http://www.moderntechno.de/index.php/meit/article/view/meit34-00-040
DOI: 10.30890/2567-5273.2024-34-00-040

DERMIS SURFACE MODIFICATION IN TISSUE ENGINEERING
МОДИФИКАЦИЯ ПОВЕРХНОСТИ ДЕРМЫ В ТКАНЕВОЙ ИНЖЕНЕРИИ

Macagonova O.V. / Макагонова О.В.
d.m.s., / д.м.н.
ORCID: 0000-0003-4414-3196
Laboratory of Tissue Engineering and Cellular Culture, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
Лаборатория тканевой инженерии и клеточной культуры, Государственный университет медицины и фармации им. Николае Тестемицану, Кишинев, Республика Молдова
Cociug A. M. / Кочуг А.М.
d.m.s.,/д.м.н.
ORCID: 0000-0001-5878-0239
Human Tissue Bank, Traumatology and Orthopedy Hospital, Republic of Moldova
Банк тканей и клеток человека, Больница травматологии и ортопедии, Республика Молдова
Taralunga T.A./ Таралунга Т.А.
ORCID: 0000-0002-8069-4975
c.m.s., / к.м.н.
Laboratory of Tissue Engineering and Cellular Culture, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
Лаборатория тканевой инженерии и клеточной культуры, Государственный университет медицины и фармации им. Николае Тестемицану, Кишинев, Республика Молдова
Braniste T.I./ Браниште Т. И.
ORCID: 0000-0001-6043-4642
National Center for Materials Study and Testing, Technical University of Moldova
Национальный центр исследования и испытания материалов, Технический университет Молдовы
Nacu V.E./ Наку В.Е.
ORCID: 0000-0003-2274-9912
Laboratory of Tissue Engineering and Cellular Culture, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
Лаборатория тканевой инженерии и клеточной культуры, Государственный университет медицины и фармации им. Николае Тестемицану, Кишинев, Республика
Human Tissue Bank, Traumatology and Orthopedy Hospital, Republic of Moldova
Банк тканей и клеток человека, Больница травматологии и ортопедии, Республика Молдова

Annotation. *The work considers the methods of dermis surface modification to optimize and improve the performance of biomaterials derived from the dermis, protein absorption and sedimentation, formulation and combination with drugs, and to adapt to tissue defects and their regeneration.*

Keywords: *dermis, surface modification, in vitro scaffolds, tissue engineering*

Introduction

Tissue engineering is an interdisciplinary field that aims to regenerate tissues and organs using cells, biomaterial scaffolds and signaling molecules. The development of biomaterials has attracted much attention for wound healing and drug delivery through biopolymers [1, 2]. Tissue engineering is a promising branch of regenerative medicine that helps replace damaged tissue using appropriate scaffolds, living cells, and growth factors [3]. The physicochemical properties of the biomaterial greatly influence cell adhesion, proliferation and differentiation on the scaffold [4, 5] The properties and grown of the cells depend of structure of the

surface of the scaffold and they are guided by growth factors. For example, Kim et al. reported that fibrinogen coating of the biomaterial surface significantly changed the adhesion and proliferation of human mesenchymal stem cells. The process was affected by the change in surface roughness due to the function of the β15-42 epitope region contained in fibrinogen [6]. Scaffolds can be made from natural and synthetic biomaterials. Synthetic materials have polymeric properties that are easy to control, but lack biochemical activity compared to natural materials. Many biological materials, such as collagen, can provide the extracellular matrix (ECM) components required for cell adhesion, thereby stimulating cell growth and viability. For synthetic polymer materials, although cells can adhere, they require additional energy to generate ECM [7]. Natural biomaterials have good biochemical activity and biological compatibility. However, in the process of handling natural materials such as decellularized tissues, the normal three-dimensional structure is altered or some growth factors are lost [8]. Material property requirements vary with different types of tissue construction. Surface modification is necessary to improve the biological activity of cells on the surface of the material, optimize porosity, solidity without changing the integrity and physical properties of the general skeleton of the material, and meet any need for skin care and adapt to tissue defects and produce wound regeneration [9]. Therefore, surface modification treatment of natural materials is necessary and very important in tissue engineering [10]. The extracellular matrix obtained from the dermis is an excellent bioscaffold. Experimental results and numerous studies show that the extracellular matrix in the dermis has great prospects for allogeneic transplantation and wound repair, rhinoplasty, gingival augmentation [11, 12]. The ECM in the dermis is a natural biomaterial. Type I collagen is the main dermal component, and its use in obtaining bio-dressings is the attraction of many researchers [13]. Collagen is a high molecular weight protein that provides structure and tensile strength. The two major components of elastic fibers are elastin and microfibrils. Fibrillins, such as fibrillin-1 and -2, are the predominant components of the microfibrils that wrap around elastin, which form the core of the elastic fiber. Elastin covalently binds to collagen, fibrillin, fibulin, and microfibril-associated glycoproteins and forms viscoelastic fibers, which surpass other ECM components in terms of biological, chemical, and thermal stability (Humphrey et al., 2014; Alfano et al., 2016). Unlike collagen, which provides tensile strength, elastin is important for tissue elasticity and strength to limit stretching. In the interstitial space of the dermis, cells such as fibroblasts, immune cells, and vascular cells are surrounded by the ECM. The surface of the scaffold provides physical support for these cells. It also allows cells to sense the continuously changing conditions in the environment and facilitates cell-to-cell communication to adapt to such changing microenvironments [13]. ECM glycoproteins have multiple functions; stabilizes collagen fibers, restores elasticity and tissue stiffness. Fibronectin is the dominant glycoprotein in the interstitial matrix of the dermis and is mainly produced by fibroblasts and keratinocytes. Laminin, like fibronectin, is a fibrous glycoprotein and a major component of sheet-like basement membranes (BM) [14, 15]. Another central component of the underlying ECM is proteoglycans (PGs), which are intercalated between and adhere to collagen fibers in the ECM. The main PGs in the skin are

