CODEN: WJAPAC Impact Factor: 3.87 ISSN: 3049-3013

World Journal of Advance Pharmaceutical Sciences

Volume 2, Issue 4. Page: 183-194 Review Article www.wjaps.com

THE ROLE OF ESSENTIAL OILS IN ENHANCING WOUND HEALING WITH POLYMERIC BIOMATERIALS

Vaishnavi Dhanedar*[1], Vaishnavi Bodkhe[2], Poonam Kodag[3], Pratiksha Kale[4], Anuja Bodkhe[5], Monika Kalamkar[6]

Rashtriya College of Pharmacy Hatnoor.

How to cite this Article Vaishnavi Dhanedar*, Vaishnavi Bodkhe, Poonam Kodag, Pratiksha Kale, Anuja Bodkhe, Monika Kalamkar (2025). THE ROLE OF ESSENTIAL OILS IN ENHANCING WOUND HEALING WITH POLYMERIC BIOMATERIALS, 2(4), 183-194.

Article Info

Article Received: 16 October 2025,

Article Revised: 06 November 2025,

Article Accepted: 26 November 2025.

DOI: https://doi.org/10.5281/zenodo.17767022

***Corresponding author:**

***Vaishnavi Dhanedar**

Rashtriya College of Pharmacy Hatnoor.

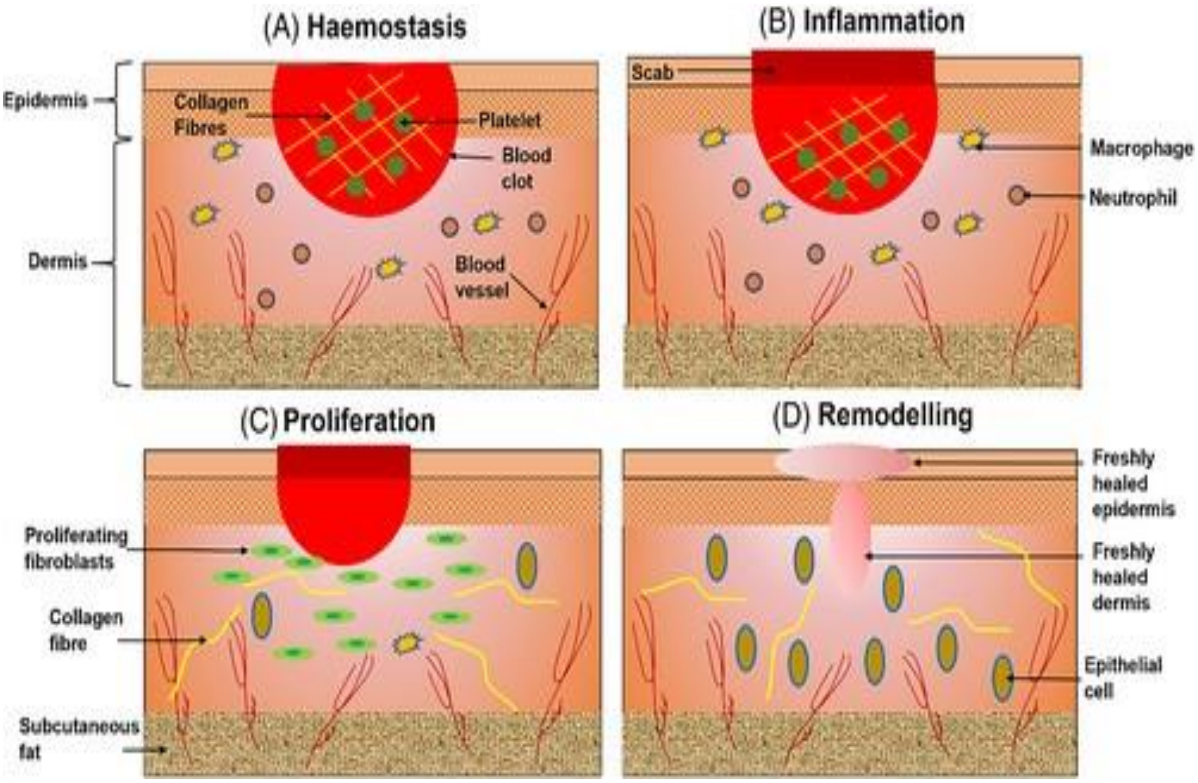
1. ABSTRACT

Wound healing can result in complex problems, and discovering an effective method to improve the healing process is essential. Polymeric biomaterials have structures similar to those identified in the extracellular matrix of the tissue to be regenerated and also avoid chronic inflammation, and immunological reactions. To obtain smart and effective dressings, bioactive agents, such as essential oils, are also used to promote a wide range of biological properties, which can accelerate the healing process. Therefore, we intend to explore advances in the potential for applying hybrid materials in wound healing. For this, fifty scientific articles dated from 2010 to 2023 were investigated using the Web of Science, Scopus, Science Direct, and PubMed databases. The principles of the healing process, use of polymers, type and properties of essential oils and processing techniques, and characteristics of dressings were identified. Thus, the plants Syzygium romanticum or Eugenia caryophyllata, Origanum vulgare, and Cinnamomum zeylanicum present prospects for application in clinical trials due to their proven effects on wound healing and reducing the incidence of inflammatory cells in the site of injury. The antimicrobial effect of essential oils is mainly due to polyphenols and terpenes such as eugenol, cinnamaldehyde, carvacrol, and thymol.

KEYWORDS: Wound healing, Polymeric biomaterials, Hybrid materials, Essential oils, Bioactive dressings, Eugenol.

2. INTRODUCTION

pastes, were commonly used in the past as wound dress-ings (Thomas1990). A few years later, materials like cotton wool, lint, and gauzes started being used as dressings, and their main function was to keep the wound dry by allow-ing wound exudates to evaporate and inhibiting invasion of bacteria from the surrounding environment (Thomas 1990). Recent studies have proven that a moist and warm environ-ment provides a better alternative to the previous wound-healing therapies. The compatibility of the physical and chemical properties of the dressing towards the nature of the wound must take into account the designing a bandage for wound healing. An active wound dressing controls the biochemical state of the wound to aid the healing process. No wound dressing is ideal, but the minimum requirements of rapid healing, affordable cost to the patient, aesthetics, and prevention of infection, must be fulfilled during wound management (Helfman etal. 1994).[1]



The convergence of tissue engineering, biomaterials science, and wound healing has led to significant advances in developing novel therapeutic strategies for skin injuries. Traditional pharmaceutical treatments are no longer viable when tissues or organs are severely diseased or lost due to trauma. In such cases, the option of artificial organs (including tissues) or organ transplantation arises to reconstruct these compromised tissues or organs. Chronic wounds and tissue defects present significant clinical challenges, requiring ongoing efforts to promote effective healing and tissue regeneration Tissue engineering aims to repair, replace, maintain, or enhance the function of a specific tissue or organ.

