

Review

Not peer-reviewed version

An Overview on Wound Dressing Materials

Tânia Lagoa , [Maria Cristina Queiroga](#) ^{*} , [Luís Martins](#)

Posted Date: 11 July 2024

doi: 10.20944/preprints202407.0881.v1

Keywords: skin; wounds; healing; wound dressings; biomaterials



Preprints.org is a free multidiscipline platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Review

An Overview on Wound Dressing Materials

Tânia Lagoa ¹, Maria Cristina Queiroga ^{1,2*} and Luís Martins ^{1,2}

¹ MED—Mediterranean Institute for Agriculture, Environment and Development & CHANGE—Global Change and Sustainability Institute, Institute for Advanced Studies and Research, Universidade de Évora, Pólo da Mitra, Ap. 94, 7006-554 Évora, Portugal; d50889@alunos.uevora.pt (T.L.); lmlm@uevora.pt (L.M) crique@uevora.pt (M.C.Q.)

² Departamento de Medicina Veterinária, Escola de Ciências e Tecnologia, Universidade de Évora, Pólo da Mitra, Ap. 94, 7006-554 Évora, Portugal

* Correspondence: crique@uevora.pt

Abstract: Wounds are an increasing global concern, mainly due to a sedentary lifestyle, frequently associated to the occidental way of life. The current prevalence of obesity in western societies, leading to an increase in type II diabetes, and an elderly population, are also a key factor associated to the problem of wounds healing. Therefore, it stands essential to find wound dressing systems allowing reestablishing the skin integrity in the shortest possible time and with the lowest cost, avoiding further damage and promoting patients' well-being. Wounds can be classified into acute or chronic, depending essentially on the duration of the healing process, which is associated with. It depends on the extent and depth of wound, localization, level of infection and on the patient health status. For each kind of wound and respective healing stage there is a more suitable dressing. The aim of this review was to focus on the possible wound dressing management, aiming the more adequate healing approach for each kind of wound.

Keywords: skin; wounds; healing; wound dressings; biomaterials

1. Introduction

The skin is the largest organ in the body and the most exposed to aggressions from the external environment, shielding from physical, biological, and chemical damages. It protects the body against invasive microorganisms and allergen penetration, contributes to the regulation of body temperature and homeostasis [1–4]. Wounds are, one of the most frequent clinical conditions observed by doctors and veterinarians, often associated to serious clinical complications in human and animal health [5,6]. The development of new drugs and covering materials is under increasing study, aiming to promote the healthy skin state in the shortest possible time. To prevent contamination and dehydration, wounds need effective and simultaneously comfortable covering. It is crucial to avoid the use of antibiotics and antiseptics, both due to growing bacterial resistance and because of the harmful effect of disinfectants on cells, which, by favoring necrosis, promotes bacterial growth. Lately, a large variety of biomaterials have been tested for their antimicrobial and wound-healing properties.

The aim of this review was to systematize the latest developments on wound dressing investigation, focusing on the most popular and promising methods of healing promotion.

2. Wound Pathogenesis

The rapid emergence of antimicrobial resistance by pathogens has become an alarming public health problem, leading to chronic infections and high morbidity and mortality rates. For this reason, the focus on the wound treatment process, aiming a faster healing stage, with less discomfort to the patient, should block contamination, preventing systemic antimicrobial therapy [7].

Recent studies argue that the most suitable materials for wound healing are those that provide a physiological environment at the wound level, preventing contamination and providing physical

support. Wound dressings must provide comfort to the patient and promote debridement of necrotic tissue, allowing the absorption of exudate, facilitating the propagation of oxygen, and providing a moist environment, with minimum toxicity, which stands essential to the healing process [8].

Healing is a dynamic process [2,8] so the choice of the best covering material depends on the healing phase and the type of wound addressed [9]. So far, there is no ideal material that meets all the requirements for all stages of wound healing, therefore it is necessary to produce a coverage, resulting from the association of several biomaterials [10].

2.1. Skin Structure and Its Functions

The skin is the largest organ of animals. It is rather complex, providing an effective defense barrier regarding the external environment, protecting the body from physical, chemical, and microbial aggressions. The skin also participates in the regulation of body temperature, sensitive perception of pain, heat, cold, pressure, and itching [1,2]. Precisely because it is an external and extensive organ, it is exposed to constant aggression, explaining the high number of dermatology cases in human and veterinary medicine, when compared to other systems. This organ also reflects the general state of health, acting like a “mirror of the organism”.

The skin is divided into three layers: epidermis, dermis, and hypodermis [2,3]. The epidermis is composed of several layers, the deeper ones show a high cell-replication rate, being responsible for cell renewal. The newer cells push the older ones towards the surface, undergoing changes in shape and chemical composition, secreting and accumulating keratin, in a process known as keratinization, during which the cells die and form a resistant outer layer. From the most superficial to the deepest, epidermal layers are known as stratum corneum, translucent, granular, spinous, and basal sheet. The dermis is responsible for the greater structural strength of the skin, nutrition of the epidermal cells and removal of waste products. The hypodermis, also called the subcutaneous layer, is mostly formed of lipid cells, presenting a role as protective padding, insulator, and energy reservoir [3].

2.2. Wounds and Their Characterization

Wounds may be caused by infection, burns, illness or accidental damage to the skin, and are frequently associated with pain, disability and bleeding. Wounds may be classified as open (when there is a break in the skin, leaving the internal tissue exposed) or closed (with no clear disruption of the continuity of the skin, hence without exposure of the underlying tissues). An impaired skin barrier function may lead to an imbalance in skin homeostasis, which may evolve to inflammatory exudative conditions, creating the adequate environment for bacterial, viral and fungal growth [11,12].

Wounds may be also classified according to their etiology, duration, degree of contamination, depth, extent, location, and according to specific morphological characteristics [11,13,14]. The healing time will also depend on those factors, allowing its classification into acute, sub-acute and chronic. Acute wounds may exhibit various manifestations, ranging from superficial scratches to deeper wounds. It is essential to assure that their evolution does not comprise the formation of a substantial crust extension and that the healing does not extend beyond 3 weeks [14]. Subacute wounds will last between 3 weeks and 3 months [13]. Chronic wounds are usually infected wounds, occurring oftenly in immunocompromised patients. These are wounds exposed to factors causing tissue hypoxia and oxidative stress as in diabetes, cardiovascular disease, hypothyroidism, hyperadrenocorticism, and malnutrition with hypoproteinemia or vitamin and mineral deficiency} [15–17]. Extensive and deep wounds or located in areas of great tension may become chronic as well [14]. Wounds subjected to radiation and hypothermia conditions, may also become persistent or chronic [16,18]. Infection represents the highest risk factor for wound healing with *Staphylococcus pseudintermedius* being the most common bacterium in wound colonization [6]. Infected wounds, ~~there is~~ show a greater chance of developing ischemia, leading to necrosis [6]. A major concern is the development of biofilms, consisting in multicellular bacterial communities, with greater resistance to both antimicrobials and the host's immune system [13]. Resistance to antimicrobials is frequently related to dehiscence of sutures with prolonged healing time (3-months minimum duration) and higher cost

of treatment with an increased zoonotic risk [6] bacteremia, endocarditis, and bone, joint and central nervous system (CNS) infections increases [19]. It is, therefore, essential to adequate the therapeutic approach to the specific classification of each wound.

2.3. Healing Stages

Wound healing is an inflammatory process mediated by cytokines and growth factors, and is a four-stage event: hemostasis, inflammation, proliferation and remodelling [2]. Briefly, the healing process is marked by an initial inflammatory response in which hemostasis occurs by platelet activation and fibrin formation, followed by the migration of neutrophils, in the acute inflammatory phase, and later of lymphocytes and macrophages, in the chronic inflammatory phase. A phase of cell proliferation and migration follows, where the migration of keratinocytes from the dermis occurs, and the formation of new blood vessels takes place. Thanks to the displacement of healing mediators, fibroblasts and keratinocytes, a replacement of the fibrin-rich matrix by granulation tissue arises. Macrophages stimulate fibroblasts to differentiate into myofibroblasts as contacting-cells, allowing the attachment of wound edges. Those cells, along with the fibroblasts, will form the extracellular collagen-rich matrix. In the last phase there is a reorganization and remodeling of this matrix, and the healing process becomes completed [5,16,17,20,21].

Some traumas require stabilization of the patient, followed by cleaning and management of the wounds, through disinfection with antiseptic solutions, debridement, wound closure, topical antimicrobial treatment, and coverage.