biglycan, decorin, versican, fibromodulin and lumican in the interstitial matrix of the dermis and perlecan and agrin in basement membranes. PGs are highly glycosylated and decorated with with glycosaminoglycan (GAG) side chains. PG/GAGs can interact with and sequester matrix-associated proteins such as growth factors, signaling molecules and chemokines and are involved in the synthesis of matrix-dependent growth factors [16, 17]. Matricellular and matrix-associated proteins primarily have regulatory roles on matrix-embedded fibers and cells. These proteins have key features such as secretion by certain cells, interaction with ECM fibers during wound development and healing [18]. The ECM actively modifies the activity of growth factors and cytokines. The ECM can also protect growth factors from degradation. The ECM surface provides the host cell with a natural attachment and migration environment, increases its biocompatibility with the host cell, and can rapidly bind to the host tissue, promote angiogenesis, and restore tissue function [20, 21].

The above features of dermal ECM show significant advantages in regenerative medicine and tissue engineering. In addition, the recent progress of ECM-based biomaterials applied in skin regeneration and future perspectives are summarized.

Aim of the study

This article discusses methods for modifying the dermis surface to optimize and improve the performance of dermis-derived biomaterials, protein absorption and sedimentation, formulation and combination with drugs, and adaptation to tissue defects and their regeneration.

Materials and Methods

The material of the study was pig skin processed by physicochemical methods with the removal of all epidermal and dermal cells.

Preparation

The ECM preparation method consists in obtaining an acellular tissue by physicochemical processing removing all epidermal and dermal cells while preserving the remaining bioactive dermal matrix. The physico-chemical method consists in physically removing the epidermis and hypodermis and separating the dermis. The main purpose of the chemical method is to remove cells from the tissue and avoid immune rejection after skin application. The chemical method involves immersing the dermis in different solutions. First, the tissue was soaked in a solution containing 0.25% trypsin for 1 h in the incubator at 37°C, then in a solution of 0.01 M PBS for 6–8 h, then in -a 1% Triton X-100 solution for 72 h and finally incubate in PBS (PH = 7-7.4) for 2 h. After rinsing with deionized water, the tissue was immersed in 20% ethanol for of 8 h, rinsed with sterile water for 2 h and stored at −80°C or used immediately. Fig. 1 shows the macroscopic surface morphology of porcine dermis after decellularization Fig. 1 (a) and the microscopic surface morphology of the SEM image Fig. 1(b).

Decellularized biomaterials do not have immunological rejection and become an ideal material for biological scaffolds [22]. Histological and genetic analysis showed that physical and chemical treatment removed the cells contained in the dermis, and the ECM is constituted by collagen fibers. The ECM preserved the normal 3D structure, is rich in continuously arranged fibers, so it could promote cell adhesion

and proliferation. Therefore, ECM is non-immunogenic and will have good biocompatibility and when repairing tissue defects will not cause immune rejection [23, 24.]. ECM plays an important role in tissue repair and reconstruction and is an excellent natural material derived from porcine dermis [25].

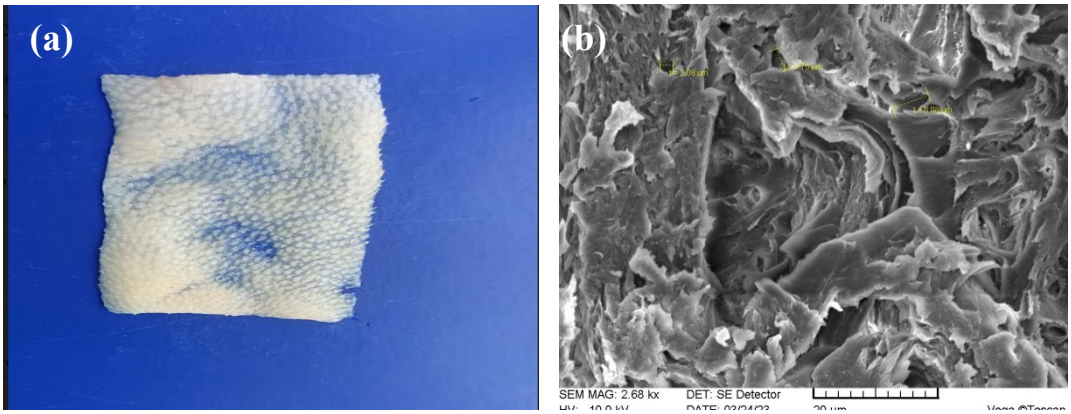

Figure 1. a) Macroscopic image of the surface morphology of the decellularized dermis; b) SEM image of the dermis after decellularization.

To some extent, porcine dermal ECM is widely used due to the easy surface modification and fabrication of biomaterials based on dermis ECM. ECM has a variety of manifestations depending on the handling process, including membrane, sponge, and hydrogels [26-28].

