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Review Article

SKIN TISSUE ENGINEERING: A REVIEW

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ABSTRACT
Tissue engineering (TE) for skin grafting, also known as skin tissue engineering (STE) is a strategy involving the generation of artificial skin by using widely available natural or synthetic materials as substitutes that resemble the native skin *i.e.,* it involves *in-vitro* fabrication of the biocompatible scaffolds. Earlier the skin grafting needed a healthy donor making the therapy limited due to the chances of immune rejection. Besides this, skin grafting may often result in poor healing in diabetic patients and bleeding problems in the individuals suffering from hemophilia. It may often result in infection of either the donor or the recipient at transplantation site. The emergence of novel methods of TE has overcome the limitations associated with the conventional methods. Various tissues and organs like the heart, skin, lung, liver, cartilage, etc, can be regenerated using TE. TE can be facilitated with the aid of nanotechnology for the generation of scaffolds due to various properties it possess, of which, the major advantageous property involves a large surface area to volume ratio to serve wider range function as well as antimicrobial properties to prevent infections near the damaged area. Often, the different types of stem cells can be used for tissue repairing, due to their self-renewable properties. The skin mimics are often prepared using 3-dimensional bioprinting. This review deals with the applications of TE in skin grafting, typically by manipulation of naturally available materials.

Keywords: Nanofibers, Electrospinning, Nanoparticles, Sutures, Autografts, Stem cells.

1. INTRODUCTION
According to the National Institutes of Health (NIH), tissue engineering (TE) is a technique that falls under regenerative medicines and is defined as the strategy that involves the formation of functional tissues by combining cells, scaffolds and biologically active materials to fabricate functional constructs to repair and sustain the impaired tissues or organs as well as to enhance the healing process. The skin was the first organ to be engineered among the various organs being produced through TE [1]. Food and Drug Administration (FDA) has approved two of the engineered tissues that are artificial skin and cartilage. Along with burn injuries due to fires, various other reasons contribute to skin lesions typically because of pollution as a result of urbanization, exposure to UV and other harmful radiations, acids, chemicals, and others. Overuse of tobacco or nicotine often leads to damage to the skin around the oral mucosa. As per the report of the World Health Organization (WHO), 2,65,000 deaths occur per year due to burn injuries that include around 96% of cases from low- and middle-income countries. Due to these ever-increasing cases of skin damages and casualties, it is crucial to find an effective solution. Hence, to meet up these requirements researchers came up with a novel idea of tissue engineering. Artificial skins, cartilages, or whole organs can be produced with the TE. Various methods have been developed to execute this by exploiting either naturally available materials or synthetic preparations.
The approach of TE has been focused to overcome the disadvantages associated with the conventional methods of skin grafting, which had various limitations such as difficulty in finding a healthy donor, and if found, then there is a chance of immune rejection by the recipient [2]. The most common method for TE includes the cell-based approach, which involves the application of induced pluripotent stem cells (iPSCs) for tissue regeneration by stimulating the growth and differentiation of keratinocytes. Epithelial autografts are

another approach for skin grafting; it is significant for the cases involving damage through burns [3]. Such autografts are constructed using keratinocytes [4, 5]. Mesenchymal stem cells (MSCs) can also be used for skin grafts. MSCs are multipotent cells that are self-renewable and can differentiate to form cells that belong to skeletal tissues [6-8].

Nanofibers account for the advanced approach that contributes to TE either through the formation of scaffold or by serving as a delivery system for drugs, cytokines, and growth factors (GFs) that play significant role in skin recovery [9]. Exploiting the idea of naturally occurring sutures for wound healing, nanofiber yarns are made through electrospinning of silk fibers synthesized by silkworms or spiders that can be used as surgical sutures [10-12]. It endows tremendous advantages in the treatment of skin lesions. Figure1 provides a comprehensive idea of the available techniques for STE.

Apart from the fibers, various other biomaterials are available that can be used as skin substitutes such as collagen, calcium hydroxyapatite, polylactic acid, polymethylmethacrylate [13]. Cellular skin-substitutes such as EPIBASE [14, 15]; Recell [16]; non-cellular skin substitutes that include Suprathel, Biobrane, Pelnac [17-20], and the Composite skin substitute that includes Apligraf [21, 22], and CryoSkin etc.

