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THE USE OF SERICIN OBTAINED ON THE BASIS OF LOCAL RAW MATERIALS TO TREAT SKIN BURNS AND ITS SCARS

Resume: A burn is a type of injury to the skin, or other tissues, caused by heat, cold, electricity, chemicals, friction, or radiation. Most burns are due to heat from hot liquids (called scalding), solids, or fire. Compared to first- and second-degree burns, third-degree burns pose a greater risk for complications. However, all burns increase the risk of infection. So the difficulties of burns are hazardous and can lead to disability and death, along with several pathologies (tetanus, sepsis, hypothermia, hypovolemia, etc.). Sericin, a substance derived from silk, may have advantages in the treatment of burns. We will discuss this in this article.

Keywords: Burns, electricity, chemical, friction, radiation, pathology, tetanus, sepsis, hypothermia, hypovolemia, sericin.

ПРИМЕНЕНИЕ СЕРИЦИНА, ПОЛУЧЕННОГО НА ОСНОВЕ МЕСТНОГО СЫРЬЯ, ДЛЯ ЛЕЧЕНИЯ ОЖОГОВ КОЖИ И ЕЕ РУБЦОВЫХ ПОВРЕЖДЕНИЙ

Резюме: Ожоги - это тип повреждения кожи или других тканей, вызванный жарой, холодом, электричеством, химическими веществами, трением или радиацией. Большинство ожогов вызвано горячими жидкостями, твердыми телами или огнем. По сравнению с ожогами первой и второй степени ожоги третьей степени представляют больший риск осложнений. Однако все ожоги в целом увеличивают риск заражения. Таким образом, осложнения ожогов очень опасны и могут привести к инвалидности и летальному исходу наряду с рядом патологий (столбняк, сепсис, переохлаждение, гиповолемия и др.). Серицин как вещество,

получаемое из шелка, может иметь ряд преимуществ при лечении ожогов. В этой статье освещается ряд вопросов о преимуществах применения данного вещества при указанной патологии.

Ключевые слова: ожоги, электричество, химия, трение, радиация, патология, столбняк, сепсис, гипотермия, гиповолемия, серицин.

Introduction: A burn is a type of injury to the skin, or other tissues, caused by heat, cold, electricity, chemicals, friction, or radiation. Burns can also occur as a result of self-harm or violence between people. Sericin is a protein created by Bombyx mori (silkworms) in the production of silk. Silk is a fiber produced by the silkworm in production of its cocoon. It consists mainly of two proteins, fibroin, and sericin.

Levels of burns. [1] Burns that affect only the superficial skin layers are known as superficial or first-degree burns [2,3]. They appear red without blisters, and pain typically lasts around three days. When the injury extends into some of the underlying skin layers, it is a partial-thickness or second-degree burn. Blisters are frequently present, and they are often very painful. Healing can require up to eight weeks, and scarring may occur. In a full-thickness or third-degree burn, the injury extends to all layers of the skin. Often there is no pain, and the burnt area is stiff. Healing typically does not occur on its own. A fourth-degree burn additionally involves injury to deeper tissues, such as muscle, tendons, or bone. The burn is often black and frequently leads to loss of the burned part (Fig.1).

Complications of burns. Several complications may occur, with infections being the most common. [4] In order of frequency, potential complications include pneumonia, cellulitis, urinary tract infections, and respiratory failure. Risk factors for the disease include burns of more than 30% TBSA, full-thickness burns, extremes of age (young or old), or burns involving the legs or perineum. [5] Pneumonia occurs particularly common in those with inhalation injuries. Anemia secondary to full-thickness burns of greater than 10% TBSA is common. [6] Electrical burns may lead to compartment syndrome or rhabdomyolysis due to muscle breakdown. [7] Blood clotting in the veins of the legs is estimated to occur in 6 to 25% of people. The hypermetabolic state that may persist for years after a significant burn can decrease bone density and a loss of muscle mass. [8] Keloids may form after a burn, particularly in those who are young and dark-skinned. [9] Following a burn, children may have significant psychological trauma and experience post-traumatic stress disorder.

Type	Layers involved	Appearance	Texture	Sensation	Healing Time	Prognosis
Superficial (first-degree)	Epidermis	Red without blisters	Dry	Painful	5–10 days	Heals well. Repeated sunburns increase the risk of skin cancer later in life.
Superficial partial thickness (second-degree)	Extends into superficial (papillary) dermis	Redness with clear blister. Blanches with pressure.	Moist	Very painful	2–3 weeks	Local infection (cellulitis) but no scarring typically
Deep partial thickness (second-degree)	Extends into deep (reticular) dermis	Yellow or white. Less blanching. May be blistering.	Fairly dry	Pressure and discomfort	3–8 weeks	Scarring, contractures (may require excision and skin grafting)
Full thickness (third-degree)	Extends through entire dermis	Stiff and white/brown. No blanching.	Leathery	Painless	Prolonged (months) and incomplete	Scarring, contractures, amputation (early excision recommended)
Fourth-degree	Extends through entire skin, and into underlying fat, muscle and bone	Black; charred with eschar.	Dry	Painless	Requires excision	Amputation, significant functional impairment and in some cases, death.

Figure 1. Primary data on burns are shown in tabular form.