Thus, dECM-based biomaterials are a useful tool for replicating human skin physiology *in vitro* and developing advanced human skin models for therapeutic discovery and testing.

Results

Forms of dermal ECM

Membrane. This is the simplest of the three forms of ECM. The dermis is decellularized through physical and chemical steps to obtain a membrane-like SIS [29-32]. Decellularized dermis is translucent white, with a thickness of approximately 0.3 mm. The surface has a few lines of fibers. As shown in Fig. 2 (b), after the removal of the cellular content, the ECM is converted into the decellularized extracellular matrix (dECM). Since decellularization was first reported in 1948 [33], decellularization technologies have developed rapidly in recent decades. Complete removal of nuclear and cytoplasmic components is difficult, and cellular debris of decellularized ECM can cause an inflammatory response at implantation sites and ultimately lead to repair failure. Therefore, it is very important to perform some evaluations for cellular debris before use. Currently, there is no unified standard procedure for the characterization of cellular debris after decellularization, but a qualitative and quantitative analysis of the remaining cellular components can be performed [34]. Qualitative assessments mainly consisted of immunofluorescence Figure 2 (a, b) and histological staining. Immunofluorescence staining, including DAPI staining was used to observe the existence of obvious nuclei and constitutive cell debris. As shown in Fig. 2 (a), fluorescent cells in the intact dermis were removed after decellularization Fig. 2 (b) [35]. Figure 3 shows hematoxylin-eosin (HE) staining images and SEM images before and after decellularization of the

dermis. Through SEM, a loose 3D network structure is visible, which will be used as a scaffold material [36].

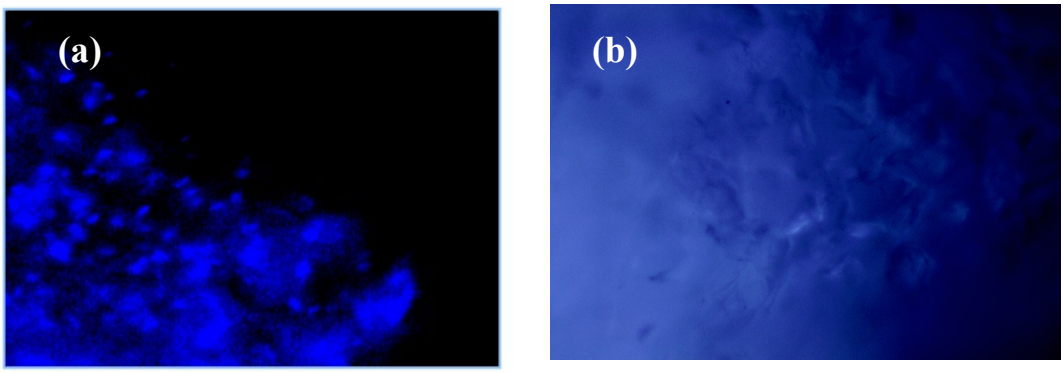

Figure 2 a) DAPI image of natural dermis, showing fluorescent cells; b) DAPI image of decellularized, almost cell-free dermis.

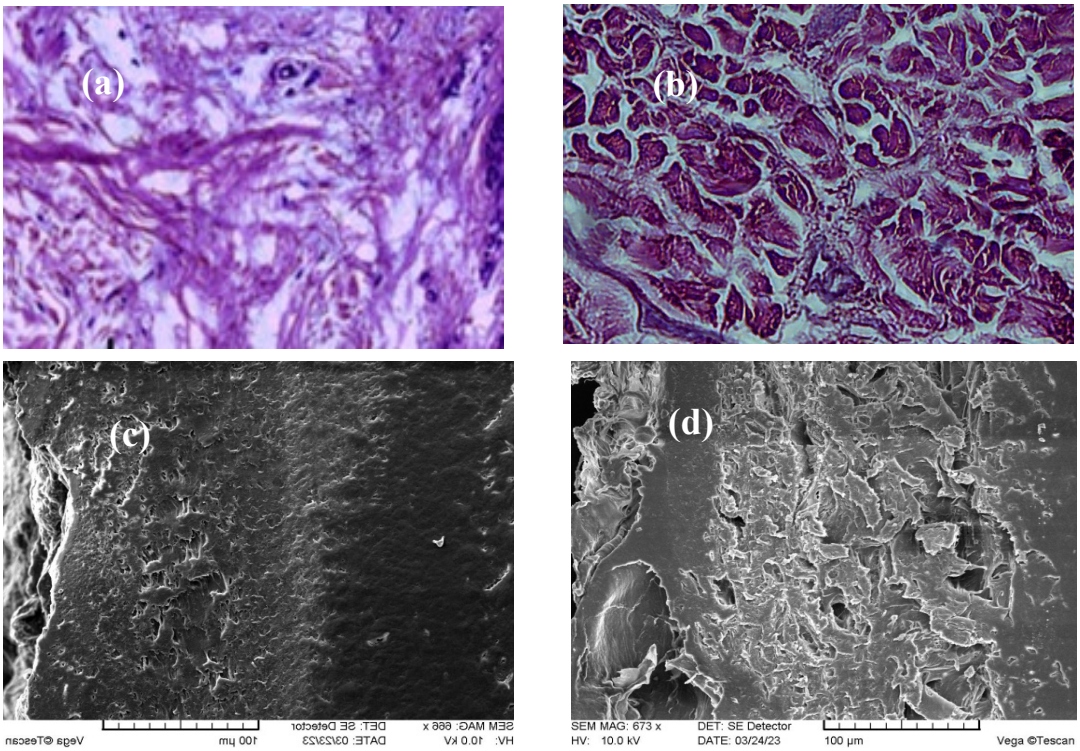

Figure 3. a) H-E image of dermis without decellularization, showing many blue nuclei; b) H-E image of decellularized dermis, almost without nuclear signs; c) SEM image of decellularized dermis showed thick, dense, nonporous tissue; d) SEM image of decellularized SIS shows a loose 3D network. structure.