There are different debridement techniques, such as surgical, which involves tools such as scissors, scalpels, and curettes; autolytic, where there is no removal of exudate so that white blood cells and proteolytic enzymes may promote the removal of bacteria and small amounts of necrotic tissue; biological, using larvae and worms to remove dead tissue; enzymatic, through the use of proteolytic enzymes such as Streptokynases, trypsin, proteinases and collagenases, to remove devitalized tissue and destroy bacterial biofilm; and mechanical, where force is involved to remove tissue or gauze adherent to the wound. According to Kietzmann, debridement is increasingly recommended to remove necrotic tissue, without resorting to antiseptics, as these may promote necrosis, fostering the growth of bacteria, and delaying the normal healing process [22]. Silvestro et al. [17] also argued that topical antimicrobials could delay the healing process and should only be used when there is confirmation of infection or in cases of immunosuppressed animals [17].

3. Types of Covers

Wounded skin should be coated to minimize damage and the risk of infection, to decrease available oxygen, to reduce pH, and to promote restoration integrity of the damaged tissue as quickly as possible. In the last decades, many biomaterials have been developed and introduced in the market, aiming to act as skin substitutes [23].

Among the available dressings, the choice of the ideal dressing will depend on the type of wound, its depth, location, extent, as well as the degree of exudation, presence of infection and level of adhesion to the wound, of the dressing material. Traditional cotton and gauze bandages, for instance, are able to absorb large amounts of exudate, which, in turn, may cause wound dryness and pain when detaching the dressing, leading to slower healing process. Generally, a coating with a high water vapor transmission rate is more likely to lead to wound dehydration, while a coating with a poor transmission rate tends to allow the accumulation of exudate. The presence of exudates in the wound promotes maceration and excoriation of the surrounding skin, and poor cohesion of the newly formed tissue layers, slowing down the healing process [9,24,25]. The dressings should be soft and flexible to allow easier and painless application and removal. Dryer environments favor cell adhesion [9].

An ideal coating must therefore have different properties, including being inexpensive, non-antigenic, durable, flexible, non-toxic, non-adherent, easy to place on lesions, applicable in a single operation, easy to remove, non-traumatic, and comprising of biological material (which requires minimal processing), not allowing water loss, adaptable to irregular lesion surfaces, allow gas exchange and removal of excess exudate, offer mechanical protection, protect from contamination,

being biodegradable and enhance the skin-inherent healing process. Comprising biological material also requires less processing with less adverse reactions [2,8–10,14]

Dressings are classified according to their antimicrobial role, absorbent and occlusive action on the wound or according to the ability to adhere and promote debridement. Covers allowing debridement contain hypertonic solutions such as sugar or honey, polyhexanides, silver salts, copper tripeptide complex, acemannan, resulting from the fermentation of aloe vera, platelet derivatives, chitosan or maltodextrin (–oligomers from glucosis).

According to the nature of the material they are made of, and its physical form, dressings can also be classified into three categories: biological (from animal or plant origin), biological-synthetic or just synthetic. According to its physical form, available coatings can be oils, films, foams, hydrogels, hydrocolloids or membranes [26]. Ndlovu et al. [24] grouped dressings into four groups: traditional, synthetic, biological dressings or skin substitutes, and bioactive [23].

3.1. *Traditional Dressings*

Traditional dressings (e.g., gauzes, cotton composites, among others) are primarily used at an early stage to promote hemostasis and are mostly used in dry and clean wound [27]. This type of dressing is affordable but present several limitations such as poor permeability to gases and the damaging of newly formed epithelium. Their fibers stick to the granulation tissue, causing pain when removing the dressing, eliminating the new tissue formed and delaying the healing [24,28].

3.2. *Synthetic Dressings*

Synthetic dressings are usually based on synthetic polymers and biopolymers. Synthetic coatings include hydrogels, hydrocolloids, paraffin gauzes, foams, semi-permeable films and silicone blends [15].

3.2.1. *Sponges*

Sponges are made of solid materials with a porous matrix, usually composed of polyurethane and, sometimes, a layer of soft silicone. Polyurethane-based products are covers mostly used for their biocompatibility, favorable mechanical properties, low toxicity, softness, flexibility, gas permeability and moisture retention [14]. The polyurethane sponges have a good absorption capacity, being useful in wounds with higher levels of exudation. These non-adherent materials are particularly adequate for promoting the formation of healthy granulation tissue.

3.2.2. *Films*

Semi-permeable films are thin, flexible, semi-occlusive, transparent, porous, and non-absorbable coatings. They allow the transmissibility of water vapor and the oxygenation of the wound, and provide a barrier against external contamination. These coatings are indicated for wounds with little or no exudate. Their use is indicated in the final stage of healing to promote epithelialization. In hairy body sites its adhesion is compromised, and the removal of the cover is usually traumatic [14].

3.2.3. *Hydrogels*

Among the various coatings available, hydrogels are the class of materials that best mimic the structure of the extracellular matrix of tissues, due to their ability to retain large amounts of water and their soft consistency [29]. Hydrogels are usually transparent and consist of polymeric networks, capable of absorbing large amounts of water or biological fluids, with simultaneous moisturising, allowing tissue rehydration [8,30]. These materials have different applications in medicine or the pharmaceutical industry. Hydrogels allow good biocompatibility, anti-inflammatory activity, promote cellular immunological activity, owing low toxicity, low allergenicity, and are easy to remove from the wound [1,8,30]. They present excellent tissue adhesion, allowing not only a stable protective barrier but also interact with different wound components and surrounding tissues. Moreover, hydrogels favor cell adhesion, vascularization, migration and proliferation of fibroblasts

and other growth factors. Hydrogels shorten the healing period by reducing the formation of granulation and necrotic tissue, through their autolytic activity [30] also assisting in the delivery of the nutrients and oxygen required for the healing process [1,8,31]. However, the highly hydrated environment may facilitate microbial colonization. Hydrogels are also used for controlled drug delivery systems, which may be additionally useful for wound management [32].

Hydrogels can be considered reversible or physical gels, based on their polymer arrangement, crosslinking procedure and external stimuli like temperature and pH. These networks are held together by molecular bonds, and/or secondary forces such as ionic, hydrogen bonding, and hydrophilic forces [8,33]. On the other hand, hydrogels can be permanent or chemical when the networks are covalently linked. The polymers used to synthesize hydrogel networks can be divided into two groups, according to their synthetic or natural origin. The synthetic polymers most commonly used to prepare hydrogels are polyethylene glycol and polyhydroxyethyl methacrylate. Besides being easily reproducible, the use of synthetic polymers generally results in hydrogels with high mechanical strength [33]. Comparatively, hydrogels from natural polymers easily lose their characteristic viscosity due to the destruction of the molecular bonds responsible for keeping the network/matrix intact, showing a critical biodegradability [1,34]. Some examples of natural polymers giving rise to hydrogels are dextran, agarose, hyaluronic acid, collagen, alginate, gelatin, cellulose, starch, chitosan and xanthan [31]. Some associations such as chitosan with gelatin, are specially useful as the resulting hydrogel presents increased resistance to degradation by collagenases [1,8].

3.2.4. Hydrocolloids

Hydrocolloids originate from a mixture of colloidal compounds with elastomers and alginates. These mixes are generally biodegradable, biocompatible and stimulate autolytic debridement, also favoring inflammation, angiogenesis, collagen synthesis and epithelialization [18,35]. Hydrocolloids are not suitable for deep wounds, especially if infected, as they reduce the amount of available oxygen required for healing. These formulas are able to absorb minimal to moderate amounts of exudate and inhibit bacterial multiplication by lowering the pH [18,35]. They contribute to pain control [31,32] but may inhibit wound contraction in the area where the skin adheres to the dressing, limiting its use in the final phase of healing. [33,34].

3.3. *Biological Dressings and Skin Substitutes*

Different research is currently in process dedicated to the production of new coatings through the synthesis and modification of biocompatible materials [23]. These coatings may originate from biopolymers such as collagen, gelatin, alginate, chitosan, dextran, cellulose and elastin [29] and present relevant advantages such as permeability to water vapor and oxygen, high biocompatibility, non expensive, highly-durable, with good ability to induce tissue regeneration, and preventive of microorganism colonization, and trauma [36].

Several skin substitutes (SS) are commercially available, being used for different clinical purposes [37]. The SS, mainly composed by collagen, may function as autografts, but despite being inexpensive, limitations have been shown, associated with the risk of infection and disease transmission [24,37,38]. Therefore, the good use of biological dressings and skin substitutes should be limited to low-exuding wounds [24,29]

3.3.1. Collagen

The main coverings from animal origin are essentially collagen-based. Collagen is the most abundant protein in connective tissue and can be extracted from bovine or porcine skin, tendons, intestine or bladder mucosa, or from rat tail [38]. This collagen from natural sources is quite versatile, allowing processing (extraction, purification, and polymerization) to undergo physical changes (under high pressure and low temperature), chemical modifications (by the addition of detergents and high osmolarity solutions of, chelation with EDTA, and basic or acid treatment) and enzymatic transformations (by trypsin digestion) giving rise to several biomaterials, with different applicability.

