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HEALING OF WOUND BY TISSUE ENGINEERING AND NANOPARTICLES: A REVIEW

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ABSTRACT

Wound healing still remains a challenging problem that is why wound management is necessary. Metal nano particle like, gold and silver shows bacteriostatic and bactericidal activities. Biomaterials like chitosan and collagen play an important role as wound dressing materials. It stimulates wound healing by fibro genesis and increases the development of skin .When we embed any biomaterial with nanoparticles then it used as a potential wound dressing materials. Nanomaterials enhance the wound healing and burn treatment. We know that silver has been used as a bactericidal agent. We can also introduce tissue engineering in case of wound healing. There are various substitutes which increases the healing of wound. Tissue engineering involves the application of biology and engineering for innovation of tissue substitute that can maintain, restore and improve the function of ruptured human tissue and it uses biomaterials and cells to produce new tissues.

Keywords: Biomaterials, Nanoparticles, Skin,Tissue engineering, Wound healing.

I. INTRODUCTION

Tissue engineering is emerging as an interdisciplinary field in biomedical engineering that aims to regenerate new biological material for replacing diseased or damaged tissues or organs and it is the in vitro development (growth) of tissues or organs to replace or support the function of defective or injured body parts. It involves the application of biology and engineering for innovation of tissue substitute that can maintain, restore and improve the function of ruptured human tissue. It is gaining its popularity in various areas such as burn treatment or wound care, neurology product orthopedics, urological products and others. It thus calls for close collaboration between cell biologists, geneticists, clinicians and other experts. It uses biomaterials and cells to produce new tissues. Stem cells have infused great excitement in the field as a powerful cell source to rebuild tissues. In past decades research in human skin equivalent has advanced in with tissue engineering and regenerative medicine. Burns destroy the barrier function of the skin and also alter the perceptions of pain, temperature and touch.

Wound repair is an essential process in maintaining tissue homeostasis in response to injury while wound management is a complex and challenging area of research. Nanotechnology is an emergingfield. Many nanoscale materials used in biomedical applications for preventing variousdiseases. The sizes of nanomaterials are 10^{-9}m (1nm). The drugs include the nanoparticles of polymers, metals, ceramics which can fight against human pathogens like bacteria and even cancer. Nanoparticles increase the chemical activity due to their large surface volume ratio.

II. STRUCTURE OF SKIN: [12, 13]

Skin is the largest organ of the human body. It has sensory nerve endings of pain, temperature and touch. Skin is composed of three distinct layers:

- Epidermis
- Dermis
- Hypodermis

Epidermis is the upper layer of the skin. It is composed of stratified squamous epithelium. Its thickness is different on different parts of body. It has several layers:

- Stratum germinativum
- Stratum spinosum
- Stratum granulosum
- Stratum lucidum
- Stratum corneum

2.1 Dermis

It is the inner layer of the skin. It is composed of dense connective tissue containing different type of cells such as fibroblasts, histocytes and mast cells. It is tough and elastic. It has two layers one is Papillary layer and the another one is Reticular layer. Dermis is consisting of:

2.2 Blood vessels

In this there is a network of arterioles with capillaries branches supplying sweat glands, sebaceous glands, hair follicles and the dermis. As we know, epidermis has no blood supply so it obtains nutrients and oxygen from the interstitial fluid which is derived from blood vessels in the papillae of dermis.

2.3 Sensory nerve endings

It contains some sensory receptors which are sensitive to touch, change in temperature, pressure and pain.
Lymph vessels, Hairs, sebaceous glands and Arrector pilli muscle.

2.4 Hypodermis

The deepest and third layer of skin is called the hypodermis. It is deeper subcutaneous tissue and is made of fat and more connective tissue. This layer contains blood vessels which also reach into the dermis and epidermis. These blood vessels are important in the transmission of medication from a patch to the bloodstream.

III.TISSUE-ENGINEERED SKIN SUBSTITUTES

Skin substitutes can be classified intoepidermal, dermal and epidermal-dermal (composite) tissue engineeredconstructs.

3.1 Epidermal Skin Substitutes

Epidermal substitutes contain only keratinocytes and can be applied onto the wound site [14].In epidermal skin replacements a 2–5 cm^2 skin biopsy is required from which the epidermis is separatedand the keratinocytes are isolated and cultured on top of fibroblasts [7].Culturedautologous keratinocytes can be applied onto the wound bed directly after having been prepared from biopsy in the operation room. This method has shown faster epithelialization and epidermal maturation in wound models [10].

