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Review Article

Impact of Antibacterial Films in Wound Healing: Literature Review

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Abstract

Antimicrobial films and coatings have revolutionized the concept of active packaging by reducing, inhibiting, or stopping the development of microbes on food surfaces. This review was designed to unfold the facts about antibacterial films, polymers used, wound healing mechanism, parameters of evaluation and applications. Early in the inflammatory stage, attempts to restore the damage caused by local aggression begin. Finally, they result in repair, which is the replacement of specialised structures caused by collagen deposition, and regeneration, which is the process of cell multiplication and posterior differentiation by existing cells in the tissues and/or stem cells. Inflammatory reaction, cell proliferation, and synthesis of the extracellular matrix elements, as well as the post-healing period, known as remodelling, are the stages of cell and biochemical actions in wound repair. This review consists an extensive survey of literature from the Scopus, PubMed, Springer Nature and other international reputed sources. Foodborne pathogens and other germs on food surfaces are reduced, inhibited, or stopped with this approach. An extensive interaction between the product and the antimicrobial ingredient is required in these circumstances. Antimicrobial agents are chosen based on their ability to kill a specific microorganism. Food product properties include pH, water activity, content and storage conditions. Antimicrobial packaging in films reduces microbial development on food surfaces by bringing the packaging material into direct touch with the food surface. It concludes that formulation of antibacterial films is very promising research domain due to its diverse beneficial properties and easy to use.

Keywords: Antibacterial Film; Wound Healing; Review; Application; Polymer

Introduction

The use of active packaging to increase the safety margin and ensure high-quality products is a new trend in food preservation, as is the incorporation of antimicrobial agents in films that can be used as active packaging [1]. Antimicrobial films and coatings have revolutionized the concept of active packaging by reducing, inhibiting, or stopping the development of microbes on food surfaces. The microbial contamination with the highest intensity is observed on the surface of most fresh or processed items. Antimicrobial chemicals used into films result in lower diffusion rates from the packaging material into the product, resulting in the maintenance of high active ingredient concentrations where they are needed. Antimicrobial agents incorporated into edible films and coatings have been shown in numerous studies to be efficient in lowering levels of pathogenic organisms i.e., *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Salmonella Typhi*, and *Staphylococcus aureus* [2]. Wounds can sometimes cause an overly aggressive healing reaction, resulting in keloids and hypertrophic scars. Hypertrophic scars, by definition, are contained within the boundaries of the original wound bed, whereas keloids expand beyond them. Excess stress from excessive movement over a joint, underlying bony structures, or tissue loss are thought to have a role in the formation of these scars [3].

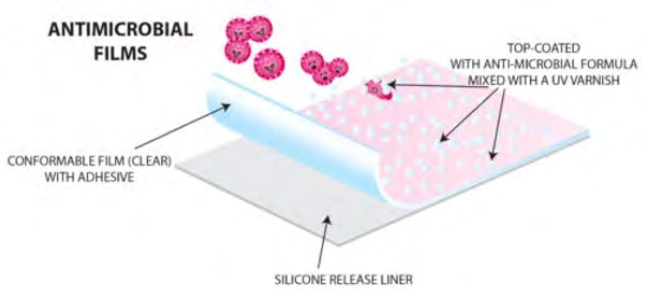

Figure 1: Antibacterial film with matrix.

Wound healing

Cutaneous healing process is a vital physiological process that involves the cooperation of a variety of cell types and their products. Early in the inflammatory stage, attempts to restore the damage caused by local aggression begin. Finally, they result in repair, which is the replacement of specialised structures caused by collagen deposition, and regeneration, which is the process of cell multiplication and posterior differentiation by existing cells in the tissues and/or stem cells [4]. Tissue repair is a straightforward linear process in which growth factors drive cell proliferation, resulting in the integration of dynamic changes involving soluble mediators, blood cells, extracellular matrix synthesis, and parenchymal cell proliferation. According to Mitchel., *et al*. the skin healing process exemplifies the principles of tissue repair for the vast majority of tissues [5].

Hemostasis occurs as soon as the injury occurs. The creation of a platelet thrombus, propagation of the coagulation cascade, cessation of clotting, and finally removal of the clot via fibrinolysis are all used to control bleeding from the wound. The vascular endothelium is damaged, allowing blood to flow to the wound site and exposing the basal lamina. Activated platelets subsequently connect to the exposed collagen, causing a cascade of growth factors, inflammatory mediators, and cytokines to be released [6].

Inflammatory reaction, cell proliferation, and synthesis of the extracellular matrix elements, as well as the post-healing period, known as remodelling, are the stages of cell and biochemical actions in wound repair [7].