It is also possible to associate other biomaterials with collagen, like elastane, chitosan and glycosaminoglycans. From collagen processing, it is even possible to obtain sponges, films, membranes, spheres, and hydrogels [18,38]. Collagen participates in the process of hemostasis and tissue repair, it is biocompatible, biodegradable, has low allergenic power, is non-toxic, and shows high tensile strength [38]. Commercial collagen sponges are useful for burn and ulcer dressing as they have high porosity and high-water absorption capacity. Several studies evidenced that collagen-based dressings promote cellular recruitment, activate the inflammation phase of wound wealing and stimulate the formation of new granulation tissue and epithelial layers. Macroscopically, studies carried out in vitro and in vivo with rabbits, revealed great stability of these materials to thermal variations and in the presence of edema. However, microscopically, foci of necrosis were detected, both in the epidermis and dermis [18]. Collagen may be also extracted from marine invertebrates and plants such as undersized fish, jellyfish, sharks, starfish and sponges. These organisms are promising sources of collagen, because there is no religious limitations for its use, and there are no reports of possible transmissible diseases [39]. However, collagen from fish origin shows limitations related with less crosslinked with its mammal equivalent and reduced mechanical strength, resulting difficult to preserve this type of material [18,21,39]. Collagen-derived products find wide applications as membrane, bone graft material, agent for local drug delivery and as hemostatic agent. Liposomes can be added to collagen gels, under encapsulation and may be used for the controlled release of insulin, and growth factors, among other drugs. There are also associations of collagen with alginate to promote the inflammatory and healing phases of wound healing [38].

3.3.2. Gelatin

Gelatin results from the denaturation of collagen obtained from the skin and bones of animals. This material offers good biocompatibility, shows hemostatic action, low toxicity and antigenic properties, is biodegradable, and presents good plasticity and adhesion capacity [38]. Gelatin shows poor mechanical and antimicrobial properties [24], however, associating sodium alginate to gelatin allows will allow greater elasticity with less resorption power and toxicity [40,41].

3.3.3. Cellulose

Cellulose is a biopolymer, mostly obtained from wood, also used in the paper industry, due to its high availability. Cellulose may come from plants, or be produced by algae, fungi, and some species of bacteria. Cellulose brings numerous advantages such as high porosity, permeability to liquids and gases, high water holding capacity, it is biodegradable, non-toxic and soft. Bacterial cellulose has good biocompatibility when compared to plant cellulose and provides extracellular protection for its producing bacteria, through a kind of biofilm that works as a protective barrier [25]. It is suitable for wound dressing due to its capacity to enable autolytic debridement, relieve pain and promote the formation of granulation tissue. Portela et al. [25] compared different treatment approaches for the healing of wounds with similar characteristics and about 15 mm in diameter. The authors reported the highest healing rate in wounds treated with mesenchymal stem cells, in association with bacterial cellulose, followed by the ones treated with a bacterial cellulose hydrogel, both with better results than the control group [25].

3.3.4. Bamboo

Plants have been crucial as natural medicines, both for local application and development of therapeutic foods. Bamboo fibers contain cellulose, lignin, hemicellulose and extractives identical to other natural fibers [42,43] Bamboo medical textil are used for controlled release of herbal extracts and show potential antimicrobial, anti-inflammatory and wound healing properties. These fibres enhance wound contraction and increase epithelialization [44]. Herb-based dressings are non-toxic, allowing using for long periods. Absorptive capacity is determined by its hydrophilic abilities and porosity. Dressings with bamboo provide high strength, besides economic viability and sustainability extraction, due to its environmental-friendly nature and rapid growing properties [42,43,45].

3.3.5. Hyaluronic Acid

Hyaluronic acid is a polysaccharide, belonging to the glycosaminoglycan family and a key-component of joint synovial fluid, cartilage, vitreous humor of the eye and skin of vertebrates. It is involved in the inflammatory response, angiogenesis, cell adhesion and regeneration process. Thanks to the intrinsic properties of hyaluronic acid, such as biocompatibility, biodegradability and hydrophilic character, it is used to produce various types of coverage like hydrogels, sponges, and films [34,46].

3.3.6. Sodium Alginate

Sodium alginate is a natural fibrous polymer derived from brown algae. When compared to synthetic coatings it has some short comings such as poor thermal stability, high hydrophilic power, and poor mechanical properties [20,47]. Alginate forms a gel when it comes in contact with wound exudate, and can absorb twenty times its weight, due to the high porosity. As alginate needs moisture to improve its performance, it is not suitable for dry wounds. Hence, to prevent excessive wound desiccation, alginate dressings should have a second layer of foam or hydrocolloid, which should not be occlusive in case of infection [18]. Thanks to the presence of calcium in its composition, it is useful for clot formation and consequently to the hemostatic process. Ambrogi et al., in 2020 [48] developed alginate films with silver nanoparticles, presenting good moisturizing properties, and, due to the slow release of silver nanoparticles, it was shown able to promote antimicrobial and anti-biofilm activity [48]

3.3.7. Extracellular Matrix Bands

Extracellular matrix bands are acellular, biodegradable and sterilized sheets, most commonly made from porcine small intestinal submucosa or urinary bladder submucosa matrix. These bands provide structural proteins, growth factors, cytokines and their inhibitors in physiological proportions, allowing stimulation of angiogenesis and presenting antibacterial properties. However, this product requires specific techniques for application, such as a well-prepared bedding with debridement, no other topical medication or cleaning agents, and no exudates. Drainage is essential, demanding fenestrated band material when exudation is relevant [49,50].

3.3.8. Omentum Flaps

Omentum flaps are used to cover tissue defects, promoting a vascular bed, controlling adhesions and fighting infections. These materials allow establishing of circulation and exudate drainage [5]. The omentum also aids in wound healing and regeneration due to its unique milky spots that produce immunomodulatory cells. Activated omentum stromal cells secrete cytokines that promote tissue repair. Recent research by Liu et al., [51] showed that omental-derived cells may help reducing open epidermis length and increase epidermal cell layers in burn wounds, underscoring the omentum's regenerative capabilities [51]. Laparoscopically harvested omentum flaps were effectively used to reconstruct extensive and complex wounds, providing well-vascularized, pliable tissue with reliable vascular anatomy [51].

3.3.9. Autologous Platelet-Rich Plasma

The autologous platelet-rich plasma favors epithelialization, contraction and neovascularization in the healing process and, being autologous, it does not present biological risks concerning the transmission of diseases. Autologous platelet-rich plasma is usually used in wounds with associated vascular problems and therefore with a high rejection rate. Gupta et al., [52] followed two groups of patients who presented chronic wounds and were subjected to skin grafts. In one of the groups, the autologous platelet-rich plasma was injected daily, showing significant improvements in the graft uptake rate, when compared to the control group, undergoing a standard method [52].

3.4. Bioactive Wound Dressings

Bioactive dressings can be used for the transport and delivery of drugs (antimicrobial or anti-inflammatory agents, growth factors and other bioactive agents) to specific tissues or organs at the right time [24,26,53]. In drug delivery systems, encapsulated therapeutics can be released through various mechanisms, widely classified as active or passive delivery. In active delivery, the release is triggered by environmental stimuli (such as pH, temperature, enzymes, chemical reactions, redox reactions, etc) or external stimuli (such as magnetic fields, electric fields, light ultrasound, etc). In contrast, passive delivery relies on the diffusion of the drug through the carrier matrix into the surrounding medium from the high drug concentration region to the low concentration region (such as blood). The rate and extent of drug absorption depend on several factors, such as route of administration, physicochemical properties of the drug, type of formulation and drug-food interactions [54,55]. These systems reduce systemic toxicity and deliver maximum drug levels directly on the target site. The main materials used for controlled and targeted drug delivery are poly(lactic-co-glycolic), poly(vinylpyrrolidone), poly(vinyl-alcohol), poly(hydroxyalkylmethacrylates), hydrocolloids, alginate, hyaluronic acid and collagen [24]. Different agents such as antimicrobials, nanoparticles and natural products (essential oils, honey, propolis and chitosan) have been incorporated within these structures allowing to improve antimicrobial properties [26].

