Journal of Computers, Mechanical and Management
Journal homepage: www.jcmm.co.in
e-ISSN: 3009-075X
AAN PUBLISHING

Volume 3 Issue 3

Article Number: 240124

The Applications of Tissue Engineering: A Beginner's Perspective on Burn Treatment and Cancer Drug Delivery

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Abstract

This short communication article provides a beginner's perspective on tissue engineering, elucidating its applications in burn skin treatment and drug delivery systems for cancer therapy. The first part discusses the challenges and current issues related to burn injuries, exploring engineered techniques for their treatment. It emphasizes the need for scaffolds in skin tissue regeneration, detailing the materials and methods used. The second part focuses on drug delivery mechanisms in tissue engineering, specifically in cancer treatments. It explains the carrier and release mechanisms of drugs targeting cancer cells and reflects on personal learning experiences from the course. The article synthesizes personal comments and learning reflections in the conclusion, making it accessible for those who wish to grasp the concept of tissue engineering at a glance.

Keywords: Burn Injuries; Drug Delivery; Artificial Tissues; Scaffolds; Tissues Engineering

Introduction

Tissue engineering is a multidisciplinary field that redefines treatment methods for biological complications through technological advancements. In recent years, tissue engineering has undergone significant changes due to discoveries in additive manufacturing, biomaterials, and cellular reprogramming. Burns are physical injuries caused by exposure to heat, friction, chemicals, electrical discharge, or radiation. According to the Global Burden of Disease (GBD), approximately 8.3 million cases of burns were reported globally in 2019 [1]. Burn injuries are classified into four degrees based on the depth of the injury, as illustrated in Figure 1. Medical or surgical interventions are determined accordingly. The healing process is complex and time-consuming, often requiring expensive interventions such as plastic surgery. Conventional burn treatments include wound care, skin grafting, and surgical procedures. Scarring is inevitable in the healing process, leading to psychological challenges for burn survivors in societies where aesthetic concerns are prominent. Burn injuries result in lifelong physical and psychological scarring, causing pain, affecting mental health, quality of life, the ability to return to work, and increasing mortality [2]. Treating burn injuries presents numerous challenges, including skin infection, prolonged healing time, intense pain, functional impairments, the need for intensive care facilities, fluid and electrolyte imbalances, poor grafting, graft rejections, and increased treatment costs. Skin grafts often require donor tissue from the same person, a biologically identical person, or animals, leading to complications such as infection, cell rejection, and donor site morbidity. Tissue engineering offers solutions that address many challenges posed by conventional burn injury treatments. Its applications in skin treatment can be categorized into four methods: tissue scaffolds, healing promotive factors, stem cells, and gene therapy [3].

*Corresponding author: snilakshman1@gmail.com
Received: 19 May 2024; **Revised:** 25 June 2024; **Accepted**: 21 July 2024; **Published:** 04 August 2024

DOI: 10.57159/gadl.jcmm.3.3.240124.

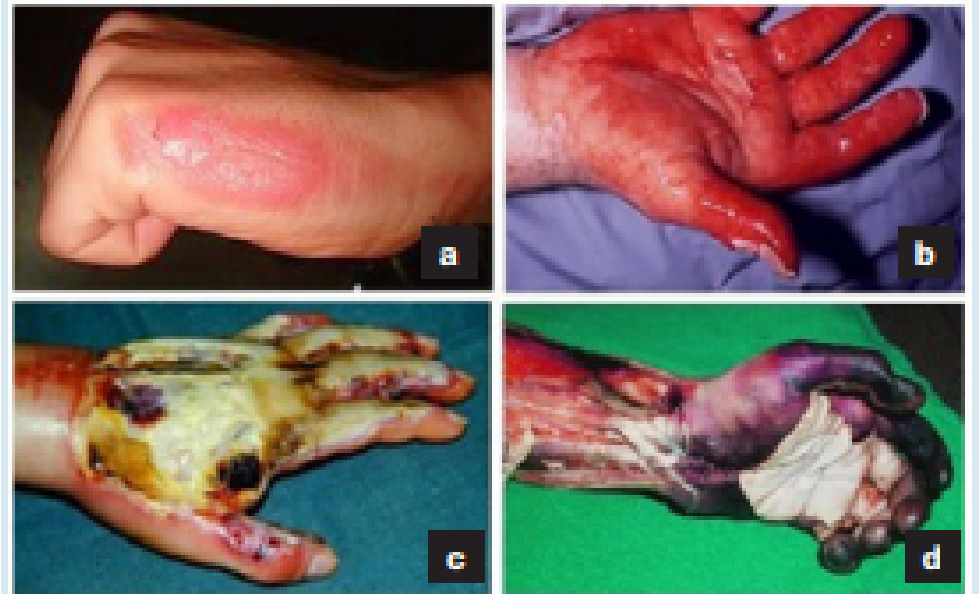

Figure 1: Classification of burn wounds by depth. Clinical examples of burn degrees: (a) First-degree burn, (b) Second-degree burn, (c) Third-degree burn, (d) Fourth-degree burn.