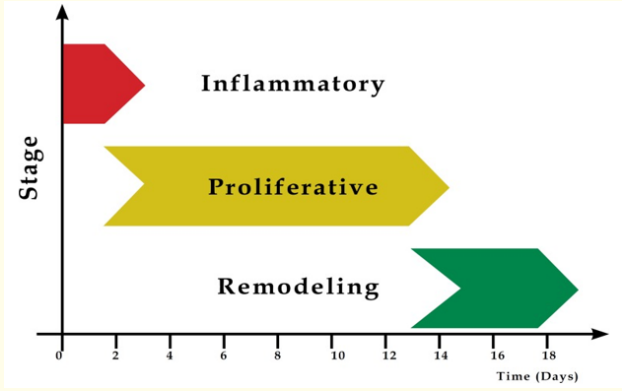

Figure 2: Stages in wound healing.

Inflammatory stage

The infarcted blood vessels constrict and the lost blood coagulates in a vascular inflammatory reaction, helping to maintain the integrity of the vessel. Coagulation is the accumulation of thrombocytes as well as platelets in a fibrin matrix, which is based on the activation and accumulation of these cells by specific factors. This also allows for cell migration into the lesion's microenvironment and fibroblast proliferation promotion [8]. This is a rapid response that correlates with the major indications of inflammation, which are edoema and erythema at the site of the lesion. Cell response is often developed within first 24 hours that can last up to two days. Mastocytes, gamma-delta cells, and Langerhans cells, which release chemokines and cytokines, may cause a rapid activation of immune cells in the tissue. The lesion causes tissue destruction by producing inflammation, which is a limited and protective tissue response. Inflammatory cells aid wound healing by releasing lysosomal enzymes and oxygen radicals, as well as cleaning up different cell debris [9].

Proliferative stage

Angiogenesis, fibroplasia, and re-epithelialization are all part of this stage, which is responsible for the lesion's closure. Within the first 48 hours after the development of the lesion, these processes start in the microenvironment of the wound and can last up to 14 days. Blood flow changes as a result of vascular remodelling. Angiogenesis is a coordinated process including endothelial cellular growth, basal membrane rupture and rearrangement, tubular structure movement and connection, and perivascular cell

recruitment. Angiogenesis has long been thought to be important in a variety of physiological and pathological processes, including embryogenesis, tumour growth, and metastasis [10].

Nearly 4 days after the lesion, granulation tissue starts to build. The new stroma gets its name from the granular presence of newly formed tissue. The granulation tissue is formed by the following mechanisms, according to Calin., *et al*. increased fibroblastic proliferation; collagenous and elastic biosynthesis, which creates a three-dimensional extracellular network of connective tissue; and fibroblast production of chemotactic factors and IFN-beta. Integrin receptors are expressed by fibroblasts and endothelial cells, which allow them to invade the coagulation in the lesion [11].

Remodelling stage

Remodelling is the third phase of healing, which starts two to three weeks after the initiation of the lesion and can last a year or more. The remodelling stage's main goal is to maximise tensile strength by reorganising, degrading, and re-synthesizing the extracellular matrix. At this point in the healing process, an attempt is made to restore normal tissue structure, and the granulation tissue is gradually reformed, resulting in scar tissue that is less cellular and vascular and has a progressive rise in collagen fibre concentration [12].

Due to migration phases, apoptosis, or other unknown mechanisms of cell death, the majority of vascular system, fibroblasts, and inflammatory cells leave from the wound region during the maturation and remodelling processes. This results in the creation of a scar with a lower cell count. Later, the granulation tissue fibroblasts change their morphology and begin to express smooth muscle actin, earning the moniker myofibroblasts [13].

Antibacterial films

Antibacterial, for example, can be integrated into biodegradable films and used as active packing. Foodborne pathogens and other germs on food surfaces are reduced, inhibited, or stopped with this approach [14]. Microbial contamination is present in the highest concentration on the surface of processed or fresh items, necessitating the need of a system to restrict microorganism development. Because diverse components of these foods can reduce their efficiency, adding antimicrobial drugs directly to foods can diminish their antibacterial impact. Films as active packaging can be more effective than antibacterial additives in meals because they can travel selectively and gradually from active film chemicals to the food's surface [15].

An extensive interaction between the product and the antimicrobial ingredient is required in these circumstances. Antimicrobial films are split into two categories [16] as below-

- They migrate to the product's surface
- They are effective against microbial growth on the surface without requiring migration inside the product.

Antimicrobial agents are chosen based on their ability to kill a specific microorganism. Food product properties include as following-

- pH
- Water activity
- Content
- Storage conditions.

All these factors influence the growth of potentially spoiling bacteria. Antimicrobial activity can be obtained by directly incorporating additives into packaging films, which is a straightforward way [17].