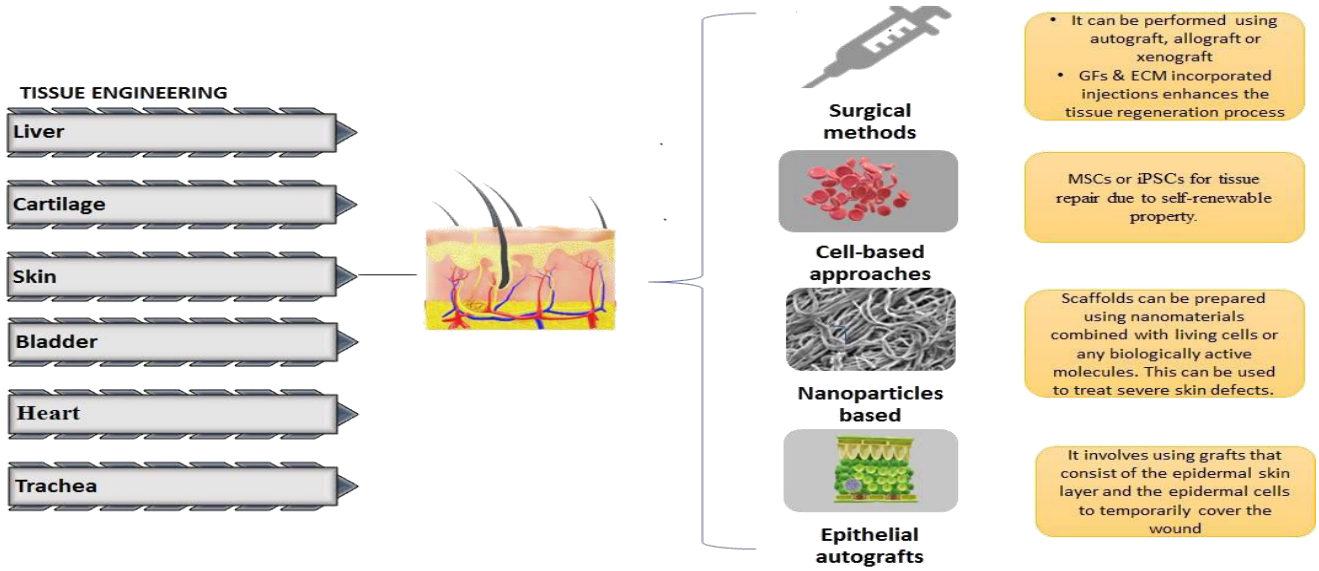

Fig. 1: Different techniques used in tissue engineering

2. BIOMATERIALS FOR TE

Numerous biomaterials are being developed for making skin sutures. Dermal fillers and fat grafting are the two strategies used for healing small wounds, specifically the injuries in the soft tissues. Dermal filler can be obtained either from natural sources such as collagen, cross-linked forms of hyaluronic acid (HA), and calcium hydroxyapatite or the synthetic sources that include polymers of polylactic acid and polymethylmethacrylate [13]. This conventional method to fill the defect has limitations that include repeated injections as they are not permanent and can result in various complications [24]. The autologous fat grafting involves using liposuction for harvesting tissues to inject it (lipoaspirate) to the injury site to facilitate filling the defect but this may often result in complications due to uneven resorption of lipoaspirate [25, 26]. After transplantation adipocyte rupture and oxygen scarcity may occur, resulting in necrosis of the lipoaspirate being transplanted [27]. Another problem associated with fat grafting is the calcification or formation of a cyst, interfering in imaging [28].

Synthetic polymers such as polylactic acid, polyglycolic acid, and copolymers possess a significant advantage as they are manufactured in a way to match the chemical composition of the skin and degenerate over time by the degradation of the ester bonds through hydrolysis. The degradation rate can often be controlled by modulating the monomer's molar ratio and mass [29]. Cells can be fused with seeded 3T3-L1 preadipocytes [30-32], or adipose-derived stem cells (ADSCs) [33, 34] over a matrix prepared from polyglycolic acid for creating

tissue scaffold, this facilitates stimulation of adipogenesis [29]. Stem cells (SCs) when injected attached to polylactic-co-glycolic acid (PLGA) spheres, whether in the form of hollow fibers or solid forms, it enhances the rate of adipogenesis [36-41]. Polymers can often form hydrophilic material by crosslinking called the hydrogel, which is usually made from Polyethylene glycol (PEG). Hydrogels encapsulate the cell and exhibits eminent swelling when introduced in the aqueous medium [29, 42].