Tissue Engineering in Skin Treatment

Skin, being the largest organ of the body, serves as an ideal candidate for tissue engineering applications aimed at regeneration and repair. The three major components in tissue engineering are:

1. **Cells**: Functional cells used for regeneration.
2. **Scaffolds**: Structures for cell-matrix adhesion.
3. **Signals**: Factors that direct growth and cell differentiation, originating from immune and damaged cells.

Advancements in stem cell technology have enabled the use of proliferated stem cells to promote cell differentiation near the extracellular matrix, facilitating the repair of burned skin through cell transplantation. Precise localization of stem cells at the wound site is crucial for effective regeneration. However, challenges such as host immune system rejection and chemical composition can lead to treatment failure. Scaffolds act as replicas of the extracellular matrix, functionally mimicking tissues at the defect site. They provide infrastructure for cell growth and differentiation, leading to proper tissue regeneration. Figure 2 compares wound closure with and without scaffold intervention.

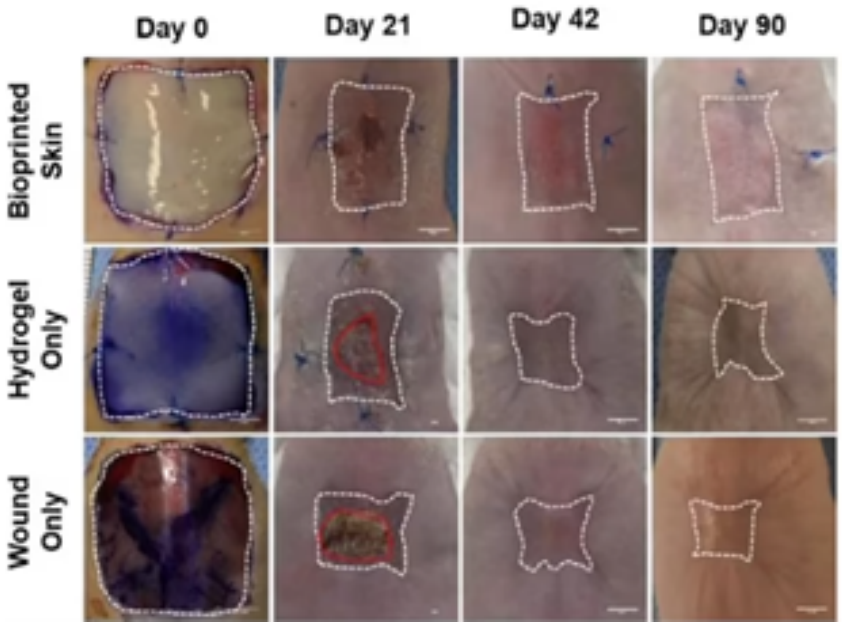

Figure 2: Comparison of wound closure: (a) Traditional healing process without scaffold intervention, (b) Enhanced healing with scaffold-based tissue engineering approaches.

Materials used as scaffolds include natural polymers such as collagen, chitosan, gelatin, elastin, fibrin, keratin, and fibropin, as well as synthetic polymers like Poly(lactic-co-glycolic acid) (PLGA), Polyethylene Glycol (PEG), Polycaprolactone (PCL), Polyethylene Terephthalate (PET), Polyvinyl Alcohol (PVA), Polyglycolic Acid (PGA), Poly(ϵ-caprolactone-co-lactide) (PCLA), and Polyacrylonitrile (PAN). Growth factors and peptide-loaded hydrogels, including Epidermal Growth Factor (EGF), Fibroblast Growth Factor (FGF), Platelet-Derived Growth Factor (PDGF), Vascular Endothelial Growth Factor (VEGF), Insulin-like Growth Factor (IGF), Hepatocyte Growth Factor (HGF), Transforming Growth Factor-beta (TGF-β), and Keratinocyte Growth Factor (KGF), are also utilized [4, 5]. The selection of cells, scaffolds, and growth factors—or combinations thereof—is based on individual cases and the injury location. Scaffolds can be 3D porous, fibrous, or particulate structures that promote cell growth. Cells extracted from the body, such as keratinocytes, fibroblasts, melanocytes, adipocytes, induced pluripotent stem cells, and mesenchymal stem/stromal cells, serve as precursors for regeneration. The effectiveness of scaffolds is determined by their biocompatibility, cell attachment and proliferation in the extracellular matrix, replication of nearby tissue's mechanical properties, surface topology, extent of vascularization, and inflammatory responses.