The process of wound healing is a fascinating and intricate mechanism encompassing four distinct phases: hemostasis, inflammation, proliferation, and remodeling. Coagulation factors are activated, forming a clot of platelets to minimize blood loss at the wound site (hemostasis). This is followed by an inflammatory response, characterized by the release of proteolytic enzymes and pro-inflammatory cytokines (inflammation). Subsequently, angiogenesis is stimulated, leading to scar formation (proliferation). Finally, the newly formed capillaries regress, and the majority of macrophages and fibroblasts undergo apoptosis (remodeling). In addition to these processes, a suitable sterile covering (dressing) is also crucial, providing the characteristics of skin tissue regeneration and a natural barrier to the external environment, mimicking the epithelium.

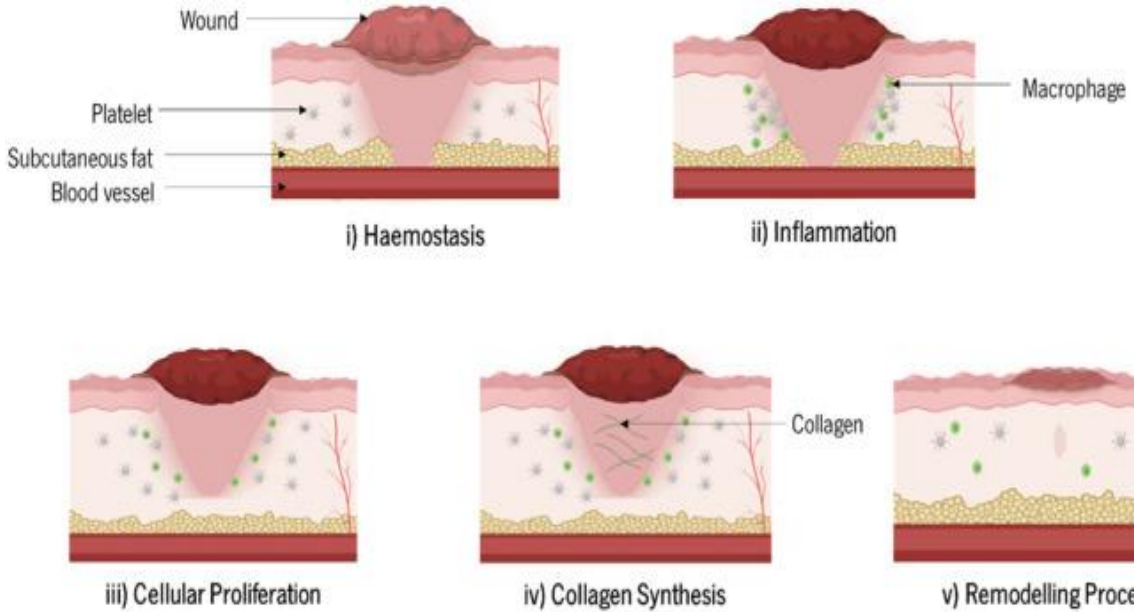
Biomaterials can be used to create wound dressings. Both natural and synthetic polymers have beneficial characteristics such as adjustable biodegradation rates, mechanical properties, high porosity with varying pore sizes, and a high surface-to-volume ratio based on the synthesis technique. Chitosan is a polymeric, antimicrobial, antioxidant, biocompatible, and biodegradable material with low toxicity and the ability to accelerate dermal regeneration usually used in biomedical areas such as wound healing and tissue engineering.

Antibacterial properties aim to reduce inflammation caused by infections, slowing the healing process. One strategy to improve biological properties is to produce smart or modern dressings interspersed with essential oils (EOs), which act as bioactive agents.

Essential oils (EOs) are volatile secondary aromatic compounds characterized by the presence of phenylpropanoids and terpenoids. They have antioxidant and antibacterial effects, as well as antiviral, insecticidal, analgesic, and anti-inflammatory properties. In the healing process, EOs can accelerate wound closure, improve collagen deposition, and increase fibroblast proliferation.

This review, therefore, elucidates recent advances in the potential application of hybrid materials (biomaterials/EO) in the process of healing skin wounds, based on the investigation of fifty scientific articles evaluated in the following databases: Web of Science, Scopus, Science Direct, and PubMed. This study covers the principles of the healing process, the use of natural

and synthetic polymers, the type and properties of essential oils and processing techniques, and the characteristics of dressings, emphasizing the chitosan biomaterial and its properties. The aim here is to provide insights into new wound treatment and tissue regeneration approaches.[2]



3. ACUTE WOUND HEALING

Acute wound healing follows a physiological and dynamic signaling cascade upon injury that can be broken down into four component phases. Starting with the *hemostatic phase*, which is the immediate response of the local tissue vasculature to activate platelets and generate a clot via formation of a provisional fibrin-platelet matrix. The goal of this phase is to prevent excessive blood loss and exsanguination, while also serving as an initiation signal for wound healing to commence. Next, is the *inflammatory phase*, which is a series of immunomodulatory signaling cascades that results in immune cell migration (neutrophil and monocyte/macrophage) into the wound tissue to begin removing damaged debris, foreign objects, or bacteria. The previously deposited fibrin-platelet clot serves as a biological signal as well as a temporary scaffold for invading cell populations into the wound site. The inflammatory phase typically culminates in about one week. Subsequently, is the transition into the *proliferative phase*, which is the stage of neovascularization, re-epithelialization, fibroblast proliferation, and wound contraction. The key modulators of this phase of healing are fibroblasts and keratinocytes, and the main outcomes are formation of granulation tissue and a restored epidermal barrier, respectively. The final stage is the *remodeling phase*, which does not occur until the wound has been sufficiently closed via reestablishment of the external epidermal barrier. Fibroblasts are the main cells participating in the remodeling phase and are involved in both the deposition of new matrix and the enzymatic degradation of old matrix in order to ultimately restore a state of anatomical homeostasis and function.

4. CHRONIC WOUNDS HEALING

Prolonged or abnormal progression through the stages of wound healing results in pathological, chronic, non-healing wounds. There are a variety of factors that can promote the progression towards pathological healing, such as trauma (particularly recurring trauma), nutritional deficits, infection, surgery, chronic disease, and radiation. Moreover, most chronic wounds tend to be stuck in a perpetual cycle of the inflammatory and proliferative phases of wound healing. Ultimately, this leads to wounds that fall within the continuum of excessive scar tissue formation and fibrosis or insufficient scar tissue formation and ulceration. Unfortunately, chronic wounds remain a significant burden on the healthcare system, affecting over 8 million people in the US at a cost of over $30 billion annually.