Scaffolds can be derived from natural sources such as alginate, silk, and chitosan, which are acquired from seaweed, silk-producing organisms, and chitin respectively. These naturally derived scaffolds are highly biocompatible and biodegradable [43-46]. Adipose tissue engineering strategy typically involves availing biocompatible seed cells to heal injuries. Alginate is used for scaffold production due to its properties such as biodegradability, injectability, and biocompatibility. Using divalent cations such as Ca^{2+}, they can easily be processed in desirable shape hence making them pertinent to customize the treatment [47, 48]. Adipose-derived stem cells (ASCs) hydrogels are injectable and are considered a novel technique for adipose tissue engineering [49-52]. Silk fibers obtained from the silk of spiders and silkworms are often used for tissue engineering due to their high mechanical strength [45].

Various cellular skin-substitutes that are sprayed over the wound to cover the affected area are used that includes, EPIBASE where autologous keratinocytes are used at the confluent stage. This is a preferable choice in severe burn injuries, as it provides outer cell covering for wounds [14, 15]. Spraying cultured keratinocyte and melanocyte isolated from the individual to permanently heal the affected area is another strategy that usually helps to treat the scars [16, 53].

Non-cellular skin substitute includes Suprathel made from polymer and is an absorbable material. They are used to treat surgical wounds and minimize bleeding [17-19]. Biobrane, a material having a mesh prepared from nylon and a porous structure, is used for dressing that has collagen and silicone in its inner and outer surface respectively. It is used for temporarily covering the wound till the graft is prepared [55]. Pelnac, a matrix formed of bilayer having porcine tendon collagen as an inner layer and silicone film as the outer one, is preferred in lesions caused by cancer [20, 53].

A composite skin substitute that includes Apligraf is a scaffold prepared from bovine collagen. It is a gel-like material incorporated with natal foreskin fibroblasts and keratinocytes, and is used in the dressing of wounds resulting from ulcers or surgeries [21-22, 56] Bioseed-S is a matrix prepared from the individual's self-keratinocytes over fibrin sealant and used as a skin substitute for ulcers [56, 57]. CryoSkin is an allogeneic keratinocyte over the silicone and is non-cultured cells that have been cryopreserved [23, 53].

3. METHODS FOR TISSUE REPAIR

3.1. Conventional methods

A treatment method is designed depending on the severity of damage in the patient. As skin can regenerate itself, the small wounds or lesions are healed usually in a short period but in cases where the damage is severe skin grafts are required. The grafting can be performed using surgical methods to restore the normal functional skin [58, 59]. Graft covers the wound hence protecting it from infection as well as provides the matrix for regeneration of tissue more rapidly. This conventional method includes autograft (graft using the individual's tissue), allograft (a donor is required to derive the tissue for grafting), xenograft (the tissue is derived from animals), and few artificially developed materials. The autografts are preferable choice for grafts as there is no chance of immune rejection but in case of deep injuries, there is a limitation of availability of autologous skin making this strategy limited. Both allograft and xenograft require a donor, from the same and different species respectively, hence there is a chance of immune rejection in them, especially a high chance of rejection in xenografts as the donor is from another species [53, 60].

3.2. Approaches for skin grafting through TE

Nanotechnology can aid TE, as the nanostructures can mimic the bio environment that is tissue-specific; this makes it to serve a wide range of functions in tissue repair or replacement as well as can be used to generate new cells or tissues as mentioned in Table1. It facilitates a faster healing process, unlike the conventional ones where tissue repair is time-consuming [61].

3.2.1. Cell-based approach

There are various approaches available for skin grafting, one of them being the cell-based approach, which majorly involve the application of iPSCs for tissue regeneration or wound healing via secretion of GFs, through cell-cell interactions that are being stimulated by fibroblasts which in turn stimulates growth and differentiation of keratinocytes [62]. The keratinocytes

are the cells that inhibit the entry of foreign materials and decrease the loss of cell constituents to the outer environment; hence the constituents required for skin repair are retained leading to faster recovery.