3.4.1. Curcumin

Curcumin is the main bioactive component present in the rhizomes of *Curcuma longa* Linn (turmeric) [56]. Curcumin is a bioactive phenol exhibiting anti-inflammatory, antioxidant, tissue protective, chemoprotective, antiviral and immunomodulatory properties. Curcumin also presents a broad spectrum of antibacterial actions including bacterial membrane disruption, disruption of biofilm formation and exerts potent antioxidant effects by scavenging reactive oxygen species (ROS) [56]. Studies in animals revealed low toxicity, demonstrating good tolerability of daily doses between 4000 and 8000 mg [57]. Curcumin promotes cell proliferation and migration by activating growth factor signaling pathways, such as the epidermal growth factor receptor (EGFR) pathway, and modulating the expression of extracellular matrix (ECM) components [57]. Fu et al., [58] reported that mice treated with curcumin-loaded poly(ϵ -caprolactone)-poly(ethylene glycol)-poly(ϵ -caprolactone) (PCEC) fibers exhibited faster re-epithelialization and blood vessel formation as well as an increase in collagen deposition over time [57,58]. Ranjbar-Mohammadi et al., [59] demonstrated that curcumin-loaded poly(ϵ -caprolactone)/gum tragacanth (PCL/GT/Cur) electrospun fibers increased collagen content and accelerated the wound healing process in diabetic male Sprague-Dawley rats [57,59]. In a comparative study utilizing a skin incision model, it was observed that curcumin facilitated complete epithelial repair, promoted angiogenesis during the proliferative phase of wound healing, and accelerated wound closure [60]. Curcumin possesses potent anti-inflammatory properties by inhibiting the activity of pro-inflammatory mediators, such as cyclooxygenase-2 (COX-2), interleukin-1 (IL-1), interleukin-8 (IL-8) tumor necrosis factor-1 (TNF-1), matrix metalloproteinase 9 (MMP-9) and matrix metalloproteinase 3 (MMP-3) [60]. The ability of curcumin to inhibit the function of NF-(κ)B (Nuclear factor kappa B), a regulatory protein central to inflammatory responses initiation, is also remarkable [60]. By attenuating inflammation, curcumin promotes a conducive microenvironment for optimal wound healing, and falls under class IV of the biopharmaceutical classification system, characterized by low solubility and poor permeability [57,60,61]. These attributes contribute to a diminished absorption, limited bioavailability, and stability concerns. Additionally, curcumin undergoes rapid metabolism at specific intervals. To address these challenges, various formulations have been explored, such as nanoparticles, liposomes, nanogels, nanoemulsions, and the use of adjuvants and nanocrystals, reporting promising results in promoting wound healing in patients with acute wounds, chronic wounds, and burns [60,62].

3.4.2. Chitosan

Chitosan is a naturally occurring glycosaminoglycan, derived from the exoskeleton of crustaceans, molluscs, insects and the cell walls of some fungi. Obtained through the alkaline deacetylation of chitin, is biodegradable, biocompatible and has a good function as an antimicrobial agent (bactericidal, bacteriostatic, fungicidal and fungistatic) [63–65]. Studies state that chitosan favors hemostasis and promotes the infiltration and migration of polymorphonuclear neutrophils and macrophages [64]. In trials with diabetic rats, chitosan accelerated the healing phase, allowing increased migration of fibroblasts, deposition of collagen and growth factors in their matrix, accelerating the speed of healing and maintenance of homeostasis [13,66]. This material has osteoinductive and cartilage-inducing activity as well as non-toxic, mucoadhesive, non-carcinogenic, immunostimulant, biocompatible, bioresorbable and bioactive properties [63,64]. However, it is susceptible to structural changes due to two reactive groups – hydroxyl and amino [67]. The free binding of amino group is also related to its antibacterial properties [10,68]. Besides the microbial agent present and the cell age, the effectiveness of chitosan action also depends on the solvent used, concentration of chitosan and its degree of deacetylation, presence of a plasticizer, hydrophilic/hydrophobic characteristics, influencing its solubility, chelating effect, and the mixing process used. Although owning a broad spectrum of antimicrobial activity, chitosan exhibits differing inhibitory efficiency against different fungi, virus, Gram-positive and Gram-negative bacteria. The mode of action of chitosan against microorganisms can be classified based on extracellular effects, intracellular effects, or both [68–72]. The chelant effect of amino groups can cause electrostatic attraction of anionic compounds, such as lipids, cholesterol, metal ions, proteins and macromolecules anionic residues, by altering their normal function [66,69,70,73]. This activity is affected by pH, being higher at lower pH (4.5-5.9). Diluted with acidic solutions, the positive charges of chitosan compete with Ca^{+} for electronegative sites on the membrane, conferring instability, weakness and increased permeability of the cell membrane, leading to cell death [73,74].

3.4.3. Xanthan Gum

Xanthan gum is a high molecular weight natural polysaccharide, obtained from the bacterium *Xanthomonas campestris* after a fermentation process [31,75]. It has good rheological properties and works as a stabilizer for water-based products, allowing their retention. Ilomuanya et al. (2020) evaluated the effectiveness of various formulations of a xanthan-rich hydrogel, and different concentrations of hyaluronic acid and silver sulfadiazine, concluding that the incorporation of 0.1% silver sulfadiazine and 1.5% hyaluronic acid in the xanthan-rich hydrogel led to the best results in terms of healing rate after 14 days [75].

3.4.4. Nanomaterials

Gold, silver, copper, zinc, titanium and magnesium nanomaterials are used for their bioavailability, absorption capacity, mucoadhesive, protective properties and as antimicrobial therapy [8]. Nanomaterials allow the controlled release of drugs trapped in capsules or through the surface membrane [7]. Silver nanoparticles are the most used as they present less toxicity to the patients' cells and greater antibacterial effect against Gram-positive and Gram bacteria [76], antiviral and fungicidal activity [77]. Silver affects microbial plasma membrane proteins, interfering with transmembrane transporting systems and causing "perforation" in their structure, with the dissipation of H^{+} ions and consequently cell death [7]. Diniz et al., [47] followed the evolution of wounds in Wistar rats for 14 days, and concluded that wounds covered with hydrogel rich in silver nanoparticles produced new granulation tissue and developed collagen-rich crusts in a shorter time than the control group [47]. Silver nanoparticles can be made available in the form of hydrocolloids, hydrogels and alginates. The disadvantage in using these nanoparticles is the difficulty in controlling their shape, size, and stability as they oxidize easily and tend to form aggregates [74]. Furthermore, in higher concentrations, heavy metals are toxic to tissue cells [78,79], having shown in vitro cytotoxicity against keratinocytes and fibroblasts and, consequently, delaying healing in vivo [79].

For this reason, slow-release systems for nanoparticles are crucial. The degree and nature of polymer matrix bonds are key-issues for the regulation of nanoparticle release.

3.4.5. Essential Oils

Essential oils (EOs) are obtained from plant extracts and have antimicrobial activity against Gram-positive and Gram-negative bacteria, fungi and virus, in addition to antiparasitic, insecticidal, anti-inflammatory, and immunostimulant properties. These oils present antioxidant action, stimulate blood circulation at skin level, reduce fluid retention and can reduce the development of bedsores and wrinkles [19,80]. However, as they are highly lipophilic components, the poor solubility in aqueous media renders contact and permeabilization of cell membranes difficult [81]. Other studies proved the beneficial action of combinations of EOs (in the form of spot-on or shampoos) as a new strategy against bacterial infections, allowing the restoration of the cutaneous barrier and the characteristic microbiome of the skin, also preventing the use of antibiotics and the resulting development of antimicrobial resistance [82–85]. Furthermore, essential oils have an anti-inflammatory activity, by inhibiting the production of tumor necrosis factor and interleukins, promoting angiogenesis and consequently accelerating healing [15]. According to Elaine dos Santos [86], it might be worth to use hydrogels with the association of EOs and nanoparticles, or nanoemulsions to increase the stability of the compound [86]. However, these materials have inherent disadvantages because they fight both microbial and the patient cells [7].

As with vegetable oils, Omega 6 - fatty acids also allow the maintenance of a moisturized environment in the wound, accelerating angiogenesis, preventing dehydration and local tissue death. Furthermore, essential oils also promote autolytic debridement and reduce local pain [87].

3.4.6. Honey

Honey is a supersaturated solution of natural sugar, with about 17% water content, fructose, glucose, maltose, sucrose, and other types of carbohydrates. The biological variety of honey depends on the floral resources. Not all honeys are equally effective in healing wounds. Physical characteristics of Manuka Honey, such as high osmolarity, acidity, an enzyme composition, that produces hydrogen peroxide and methylglyoxal – (MGO) (non-hydrogen peroxide components), contribute to its antimicrobial [76,88], anti-inflammatory, immunostimulant and antioxidant action, alone or associated with conventional therapy [8,10,89,90]. Bulman et al., [88] incorporated MGO in polyvinil alcohol fibers composition and confirmed bactericidal activity against *E.coli* and *S. aureus* [26,88]. Some authors believe that the acidic pH of honey may enhance macrophages killing of bacteria and inhibit microbial biofilm formation. Additionally, the high osmolarity of honey provides an unfavorable environment for microorganism survival and growth. Furthermore, the hydrogen peroxide forms highly toxic hydroxyl radical, which is involved in microbial killing. Many studies prove that exposure of *E.coli* to low concentrations of hydrogen peroxide results in DNA damage, that causes mutagenesis and kills the bacteria [26,91].