There are a variety of local and systemic factors that can have a detrimental impact on wound healing and subsequently result in non-healing wounds. Locally, chronic wounds tend to maintain a highly inflammatory, oxidative, alkaline, and proteolytic tissue environment, in addition to having a higher propensity for microbial colonization (especially biofilm) and infection, which ultimately results in obstruction of physiological healing. Notably, wound fluid from chronic wounds demonstrated the ability to rapidly degrade matrix structural proteins (e.g. collagen) and key signaling factors, further demonstrating the destructive capacity of the proteolytic imbalance of chronic wounds. Systemically, comorbid conditions that are associated with inadequate supply of nutrients and waste transport (e.g. cardiovascular disease) and states of chronic inflammation (e.g. obesity and diabetes) contribute to non-healing wound progression. Similarly, complex wounds that result in

significant tissue involvement and destruction, such as those from extensive burns, traumas, or military-based incidents, are also highly prone to progression towards non-healing chronic wounds and require special attention.

All of the above-mentioned factors are important to consider when generating a wound treatment plan for a patient who may have varying degrees of each. However, comorbid health conditions, such as diabetes, are considered to play one of the most significant roles in the development and progression of chronic, non-healing wounds, where up to 15% of diabetics develop ulcerative wounds with a greater than 50% recurrence rate. Diabetic wounds inherently have an improper balance and composition of bioactive compounds within the tissue, resulting in inadequate neotissue formation. Consequently, lack of wound closure results in polymicrobial infections, desiccation, and reinjury of the diabetic wounds, which remain the leading cause of non-traumatic lower limb amputations. Overall, chronic wounds are highly complex and variable, though they are often treated in a similar fashion with labor intensive and non-specific treatment modalities that can include continuous wound cleaning, debridement, surgery, antibiotics, oxygen therapy, and dressing changes. Thus, developing more effective personalized wound therapies is a critical area of research.[3]

5. WOUND HEALING PROCESS

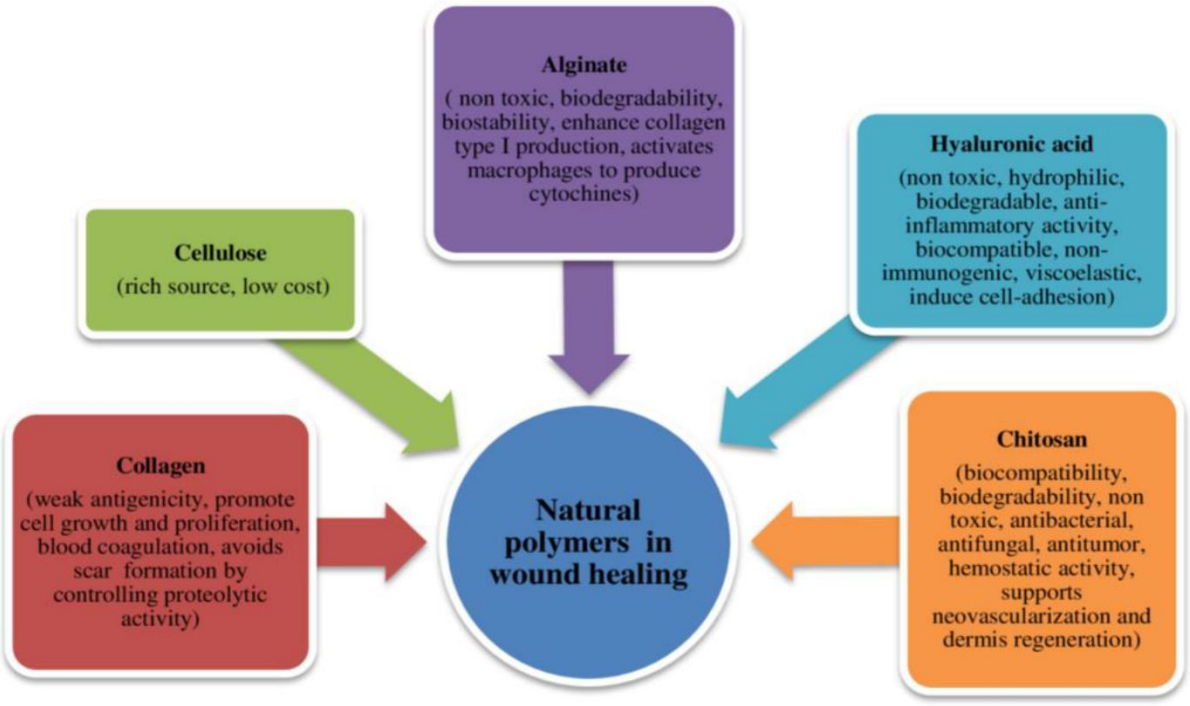
Wound healing is a complex and dynamic process that involves four continuous and overlapping phases. These phases occur in a precise and regulated manner. The wound healing process can be delayed by certain interruptions and aberrancies. The four phases of wound healing are as follows. The first phase is hemostasis which occurs immediately when blood leaks out of the body. Hemostasis is a process in which the wound is closed by vascular constriction and fibrin clot formation. The next stage is inflammatory which begins when the injured blood vessels leak an exudate resulting in localized swelling. This exudate comprises water, salt, and proteins. The role of the exudate is to remove damaged cells, pathogens, and bacteria from the wound area, and the inflammation stage is when bleeding stops and wound infection should be prevented. This phase also helps repair cells to move to the site of the wound to commence healing. The third stage is the proliferative phase in which the wound is rebuilt with the formation of the new tissue contains collagen and an extracellular matrix. In the proliferative phase, the wound begins to close as new tissues are produced. In addition, new blood vessels are constructed resulting in the generation of the healthy granulation tissue which can then receive sufficient oxygen and nutrients. Granulation tissue is composed of fibroblast cells, endothelial cells, capillaries, and keratinocytes. If the granulation tissue is pink and does not bleed easily, it is a sign of healthy wound healing. However, dark granulation tissue is a sign of infection, ischemia, or poor perfusion. In the final phase of the proliferative stage of wound healing, the wound surface will be closed by epithelial cells. Epithelialization occurs faster if the wound is kept moist and hydrated. The final stage is the maturation phase in which the remodeling of collagen from type III to type I occurs, and the wound should fully close. The cells which are no longer needed to repair the damaged tissue are removed by apoptosis. In the maturation phase, collagen tends to align in tension lines, and water is reabsorbed making the collagen fibers closer together and cross-linking occurs. Cross-linking of collagen helps in reducing the scar thickness and also makes stronger skin in the area around the wound.[4]

6. POLYMERIC-BASED BIOMATERIALS FOR WOUND HEALING

Materials to be used for wound treatment must have biocompatibility, like chitosan (Liu, 2018). Polymers have interesting properties. They are easily modified through chemical processes, with the ability to form 3D structures for scaffolds and tailor their surface functionality (Paul and Sharma, 2004). Polymers flexibility in terms of topology, dimensions, and chemistry make them suitable to act as a drug delivery system enhancing wound repair. Therefore, polymers are great candidates to be used as skin substitutes (Talikowska et al., 2019), (Negut et al., 2020). Table 1 describes the application of different polymers for wound healing and skin applications.