3.2.1.1. MSCs in tissue engineering

MSCs are the multipotent cells that are self-renewable and can differentiate to form cells that belong to skeletal tissues that include osteoblasts, myocytes, chondrocytes as well as adipocytes. MSCs along with the secretion of materials responsible for immunomodulatory effects such as GFs, cytokines, and chemokines, also secret extracellular vessels that are involved in communication via cellular signals and are responsible for providing trophic support [6-8]. The MSCs can be derived from different sources including bone marrow (BM) and placenta, which are significant in the repair and regeneration of tissue.

3.2.1.1.1. BM-derived MSCs

MSCs derived from BM, when labeled with Fe_3O_4 nanoparticles (NPs) were found to be more significant in healing the injury. When an external magnetic field (MF) induced through laser is applied to these labeled NPs, towards the wound *in-vivo*, it was observed that the NPs- labeled MSCs moved towards the injury site more rapidly compared to the unlabeled one. Along with this rapid movement, such MSCs are often found to enhance the angiogenesis process while minimizing the inflammatory effect [8].

In an experiment performed to check what affects the process of wound healing, non-obese diabetic (NOD) mice were injected with the bone marrow-derived allogeneic MSCs (allo-mBM-MSCs) and their acellular derivatives (allo-acd-mMSCs). On observation at 4^{th}, 6^{th} and 8^{th} day, it was found that the allo-acd-mMSCs had a high percentage of wound healing rate compared to allo-mBM-MSCs, while an observation made on the 16^{th} day showed both the allo-acd-mMSCs and allo-mBM-MSCs had almost similar wound healing rate, suggesting that the growth factors and proteins such as insulin-like GF-1 (IGF-1), keratinocyte GF (KGF), hepatocyte GF (HGF), vascular endothelial GF (VEGF), angiotensin-2 (ANG-2), matrix metalloproteinase-1 (MMP-1), colicinogenic (CoL-1), and Prostaglandin E2 (PGE2) that are required for wound healing are present on the allo-acd-mMSCs, which can be utilized by allo-mBM-MSCs to further enhance the wound healing process, but the allo-mBM-MSCs solely cannot perform wound healing. Soluble factors of BM-MSC that include interleukin-6 (IL-6), macrophage colony-stimulating factor (M-CSF), IL-10, transforming GF (TGFβ), HGF, and PGE2 enhances the recovery rate as they can trigger the innate as well as the adaptive immune system [63-65]. The other diseases that can be treated by BM-derived MSCs include hematopoietic disorders and autoimmune diseases (ADs) [66].

3.2.1.1.2. Placental derived MSCs

SCs derived from the placenta are highly potent due to their elementary genesis [67] and endows a benefit over the MSCs derived from other organs due to lack of the MHC class II antigens that are responsible for graft versus host disease (GVHD) [68], hence provides diversity in the treatment. Moreover, they often become vestigial after the parturition hence eliminates the ethical issues associated with their application [69].

Duchenne muscular dystrophy (DMD), an X-linked genetic disorder caused by a mutation in a gene called dystrophin, leads to progressive muscle degeneration [70] as a result of a loss of functional dystrophin protein which is responsible for the integrity of muscle cells and also plays a vital role in the functioning of muscle cells [71]. Unlike the normal condition, where the satellite cells get activated on muscle degeneration and differentiate into mature muscle cells, in the defective conditions the degenerated muscles are replaced by fibrotic and fat tissues [70]. Transplantation of MSC in animal models has been demonstrated to promote regenerative activity in muscles that get damaged [72]. The differentiation of muscle cells from patients with DMD was found to be enhanced with the aid of placental-derived MSCs (PL- MSCs) with the mediator being exosomal miR-29. Placental-derived MSCs (PL-MSCs) and PL-exosomes (vesicles secreted by PL-MSCs) along with utrophin (a protein resembling amino acid sequence of dystrophin) expression was found to be responsible for inhibiting fibrosis as well as inflammation. When gold NPs were used for labeling MSCs, it demonstrated localization of cells in the muscle tissues after treatment showing that PL-MSCs and PL-exosomes are significant in cell therapy of DMD [73].