ECM in the membranous aspect can be directly squeezed into a small tubular structure and transplanted directly into the skin wound as a scaffold material or biological dressing. In recent years, ECM membranes have been widely used in the study of tissue defect repair *in vivo* [37, 38] and supports for cell growth [39]. The ECM membrane has been used for skin reconstruction [40].

Sponge. The ECM membrane is broken to obtain powder, mixed with a solution containing acetic acid and pepsin, stirred and lyophilized in sponges fig.4 (a), [41,

42]. Sponge based on dermal ECM is elastic and flexible, easy to handle and has interconnected porous structures, visualized by SEM Fig. 3 (b). Data show that dermal collagen sponge can play a huge role in wound healing and can adhere uniformly to the wound surface and show better absorption of wound exudation than covered with polyurethane film [43]. Therefore, it can be used to regenerate skin tissue in the wound area. Based on this finding, we can predict that the dermal ECM-based sponge also has great prospects in vascular endothelialization. Some researchers cultured rat bone marrow stem cells on dermal ECM-based sponges [44], which have also been shown to promote cell proliferation.

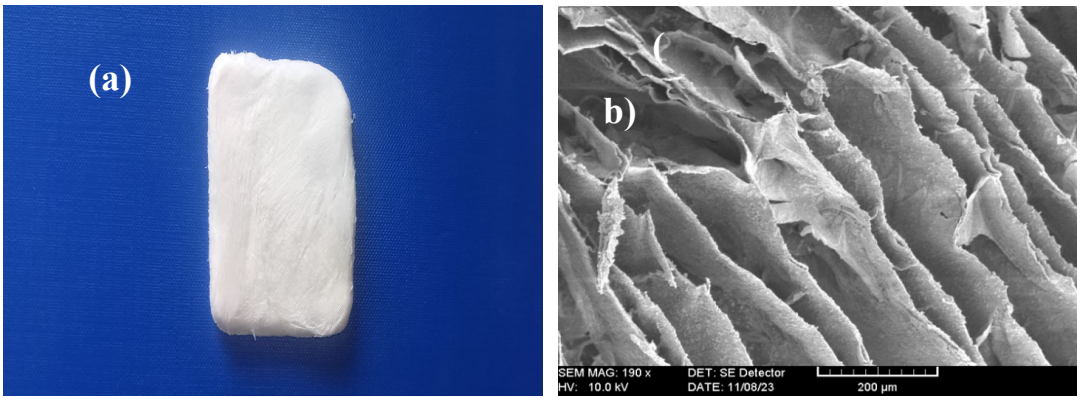

Figure 4. a) Collagen sponge based on dermal collagen from ECM; b) SEM image of collagen sponge based on dermal ECM.

Hydrogel. In addition to membrane and sponge, another common form of derm application is hydrogel. Hydrogels are the most suitable tissue filling materials because hydrogels can be formed into various shapes by syringes to accommodate tissue defects and regeneration [45]. Brief preparation of the hydrogel is as follows. Porcine ECM membrane was pulverized, suspended in porcine pepsin HCl solution, stirred at room temperature, adjusted to pH 7.4, lyophilized, and pulverized to obtain a dermis powder. The resulting powder was dissolved in PBS at 20% w/v overnight at 37°C and can be molded into a gel of any shape [46]. For example, ECM hydrogel placed on the bottom of the culture dish forms a flat shape [47] or placed in a small bottle forms a thicker cylindrical shape Fig. 5 (a). The hydrogel can also be injected into a specific area with a syringe having good fluidity.

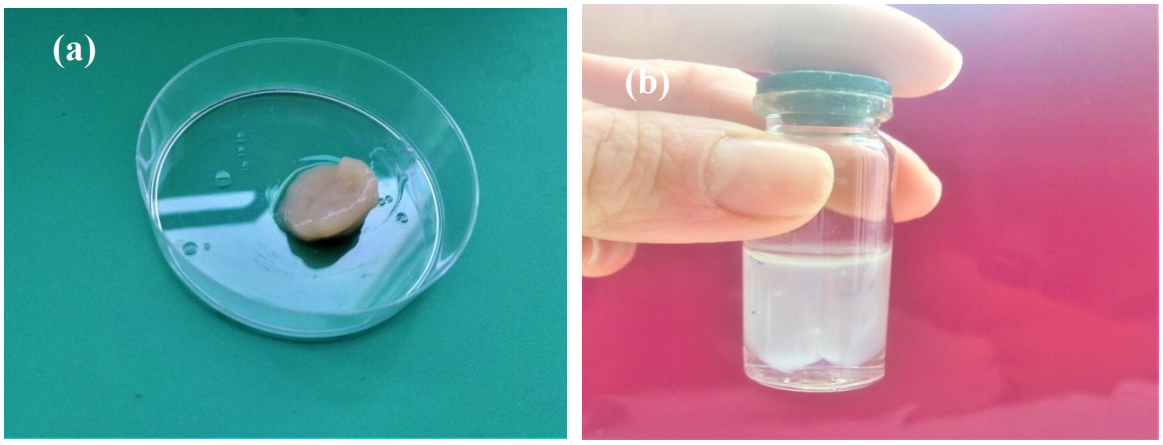

Figure 5. a) Image of hydrogel on Petri dish and b) in a tube.