3.4.7. Propolis

Propolis is a natural resinous product produced by honeybees, using substances collected from plants, which are changed by the bee salivary secretion. Propolis contains flavonoids, terpenes, phenolic acids, aldehydes and ketones, and promotes tissue healing, by granulation growth and limitation of scar formation. Many studies have confirmed that propolis contains bioactive compounds with antibacterial [92], antiviral [93], antifungal [93] and antibiofilm activity [92]. The exact way propolis fights off microorganisms is still not entirely clear [94]. It seems to work through a combination of its various components, working together, rather than one specific mechanism. However, certain species of microorganisms are more vulnerable to propolis than others. Some research suggests that propolis might damage the structure of microorganisms, hampering their normal metabolism. This natural substance seems to have multiple targets regarding bacterial cells. By creating a physical barrier and interfering with enzymes and proteins that are necessary for the

bacterial invasion process, propolis seems to hinder microorganisms, blocking their ability to replicate and preventing them from invading host cells. Additionally, propolis disrupts the metabolic processes of microorganisms by interfering with cellular structures and components responsible for energy production [94]. Numerous in vitro and in vivo studies have investigated the effects of propolis on different aspects of the wound healing process. In the inflammatory phase, propolis has shown to modulate immune responses, reduce inflammatory cytokine levels, and promote M2 macrophage polarization, leading to accelerated wound closure and resolution of inflammation. Propolis has analgesic and antioxidant action, after acute trauma and burn [92–96]. It inhibits the occurrence of reactive oxygen species and consequent tissue damage [97]. In the proliferation phase, propolis stimulates fibroblast proliferation and collagen synthesis, enhances angiogenesis, and accelerates re-epithelialization, thereby promoting tissue regeneration and granulation tissue formation. In the remodeling phase, propolis facilitates the remodeling of newly formed tissue, promotes wound contraction, and improves the tensile strength of healed wounds. Ibrahim et al., [98] tested a sponge matrix from collagen hydrolysates and honey-propolis wax (HPW) on wound healing, in a mouse model, revealing that HPW increased the re-epithelialization and the overall wound healing rate in mice [98].

4. Conclusion

Skin is the biggest organ of the body and, consequently, wounds are between the most frequently situations attended in veterinary medicine. In a growing urban lifestyle, with a higher prevalence of obesity and diabetes, wound handling became vital both for humans and companion animals. The longer the wound takes to heal, the higher the cost, the greater the morbidity and the higher the zoonotic risk. Furthermore, the use of antibiotics increases the selection for resistant bacteria. Topical adjuvant therapies with dressings from natural products, prevent biofilm formation and do not promote antimicrobial resistance, which is a growing concern nowadays and a current and future research topic.

We believe that this review may result truly useful for choosing the right wound handling procedures to be implemented in each wound, depending on its characteristics.

Author Contributions: Conceptualization, T.L., M.C.Q. and L.M.; writing—original draft preparation, T.L.; writing—review and editing, M.C.Q.; supervision, M.C.Q. and L.M.; funding acquisition, M.C.Q. and L.M. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by National Funds through FCT – Fundação para a Ciência e a Tecnologia, Portugal, under the projects UIDB/05183/2020 and LA/P/0121/2020.

Acknowledgments: The authors wish to thank MED (<https://doi.org/10.54499/UIDP/05183/2020>) & CHANGE (<https://doi.org/10.54499/LA/P/0121/2020>).

Conflicts of Interest: The authors declare no conflicts of interests.

References

1. Firlar, I.; Altunbek, M.; McCarthy, C.; Ramalingam, M.; Camci-Unal, G. Functional Hydrogels for Treatment of Chronic Wounds. *Gels* **2022**, *8*, 127, <https://doi.org/10.3390/gels8020127>.
2. Liang, Y.; Liang, Y.; Zhang, H.; Guo, B. Antibacterial Biomaterials for Skin Wound Dressing. *Asian J Pharm Sci* **2022**, *17*, 353–384.
3. Souci, L.; Denesvre, C. 3D skin models in domestic animals. *Veter- Res.* **2021**, *52*, 1–15, <https://doi.org/10.1186/s13567-020-00888-5>.
4. Paixão, A.; Caldeira, J.; Leocádio, J.; Martins, L.; Gama, F.d.C.C.V.V.d. A importância da integridade da barreira cutânea na prevenção da alergia veterinária. *Rev. Port. de Imunoalergologia* **2022**, *30*, 9–20, <https://doi.org/10.32932/rpia.2022.03.074>.
5. S W A I M, S.F. Advances in Wound Healing in Small Animal Practice: Current Status and Lines of Development; 1997; Vol. 8;.
6. Kožár, M.; Hamilton, H.; Koščová, J. Types of Wounds and the Prevalence of Bacterial Contamination of Wounds in the Clinical Practice of Small Animals. *Folia Veter-* **2018**, *62*, 39–47, <https://doi.org/10.2478/fv-2018-0036>.

7. Yang, K.; Han, Q.; Chen, B.; Zheng, Y.; Zhang, K.; Li, Q.; Wang, J. Antimicrobial hydrogels: promising materials for medical application. *Int. J. Nanomed.* **2018**, *ume* 13, 2217–2263, <https://doi.org/10.2147/ijn.s154748>.
8. Zhang, X.; Qin, M.; Xu, M.; Miao, F.; Merzougui, C.; Zhang, X.; Wei, Y.; Chen, W.; Huang, D. The fabrication of antibacterial hydrogels for wound healing. *Eur. Polym. J.* **2021**, 146, <https://doi.org/10.1016/j.eurpolymj.2021.110268>.
9. Campbell, B.G. Dressings, Bandages, and Splints for Wound Management in Dogs and Cats. *Veterinary Clinics of North America - Small Animal Practice* 2006, 36, 759–791.
10. Wang, T.; Zhu, X.-K.; Xue, X.-T.; Wu, D.-Y. Hydrogel sheets of chitosan, honey and gelatin as burn wound dressings. *Carbohydr. Polym.* **2012**, 88, 75–83, <https://doi.org/10.1016/j.carbpol.2011.11.069>.
11. Miniño AM, Anderson RN, Fingerhut LA, Boudreault MA, Warner M. Deaths: injuries, 2002. *Natl Vital Stat Rep.* 2006 Jan 31;54(10):1-124. PMID: 16485447;
12. Matias, D.F.; Paixão, A.R.C.; Martins, L. Skin barrier in veterinary allergy or the animal [and human] skin protective hat. *J. Dairy, Veter- Anim. Res.* **2023**, 12, 82–84, <https://doi.org/10.15406/jdvar.2023.12.00328>.
13. Patrúlea, V.; Ostafe, V.; Borchard, G.; Jordan, O. Chitosan as a starting material for wound healing applications. *Eur. J. Pharm. Biopharm.* **2015**, 97, 417–426, <https://doi.org/10.1016/j.ejpb.2015.08.004>.
14. Niculescu, A.-G.; Grumezescu, A.M. An Up-to-Date Review of Biomaterials Application in Wound Management. *Polymers* **2022**, 14, 421, <https://doi.org/10.3390/polym14030421>.
15. Li, Q.; Liu, X.; Yang, S.; Li, C.; Jin, W.; Hou, W. Effects of the Chinese Herb Medicine Formula “She-Xiang-Yu-Hong” Ointment on Wound Healing Promotion in Diabetic Mice. *Evidence-Based Complement. Altern. Med.* **2022**, 2022, 1–8, <https://doi.org/10.1155/2022/1062261>.
16. Zielins, E.R.; A Brett, E.; Luan, A.; Hu, M.S.; Walmsley, G.G.; Paik, K.; Senarath-Yapa, K.; A Atashroo, D.; Wearda, T.; Lorenz, H.P.; et al. Emerging drugs for the treatment of wound healing. *Expert Opin. Emerg. Drugs* **2015**, 20, 235–246, <https://doi.org/10.1517/14728214.2015.1018176>.
17. Silvestro, I.; Lopreiato, M.; D’abusco, A.S.; Di Lisio, V.; Martinelli, A.; Piozzi, A.; Francolini, I. Hyaluronic Acid Reduces Bacterial Fouling and Promotes Fibroblasts’ Adhesion onto Chitosan 2D-Wound Dressings. *Int. J. Mol. Sci.* **2020**, 21, 2070, <https://doi.org/10.3390/ijms21062070>.
18. Ghomi, E.R.; Khalili, S.; Khorasani, S.N.; Neisiany, R.E.; Ramakrishna, S. Wound dressings: Current advances and future directions. *J. Appl. Polym. Sci.* **2019**, 136, 47738. <https://doi.org/10.1002/app.47738>.
19. Vasile, B.S.; Birca, A.C.; Musat, M.C.; Holban, A.M. Wound Dressings Coated with Silver Nanoparticles and Essential Oils for The Management of Wound Infections. *Materials* **2020**, 13, 1682, <https://doi.org/10.3390/ma13071682>.
20. Siliane Batista de Souza -Professora Associada, M.B.; Vicky Bahr Arias -Professora Associada, M.C. Use of Wound Dressing for Treatment of Wounds in Dogs and Cats: Literature Review Daniela Scapini Mendes-Médica Veterinária Autônoma Resumo; 2014;
21. Boucard, N.; Viton, C.; Agay, D.; Mari, E.; Roger, T.; Chancerelle, Y.; Domard, A. The use of physical hydrogels of chitosan for skin regeneration following third-degree burns. *Biomaterials* **2007**, 28, 3478–3488, <https://doi.org/10.1016/j.biomaterials.2007.04.021>.
22. Kietzmann, M. Improvement and retardation of wound healing: Effects of pharmacological agents in laboratory animal studies. *Vet. Dermatol.* **1999**, 10, 83–88, <https://doi.org/10.1046/j.1365-3164.1999.00155.x>.
23. Sheikholeslam, M.; Wright, M.E.E.; Jeschke, M.G.; Amini-Nik, S. Biomaterials for Skin Substitutes. *Adv. Heal. Mater.* **2017**, 7, 1700897, <https://doi.org/10.1002/adhm.201700897>.
24. Ndlovu, S.P.; Ngece, K.; Alven, S.; Aderibigbe, B.A. Gelatin-Based Hybrid Scaffolds: Promising Wound Dressings. *Polymers* **2021**, 13, 2959, <https://doi.org/10.3390/polym13172959>.
25. Portela, R.; Leal, C.R.; Almeida, P.L.; Sobral, R.G. Bacterial cellulose: a versatile biopolymer for wound dressing applications. *Microb. Biotechnol.* **2019**, 12, 586–610, doi:10.1111/1751-7915.13392.
26. Simões, D.; Miguel, S.P.; Ribeiro, M.P.; Coutinho, P.; Mendonça, A.G.; Correia, I.J. Recent Advances on Antimicrobial Wound Dressing: A Review. *European Journal of Pharmaceutics and Biopharmaceutics* 2018, 127, 130–141.
27. Mani, M.P.; Faudzi, A.A.M.; Ramakrishna, S.; Ismail, A.F.; Jaganathan, S.K.; Tucker, N.; Rathanasamy, R. Sustainable electrospun materials with enhanced blood compatibility for wound healing applications—A mini review. *Curr. Opin. Biomed. Eng.* **2023**, 27, <https://doi.org/10.1016/j.cobme.2023.100457>.
28. Nguyen, H.M.; Le, T.T.N.; Nguyen, A.T.; Le, H.N.T.; Pham, T.T. Biomedical materials for wound dressing: recent advances and applications. *RSC Adv.* **2023**, 13, 5509–5528, <https://doi.org/10.1039/d2ra07673j>.
29. Revete, A.; Aparicio, A.; Cisterna, B.A.; Revete, J.; Luis, L.; Ibarra, E.; González, E.A.S.; Molino, J.; Reginensi, D. Advancements in the Use of Hydrogels for Regenerative Medicine: Properties and Biomedical Applications. *Int. J. Biomater.* **2022**, 2022, 1–16, <https://doi.org/10.1155/2022/3606765>.
30. Zeng, D.; Shen, S.; Fan, D. Molecular design, synthesis strategies and recent advances of hydrogels for wound dressing applications. *Chin. J. Chem. Eng.* **2020**, 30, 308–320, <https://doi.org/10.1016/j.cjche.2020.12.005>.