3.2.1.2. Adipose tissues

An autologous split-thickness skin graft (STSG) is a promising strategy that includes grafts made from dermal or epidermal layers, providing sufficient tissue as well as excellent flexibility for the coverage of large

defects amid complex topography [74], but the STSG possess few disadvantages, such as- contracture, poor cosmetic outcome, and physical disability [75]. Moreover, such skin grafts have poor vascularization leading to hypoxic conditions and an ischemic period following surgery, which eventually leads to cell death [76]. This can be improved by engineering it with adipose tissue-derived microvascular fragments (ad-MVF). Adipose tissues can be used to observe the effect of prevascularization while treating bradytrophic wounds such as full-thickness skin defects having an impaired vascularization. In a study conducted for improving STSG, dermal matrices were seeded with ad-MVF, and its effect was compared with the non-seeded control. It has been found that the microvascular and lymphatic networks were denser in prevascularized matrices, and through prevascularization with ad-MVF, autologous skin grafting can be achieved at a faster rate [77].

3.2.1.3. Epithelial autografts

Tissue-engineered skin substituents became an efficient approach for skin regeneration nowadays, as they temporarily cover the wounds and protect them from infections as well as the loss of cellular constituents, hence accelerating the rate of wound healing by the promotion of cytokine and GF release at the affected site [78]. Tissue-engineered skin provides dermal as well as epidermal components that are essential for the healing process, even for deep cuts or burns [79-82].

Epidermal skin grafts (ESGs) consist of the epidermal skin layer and the epidermal cells [83-85]. ESGs are considered to be an alternative to conventionally harvested skin grafts when the wound is minor, and are dependent on the wound bed receptiveness and presence of sufficient tissue for granulation with minimum burden [85]. The phenotype of cells in newly incorporated grafts is highly influenced by the recipient environment [84-85]. ESGs are cost-effective as there is no need for anesthesia or any specialized equipped room for its setting [86]. For preparing the graft, interstices are made through meshing or fenestration, facilitating flexibility of skin and passage of fluids that allows more efficient interaction between the graft and the wound. On the other hand, the pinch graft technique is used for small defects. In such grafts, an area of donor skin is harvested using a scalpel or a biopsy tool and then transplanted to the damaged skin [83].

3.2.2. Nanofibers

Current development in technology has allowed the use of nanofibers in TE. Nanofibers contribute either through the formation of a scaffold or by serving as a delivery system for drugs, cytokines, and GFs which stimulates rapid growth of the tissue. The scaffolds for skin are being generated with the help of nanofibrous materials that imitate the native extra cellular matrix (ECM) and regenerates or repairs the cells/tissues when combined with the living cells or any biologically active molecules. The scaffold should possess few properties like controllable porosity, biocompatibility, and high tensile strength to provide support for cell adhesion and proliferation. The addition of nanotopographies to the biomaterial surface enhances bioadhesive property. The nanomaterials due to their small size have a larger surface area, this facilitates increased adsorption of adhesive proteins like vitronectin and fibronectin, mediating cell-surface interactions via integrin cell surface receptor [9, 87-88]. Nanofibers also serve as a delivery system for drugs, cytokines, and GFs that promote cell function and hence rapid tissue regeneration [9, 89].

3.2.2.1. Electrospun nanofibers as a potential scaffold for cell or tissue regeneration

Electrospinning involves the application of nanotechnology for the production of biomimetic nanofibrous material, having biologically relevant features, with the help of various natural and synthetic polymers [90]. Electrospun nanofibers present a great advantage in TE or wound healing. They possess certain properties that make them a relevant choice for skin repair, such as compositional mimicry, structural mimicry, ease of incorporation of bioactive materials as well as mechanical mimicry [91]. Moreover, electrospinning allows the production of type I and III collagen (structural protein present in the ECM of the skin) nanofibers [92, 93]. For continuous and homogenous production of polyethylene (PE) blended collagen, elastin, and collagen-elastin nanofibers, incorporation of NaCl and polyethylene oxides are essential [94].