3.2 Dermal Skin Substitutes

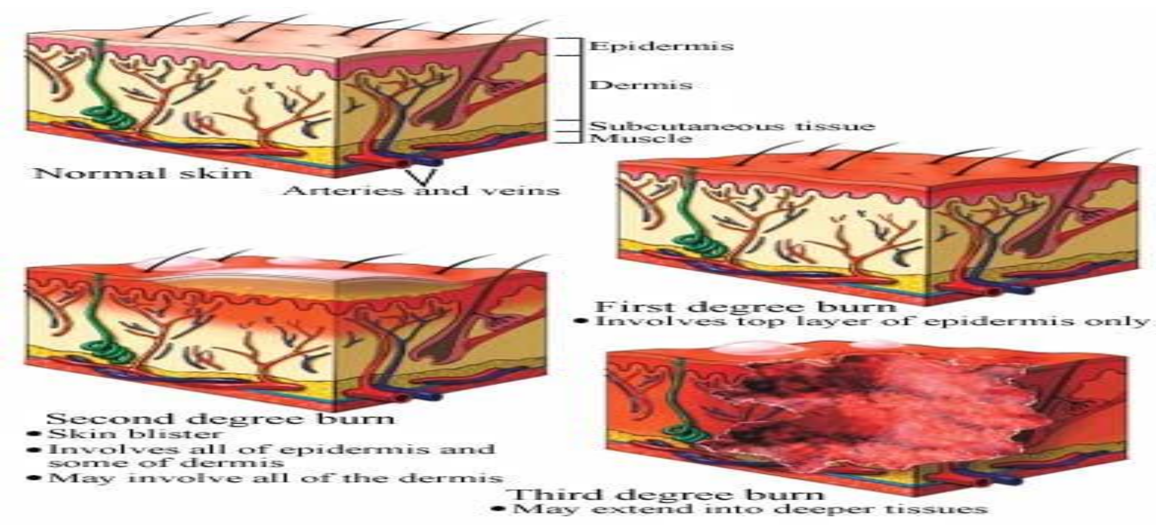
The biomaterials in dermal skin substitutes help in woundbed preparation and provide temporary scaffolds for cellattachment and proliferation. Fibroblasts found in the dermis of human skin produce collagen, growth factors,glycosaminoglycans (GAGs), and fibronectin to initiate woundhealing[3].Dermal substitutes try to restore dermal growth with less scarring. It is applied to the wound site and the skin regenerates and grows naturally[15]. Dermal skin replacements aid in greater mechanical stability and prevent the wound from contracting[7].

3.3 Epidermal-Dermal Skin Substitutes

Epidermal-dermal skin substitutes comprising both epidermal and dermal layers it is the most sophisticated tissue-engineered skin product that closely resembles the structure of native human skin. The presence of both keratinocytes and fibroblasts within theepidermal-dermal skin substitutes leads to the production of a variety of growth factors. These epidermal-dermal skin substitutes have been utilized for treatment of chronic wounds and ulcers with higher incidences of wound closure were reported [3].

Recently military researchers are putting the final touches on the study of a skin substitutes grown from a patient own cells to treat complex burns and soft tissue injury. The treatment called **"Engineered Skin Substitute"** or **ESS** combines tissue cultivated from a patient's own skin along with collagen producing cells to replace the two components of skin, the epidermis and dermis [15].

IV. BURN [11]



Burn is a kind of wound that occurs by excessive heat, electricity, radioactivity, or corrosive chemicals that denaturetheproteins in the skin cells. Burns destroy some of the skin's importantcontributions to homeostasis—protection against microbial invasionand desiccation, and thermoregulation. Burn causes changes of vascular permeability and aggregation of platelets.Burns are graded according to their severity:

A first-degreeburn involves only the outer layer ofepidermis and there is no damage in the dermis.it generally occurs as a result of short term heat or long term exposing to sunlight.Generally healing of afirst-degree burn will occur in 3 to 6 days and may be accompaniedby flaking or peeling. At this stage skin begins to dry and sometimes infection is not seen.

A Second-degree burn is deeper than first degree burn. Generally, Second degree burn, heal spontaneously in a short period if infection does not occur. If infection occurs it converts into third degree burn. Itdestroys the epidermis and part of the dermis, second-degree burns heal without skin grafting inabout 3 to 4 weeks, but scarring may result.