6.1 NATURAL POLYMERS

Natural polymers, as the name states, are obtained from natural sources such as microbial, vegetable, and animal biomass. The characteristics of these polymers, namely biodegradability, biocompatibility, and biological activity, make them ideal for health-related applications (Negut et al., 2020). Moreover, natural-derived polymers can be used to replace natural ECM structural components and skin cellular background (Negut et al., 2020), (Portela et al., 2019). Indeed, these biopolymers are an asset for the design of versatile materials, as they meet the requirements for tissue engineering applications. When subjected to enzymatic degradation, natural polymers form by-products with low toxicity, which in most cases are well accepted by living organisms. However, natural polymers have some limitations, namely the difficulty to control their degradation rates/processes (Negut et al., 2020), (Bao et al., 2009), (Sill and von Recum, 2008). Regarding wound healing applications, natural polymers can be used as bioactive materials enhancing regeneration, as vehicles for drug delivery, and as scaffold formations with 3D networks promoting local tissue regeneration. When selecting polymeric materials for biomedical applications, several characteristics must be considered, including architecture, solubility, pore size, degradability, water absorption capacity, and electrical charge (ter Horst et al., 2019).[5]



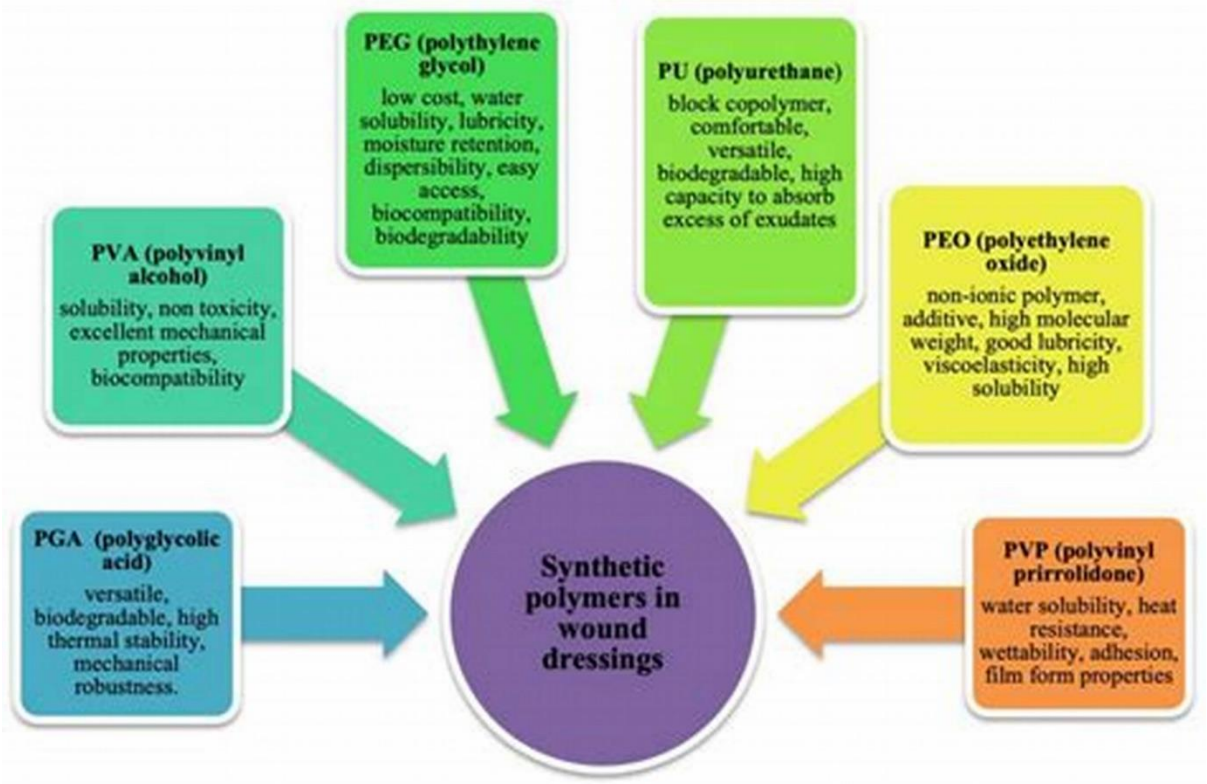
6.2 SYNTHETIC POLYMER

Polymer films have been initially introduced as drapes for surgical incisions. Studies have documented the use of polymers in dressings or as medical devices for potential improvement in controlling wound healing (Mir et al. 2014a, b, 2016). However later they have now carved a niche in wound-healing management as occlusive dressings.

During the past years wound dressing has been modernized which now mainly consist of synthetic polymers for wound management. Synthetic polymer dressings can be classified as passive and interactive. Passive synthetic polymer dressings are non-occlusive, used for covering wound and help in restoring function under the polymer film. Example of such passive synthetic polymers is gauze and tulle. Interactive synthetic polymer dressings are occlusive or semi-occlusive which provide a barrier against bacterial penetration to the wound. They can be in the form of films, foams, hydrogel or hydrocolloids (Dhivya et al. 2015).

Polymer films trap exudates, hence providing a moist environment for wounds. Polyurethane (PU) is used in many semi-permeable dressings because of its ability to provide good barrier and permeability to oxygen. One main feature is that these films are impermeable to bacteria and liquid but are permeable to moisture vapor and air. Exudates from wounds may accumulate underneath such semi-occlusive film since these dressings are non-absorbent which is a major drawback of such dressings. Although this does not appear to encourage bacterial growth in the wound, the seeping fluid pressure may cause a break in the environment maintained by the occlusive dressing.

In one of the experiment, synthetic polyurethane films have been analyzed as potential polymeric wound dressings. As compared to the control dressing Tegaderm that is commercially in use for healing of wounds and it is considered as standard dressing (Jenks et al. 2016), wounds covered with polyurethane films form a thinner scab, with lower inflammatory cell infiltration. The study also shows earlier formation of granulation tissue on the wound site, which is vascularized and rich with collagen. Wound healing also depicts a better rate of epithelial cell organization as compared to Tegaderm™ which has been used as a the control (Khil et al. 2003).[6]



7. ESSENTIAL OILS AND BIOLOGICAL PROPERTIES

When the skin is compromised due to injury or damage, it becomes more vulnerable to microbial infections. These infections are often caused by different types of bacteria, including Gram-positive bacteria such as Staphylococcus aureus and Staphylococcus epidermidis, as well as Gram-negative bacteria like Escherichia coli and Pseudomonas aeruginosa. Gram-negative bacteria have two lipid membranes and a thin layer of peptidoglycan, while Gram-positive bacteria have a single bilayer membrane surrounded by a thick layer of peptidoglycans.