Environment-responsive electrospun nanofibers unlike the conventional ones for drug delivery enable rapid response time and more targeted release for recovery of the wound [95-96]. The scaffolds are capable of modulating the cellular processes [97]. The electrospun poly(ε-caprolactone-co-lactide)/Poloxamer

(PLCL/Poloxamer) nanofibers fabricated with varying PLCL to poloxamer ratios were found to have high tensile strength and young's modulus in the human skin range [98]. The electrospun nanofibers are capable of regulating the behavior of a skin cell either through intracellular signaling pathways or through the transmembrane receptor. Collagen, laminin, and integrin ligands coated electrospun nanofibers promote the adhesion of native human keratinocytes [99]. Collagen nanofiber membrane blended with a polycaprolactone (PCL) serves as a support for human dermal fibroblasts for attachment and proliferation [100]. The fibrin coating on electrospun polylactic acid (PLA) was found to enhance the cell spreading and proliferation of human dermal fibroblasts as well as the synthesis of type I collagen in human dermal fibroblasts [101]. The PCL fiber meshes were found to provide an area for normal human epidermal melanocytes, facilitating their differentiation [102].

3.2.2.2. Sutures in tissue engineering

Sutures made by electrospinning of the silkworm or spider silk are used in the TE process. Scaffold prepared by electrospinning of nanofibers can efficiently heal the skin damages [10-12] with no deleterious effect to the host.

3.2.2.3. Silk fiber from silkworm

Silk fiber derived from silkworm (commonly from *Bombyx mori*), is specially used for making scaffolds *in-vitro*, because of their unique mechanical property imparted by extensive hydrogen bonding. In TE, silk fiber can be used for designing scaffolds as it possesses properties like high tensile strength and variable side chain which imparts a high diversity [103].

For clinical applications the sutures should possess additional properties such as biodegradability, elasticity, high tensile strength, and should be non-irritant, making silk fiber a preferred entity for aspects of TE. Such properties of sutures allow controlled release of skin recovery medications and making them excellent biomaterial to be used as a scaffold. The composition of silk fibers can often be tailored providing a medium for exploiting these proteins for application in the biomedical field. For example, sericin, a glue-like protein in the silk is known to have adverse effects like hypersensitivity, this restricts it from being biocompatible, so the removal of sericin is essential for making silk fiber a biocompatible material. Silk sutures induce angiogenesis and elicit a high response from macrophages to phagocytose. Such response was assumed to be the function of produced particles and not of actual silk fibroin material [103-106]. The silk takes a long time to degrade. This degradation takes place by cleavage of less-crystalline regions of the proteins through protease enzymes, that are phagocytosed for further biological processes [107-110] and providing long term reliability.

3.2.2.4. Spider silk

Spider silks are of low density as well as are highly biocompatible and biodegradable. Moreover, they also exhibit high mechanical strength and significantly high surface-to-volume ratio [111], making them suitable for forming sutures. However, the natural production of spider silk is limited, so now-a-days, it is being recombinantly modified to enhance its production for the intended applications [112, 113], using Escherichia coli (*E. coli)* as a host. *E. coli* is used due to its rapid growth kinetics and ease of transformation [114]. Out of various types of silk produced by the spider, Major ampullate (MA) silk, which is the silk produced by adult female *Nephila* spider also called dragline silk, contains at least two protein classes- the first being, proline-free major ampullate skin protein1 (MaSp1) that is hydrophobic and the other being proline-rich and more hydrophilic MaSp2. Such proteins were widely studied and potentially used as sutures in the treatment of tendon rupture [115-118]. Spidroins is the term used to denote the main proteins in spider silk. MaSp1 and MaSp2 are two important spidroins. MaSp3 is a recently identified spidroin type [119] from *Argiope argentata* and *Latrodectus hesperus*. Unlike MaSp1 and MaSp2, this spidroin is deficient in polyalanine and glycine-proline-glycine motifs and have more polar amino acids. The ampullate spidroins gather to form hierarchically structured fiber [112, 120]. The properties of spider silk can be tuned with the aid of either genetic manipulation or via amino acid sequences such as the RGD (arginine, glycine, and aspartic acid) motif by their chemical modification. The functional groups are provided through amino acids such as cysteine [121-123], [112]. Braiding fiber of natural spider silk causes stabilization of the tendon injuries by imparting mechanical strength and leads to slow degradation of spider silk. This braided silk is stiffer and is highly effective. The spider silk fibers woven on steel frames serve as an excellent matrix in plastic reconstructive surgeries for skin repair [124, 125].