A third-degree burn or full-thickness burn destroys the epidermis, dermis, and subcutaneous layer .Skin grafting may be requiredto promote healing and to minimize scarring. These kinds of burns result from hot water, fire, and with prolonged electrical current.

V. NANOPARTICLES USED IN WOUND HEALING [2, 5, 6]

Wound healing still remains a challengingproblem for which wound management is necessary. When we embed any biomaterial with nanoparticles then it used as a potential wound dressing materials. Nanomaterials enhance the wound healing and burn treatment. Metal nanoparticles like gold and silver show splendid properties such as low toxicity in vivo, bacteriostatic and bactericidal activities. The process of wound healing involves 4 main stages: Haemostasis, inflammation, proliferation and remodeling.

The main purpose of wound healing is to have efficient recovery with minimal scarring. The sizes of Nonmaterial are 10^{-9} m (1nm). Nanotechnology and use of nanomaterials is a rapidly expanding field, it encompasses the development of man-made materials in the nanometer size range or molecular scale.In this the development of nanoscale materials used in many biomedical applications for preventing various diseases.After decreasing material size into the nanoscale, dramatically increased surface area, surface roughness and surface area to volume ratios can be created which lead to superior physiochemical properties.The drugs which include the nanoparticles of polymers, metals, ceramics which can fight against human pathogens like bacteria and even cancer.

5.1 Nanoparticles

5.1.1 Silver

Silver has been used as a bactericidal agent because of its bactericidal property, silver is used to treat burns and a variety of wound infections. However, it is used in different biomedical fields, especially in wound healing and burn treatment.Chronic wounds are still treated with silver nitrate. Now a day, different formulations of silver coatings, is used in wound dressings for efficient distribution of drug, affinity of dressing to the wound and it also plays a major role in wound management [2].

Silver nanoparticles based dressing does not create an obstacle to the recovery of severe partial thickness burns. The advantage of silver Nanoparticles-based dressings, even for a prolonged time, does not seem to negatively affect the proliferation of fibroblasts and keratinocytes, which leads the healing of wound. When we embed Collagen with silver nanoparticles it shows the antibacterial activity and makes it an eligible component for wound dressing material [5, 11].

5.1.2 Gold

Gold nanoparticles are biocompatible. They can be used in drug delivery and wound healing. The cross linking of collagen with gold nanoparticles which allowed the easy incorporation of biomolecules like growth factors, peptides, cell adhesion molecules by their immobilization at the Gold surface without additional altering of collagen structure. Collagen is used mostly in a gel form which could be used for drug delivery and tissue engineering applications. When we embed collagen with gold nanoparticles it shows the properties like biocompatibility, antibacterial, biodegradability. That's why it is used in wound healing. When we combine gelatin chitosan with gold nanoparticles it shows safe and good work in wound healing [2, 11].

5.1.3 Zinc Oxide

Zinc is normally required for wound healing, especially burns. It enhances the wound healing process by remaining at the site for a maximumperiod of time. Zinc oxide nanoparticles possess antibacterial properties so; we can easily use Zinc oxide in case of wound healing. Zinc oxide nanoparticles are widely used in cosmetics. Mainly, it is used in skin creams because it has anti-inflammatory and antiseptic properties. The size and concentration of nanoparticles also influence the wound healing process. When we embed Zinc oxide nanoparticles with chitosan hydrogelit shows the antibacterial activity and makes it an eligible component for wound dressing material. Hydrogel based dressing has so many advantages like, it is soft and water retention quality of hydrogels prevents tissue dehydration. Moist dressing accelerates the rate of fibroplasia angiogenesis. It also shows enhanced swelling, blood clotting, and antibacterial activity. Because of so many advantages we can use it as composite bandages for burns, chronic wounds, and diabetic foot ulcers. [1, 2, 11]

VI. CONCLUSION

The main aim of the review is to highlight how wound can be healed with the use of tissue engineering substitutes and with the nanoparticles. Tissue engineering involves the application of biology and engineering for innovation of tissue substitute that can maintain, restore and improve the function of ruptured human tissue and it uses biomaterials and cells to produce new tissues.The combination of nanoparticles and biopolymers would have a high chance of faster wound healing. When we embed any biomaterial with nanoparticles then it used as a potential wound dressing materials. Nonmaterial enhances the wound healing and burn treatment.

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