Staphylococcus aureus, commonly found on healthy and damaged skin. poses a significant challenge due to its antibiotic resistance, which can impede the natural healing processes. On the other hand, Staphylococcus epidermidis is beneficial in preserving the skin's integrity and producing antimicrobial molecules that hinder the formation of biofilms by S. aureus. Escherichia coli is known for its ability to form biofilms on various surfaces. At the same time, Pseudomonas aeruginosa is notorious for causing persistent infections and delayed wound healing, mainly due to its high antibiotic resistance and strong biofilm-forming capacity.

Antibacterial properties are fundamental in biomedical applications, aiming to reduce inflammation caused by infections, which delay healing. In this context, the emergence of resistant bacteria has spurred studies on therapeutic alternatives and the incorporation of antimicrobial agents that can enhance the efficiency of dressings. Among these alternatives, essential oils (EOs) stand out due to their high capacity to control microbial infections. EOs have shown promising potential in the eradication of multi-drug-resistant pathogens, as they inhibit the growth of microorganisms, creating disturbances in the cytoplasmic membrane; interrupting the proton motive force, the flow of electrons, and active transport; and hindering protein synthesis.

EOs are volatile compounds of low molar mass extracted from aromatic plants from different tissues (roots, flowers, stems, leaves, seeds, fruits, or the entire plant). They present excellent antimicrobial, antifungal, antioxidant, and anti-inflammatory properties. In addition to being biodegradable and lipophilic, they are also sedatives and analgesics with a low degree of toxicity.

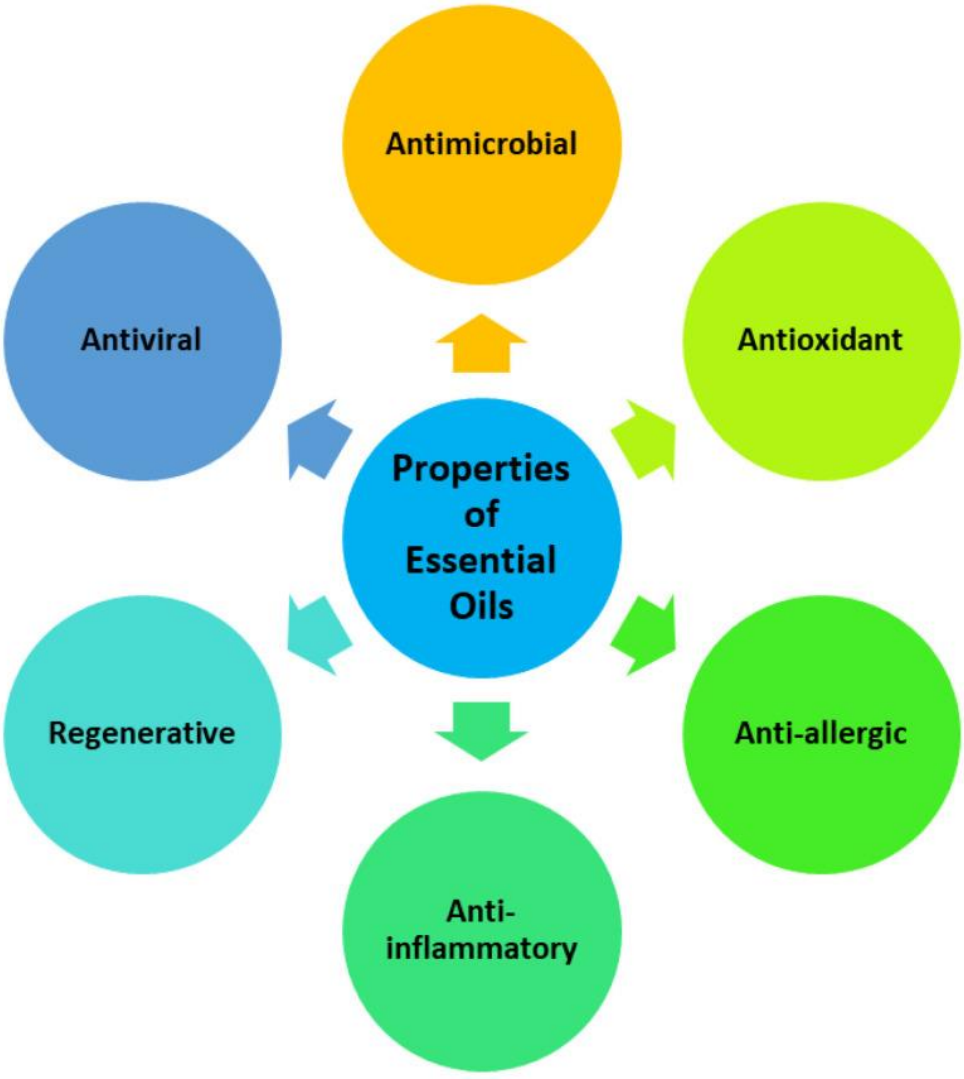
Chemically, EOs are characterized by terpenes and phenylpropanoids. Terpene compounds can be divided into two main categories: terpenes with a hydrocarbon structure (mono-, sesqui-, and diterpenes) and their oxygenated derivatives (alcohols, oxides, aldehydes, ketones, phenols, acids, esters, and lactones). The antimicrobial properties of EOs are attributed to active constituents, mainly related isoprenes, along with other hydrocarbons and phenol. Therefore, the presence of phenolic compounds (carvacrol, eugenol, and thymol, among others) generates a rupture of the cytoplasmic membrane by the proton motive force, by the flow of electrons, by active transport, and also by the coagulation of cellular contents. Therefore, essential oils characterized by a high level of phenolic compounds,

such as carvacrol, eugenol, and thymol, have important antibacterial activities resulting in essential antibacterial properties. Given these characteristics, between 2020 and 2023, recent studies reported using essential oils (clove, tea tree, and oregano) in wound healing.

The EO composition also influences its antioxidant potential. Phenolics and secondary metabolites with conjugated double bonds generally exhibit considerable antioxidant properties. These phenolic compounds possess redox properties and are essential in neutralizing free radicals and decomposing peroxides. The antioxidant activity of essential oils is also associated with some alcohols, ethers, ketones, aldehydes, and monoterpenes: linalool, 1,8-cineole, geranial/neral, citronellal, isomenthone, and menthone. EOs of α-terpineol, linalool, linalyl acetate, limonene, δ-3-carene, α-pinene, and 1,8-cineole have important anti-inflammatory activity. These compounds act by inhibiting histamine release or reducing the production of inflammatory mediators. Therefore, the anti-inflammatory activity of EOs can be attributed to their antioxidant activities and their interactions involving cytokines, regulatory transcription factors, and the expression of pro-inflammatory genes.