As a collagen scaffold, dermis has been successfully used for skin wound repair. In 2009, Hsu P.W et al. applied porcine dermis to reconstruct the abdominal wall [48]. Other researchers have conducted a series of organ and tissue repair studies using porcine or bovine dermis [49]. Others have used cadaveric human dermis to obtain biomaterials with regenerative effects [50], for orthopedic applications [51]. In 2021, the dermis was used in breast reconstruction [52] and the treatment of diabetic ulcers [53].

Discussions

The application of dermis in tissue engineering and regenerative medicine is limited by its mechanical properties. The modification of the dermis surface has greatly improved its application in tissue engineering. Easy surface modification means that the dermis film can be subjected to various forms of surface modification, such as composite cells on the surface of the collagen sponge, growth factors or high molecular weight polymers, etc. This will be described in detail below.

Collagen is widely used in tissue regeneration and repair due to its excellent biological properties. Currently, commercial collagen products such as gelatin sponges have been used in tissue repair and other fields. The use of other materials to modify collagen and loading factors to make it more suitable for wound repair is an important point of research. Thones et al. constructed an HA/collagen hydrogel containing hyaluronic acid (HA) sulfate to promote wound healing through the continuous release of heparin-binding EGF-like growth factor. In vitro experiments showed that hydrogels containing heparin-bound EGF induced keratinocyte migration, EGFR signaling, and HGF expression in dermal fibroblasts. In a culture model grown on pig skin, it was found that epithelial growth could be significantly enhanced [54]. Kondo et al. constructed a HA collagen sponge dressing consisting of HA and collagen of different molecular weights and added EGF to it. They found that EGF-loaded dressings significantly increased the release of VEGF and HGF in fibroblasts, promoting wound healing and granulation tissue formation [55]. Niiyama and Kuroyanagi constructed a new wound dressing composed of HA and collagen loaded with vitamin C and EGF and found that the new wound dressing promoted granulation tissue and angiogenesis and accelerated epithelial formation in SD rats and diabetic mice [56]. Cheng et al. They prepared a freeze-dried hybrid dressing composed of EGF and recombinant human collagen and found that this dressing significantly improved fibroblast proliferation adhesion and migration to the wound. Immunohistochemical results showed that wound healing rate, epithelial regeneration, and orderly arrangement and collagen deposition were significantly accelerated in rats [57].

The fabrication of hybrid scaffolds based on dECM and other natural macromolecules is considered as a candidate strategy for improving the mechanical properties of dECM. Nyambat et al. [58] developed a hybrid dECM sponge (HEMS) by incorporating rabbit dECM ADSCs with graphene oxide and genipin. This hybrid sponge has been proven in vitro to have better mechanical properties and a longer degradation time (4 weeks) than non-crosslinked ECM sponges, which are suitable for skin regeneration. Similarly, Rameshbabu et al. [59] introduced a hybrid dECM scaffold by coupling a placenta-derived dECM with SF, which integrated the

advantages of dECM and SF. This hybrid scaffold promoted the regeneration of full-thickness skin defects by stimulating cell migration and neovascularization. In another study, Kim et al. [60] combined human lung fibroblast dECM (fdECM) and porcine type I collagen to prepare bio scaffolds for skin wound healing and remodeling. Advanced skin healing with restoration of epidermal barrier function and restoration of collagen, hair follicle, and subepidermal plexus was observed in full thickness wound and diabetic ulcer models.

Conclusions

Dermis can be easily obtained from pig skin, and in the decellularization process, the resulting ECM can be surface modified in various ways to adjust mechanical properties and biological properties. It can be widely used in tissue engineering of various tissues and organs, such as chronic wounds, breast reconstruction, and abdominal wall. To summarize the 3 methods of dermis surface modification, our own results and existing literature in this field were reviewed, and the unique objectives and characteristics of each method were discussed. Each approach has an important impact on dermis surface modification, all methods and their respective combinations deserve further exploration and application. The modification of the dermis surface and the application of tissue engineering still have a long way to go. Dermis is expected to be one of the suitable materials for repairing damaged tissues and organs in tissue engineering. Researchers should strive to develop more dermis-modified methods to improve the performance of the resulting simple-to-composite biomaterials.

Reference:

1. Variksha S., Thashree M., Maya M.M. et al. (2022). Biopolymer-Based Wound Dressings with Biochemical Cues for Cell-Instructive Wound Repair. *Polymers*, *14*(24), 5371; DOI: 10.3390/polym14245371.

2. Mantha S., Pillai S. Khayambashi P. et al. (2019) Smart Hydrogels in Tissue Engineering and Regenerative Medicine. Materials, 12, 3323.

3. Viet-Nhi N. K., Chen Y. C., Dang L. H, et al. (2023) Degassing a Decellularized Scaffold Enhances Wound Healing and Reduces Fibrosis during Tracheal Defect Reconstruction: A Preliminary Animal Study. J Funct Biomater. 14(3):147. DOI: 10.3390/jfb14030147.