31. Alves, A.; Miguel, S.P.; Araujo, A.R.; Valle, M.J.d.J.; Navarro, A.S.; Correia, I.J.; Ribeiro, M.P.; Coutinho, P. Xanthan Gum–Konjac Glucomannan Blend Hydrogel for Wound Healing. *Polymers* **2020**, *12*, 99, <https://doi.org/10.3390/polym12010099>.
32. Veiga, A.S.; Schneider, J.P. Antimicrobial hydrogels for the treatment of infection. *Biopolym.* **2013**, *100*, 637–644, <https://doi.org/10.1002/bip.22412>.
33. Nasra, S.; Patel, M.; Shukla, H.; Bhatt, M.; Kumar, A. Functional hydrogel-based wound dressings: A review on biocompatibility and therapeutic efficacy. *Life Sci.* **2023**, *334*, 122232, <https://doi.org/10.1016/j.lfs.2023.122232>.
34. Davachi, S.M.; Haramshahi, S.M.A.; Akhavirad, S.A.; Bahrami, N.; Hassanzadeh, S.; Ezzatpour, S.; Hassanzadeh, N.; Kebria, M.M.; Khanmohammadi, M.; Bagher, Z. Development of chitosan/hyaluronic acid hydrogel scaffolds via enzymatic reaction for cartilage tissue engineering. *Mater. Today Commun.* **2022**, *30*, 103230, <https://doi.org/10.1016/j.mtcomm.2022.103230>.
35. Pott, F.S.; Meier, M.J.; Stocco, J.G.D.; Crozeta, K.; Ribas, J.D. A Efetividade Do Hidrocoloide versus Outras Coberturas Na Cicatrização de Úlceras Por Pressão Em Adultos e Idosos: Revisão Sistemática e Metanálise. *Rev Lat Am Enfermagem* 2014, *22*, 511–520.
36. May, S.R. The Effects of Biological Wound Dressings Healing Process; 1991; Vol. 8;.
37. Tran, A.; Desai, S.; Robinson, D.M. From ancient Egypt to the dermatologic office: An overview of skin substitutes and modern-day applications in dermatologic surgery. *Heal. Sci. Rep.* **2023**, *6*, e1067, <https://doi.org/10.1002/hsr2.1067>.
38. Chattopadhyay, S.; Raines, R.T. Review Collagen-Based Biomaterials for Wound Healing. *Biopolymers* 2014, *101*, 821–833.
39. Coppola, D.; Oliviero, M.; Vitale, G.A.; Lauritano, C.; D'ambra, I.; Iannace, S.; de Pascale, D. Marine Collagen from Alternative and Sustainable Sources: Extraction, Processing and Applications. *Mar. Drugs* **2020**, *18*, 214, <https://doi.org/10.3390/md18040214>.
40. Labowska, M.B.; Cierluk, K.; Jankowska, A.M.; Kulbacka, J.; Detyna, J.; Michalak, I. A Review on the Adaption of Alginate-Gelatin Hydrogels for 3D Cultures and Bioprinting. *Materials* **2021**, *14*, 858, doi:10.3390/ma14040858.
41. Serafin, A.; Culebras, M.; Collins, M.N. Synthesis and evaluation of alginate, gelatin, and hyaluronic acid hybrid hydrogels for tissue engineering applications. *Int. J. Biol. Macromol.* **2023**, *233*, 123438, <https://doi.org/10.1016/j.ijbiomac.2023.123438>.
42. Abdul Khalil, H.P.S.; Alwani, M.S.; Islam, M.N.; Suhaily, S.S.; Dungani, R.; H'ng, Y.M.; Jawaid, M. The Use of Bamboo Fibres as Reinforcements in Composites. In *Biofiber Reinforcements in Composite Materials*; Elsevier Inc., 2015; pp. 488–524 ISBN 9781782421276.
43. Hasan, K.F.; Al Hasan, K.N.; Ahmed, T.; György, S.-T.; Pervez, N.; Bejó, L.; Sándor, B.; Alpár, T. Sustainable bamboo fiber reinforced polymeric composites for structural applications: A mini review of recent advances and future prospects. *Case Stud. Chem. Environ. Eng.* **2023**, *8*, <https://doi.org/10.1016/j.cscee.2023.100362>.
44. Ahmed, S.S.Z.; Balu, N.; Khader, S.Z.A.; Mahboob, M.R.; Lakshmanan, S.O.; Vetrivel, M. Fabrication and evaluation of bamboo fabric coated with extracts of *Curcuma longa*, *Centella asiatica* and *Azadirachta indica* as a wound dressing material. *Orient. Pharm. Exp. Med.* **2020**, *21*, 83–95, <https://doi.org/10.1007/s13596-020-00503-0>.
45. Silva, M.F.; Menis-Henrique, M.E.C.; Felisberto, M.H.F.; Goldbeck, R.; Clerici, M.T.P.S. Bamboo as an eco-friendly material for food and biotechnology industries. *Curr. Opin. Food Sci.* **2020**, *33*, 124–130, <https://doi.org/10.1016/j.cofs.2020.02.008>.
46. Neuman, M.G.; Nanau, R.M.; Oruña-Sanchez, L.; Coto, G. Hyaluronic Acid and Wound Healing; 2015; Vol. 18;.
47. Diniz, F.R.; Maia, R.C.A.P.; Andrade, L.R.; Andrade, L.N.; Chaud, M.V.; Da Silva, C.F.; Corrêa, C.B.; de Albuquerque Junior, R.L.C.; Da Costa, L.P.; Shin, S.R.; et al. Silver Nanoparticles-Composing Alginate/Gelatine Hydrogel Improves Wound Healing In Vivo. *Nanomaterials* **2020**, *10*, 390, doi:10.3390/nano10020390.
48. Ambroggi, V.; Pietrella, D.; Donnadio, A.; Latterini, L.; Di Michele, A.; Luffarelli, I.; Ricci, M. Biocompatible alginate silica supported silver nanoparticles composite films for wound dressing with antibiofilm activity. *Mater. Sci. Eng. C* **2020**, *112*, 110863, <https://doi.org/10.1016/j.msec.2020.110863>.
49. Balsa, I.M.; Culp, W.T.N. Wound Care. *Veterinary Clinics of North America - Small Animal Practice* 2015, *45*, 1049–1065.
50. Schallberger, S.P.; Stanley, B.J.; Hauptman, J.G.; Steficek, B.A. Effect of Porcine Small Intestinal Submucosa on Acute Full-Thickness Wounds in Dogs. *Veter. Surg.* **2008**, *37*, 515–524, <https://doi.org/10.1111/j.1532-950x.2008.00398.x>.
51. Liu, J.; Han, J.; Ji, G.; Zhang, T.; Xie, S.; Liu, Y.; Li, Y.; Ma, C.; Zheng, Z.; Hu, D. Laparoscopic harvest and free transplantation of great omentum flap for extensive tissue defects in complex wounds. *JPRAS Open* **2024**, *39*, 1–10, <https://doi.org/10.1016/j.jptra.2023.10.012>.