EOs can be obtained by various extraction techniques such as pressing, hydrodistillation, and steam distillation. In the hydrodistillation technique, the sample is immersed in water in a distillation system with heating. The volatiles in the sample are boiled, forming a heterogeneous mixture at the end of the process. In extraction by steam distillation, water vapours pass through the sample, which entrains plant volatiles, as the plant sample is suspended and there is no direct contact with water.

The main disadvantages of applying EO are its volatility, low stability, high sensitivity. and degradation under the processing temperature. Therefore, to overcome these deficiencies, EOs can be encapsulated and incorporated into polymeric matrices to increase their activity and stability, improve water solubility, and facilitate their delivery in healing applications and tissue engineering.[7]



Enrollment in local colleges, 2005

Publication Year/ Species /Essential Oil	Major Compounds	Wound Dressing System	Biological Results
2010 Thymus vulgaris Thyme	carvacrol and thymol	CS (low molecular weight, degree of deacetylation ~85)	Antibacterial activities and antioxidants
2015 Copaifera Copaiba	β-cubebene, β-, α-caryophyllene, α-bergamotene, β-, δ-cadinene, β-, α-selinene, β-, α-bisabolene	PLA (Mw~66,000 g/mol) and PVP (Mw~55, 000 g/mol)	In vitro release tests of oil volatiles demonstrated a higher release rate and had greater antimicrobial action against Staphylococcus aureus in fibers containing PVP
2017 Hypericum perforatum	chemical composition not reported	CS (low molecular weight, degree of deacetylation of 85%)	The films had antimicrobial activity against the activity of Escherichia coli and Staphylococcus aureus; they had no cytotoxic effects on NIH3T3 fibroblast cells and provided a good surface for cell attachment and proliferation
2017 Rosmarinus officinalis Rosemary	1,8-cineole, α-pinene, camphor, and camphene	CS (deacetylation degree of 34% and molecular weight of 128 kg/mol)	They showed high percentages of inhibition of erythrocyte hemolysis (>63%) and relatively low antioxidant capacity by the ABTS radical (≈6 to 9%)
2017 Zataria multiflora	thymol, carvacrol, p-cymene, and γ-terpinene	PVA (60–70 kDa)/gelatin (type A, 50–100 kDa)	Considerably increased the antioxidant and antibacterial activities of the dispersions. Pseudomonas aeruginosa was the most resistant bacteria
2018 Cinnamon	cinnamaldehyde, cinnamyl acetate, caryophyllene, linalool, and eugenol	Sodium alginate/PVA (90% hydrolysed having Mw of 70,000)	Good antibacterial properties against Staphylococcus aureu
2019 Melaleuca alternifólia Tea tree	terpinen-4-ol (45.23%), γ-terpinene (23.07%), α-terpinene (10.84%)	CS (highly viscous)/PVA (molecular weight ~31,000)/glycerol	Significant increase in wound contraction percentage; decreased oxidative stress in the wound area; re-epithelialization associated with activated hair follicles
2019 Eugenia caryophyllata or Syzygium aromaticum Clove	eugenol, eugenol acetate, and β-caryophyllene	CS (shrimp shells, medium molecular weight: 230–250 kg/mol; degree of deacetylation: 85%)	Inhibition against Staphylococcus aureus, Escherichia coli, and Candida albicans
2020 Origanum vulgare Oregano	carvacrol	PLCL/cocoons of Bombyx mori silkworm	It has turned out to be biocompatible, anti-adhesive, and antibacterial against both Gram-positive and Gram-negative bacteria; accelerated wound contraction with complete epithelialization, collagen deposition, and angiogenesis

2021 Frankincense	**chemical composition not reported**	**Psyllium/Carbopol 940**	**They showed antioxidant efficiency, excellent barrier potency against external microorganism attacks, and efficient antimicrobial activities against S. aureus, E. coli, and C. albicans; induced faster wound healing with improved biochemical parameters compared with oil-free hydrogel Showed > 95% antimicrobial activity against both Gram-positive and Gram-negative bacteria Exhibited more potent antibacterial activity against S. aureus and E. coli and enhanced biocompatibility; significantly enhanced the proliferation of L929 fibroblast cell Show high antibacterial activity and cell migration activity and a significant effect on skin repair in vitro and in vivo**
2022 Thymus vulgaris Thyme	**carvacrol**	**κ-Carrageenan (Mw = 400–560 KDa)/PEG (powder, Mw = 35,000 g/mol)**	
2023 Cinnamomum cassia bark Cinnamon	**(E)-cinnamaldehyde (75.31%), (+)-3-carene (8.12%)**	**Cellulose nanofibers/CS (not mentioned information)**	
2021 Eucalyptus	**eucalyptol (83.27%), D-limonene (5.82%), o-cymene (3.46%)**	**CMC (molecular weight concentrated at 195.7 kg/mol and 2.0 kg/mol; the degree of substitution was 73.73%)/CBM 940 (molecular weight concentrated at 1894.7 kg/mol and 15.8 kg/mol)**	

8. WOUND DRESSINGS

8.1) GAUZE DRESSINGS

The gold standard for minor wound treatment is the application of soft paraffin as an occlusive layer and the use of a frequently changed sterile nonadherent dressing pad or cloth according to the American Academy of Dermatology Association. The choice of the type of dressing depends on various factors, such as the cause, size and depth of the wound; whether the wound is exuding/contaminated; and availability and economic factors. A recent report compared several marketed gauze dressings (Johnson & Johnson, 3 M or Medtronic) in terms of market share and future estimation https://www.alliedmarketresearch.com/gauze-bandages-market. Gauze dressing pads suffer from two main disadvantages: inability to absorb wound exudates and thus inability to adhere properly to the wound tissues and pain during dressing changes.

8.2) HYDROCOLLOID DRESSINGS

These are transparent films formed by the solvent casting technique of hydrophilic polymer solutions such as gelatin, pectin, alginates, or carboxymethyl cellulose. Interestingly, the polymer used for film formation has adhesive power, so it can adhere well to tissues. The advantages of these types of dressings are that they are waterproof and clear, so healing progress can be easily monitored without removal of the dressing; moreover, the absorbing power of the polymers sets them optimal for mildly oozing wounds. Hydrocolloid dressings are available from several manufacturers, such as Johnson & Johnson and 3 M. However, hydrocolloid dressings cannot handle large-volume exudating wounds, so due to the frequent exchange rate of the dressing, the cost-effectiveness of these products has decreased.

8.3) HYDROGEL SCAFFOLDS

Hydrogels are 3D networks of hydrophilic polymers that swell but do not dissolve in water. Like hydrocolloid dressings, they are clear, but they have more flexible and malleable structures, enabling them to fill the wound space. Hydrogels are cross linked polymer chains with 3D structures that can absorb large volumes of fluid. They are similar to living tissue due to their high water content, soft struck true, and porosity.

