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REVIEW ARTICLE

Polymeric Gel Scaffolds and Biomimetic Environments for Wound Healing

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Abstract: Infected wounds that do not heal are a worldwide problem that is worsening, with more people dying and more money being spent on care. For any disease to be managed effectively, its root cause must be addressed. Effective wound care becomes a bigger problem when various traditional wound healing methods and products may not only fail to promote good healing. Still, it may also hinder the healing process, causing wounds to stay open longer. Progress in tissue regeneration has led to developing three-dimensional scaffolds (3D) or constructs that can be leveraged to facilitate cell growth and regeneration while preventing infection and accelerating wound healing. Tissue regeneration uses natural and fabricated biomaterials that encourage the growth of tissues or organs. Even though the clinical need is urgent, the demand for polymer-based therapeutic techniques for skin tissue abnormalities has grown quickly. Hydrogel scaffolds have become one of the most imperative 3D cross-linked scaffolds for tissue regeneration because they can hold water perfectly and are porous, biocompatible, biodegradable, and biomimetic. For damaged organs or tissues to heal well, the porosity topography of the natural extracellular matrix (ECM) should be imitated. This review details the scaffolds that heal wounds and helps skin tissue to develop. After a brief overview of the bioactive and drug-loaded polymeric hydrogels, the discussion moves on to how the scaffolds are made and what they are made of. It highlights the present uses of *in vitro* and *in-vivo* employed biomimetic scaffolds. The prospects of how well bioactive-loaded hydrogels heal wounds and how nanotechnology assists in healing and regeneration have been discussed.

Keywords: Wound healing, hydrogel, scaffolds, polymers, tissue regeneration, extracellular matrix.

1. INTRODUCTION

A visible disruption or a breach in continuity in skin/mucous layers, brought on by physical or thermal injury, is called a wound [1, 2]. Skin typically heals within an anticipated period of 8 to 12 weeks [3], subject to the depth, size, and breadth of the infected wound. The skin is crucial in defending the body from external environmental threats, including diseases and toxins [2, 4]. When the skin's structure or function is compromised, the body becomes vulnerable to microbial invasion and wound infection, which slows down wound healing and might put the patient's life in jeopardy. Skin integrity may be harmed, homeostasis may be disrupted, and wound infections can result in the aftermath of surgery, burns, or chronic illnesses. Microbial infections that directly contribute to the wounded state are prolonged by delayed wound healing [5, 6]. However, the treatment of acute and chronic skin injuries faces significant difficulties in clinical practice due to the complexity of wound healing. An efficient wound dressing not only consistently supports the skin's functional responses but also facilitates the future advancement of skin scaffolds [7].

There are multiple methods of classifying wounds. They can be termed as smooth or jagged, exposed or unexposed, internal or external, acute or chronic, clean or contaminated, superficial (*e.g.*, bruises, grazes, abrasions), and deep (*e.g.*, cuts, puncture or surgical wounds, *etc.*) based on origin, extent, and location of infection [8]. Healthcare costs for all forms of wounds covered by medical insurance will exceed $22 billion by 2024 [5]. The cost of treating surgical wounds and diabetic ulcers is among the highest. [9]. If a wound has many underlying issues, it might take longer for the wound bed to heal entirely, necessitating the use of clinically advanced and economically viable wound coverings. For instance, local and systemic variables disrupt the process by creating significant uncertainty in the healing time [10, 11]. Tables **1** and **2** represent cells and the growth factors involved in the wound healing process, respectively.

Table 1. Cells involved in the wound-healing process.

Cells	Purpose in Wound Healing	References
Fibroblasts	Produce many ECM elements, such as fibronectin, collagen, fibrin, hyaluronic acid, *etc.*, that aid in the formation of granulation tissue.	[12]
Neutrophils	First, cells colonize the wound site. Invading bacteria are killed intracellularly through phagocytosis.	[13]
Macrophages	Remove trash and necrotic tissue; destroy invasive microorganisms by phagocytosis; and create rich pools of inflammatory mediators (including cytokines). Activate fibroblasts, promote collagen synthesis, and quicken angiogenesis.	[14]
Platelets	Formation of a thrombus, accumulation of inflammatory mediators (including cytokines), inflammatory stimulus.	[15]

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