4. Costa A., Adamo S., Gossetti F. (2019). Biological Scaffolds for Abdominal Wall Repair: Future in Clinical Application? *Materials*, *12*(15), 2375. DOI: 10.3390/ma12152375

5. Dziki J.L., Wang D.S. Pineda et al. (2017). Solubilized extracellular matrix bioscaffolds derived from diverse source tissues differentially influence macrophage phenotype. *J. Biomed. Mater. Res. Part A*, *105*, 138–147.

6. Zhou Ji. Y., Sun T. (2018). et al. Diverse preparation methods for small intestinal submucosa (SIS): decellularization, components, and structure. *J Biomed Mater Res A*; 107:689–97.

7. Ikada Y. (1994). Surface modification of polymers for medical applications. *Biomaterials*; 15:725–36.

8. Souza J.C., Sordi M.B., Kanazawa M. (2019) et al. Nano-scale

modification of titanium implant surfaces to enhance osseointegration. *Acta Biomater*; 94:112–31.

9. Mir M., Ali M.N., Barakullah A., (2018). et al. Synthetic polymeric biomaterials for wound healing: a review. Prog Biomater, 7(1):1-21. DOI: 10.1007/s40204-018-0083-4.

10. Hien M. N., Tam Thi N., Thanh N. et al. (2023). Biomedical materials for wound dressing: recent advances and applications. RSC Adv;13(8):5509-5528. DOI: 10.1039/d2ra07673j.

11. Bonnans C., Chou J., Werb Z. (2014). Remodelling the extracellular matrix in development and disease. *Nat. Rev. Mol. Cell Biol.* 15 786–801. DOI: 10.1038/nrm3904.

12. Mansheng L., Xiao L., Bingui L. (2021) et al. Time-Resolved Extracellular Matrix Atlas of the Developing Human Skin Dermis. Front. Cell Dev. Biol., Volume 9 – 2021. DOI: 10.3389/fcell.2021.783456

13. Bonnans C., Chou J., Werb Z. (2014). Remodelling the extracellular matrix in development and disease. *Nat. Rev. Mol. Cell Biol.* 15, 786–801. DOI: 10.1038/nrm3904.

14. Quan T., and Fisher G. J. (2015). Role of Age-Associated Alterations of the Dermal Extracellular Matrix Microenvironment in Human Skin Aging: A Mini-Review. Gerontology 61, 427–434. DOI:10.1159/000371708.

15. Bonnans C., Chou J., Werb Z. (2014). Remodelling the extracellular matrix in development and disease. *Nat. Rev. Mol. Cell Biol.* 15, 786–801. DOI: 10.1038/nrm3904.

16. Dyer D. P. (2020). Understanding the mechanisms that facilitate specificity, not redundancy, of chemokine-mediated leukocyte recruitment. *Immunology* 160, 336–344. 10.1111/imm.13200.

17. Nystrom A., Bruckner-Tuderman L. (2019). Matrix molecules and skin biology. *Semin. Cell Dev. Biol.* 89 136–146. 10.1016/j.semcdb.2018.07.025.

18. Nystrom A., Bruckner-Tuderman L. (2019). Matrix molecules and skin biology. Semin. Cell Dev. Biol. *89*, 136–146. 10.1016/j.semcdb.2018.07.025.

19. Rousselle P., Montmasson M., Garnier C. (2019). Extracellular Matrix Contribution to Skin Wound Re-epithelialization. Matrix Biol. 75, 12–26. DOI:10.1016/j.matbio. 2018.01.002.

20. Brinckmann J., Hunzelmann N., Kahle B., et al. (2010). Enhanced fibrillin-2 expression is a general feature of wound healing and sclerosis: potential alteration of cell attachment and storage of TGF-beta. Lab Invest 90:739–752.

21. Yu Y., Alkhawaji A., Ding Y. et al. (2016). Decellularized scaffolds in regenerative medicine. *Oncotarget*; 7:58671–83.

22. Frantz C., Stewart K.M., Weaver V.M. (2010). The extracellular matrix at a glance. *J. Cell Sci.*;123:4195–4200. doi: 10.1242/jcs.023820.

23. Maquart F. X., Monboisse J. C. (2014). Extracellular matrix and wound healing. *Pathol. Biol.*;62:91–95. doi:10.1016/j.patbio.2014.02.007.

24. Ventura R. D., Padalhin A. R., Park C. M., Lee B. T. Enhanced decellularization technique of porcine dermal ECM for tissue engineering applications. *Mater. Sci. Eng. C.* 2019;104:109841. doi:

10.1016/j.msec.2019.109841.

25. Meyer, M. (2019). Processing of collagen based biomaterials and the resulting materials properties. *BioMed. Eng. OnLine*, *18*, 24., Meyer, M. Processing of collagen based biomaterials and the resulting materials properties. *BioMed. Eng. OnLine*,*18*, 24.

26. Gillette, B. M., Rossen, N. S., Das, N. et al. (2011). Engineering extracellular matrix structure in 3D multiphase tissues. *Biomaterials*, *32*, 8067–8076.

27. Achilli, M., Mantovani, D. (2010). Tailoring Mechanical Properties of Collagen-Based Scaffolds for Vascular Tissue Engineering: The Effects of pH, Temperature and Ionic Strength on Gelation. *Polymers*, *2*, 664–680.

28. Fernández-Pérez J., Ahearne M. (2019). The impact of decellularization methods on extracellular matrix derived hydrogels. *Sci. Rep.*;9:1–12. doi:10.1038/s41598-019-49575-2.