Natural polymers (chitosan–alginate–hyaluronic acid (HA)–collagen), semisynthetic materials (hydroxypropyl methyl cellulose) or even synthetic materials (polyvinyl alcohol–polyethylene glycol–carbomer) are used to formulate hydrogels. Hydrogels have many advantages, such as painless removal, absorption of wound exudates and preservation of the moist microenvironment provided by the hydrogel, which accelerates the healing of normal wounds, chronic wounds, and even burns. In addition, the polymeric strands of the hydrogel serve as a scaffold structure, thus promoting cell division and adhesion.

Several studies have used hydrogels as DDSs for wound treatment. Wang, H. et al. loaded 3 essential oils (eucalyptus, ginger and cumin) as antibacterial agents in a physically cross-linked hybrid hydrogel constructed of carboxymethyl chitosan and carbomer 940. In a mouse burn model, these hydrogel systems accelerated wound healing by promoting transforming growth factor-β, vascular endothelial growth factor (VEGF), and epidermal growth factor while diminishing interleukin-6 and tumor necrosis factor-α levels. They concluded that this polysaccharide hydrogel loaded with essential oils has potential for use as a promising dressing for skin burns with excellent antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*.

Diabetic wounds exhibit a slow healing pattern because the immune system is impaired. This necessitates the use of advanced drug delivery systems as 3D bioprinting materials. Although the cost of stem cells and bioengineering skin substitutes is high, their use is limited to treating large full-thickness skin defects and chronic wounds. Xia, S. et al. fabricated a 3D-printed scaffold using bioink, gelatin methacryloyl and stem cells because of their rapid proliferation rate. Curcumin was incorporated into the system because it has antioxidant activity to mitigate the generation of reactive oxidative species in the diabetic wound milieu and to decrease the apoptosis of stem cells, thus enhancing the survival of stem cells. Gelatin was chosen for the fabrication of the dressing because it comprises amino acids (aspartate, arginine and glycine) that exist in an arrangement that enhances both cell proliferation and attachment. The circular scaffold mesh showed appropriate mechanical properties and was biocompatible, and when tested in an *in vivo* diabetic wound model in mice, it was shown that it had significant healing ability.

Hydrogels, however, have some fundamental limitations, such as, low mechanical strength and poor stimulus resistance, "smart self-healing hydrogels", which can mechanically repair themselves when they are ruptured or traumatized, have been developed. Since it may restore its previous mechanical properties through stretchability, injectability, and shape-reformation, it is superior in terms of stability and durability.[8]

9. CURRENTLY COMMERCIALLY AVAILABLE WOUND DRESSING PRODUCTS

Topical wound dressings protect skin layers from microbial contamination. It aids hydration and enhances skin regeneration by preventing exposure to wound tissues. Thus, wound dressing models serve to be cost-effective, biocompatible, hypoallergenic and permeable to water and oxygen supply. Several biopolymers like elastin, Cs and collagen are used as bioactive wound dressings in biomedical applications. These biopolymers show non-toxicity, biodegradability, biocompatibility, readily availability, and non-immunogenicity that can be significantly beneficial in wound healing. Natural polymers enhance the mechanical characteristics of the material, help combat the bacterial wound infections, make the wound healing process faster, gaseous permeability and state of biodegradability.

Tetracyclines, neomycin, quinolones, cephalosporins and polymyxin B are the currently available antimicrobial agents in wound healing process due to their ability to control microbial contamination. However, inappropriate and repeated administration of antibiotics increases antibacterial resistance. Antimicrobial agents, organic and in-organic compounds such as essential oils and other nanomaterials have been used as wound dressings in order to prevent antimicrobial resistance. There are various catagories of wound dressings available in the market namely Adhesive items, Hydrofiber/alginate, Charcoal, etc. shows the different catagories of wound dressings and their respective brand names. Wound dressings namely Pathon, TPP-fibres and Surgi CLOT are used, but only Surgi CLOT is available in the market.

Spiceries regarded as a portable device for electrospinning applied directly on the wound. Surgi CLOT, extracted from dextran, is a polysaccharide and bio-based wound dressing mode. Dextran belongs to a large class of glucose linked polymers. Dextran is extracted from sucrose using certain lactic acid bacteria like *Lactobacillus spp*, *Leuconostocmesenteroides* and *Streptococcus mutan*. The biodegradation of polyurethanes is a very complex process that involves three major pathways namely enzymatic, hydrolytic and oxidative. The nature of product degradation solely depends on the chemistry of the natural polymer that can be designed for wound dressing applications. The most recurrent type of side effect found in commercialized wound dressing models is dermatitis, predominantly occurring in leg ulcers of diabetic patients. While prior conventional approaches were based on the encapsulation of therapeutic drugs/molecules within the bulk phase of the carrier substance, an alternative in the form of nanomaterials, namely therapeutics impregnated nanofibrous membranes is very much essential for developing biocompatible and efficient wound dressing models.[9]

10. FUTURE CONCEPTS FOR THE TREATMENT OF CHRONIC WOUNDS

Although the aetiologies and the physical characteristics for the various types of chronic wounds are different, there is a common trend in their biochemical profiles. The precise pattern of growth factor expression in the different types of chronic wounds is not yet known; but it has been determined that there is generally a decreased level of growth factors and their receptors in chronic wound fluids. The absolute levels of growth factors may not be as important as the relative concentrations necessary to replace the specific deficiencies in the tissue repair processes. For the treatment of chronic wounds, Robson[43] proposed that growth factor therapy be tailored to the deficiency in the repair process. Therefore, the effectiveness of the therapy is predicated on adequate growth factor levels and the expression of their receptors balanced against receptor degradation by proteases and the binding of growth factors by macromolecules such as macroglobulin and albumin.

Studies that evaluated topical growth factor treatment of chronic wounds, such as PDGF in diabetic foot ulcers and EGF in chronic venous stasis ulcers, have shown an improvement in healing. These findings have led to the hypothesis that altering the cytokine profile of chronic wounds through the use of MMP inhibitors, addition of growth factors, and the elimination of inflammatory tissue and proteases by debridement would shift the wound microenvironment towards that of an acute wound, thereby improve healing.