Drug Delivery in Oncology

Cancer is characterized by uncontrolled cell growth and proliferation, with the potential to spread to nearby tissues through metastasis. The variable nature of cancer cell growth poses significant challenges for medical interventions, leading to considerable mortality each year. The majority of cancers occur in the lungs, followed by the liver, colorectal region, stomach, and breast [6]. Chemotherapy, a common cancer treatment, is associated with side effects such as weakness, fatigue, nausea, hair loss, and vomiting [7]. Recent advancements have introduced nanoparticle drug delivery as a promising approach in oncology. Nanoparticles, characterized by their small size and unique physicochemical properties, offer a tailored and targeted approach to drug delivery, enhancing the efficacy of anti-cancer drugs while minimizing systemic side effects. Various types of nanocarriers used in medical applications are illustrated in Figure 3. These include:

- **Inorganic Nanocarriers**: Single-walled carbon nanotubes, gold nanocarriers, magnetic nanocarriers, quantum dots, mesoporous silica nanocarriers.
- **Organic Nanocarriers**: Solid lipid nanocarriers, liposomes, dendrimers, polymeric nanocarriers.
- **Hybrid Nanocarriers**: Polymeric-lipid nanocarriers.

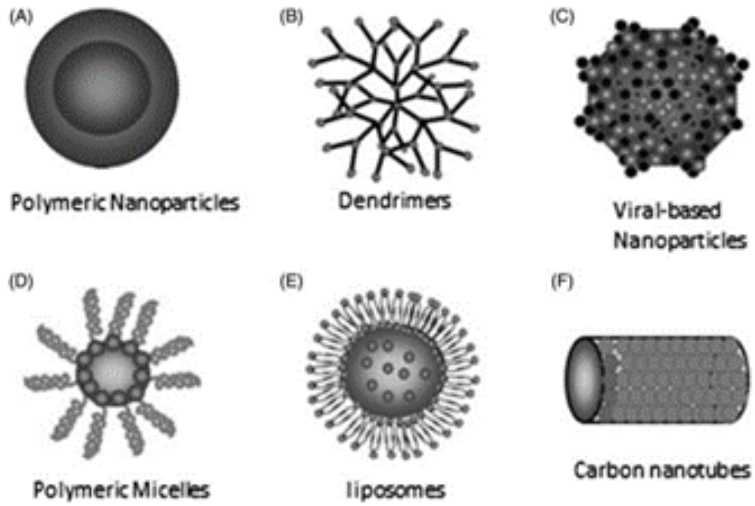

Figure 3: Types of nanocarriers used for drug delivery in cancer therapy.

These nanocarriers provide precise control over drug release, improved bioavailability, and the ability to selectively target cancer cells [8].

Drug Delivery Mechanism

Nanocarriers typically range from 1 to 100 nm and possess colloidal characteristics. They are compounds loaded with anticancer drugs and can be customized with functional groups for targeting specific environments—a process known as functionalization. Drug loading strategies include covalent bonding conjugation, encapsulation, and electrostatic interaction. Targeting mechanisms involve direct administration at the target site, directing magnetic nanocarriers using magnetic fields, active targeting, and passive targeting. The schematic of nanoparticle responses is depicted in Figure 4. Drug delivery using nanoparticles can be mathematically modeled using various kinetic models such as the diffusion model, Peppas model, first-order release kinetics, zero-order release kinetics, Weibull model, Hixson–Crowell model, Hopfenberg model, and sequential layer model [9].