52. Gupta, S.; Goil, P.; Thakurani, S. Autologous Platelet Rich Plasma As A Preparative for Resurfacing Burn Wounds with Split Thickness Skin Grafts. **2020**, 9, 29–32, <https://doi.org/10.29252/wjps.9.1.29>.
53. del Olmo, J.A.; Pérez-Álvarez, L.; Sáez-Martínez, V.; Benito-Cid, S.; Ruiz-Rubio, L.; Pérez-González, R.; Vilas-Vilela, J.L.; Alonso, J.M. Wound healing and antibacterial chitosan-genipin hydrogels with controlled drug delivery for synergistic anti-inflammatory activity. *Int. J. Biol. Macromol.* **2022**, 203, 679–694, <https://doi.org/10.1016/j.ijbiomac.2022.01.193>.
54. Saghazadeh, S.; Rinoldi, C.; Schot, M.; Kashaf, S.S.; Sharifi, F.; Jalilian, E.; Nuutila, K.; Giatsidis, G.; Mostafalu, P.; Derakhshandeh, H.; et al. Drug delivery systems and materials for wound healing applications. *Adv. Drug Deliv. Rev.* **2018**, 127, 138–166, <https://doi.org/10.1016/j.addr.2018.04.008>.
55. Adepu, S.; Ramakrishna, S. Controlled Drug Delivery Systems: Current Status and Future Directions. *Molecules* **2021**, 26, 5905, <https://doi.org/10.3390/molecules26195905>.
56. Torbat, N.A.; Akbarzadeh, I.; Rezaei, N.; Moghaddam, Z.S.; Bazzazan, S.; Mostafavi, E. Curcumin-Incorporated Biomaterials: In silico and in vitro evaluation of biological potentials. *Co-ord. Chem. Rev.* **2023**, 492, <https://doi.org/10.1016/j.ccr.2023.215233>.
57. Hamilton, A.E.; Gilbert, R.J. Curcumin Release from Biomaterials for Enhanced Tissue Regeneration Following Injury or Disease. *Bioengineering* **2023**, 10, 262, <https://doi.org/10.3390/bioengineering10020262>.
58. Fu, S.; Meng, X.; Fan, J.; Yang, L.; Wen, Q.; Ye, S.; Lin, S.; Wang, B.; Chen, L.; Wu, J.; et al. Acceleration of dermal wound healing by using electrospun curcumin-loaded poly(ϵ -caprolactone)-poly(ethylene glycol)-poly(ϵ -caprolactone) fibrous mats. *J. Biomed. Mater. Res. Part B: Appl. Biomater.* **2013**, 102, 533–542, <https://doi.org/10.1002/jbm.b.33032>.
59. Ranjbar-Mohammadi, M.; Rabbani, S.; Bahrami, S.H.; Joghataei, M.; Moayer, F. Antibacterial performance and in vivo diabetic wound healing of curcumin loaded gum tragacanth/poly(ϵ -caprolactone) electrospun nanofibers. *Mater. Sci. Eng. C* **2016**, 69, 1183–1191, <https://doi.org/10.1016/j.msec.2016.08.032>.
60. Kumari, A.; Raina, N.; Wahi, A.; Goh, K.W.; Sharma, P.; Nagpal, R.; Jain, A.; Ming, L.C.; Gupta, M. Wound-Healing Effects of Curcumin and Its Nanoformulations: A Comprehensive Review. *Pharmaceutics* **2022**, 14, 2288, <https://doi.org/10.3390/pharmaceutics14112288>.
61. Torbat, N.A.; Akbarzadeh, I.; Rezaei, N.; Moghaddam, Z.S.; Bazzazan, S.; Mostafavi, E. Curcumin-Incorporated Biomaterials: In silico and in vitro evaluation of biological potentials. *Co-ord. Chem. Rev.* **2023**, 492, <https://doi.org/10.1016/j.ccr.2023.215233>.
62. Akbik, D.; Ghadiri, M.; Chrzanowski, W.; Rohanizadeh, R. Curcumin as a wound healing agent. *Life Sci.* **2014**, 116, 1–7, <https://doi.org/10.1016/j.lfs.2014.08.016>.
63. Şenel, S.; McClure, S.J. Potential applications of chitosan in veterinary medicine. *Adv. Drug Deliv. Rev.* **2004**, 56, 1467–1480, <https://doi.org/10.1016/j.addr.2004.02.007>.
64. Cui, C.; Sun, S.; Wu, S.; Chen, S.; Ma, J.; Zhou, F. Electrospun chitosan nanofibers for wound healing application. *Eng. Regen.* **2021**, 2, 82–90, <https://doi.org/10.1016/j.engreg.2021.08.001>.
65. Alves, N.; Mano, J. Chitosan derivatives obtained by chemical modifications for biomedical and environmental applications. *Int. J. Biol. Macromol.* **2008**, 43, 401–414, <https://doi.org/10.1016/j.ijbiomac.2008.09.007>.
66. Ribeiro, M.P.; Espiga, A.; Silva, D.; Baptista, P.; Henriques, J.; Ferreira, C.; Silva, J.C.; Borges, J.P.; Pires, E.; Chaves, P.; et al. Development of a new chitosan hydrogel for wound dressing. *Wound Repair Regen.* **2009**, 17, 817–824, <https://doi.org/10.1111/j.1524-475x.2009.00538.x>.
67. Raafat, D.; Sahl, H. Chitosan and its antimicrobial potential – a critical literature survey. *Microb. Biotechnol.* **2009**, 2, 186–201, <https://doi.org/10.1111/j.1751-7915.2008.00080.x>.
68. Fathy, Y.; Azab, W.; Ebid, W.M.A.; Abdeltwab, W.M.; Abdelaliem, Y.F.; Metry, W.A.; Eldeghedy, M. Antimicrobial Effect of Chitosan and Nano-Chitosan against Some Pathogens and Spoilage Microorganisms. 2019.
69. Ardean, C.; Davidescu, C.M.; Nemeş, N.S.; Negrea, A.; Ciopec, M.; Duteanu, N.; Negrea, P.; Duda-Seiman, D.; Musta, V. Factors Influencing the Antibacterial Activity of Chitosan and Chitosan Modified by Functionalization. *Int. J. Mol. Sci.* **2021**, 22, 7449, <https://doi.org/10.3390/ijms22147449>.
70. Moratti, S.C.; Cabral, J.D. Antibacterial Properties of Chitosan. In *Chitosan Based Biomaterials*; Elsevier Inc., **2017**; Vol. 1, pp. 31–44 ISBN 9780081002575.
71. Kong, M.; Chen, X.G.; Xing, K.; Park, H.J. Antimicrobial properties of chitosan and mode of action: A state of the art review. *Int. J. Food Microbiol.* **2010**, 144, 51–63, [doi:10.1016/j.ijfoodmicro.2010.09.012](https://doi.org/10.1016/j.ijfoodmicro.2010.09.012).
72. Bano, I.; Arshad, M.; Yasin, T.; Ghauri, M.A.; Younus, M. Chitosan: A potential biopolymer for wound management. *Int. J. Biol. Macromol.* **2017**, 102, 380–383, <https://doi.org/10.1016/j.ijbiomac.2017.04.047>.
73. Matica, M.A.; Achmann, F.L.; Tøndervik, A.; Sletta, H.; Ostafe, V. Chitosan as a Wound Dressing Starting Material: Antimicrobial Properties and Mode of Action. *Int. J. Mol. Sci.* **2019**, 20, 5889, <https://doi.org/10.3390/ijms20235889>.
74. Agnihotri, S.; Mukherji, S.; Mukherji, S. Antimicrobial chitosan–PVA hydrogel as a nanoreactor and immobilizing matrix for silver nanoparticles. *Appl. Nanosci.* **2012**, 2, 179–188, <https://doi.org/10.1007/s13204-012-0080-1>.