Current treatment strategies are being developed to address the deficiencies (growth factor and protease inhibitor levels) and excesses (MMPs, neutrophil elastase, and serine protease levels) in the chronic wound microenvironment. Although the more specific and sophisticated treatments remain in the lab at this time such as the new potent, synthetic inhibitors of MMPs and the naturally occurring protease inhibitors, TIMP-1 and 1-antitrypsin, available by recombinant DNA technology, the use of gene therapy in the treatment of chronic diabetic foot ulcers is currently being evaluated in a clinical trial. A phase III clinical trial is underway to determine the efficacy of keratinocyte growth factor-2 (KGF-2) in the treatment of chronic venous stasis ulcers. The treatment strategy to add growth factor to a chronic wound has been in place for the past several years. Regranex®, human recombinant plate-let derived growth factor (PDGF-BB), has been available for the treatment of diabetic foot ulcers; demonstrated approximately 20% improvement in healing compared to controls.[44] In keeping with the strategy to restore a deficient wound environment, Dermagraph® and Apligrapf®, engineered tissue replacements, have been applied to chronic diabetic ulcers.[45,46] Although Apligrapf® is no longer available, both tissue replacements have proven to be effective in selected types of ulcers. Other approaches to the treatment of chronic wounds have been to remove the increased protease levels. This is in part the strategy of a vacuum-assisted negative pressure wound dressing[47] and in the recent development of dressings that bind and remove MMPs from the wound fluid, such as Promogran®.[48,49]

There have been some advances made in the development of new antimicrobial dressings and they have been summarized by Hamm in a recent publication (Antibacterial Dressings in Advances in Wound Care: Volume 1; Mary Anne Libert Inc. 2010, page 148).

Another strategy is to use synthetic protease inhibitors to decrease the activities of MMPs in the wound environment. Doxycycline, a member of the tetracycline family of antibiotics, is a moderately effective inhibitor of metalloproteinases, including MMPs and the TNFα converting enzyme (TACE). We have demonstrated a reduction in inflammatory cell infiltrate and extra-cellular matrix in chronic pressure ulcers treated with 100mg doxycycline twice daily. Low dose doxycycline 20mg, twice daily has been proven to be beneficial in other pathologic states such as periodontitis that are characterized by chronic, neutrophil-driven inflammation, and matrix destruction.[50] In the future, treatment of chronic wounds may require the use of specific growth factors or inhibitors unique to the type of ulcer or the use of combinations of selective inhibitors of proteases, growth factors and tissue replacements to act synergistically to promote healing.

As previously described, endocrine hormones, such as insulin, glucocorticoids, and oestrogen, play important roles in regulating wound healing. Although there is no current therapy that specifically addresses the molecular deficits created by type I or type II diabetes (inadequate insulin levels or insulin resistance), systemic insulin

injections may improve the local wound microenvironment. For patients receiving long-term corticosteroids, the use of vitamin A seems to facilitate wound healing. Studies are underway to determine the efficacy of topical oestrogen applications on skin aging.

New technologies are being developed to help researchers better understand the complex microenvironment that exists in chronic wounds.[51] A technique called Polymerase Chain Reaction (PCR) can amplify the microbial DNA that is extracted from the wound bed and then be used to identify and quantify specific organisms. The test is highly sensitive and there is a rapid turn around time. The drawback is that PCR can only be used to identify known organisms and new unknown microbes will not be detected.[10]

11. RESULTS

Treatments with EO from species of genders *Lavandula, Croton, Blumea, Eucalyptus, Pinus, Cymbopogon, Eucalyptus, Cedrus, Abies, Rosmarinus, Origanum, Salvia* and *Plectranthus,* have shown positive results in rodent wounds. All of these EO were mainly composed by monoterpenoids—thymol, 1,8-cineole, linalool—or monoterpenes, as limonene or pinenes. Experimental wounds in rodents have shown faster closure rate, better collagen deposition and/or enhanced fibroblasts proliferation. In blends with biopolymers, several EO combined with chitosan, alginate, gelatin or collagen, were processed to give active films or nanofibers, with antioxidant, anti-inflammatory or antimicrobial activities. Curiously, all of these works were carried out since 2010.

12. CONCLUSIONS

There is significant evidence about the effectivity of EO as wound healers. The incorporation of EO into a polymer matrix that contributes to wound healing is still incipient. However, scientific based evidence of the EO incorporation in resorbable polymeric scaffolds was found and analyzed herein. In summary, EO-biopolymer dressings or scaffolds have become promising artifacts regarding wound treatments, especially in chronic wounds, where treating infection and inflammation are still important issues.

13. REFERENCE

1. Synthetic polymeric biomaterials for wound healing: a review Mariam Mir, Murtaza Najabat Ali, Afifa Barakullah, Ayesha Gulzar, Munam Arshad, Shizu Fatima, and Maliha Asad.
2. Polymer-Based Wound Dressings Loaded with Essential Oil for the Treatment of Wounds: A Review by Bruna Michele A. de B. Buriti Pablo Luis B. Figueiredo Marcele Fonseca Passos and Joyce Kelly R. da Silva.
3. Evaluating polymeric biomaterials to improve next generation wound dressing design JACOB G. HODGE HTTPS://ORCID.ORG/0000-0002-6165-3932, DAVID S. ZAMIEROWSKI, JENNIFER L. ROBINSON, AND ADAM J. MELLOTT Authors Info & Affiliations.
4. Sustainable electrospun materials with enhanced blood compatibility for wound healing applications—A mini review panel Mohan Prasath Mani, Ahmad Athif Mohd Faudzi, Seeram Ramakrishna, Ahmad Fauzi Ismail, Saravana Kumar Jaganathan, Nick Tucker, Rajasekar Rathana samy.
5. Polymer-Based Wound Dressings Loaded with Essential Oil for the Treatment of Wounds: A Review by Bruna Michele A. de B. Buriti, Pablo Luis B. Figueiredo, Marcele Fonseca Passos, Joyce Kelly R. da Silva.
6. Polymeric biomaterials for wound healing by Cristiana Oliveira, Diana Sousa, José A. Teixeira, Pedro Ferreira-Santos, and Claudia M. Botelho.
7. Natural and synthetic polymers for wounds and burns dressing Author links open overlay panel George Dan Mogoşanu, Alexandru Mihai Grumezescu.
8. A Review Exploring the Wound-Healing Activity of Self-Healing Hydrogels: Fabrication, Characterization, Mechanism, and Biomedical Applications Heba-Alla, H. Abd-ElSalam, Omar A. Refaeey, Khaled G. Waked, Khaled A. Elsherbiny, Aya M. Aleam.
9. Therapeutic applications of electrospun nanofibers impregnated with various biological macromolecules for effective wound healing strategy – A review panel Lakshimipriya Sethuram, John Thomas.
10. Mechanisms of Vascular Disease: A Reference Book for Vascular Specialists [Internet]. Fitridge R, Thompson M, editors. Adelaide (AU): University of Adelaide Press, 2011.
11. Polymer-Based Wound Dressings Loaded with Essential Oil for the Treatment of Wounds: A Review Bruna Michele A. de B. Buriti 1, Pablo Luis B. Figueiredo 2, Marcele Fonseca Passos 2,3 and Joyce Kelly R. da Silva.
12. Could essential oils enhance biopolymers performance for wound healing? A systematic review Mercedes Pérez-Recalde, Ignacio E. Ruiz Arias, Elida B. Hermida.