Table 1: Approaches of tissue engineering (TE) for skin grafts and wound healing.

Approaches of TE	Description	References
Surgical methods	In this method, injections of growth factors and extracellular matrix are provided for wound healing as well as for regeneration of the tissue.	[2]
Cell and tissue based approaches	Involves using grafts that consist merely of the epidermal skin layer and the epidermal cells. For preparing the graft, interstices are made within it through meshing or fenestration, facilitating flexibility of skin and passage of fluids that allows more efficient interaction between the graft and the wound bed to be more effective. The presence of a variety of cells, specifically stem cells, in the skin being generated through tissue engineering allows the reconstruction of native-like skin. **Epithelial autografts:** Epithelial autografts are significant for the cases involving damage through burns. Such autografts are constructed using keratinocytes. **Mesenchymal stem cells (MSCs):** MSCs are the multipotent cells that are self-renewable as well as can differentiate to form cells that belong to skeletal tissues. They secrete materials responsible for immuno-modulatory effects as well as extracellular vessels that are involved in the cellular signaling process and are responsible for providing trophic support. **Autologous split-thickness skin graft (STSG):** Grafts are made from the dermal or epidermal layer, providing sufficient tissue as well as excellent flexibility allowing the coverage of large defects amid complex topography.	[3-8, 74, 83-85]
Electrospun nanofibers	It can contribute to TE either through the formation of a scaffold or it can serve as a delivery system for drugs, cytokines, and growth factors, or any biologically active molecule.	[9]
Sutures	It exploits the idea of naturally occurring sutures for wound healing. Nanofibers yarns are made through electrospinning that can be used as surgical sutures. The materials for making these sutures can be derived mainly from the silk of spiders or silkworms.	[10-12]

4. ROLE OF 3D PRINTING IN TE

Three-dimensional (3D) printing has emerged as a novel technique, used in TE scaffolds and tissue models that involve tissue and organ printing [126-130]. It performs fabrication of 3D construct from the individual's medical images obtained by diagnostic tests thus allowing tailoring of the construct with high complexity according to the individual's requirement [131]. 3D printing is a significant approach to construct the exact image of the lesion or wound and hence can be used to design a personalized treatment instead of giving a randomized available treatment. This enables the accuracy [132-133] and pre-treatment planning, ultimately decreasing chances of any harmful effects [133-134]. Along with this, it also minimizes the use of animal models [135], hence excluding the ethical concerns that restrict experimentation.

5. CONCLUSION AND FUTURE PROSPECTS

Tissue engineering is an approach designed for generating skin grafts by exploiting the idea from nature. The conventional method of skin grafting involves using the tissue from the healthy part of the same individual (autograft) or from the donor (allograft). Such conventional methods are limited due to post-operative bleeding, leaving scars in the part from where the tissue has been derived as well as the immune rejection in case of tissues derived from the other individuals. The affected individual may be administered with injections of growth factors and extracellular matrix to induce tissue repair, but this requires time, hence may result in infection if the wound is kept open for long, so now a days the scaffolds made using the tissue engineering approaches such as epithelial autografts are used to temporarily cover the wound to prevent infection as well as to inhibit the leakage of cellular constituents. Stem cells and induced pluripotent stem cells, due to their self-renewable property, can be used to efficiently treat wounds and injuries. However, the use of nanotechnology is the most effective way for skin tissue engineering that exploits the idea of natural silk from spiders or silkworms for making scaffolds that serve as a significant graft for damaged tissues to treat the lesions. It is

preferred due to no (or fewer) side-effects unlike that of conventional methods. Moreover, it often results in fast recovery of damaged skin and protection from infections as well.

Even after the availability of a wide range of skin replacement materials and novel strategies, there are still some limitations that exist with healing the scars for severe defects. For example, the approaches that completely restore the normal morphology of skin being affected through acid spills have not been yet developed. Scientists are doing research for reducing skin aging process through tissue engineering approaches.

Conflicts of Interest

The authors declare no conflict of interest.

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