75. Ilomuanya, M.; Seriki, Z.; Ubani-Ukoma, U.; Oseni, B.; Silva, B. Silver Sulphadiazine- xanthan gum-hyaluronic Acid Composite Hydrogel for Wound Healing: Formulation Development and in vivo Evaluation. *Niger. J. Pharm. Res.* **2020**, *16*, 21–29, <https://doi.org/10.4314/njpr.v16i1.3>.
76. Yousefian, F.; Hesari, R.; Jensen, T.; Obagi, S.; Rgeai, A.; Damiani, G.; Bunick, C.G.; Grada, A. Antimicrobial Wound Dressings: A Concise Review for Clinicians. *Antibiotics* **2023**, *12*, 1434, <https://doi.org/10.3390/antibiotics12091434>.
77. Mukha, I.P.; Eremenko, A.M.; Smirnova, N.P.; Mikhienkova, A.I.; Korchak, G.I.; Gorchev, V.F.; Chunikhin, A.Y. Antimicrobial activity of stable silver nanoparticles of a certain size. *Appl. Biochem. Microbiol.* **2013**, *49*, 199–206, doi:10.1134/s0003683813020117.
78. Low, W.; Kenward, K.; Britland, S.T.; Amin, M.C.; Martin, C. Essential oils and metal ions as alternative antimicrobial agents: a focus on tea tree oil and silver. *Int. Wound J.* **2016**, *14*, 369–384, <https://doi.org/10.1111/iwj.12611>.
79. Sandri, G.; Bonferoni, M.C.; D'autilia, F.; Rossi, S.; Ferrari, F.; Grisoli, P.; Sorrenti, M.; Catenacci, L.; Del Fante, C.; Perotti, C.; et al. Wound dressings based on silver sulfadiazine solid lipid nanoparticles for tissue repairing. *Eur. J. Pharm. Biopharm.* **2012**, *84*, 84–90, <https://doi.org/10.1016/j.ejpb.2012.11.022>.
80. Ebani, V.V.; Mancianti, F. Use of Essential Oils in Veterinary Medicine to Combat Bacterial and Fungal Infections. *Veter- Sci.* **2020**, *7*, 193, <https://doi.org/10.3390/vetsci7040193>.
81. Stevanović, Z.D.; Bošnjak-Neumüller, J.; Pajić-Lijaković, I.; Raj, J.; Vasiljević, M. Essential Oils as Feed Additives—Future Perspectives. *Molecules* **2018**, *23*, 1717, <https://doi.org/10.3390/molecules23071717>.
82. Stevanović, Z.D.; Bošnjak-Neumüller, J.; Pajić-Lijaković, I.; Raj, J.; Vasiljević, M. Essential Oils as Feed Additives—Future Perspectives. *Molecules* **2018**, *23*, 1717, <https://doi.org/10.3390/molecules23071717>.
83. Bensignor, E.; Videmont, E. Weekly topical therapy based on plant extracts combined with lokivetmab in canine atopic dermatitis. *Veter- Dermatol.* **2021**, *33*, 68–e22, <https://doi.org/10.1111/vde.13004>.
84. Pierozan, F.; Olivry, T.; Paps, J.S.; Lawhon, S.D.; Wu, J.; Steiner, J.M.; Suchodolski, J.S.; Hoffmann, A.R. The skin microbiome in allergen-induced canine atopic dermatitis. *Veter- Dermatol.* **2016**, *27*, 332–e82, <https://doi.org/10.1111/vde.12366>.
85. Soo Xi Yap, P.; Chin Yiap, B.; Cai Ping, H.; Hua Erin Lim, S. Send Orders for Reprints to Reprints@benthamscience.Net Essential Oils, A New Horizon in Combating Bacterial Antibiotic Resistance; 2014; Vol. 8;.
86. dos Santos, E.P.; Nicácio, P.H.M.; Barbosa, F.C.; da Silva, H.N.; Andrade, A.L.S.; Fook, M.V.L.; Silva, S.M.d.L.; Leite, I.F. Chitosan/Essential Oils Formulations for Potential Use as Wound Dressing: Physical and Antimicrobial Properties. *Materials* **2019**, *12*, 2223, <https://doi.org/10.3390/ma12142223>.
87. Silva, J.R.; Burger, B.; Köhl, C.M.C.; Candreva, T.; dos Anjos, M.B.P.; Rodrigues, H.G. Wound Healing and Omega-6 Fatty Acids: From Inflammation to Repair. *Mediat. Inflamm.* **2018**, *2018*, 1–17, <https://doi.org/10.1155/2018/2503950>.
88. EL Bulman, S.; Goswami, P.; Tronci, G.; Russell, S.J.; Carr, C. Investigation into the potential use of poly(vinyl alcohol)/methylglyoxal fibres as antibacterial wound dressing components. *J. Biomater. Appl.* **2014**, *29*, 1193–1200, <https://doi.org/10.1177/0885328214556159>.
89. Mukai, K.; Koike, M.; Nakamura, S.; Kawaguchi, Y.; Katagiri, F.; Nojiri, S.; Yamada, Y.; Miyajima, E.; Matsumoto, M.; Komatsu, E.; et al. Evaluation of the Effects of a Combination of Japanese Honey and Hydrocolloid Dressing on Cutaneous Wound Healing in Male Mice. *Evidence-Based Complement. Altern. Med.* **2015**, *2015*, 1–9, <https://doi.org/10.1155/2015/910605>.
90. Samarghandian, S.; Farkhondeh, T.; Samini, F. Honey and health: A review of recent clinical research. *Pharmacogn. Res.* **2017**, *9*, 121–127.
91. Al-Waili, N.S.; Salom, K.; Butler, G.; Al Ghamdi, A.A. Honey and Microbial Infections: A Review Supporting the Use of Honey for Microbial Control. *J. Med. Food* **2011**, *14*, 1079–1096, <https://doi.org/10.1089/jmf.2010.0161>.
92. Queiroga, M.C.; Laranjo, M.; Andrade, N.; Marques, M.; Costa, A.R.; Antunes, C.M. Antimicrobial, Antibiofilm and Toxicological Assessment of Propolis. *Antibiotics* **2023**, *12*, 347, <https://doi.org/10.3390/antibiotics12020347>.
93. Martinotti, S.; Ranzato, E. Propolis: A New Frontier for Wound Healing? *Burns Trauma* **2015**, *3*, 1–10.
94. da Rosa, C.; Bueno, I.L.; Quaresma, A.C.M.; Longato, G.B. Healing Potential of Propolis in Skin Wounds Evidenced by Clinical Studies. *Pharmaceuticals* **2022**, *15*, 1143, <https://doi.org/10.3390/ph15091143>.
95. Oryan, A.; Alemzadeh, E.; Moshiri, A. Potential role of propolis in wound healing: Biological properties and therapeutic activities. *Biomed. Pharmacother.* **2018**, *98*, 469–483, <https://doi.org/10.1016/j.biopha.2017.12.069>.
96. Yang, J.; Pi, A.; Yan, L.; Li, J.; Nan, S.; Zhang, J.; Hao, Y. Research Progress on Therapeutic Effect and Mechanism of Propolis on Wound Healing. *Evidence-Based Complement. Altern. Med.* **2022**, *2022*, 1–15, <https://doi.org/10.1155/2022/5798941>.
97. El-Sakhawy, M.; Salama, A.; Tohamy, H.-A.S. Applications of propolis-based materials in wound healing. *Arch. Dermatol. Res.* **2023**, *316*, 1–13, <https://doi.org/10.1007/s00403-023-02789-x>.

98. Ibrahim, H.-I.M.; Thangavelu, M.; Khalifa, A. Honey-Propolis-Engineered Collagen Peptides as Promising Wound-Healing Matrix in Mouse Model. *Molecules* **2022**, *27*, 7090, <https://doi.org/10.3390/molecules27207090>.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.