Antibacterial agent	Polymer	Microorganism	Reference
Nisin	Whey protein, Methylcellulose	*L. monocytogenes, L. innocua, S. aureus, M. luteus*	[18,19]
Lysozyme	Whey protein	L. monocytogenes	[20]
Lactoperoxidase	Whey protein	*L. monocytogenes, E. coli, S. enterica, P. commune*	[21]
Oregano oils garlic oils	Whey protein	*E. coli, S. aureus, S. Enteritidis, L. monocytogenes, L. plantarum*	[22]
Garlic oils	Alginate	*S. aureus, B. subtilis*	[23]

Grape seed extract	Soy protein	*L. monocytogenes, E. coli, S. Typhimurium*	[24]
Grapefruit seed extract	Alginian	*M. luteus, L. innocua, S. Enteritidis, E. coli, S. aureus*	[25]
Sorbic acid	Zein	*L. monocytogenes*	[26]
Potassium sorbate	Starch	*E. coli*	[27]

Table 1: Preparation of antibacterial films with similar agents and suitable polymers, effective against specific microorganisms.

Method of preparation-blank film

Agar is dissolved in hot water at a 1:10 ratio to make the film basis. The agar solution is homogeneously mixed with sodium alginate, pectin, propylene glycol, and glycerin. Finally, the film substrate is cast into a plate (25x30cm2) and dried for 24 hours at 50°C in a hot-air oven, resulting in the formation of a film [28].

Characterization parameters

Kirby-Bauer disk diffusion test

The experiment was carried out as reported by Semeniuc., *et al*. (2017) [29]. Using 9-mm sterile paper discs, the essential oil of tarragon was tested against all microorganisms. As a positive control, gentamicin (0.4 mg/ml) was utilised. A Drigalski spatula was used to spread 100 microliters of the inoculum solution (1.5 108CFU/ml) over the whole surface of the Mueller-Hinton agar plate. 40 litres of tarragon essential oil were released onto a sterile paper disc in the centre of a Petri plate. Plates were subsequently incubated at 37°C for 24 hours (in the case of S. aureus, E. coli, and S. enteritidis) or 48 hours (in the case of other bacteria) (in the case of L. monocytogenes). The inhibition was measured using a digital calliper.

Measurement of thickness

A digital calliper was used to measure the thickness (mm) of each film composition at 24 random sites.

Determination of Moisture Content

By weighing the film sample before and after drying, the moisture content was determined using the oven-drying method. Each quarter of the film specimen was dried in an oven at 105°C until consistent weight was achieved.

Estimation of swelling and solubility

These parameters were calculated using a slightly modified Wang., *et al*. (2010) [30] approach. Cut the film specimen into square pieces. A piece of film was properly weighed (0.1 g) and placed in a 50-mL glass beaker, followed by 40 mL of distilled water. The residual was filtered and weighed after 24 hours of immersion at room temperature (25°C) to determine swelling degree, or filtered and dried in an oven at 105°C until constant weight to determine solubility in water.

Determination of water-vapor permeability

The WVP was calculated using Ghasemlou., *et al*. (2013) approach [31], with minor modifications. With an exposed surface of 4.0 cm^2, the film was sealed on a commercially available plastic cup containing 5.0g of calcium chloride anhydrous ($CaCl_2$—0 percent RH). A desiccator with a saturated sodium chloride solution (25 C, NaCl—60 percent relative humidity) was used to keep the cup at ambient temperature. Every hour for the first 8 hours, and every day for the next 14 days, the weight of the cup (w) was recorded.

Applications of antibacterial films [32]

- Bacteriocins are being incorporated into food packaging sheets to prevent pathogenic germs from spoiling food.
- Antimicrobial packaging in films reduces microbial development on food surfaces by bringing the packaging material into direct touch with the food surface.
- In the case of bacteriocins, controlled release application provides a therapeutic method for resistant bacterial strains.
- They have been used to minimize and prevent microbial growth on the surface of food products.
- A polymer-based film solution coating has proven to be the most stable technique of attaching a bacteriocin to a plastic packaging film in terms of stability.

Conclusion

This is why the antimicrobial packaging sheet should make contact with the food surface, allowing bacteriocins to diffuse

to the surface. The controlled release of bacteriocins from food packaging film toward the food surface has a significant benefit over dipping or spraying foods. Antimicrobial agents have been successfully employed as additives in films and food products for many years. Antibacterial additives can be directly included into food packaging films made of natural and synthetic polymers, which is a straightforward means of achieving antimicrobial action. Some of these compound's affectivity as indirect food additives contained in food packaging materials has been documented in the past.

It concludes that formulation of antibacterial films is very promising research domain due to its diverse beneficial properties and easy to use.

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Nil.

Conflict of Interest

Authors have declared for none conflict of interest.

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