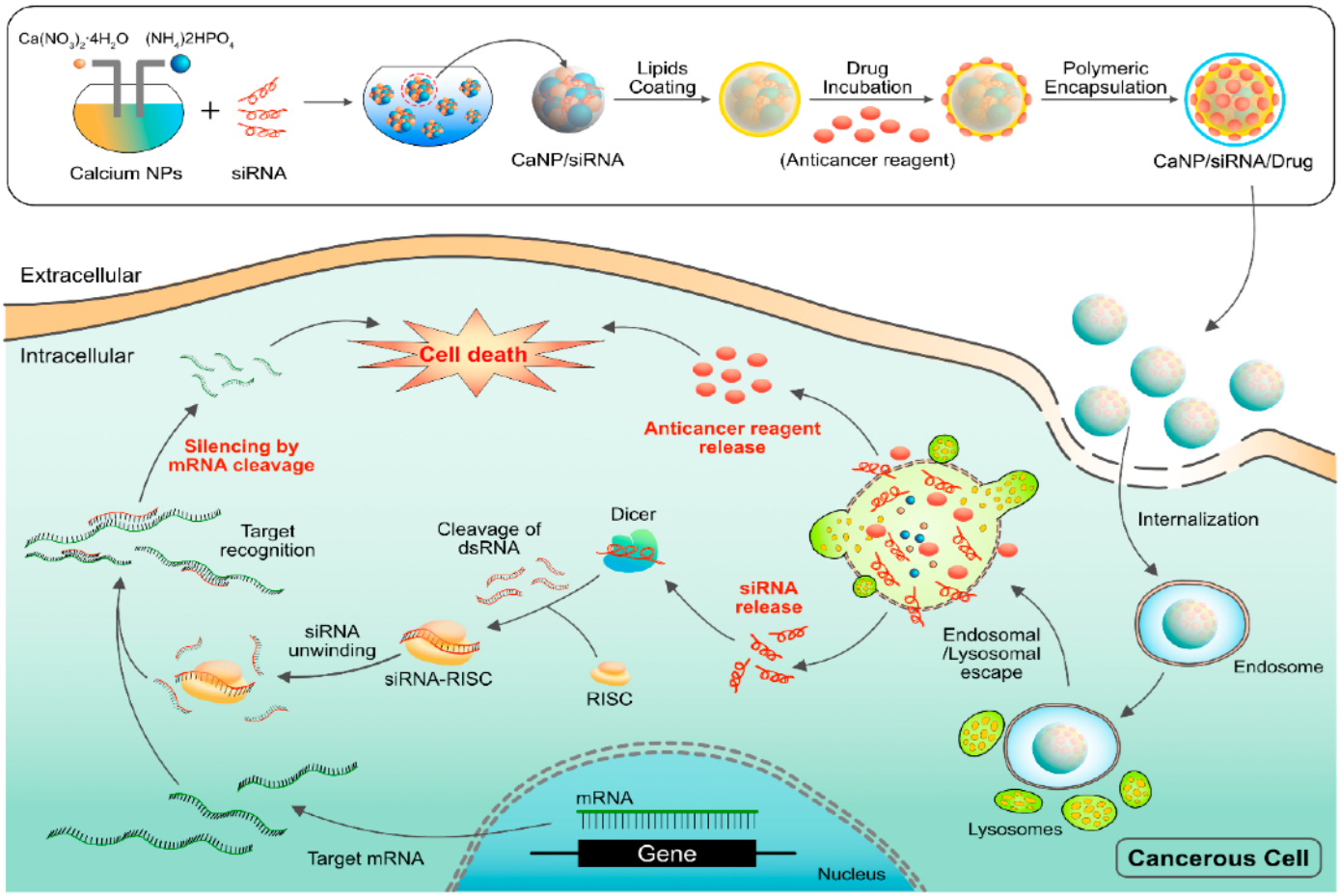

Figure 4: Schematic representation of nanoparticle responses in drug delivery systems, illustrating stimuli-responsive mechanisms for controlled drug release.

Once the nanoparticle enters cancer cells, it reaches the lysosomal compartments to release the drug. Rapid release of a drug into the interstitial space from the nanoparticles may cause premature release and systemic side effects, while slow release decreases drug efficacy and increases multidrug resistance. Therefore, the drug is designed to be released according to *in vivo* physiological conditions or external stimuli. Internal stimuli mechanisms include pH changes, redox reactions, reactive oxygen species (ROS), enzymes, hypoxia, inflammatory mediators, adenosine triphosphate (ATP), and ionic microenvironments. External stimuli include temperature, ultrasound (mechanical stress modulation), magnetic fields, electric fields, and light. The interaction efficiency of nanoparticles with biological or targeted tissues influences the overall treatment effectiveness. Biocompatibility of nanocarriers is of utmost concern. Materials that are biologically non-harmful or have low toxicity, along with surface modification, generally attract proteins onto the surface of the carrier, facilitating easier binding. The testing pipeline typically involves *in vitro* studies to assess cellular responses and drug release mechanisms, followed by *in vivo* studies in animal models to evaluate efficacy, toxicity, immunogenicity, and other factors.

Conclusion

This article provides an overview of tissue engineering applications in burn injury treatment and drug delivery systems for cancer therapy. It elucidates the basics of tissue engineering, scaffold systems, biocompatibility, and drug delivery mechanisms. By examining specific applications such as burn skin treatment and nanoparticle-mediated drug delivery to cancer tissues, the article highlights the innovative solutions that tissue engineering brings to modern medicine. The detailed analysis of materials and methods used in scaffold creation and drug delivery systems, including the use of natural and synthetic polymers, growth factors, and various types of nanocarriers, offers valuable insights into the current state and future directions of this rapidly evolving field. By translating complex scientific concepts into accessible language, this article serves as a useful resource for those seeking to understand the fundamental principles and applications of tissue engineering. Through continued research and technological advancements, the potential for improved treatments and better patient outcomes in both burn injuries and cancer therapy remains vast and promising. The integration of interdisciplinary approaches in tissue engineering holds the key to unlocking new therapeutic possibilities and enhancing the quality of life for patients worldwide.

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