29. Cichoń M. A, Elbe-Bürger A. (2023). Epidermal/Dermal Separation Techniques and Analysis of Cell Populations in Human Skin Sheets. J Invest Dermatol.;143(1):11-17.e8. DOI: 10.1016/j.jid.2022.10.012.

30. Macagonova, O., Risnic, D., Cociug, A, et al. (2021) Comparative analysis of the skin decellularization methods. Moldovan Medical Journal 64(2), 79-86. https://doi. org/10.52418/moldovan-med-j.64-2.21.14. DOI:10.1111/1523 1747.ep1268106.

31. Dar-Jen H., Periasamy S., Ko-Chung Y. (2020). Protocols for the preparation and characterization of decellularized tissue and organ scaffolds for tissue engineering. biotechniques 70 (2), 107-115. DOI.:10.2144/btn-2020-0141.

32. Liyan Jian, Yu C., Ying, Z. (2019). Dermal-Epidermal Separation by Chemical. Epidermal Cells. Methods in Molecular Biology, vol 2109. Pp. 31–33. DOI: 10.1007/7651_2019_266.

33. Yang J. Z., Qiu L. H., Xiong S. H. (2020). Decellularized adipose matrix provides an inductive microenvironment for stem cells in tissue regeneration World J. Stem. Cells, 12, pp. 585-603.

34. Dong Li, Y. Song, Y.et al. (2021): MSC-derived immunomodulatory extracellular matrix functionalized electrospun fibers for mitigating foreign-body reaction and tendon adhesion. Acta Biomater., Oct 1:133:280-296. DOI: 10.1016/j.actbio.2021.04.035.

35. Badylak S. F. (2002). The extracellular matrix as a scaffold for tissue reconstruction. *Semin. Cell Dev. Biol.*; 13:377–383. DOI:10.1016/S1084952102000940.

36. Puhl D. L., Mohanraj D., Nelson D. W., et al. (2022). Designing electrospun fiber platforms for efficient delivery of genetic material and genome editing tools. *Adv. Drug Deliv. Rev.*;183:114161. DOI: 10.1016/j.addr.2022.114161.

37. Patil P., Russo K. A., McCune J. T. et al. (2021). ROS-Degradable Polythioketal Urethane Foam Dressings to Promote Porcine Skin Wound Repair. *bioRxiv*. DOI:10.1101/2021.05.21.445175.

38. Vernon R. B., Gooden M. D., Lara, S. L. et al. (2005). Native fibrillar

collagen membranes of micron-scale and submicron thicknesses for cell support and perfusion. *Biomaterials*, *26*, 1109–1117.

39. Ventura R. D., Padalhin A. R., Park C. M. et al. (2019). Enhanced decellularization technique of porcine dermal ECM for tissue engineering applications. *Mater. Sci. Eng. C Mater. Biol. Appl.*,*104*, 1–12.

40. Araujo T. A., Almeida M. C., Avanzi, I. et al. (2021). Collagen Membranes for Skin Wound Repair: A Systematic Review. *J. Biomater. Appl.*, *36*, 95–112.

41. Hakim T. R., Pratiwi A., Jamhari N., et al. (2021). Extraction of collagen from the skin of Kacang goat and production of its hydrolysate as an inhibitor of angiotensin converting enzyme. Trop Anim Sci J. 2021;44(2):222-228. DOI: 10.5398/tasj..44.2.222. 19.

42. He L, Lan W, Zhao Y. et al. (2020). Characterization of biocompatible pig skin collagen and application of collagen-based films for enzyme immobilization. RSC Advances. 10(12):7170-7180. DOI:10.1039/C9RA10794K.

43. Sedlarik K.M., Schoots J. A., Oosterbaan, J. P. et al. (1992). Healing of a deep skin wound using a collagen sponge as dressing in the animal experiment. Aktuelle Traumatol; 22(5): 219-28.

44. Yufei S., Hongjian Z., Xin Z. (2020). A comparative study of two porous sponge scaffolds prepared by collagen derived from porcine skin and fish scales as burn wound dressings in a rabbit model. *Regenerative Biomaterials*, Volume 7, Issue 1, pp. 63–70. DOI: 10.1093/rb/rbz036.

45. Zhao Y., Fan J., Bai S. (2019). Biocompatibility of injectable hydrogel from decellularized human adipose tissue *in vitro* and *in vivo*. *J Biomed Mater Res*; 107:1684–94.

46. Yi Y., Guang-Wei Y., Jian-Juan L. (2024). Fabrication of levofloxacin-loaded porcine acellular dermal matrix hydrogel and functional assessment in urinary tract infection. *Journal of Nanobiotechnology* volume 22, Article number:52, 1167.

47. Lee C, Shim S., Jang H. et al. (2017). Human umbilical cord blood-derived mesenchymal stromal cells and small intestinal submucosa hydrogel composite promotes combined radiation-wound healing of mice. *Cytotherapy*; 19:1048–59.

48. Hsu P. W., Salgado C. J., Kent K., et al. (2009). Evaluation of porcine dermal collagen (Permacol) used in abdominal wall reconstruction. *J. Plast. Reconstr. Aesthetic Surg.*; 62:1484–1489. DOI:10.1016/j.bjps.2008.04.060.

49. Veves A., Sheehan P., Pham H.T. (2002). A randomized, controlled trial of Promogran (a collagen/oxidized regenerated cellulose dressing) vs. standard treatment in the management of diabetic foot ulcers. *Arch. Surg.*; 137:822–827. DOI: 10.1001/archsurg.137.7.822.

