(3):219-29.

9) Patel S, Srivastava S, Singh MR. Singh D. Mechanistic insight into diabetic wounds: Pathogenesis, molecular targets and treatment strategies to pace wound healing. Biomedicine & Pharmacotherapy. 2019 Apr l; 112: 108615.

10) Duarte J, Mascarenhas-Me10 F. Pires pc, veiga F. Paiva-Santos AC, Multifunctional hydrogels-based therapies for chronic diabetic wound healing. European Polymer Journal. 2024 Apr 8:113026.

12) Lu Z, Cui J, Liu F, Liang C, Feng S, Sun Y, Gao W, Guo Y, Zhang B, Huang W. A 41)
Printed Adhesive, Thermo-Contractile, and Degradable Hydrogel for Diabetic Wound Heali1V Advanced Healthcare Materials. 2024 Apr; 13(10):23

13) Zhang H, Lin X, Cao X, Wang Y, Wang J, Zhao Y. Developing naturål polymers for skin wound healing. Bioactive Materials. 2024 Mar l; 33:355-76.

14) Hao Z, Li X, Zhang R, Zhang L. Stimuli-Responsive Hydrogels for Antibacterial Applications. Advanced Healthcare Materials. 2024 May 9:2400513.

15) Fang Z, Chen P, Ji Q, Yan C, Gong A. Stimuli-responsive hydrogel for disease therapy.
Polymer Bulletin, 2024 1981-2000,

16) Hoffman AS. Hydrogels for biomedical applications. Advanced drug delivery reviews. 2012 Dec 64:18-23.

17) Shields BE. Diet in wound care: can nutrition impact healing. Current Psychiatry. 2021 Dec1;20(12).

18) Seth I, Lim B, Cevik J , Gracias D, Chua M, Kenney PS, Rozen WM, Cuomo R, The Impact of Nutrition on Skin Wound Healing and Aesthetic Outcomes: A comprehensive narrative review. JPRAS open. 2024 Jan 23.

19) Arnold M, Barbul A. Nutrition and wound healing. Plastic and reconstructive surgery. 2006 Jun1;117(7S):42S-58S.

20) Kavalukas SL, Barbul A. Nutrition and wound healing: an update. Plastic and reconstructive surgery. 2011 Jan l; 127:38S-43S.

21) Anderson B. Nutrition and wound healing: the necessity of assessment. British journal of nursing. 2005 Oct 28;14(Sup5): S30-8.

22) Clark RK, Stampas A, Kerr KW, Nelson JL, Sulo S, Leon-Novelo L, Ngan E, Pandya D. Evaluating the impact of using a wound-specific oral nutritional supplement to support wound healing in a rehabilitation setting. International wound journal. 2023 Jan;20(l):145-54.

23) Stechmiller JK. Understanding the role Of nutrition and wound healing. Nutrition in clinical practice. 2010Feb;25(1

24) Fani N, Moradi M, Zavari R, Parvizpour F, Soltani A, Arabpour Z, Jafarian A. Current advances in wound healing and regenerative medicine. Current stem cell research & therapy.
2024 Apr1;19(3):2

25) Roy R, Ashmika R. Textile Products in Healthcare: Innovations, Applications, and Emerging Trends. Emerging Technologies for Health Literacy and Medical Practice.
2024:288-314.

26) Saifullah Q, Sharma A. Current trends on innovative technologies in topical wound care for advanced healing and management, Current Drug Research Reviews Formerly: Current Drug Abuse Reviews. 2024 Nov 1;16(3):319-32.

27) Huang SW, Wu YF, Ahmed T, Pan SC, Cheng CM. Point-of-care detection devices for wound care and monitoring. Trends in biotechnology. 2024 Jan 1:42(1):74-90.

28) Fani N, Moradi M, Zavari R, Parvizpour F, Soltani A, Arabpour Z, Jafarian A. Current advances in wound healing and regenerative medicine. Current stem cell research & therapy.
2024 Apr1;19(3):

29) Roy R, Ashmika R. Textile Products in Healthcare: Innovations, Applications, and Emerging Trends. Emerging Technologies for Health Literacy and Medical Practice. 2024288-314.

30) Prakashan D, Kaushik A, Gandhi S. Smart sensors and wound dressings: Artificial intelligence-supported chronic skin monitoring—A review. Chemical Engineering Journal. 2024 Jul 29:154371.

31) Huang SW, W u YF, Ahmed T, Pan SC, Cheng CM, Point-of-care detection devices for wound care and monitoring. Trends in biotechnology. 2024 Jan1;42(1):

32) Cheng S, Gu Z, Zhou L, Hao M, An H, song K, wU X, Zhang K, Zhao Z, Dong Y, wen Y. Recent progress in intelligent wearable sensors for health monitoring and wound healing based on biofluids. Frontiers in Bioengineering and Biotechnology. 2021 Nov 1;9:765987.

33) Deliorman M, Ali DS, Qasaimeh MA. Next-generation microfluidics for biomedical research and healthcare applications. Biomedical Engineering and Computational Biology.
2023 Nov; 14:11795972231214387.

34) Choudhary BK, Durai SA, Ahmad N. Smart Microfluidic Devices for Point-Of-Care Applications. Journal of Advanced Research in Fluid Mechanics and Thermal Sciences. 2024 Feb15;114(1):119-33.

35) Myers FB, Lee LP. Innovations in optical microfluidic technologies for point-of-care diagnostics. Lab on a Chip.2008;8(12):2015-31.

36) Nasra S, Pramanik S, Oza V, Kansara K, Kumar A. Advancements in wound management:
integrating nanotechnology and smart materials for enhanced therapeutic interventions.
Discover nano. 2024 Oct2;19(1):159.

37) Yang SM, Lv S, Zhang W, Cui Y. Microfluidic point-of-care (POC) devices in early diagnosis:
A review of opportunities and challenges. Sensors. 2022 Feb 18;22(4):1620.

38) Jiang S, Xie D, Hu Z, Song H, Tang P, Jin Y, Xia J, Ji Y, Xiao Y, Chen S, Fu Q. Enhanced diabetic wound healing with injectable hydrogel containing self-assembling nanozymes. Journal of Controlled Release. 2024 Aug1;372:2

39) Wang H, Zhang LM. Intelligent biobased hydrogels for diabetic wound healing: A review. Chemical Engineering Journal. 2024 Feb 10: 149493.