50. Kuo S., Kim H. M., Wang Z., et al. (2018). Comparison of two decellularized dermal equivalents. *J. Tissue Eng. Regen. Med.*; 12:983–990. DOI:10.1002/term.2530.

51. Valentin J. E., Badylak J. S., McCabe G. P., et al. (2006) Extracellular matrix bioscaffolds for orthopaedic applications: A comparative histologic study.

JBJS; 88:2673–2686. DOI:10.2106/JBJS.E.01008.

52. Tierney B.P. (2021). Comparison of 30-day Clinical Outcomes with SimpliDerm and AlloDerm RTU in Immediate Breast Reconstruction. *Plast. Reconstr. Surg. Glob. Open.*;9:e3648. DOI:10.1097/GOX.0000000000003648.

53. Veves A., Sheehan P., Pham H. T. (2002). A randomized, controlled trial of Promogran (a collagen/oxidized regenerated cellulose dressing) vs. standard treatment in the management of diabetic foot ulcers. *Arch. Surg.*;137:822–82754.

54. Thönes S., Rother S., Wippold T., et al. (2019) Hyaluronan/collagen hydrogels containing sulfated hyaluronan improve wound healing by sustained release of heparin-binding EGF-like growth factor. Acta Biomater.;86:135–47. DOI: 10.1016/j.actbio.2019.01.029.

55. Kondo S., Kuroyanagi Y. (2012). Development of a wound dressing composed of hyaluronic acid and collagen sponge with epidermal growth factor. J Biomat Sci-Polym E.;23(5): 629–43. DOI:10.1163/092050611X555687.

56. Niiyama H., Kuroyanagi Y. (2014). Development of novel wound dressing composed of hyaluronic acid and collagen sponge containing epidermal growth factor and vitamin C derivative. J Artif Organs.;17(1):81–7. DOI: 10.1007/s10047-013-0737-x.

57. Cheng Y., Huang S., Yu F., et al. (2020) Hybrid freeze-dried dressings composed of epidermal growth factor and recombinant human-like collagen enhance cutaneous wound healing in rats. Front Bioeng Biotechnol.;8:8. DOI: 10.3389/fbioe.2020.00742.

58. Nyambat B., Chen C. H., Wong P. C. et al. (2018). Genipin-crosslinked adipose stem cell derived extracellular matrix-nano graphene oxide composite sponge for skin tissue engineering J. Mater. Chem. B, 6, pp. 979-990.

59. Rameshbabu A. P., Bankoti K., Datta S., et al. (2018). Silk sponges ornamented with a placenta-derived extracellular matrix augment full-thickness cutaneous wound healing by stimulating neovascularization and cellular migration ACS Appl. Mater. Interfaces, 10, pp.16977-16991.

60. Kim H. S., Hwang H. J., Kim H. J., et al. (2022). Effect of decellularized extracellular matrix bioscaffolds derived from fibroblasts on skin wound healing and remodeling Front. Bioeng. Biotechnol.,10, Article 865545.

Резюме.

Введение: *Тканевая инженерия со временем развивается благодаря разработке биополимерных каркасов, которые должны обладать способностью стимулировать адгезию и пролиферацию клеток in vitro и in vivo. Модификация поверхности материала каркаса оказывает большое влияние на биосовместимость и функциональность материалов. Дерма – это слой соединительной ткани между эпидермисом и подкожной клетчаткой. Он имеет волокнистую структуру, состоящую из коллагена, эластических волокон и других внеклеточных компонентов, включая кровеносные и лимфатические сосуды, нервные окончания, волосяные фолликулы и железы. Путем деэпителизации и децеллюляризации дермы получают бесклеточный матрикс, выделенный из эпидермиса и гиподермы, обладающий хорошими тканемеханическими свойствами, регенеративной активностью и пригодный для клеточной адгезии, пролиферации и дифференцировки. В последние годы внеклеточный матрикс дермы широко используется при реконструкции поврежденной кожи.*

Цель: *В данной статье обсуждаются методы модификации поверхности дермы для оптимизации и улучшения характеристик биоматериалов, полученных из дермы, абсорбции и седиментации белков, составления рецептур и комбинирования с лекарственными средствами, а также адаптации к дефектам тканей и их регенерации.*

Материалы и методы: *Материалом исследования служила свиная кожа, обработанная физико-химическими методами с удалением всех эпидермальных и дермальных клеток.*

Результаты: *получены неиммуногенные, биосовместимые и биоразлагаемые биоматериалы с сохранением оставшегося биоактивного дермального матрикса, модифицирующие форму для улучшения биологической активности клеток на поверхности материала, оптимизации пористости, прочности без изменения целостности и физических свойств материала. общий скелет материала и удовлетворяет любые потребности в уходе за кожей, а также в адаптации к дефектам тканей и регенерации ран.*

Заключение: *Оптимальное сочетание этих методов обеспечивает улучшение поверхности дермы для использования в регенеративной медицине.*

Ключевые слова: *дерма, модификация поверхности, каркасы in vitro, тканевая инженерия.*

Funding: This study was funded by the institutional project ,,Development of the three-dimensional matrices from the biological structures for the treatment of critical tissue defects" Nr. 08020, and the project for young researchers, ,,Development of the biological dressings for the regeneration of the skin wounds by the tissue engineering" with the number 23.70105.8007.02T.

Статья отправлена: 20.08.2024 г.