When quickly and adequately treated, the outlook for first- and second-degree burns are good. These rarely burn scar but can result in a change in the pigment of the skin that was burned. The key is to minimize further damage and infection. Extensive damage from severe second-degree and third-degree burns can lead to problems in deep skin tissues, bones, and organs. Therefore, it is essential to gain adequate physical treatment for burns. Patients may require: surgery, physical therapy, rehabilitation, lifelong assisted care [10].

Burns are acute traumatic wounds that can be life-threatening. Despite improvement in burn wound care, severe burns are associated with high morbidity and disability [12,13]. For partial-thickness and full-thickness burns, acute burn management involves multiple activities, including protecting the wound from further injury, initial cleansing and debridement, and determining dressings with or without a topical antimicrobial agent [14,15]. In addition, fluid resuscitation, hypothermia prevention, and pain management are also critical aspects of burn care andmanagement[13,16]. For extensive full-thickness burns, standard surgical procedures involve wound excision/debridement and coverage with an autologous split-thickness skin graft (STSG) from a donor site [17]. For patients with extensive burns and limited availability of suitable donor skin, the skin grafts are sometimes meshed and expanded to allow more excellent coverage. However, maturation of the meshed graft may take several weeks and, depending on the severity and location of the wound and the degree of meshing, the cosmetic outcome is often unsatisfactory. In addition, complications such as infection or contractures may occur, which can result in further treatments and procedures and prolongation of healing [18]. Therefore, there is a need to develop novel therapies to improve acute burn management and patient quality of life [19].

We want to suggest using a sericin substance to treat burns because this substance can have several advantages in the treatment process. Why were we interested in sericin? Because [11]: the damage to the skin is most prominent and evident as it is our first line of defense and unremittingly under attack by biological and environmental factors. The restoration of the skin is dependent on the extent of the injury. To explore the prospects of new biomimetic material, a bi-layered skin construct is fabricated in vitro with nonmulberry silk protein sericin and chitosan hydrogels using human dermal fibroblasts and keratinocytes. The in vitro analysis of the hydrogels showed enhanced adhesion, proliferation, and migration of skin cells with coordinated interaction amongst themselves, leading to the synthesis of collagen IV and matrix metalloproteinase (MMP2 and MMP9). The in vivo evaluation indicates the regeneration of skin with densely packed collagen and matured blood vessels in the animals implanted with sericin-containing hydrogels.

Moreover, the local and systemic immune response determined in vivo exhibits the biosafety of sericin-based hydrogels. In addition, the cross-sectional analysis of the implanted hydrogels displays infiltration of the skin tissue cells into the hydrogels marking their biocompatibility and non-toxicity. Finally, the cumulative research of the in vitro and in vivo observations demonstrates that the sericin-based hydrogels are non-inflammatory, supporting the skin tissue's regeneration and repair.

A group of scientists commented on sericin based on their research: [11] The fabricated hydrogels of sericin-chitosan enhance the attachment, proliferation, and migration of the skin cells (fibroblasts and keratinocytes), leading to the formation of bi-layered skin like construct. The presence of sericin enhances collagen and matrix metalloproteinase, which forms the extracellular matrix supporting skin tissue growth. When implanted subcutaneously in Wistar rats, these hydrogels show remodeling similar to the normal skin tissue with the intact epidermis and densely packed collagen fibrils in the dermis. The animals implanted with sericin-containing hydrogels exhibit more vascularisation in the dermis without any additional growth factor signifying the role of sericin in promoting the formation of blood vessels and thereby nourishing the dermal layer of the newly formed skin tissue. The infiltration of the skin cells into the hydrogels validates their biocompatibility. The in vitro and in vivo analysis show that sericin-based hydrogels are biocompatible, non-inflammatory, and promote the reconstruction of the skin tissue. The present study has established that sericin-based hydrogels promote skin repair.

According to another group of scientists: [20] Among naturally occurring polymers, silk fibroin and sericin have attracted much attention in the field of tissue engineering; however, clinical application of silk fibroin/sericin scaffolds in a combined form has been questioned due to the possible pro-inflammatory reaction against native silk and fibroin/sericin 3D constructs. The objective of this study was to fabricate 3D spongy fibroin/sericin scaffolds and to explore the structural, biological, and immunological properties of different ratios of fibroin and sericin. Structural characterization revealed a highly porous structure (>91%) with a large surface area and water uptake capacity for all different fibroin/sericin scaffolds. Notably, the scaffolds showed enhanced mechanical properties and a higher degradation rate with increasing sericin content. Excellent cell attachment and no significant cytotoxicity were observed in all scaffold types seven days after seeding of osteoblast-like MG63 cells. Gene expression of pro-inflammatory markers TNF-α, CXCL10 and CD197 as well as TNF-α secretion by THP-1-derived macrophages revealed no significant immune response to all fibroin/sericin scaffold types when compared to sericin-free F1:S0 samples and a TCP (Mϕ) control group. These results demonstrate that spongy fibroin/sericin scaffolds can support the growth of osteoblast-like cells without eliciting a pro-inflammatory response, thus being a promising material for bone tissue engineering.

Sericin is the waste by-product of silk industries and exhibits prospects to be utilized in this field, attributing its beneficial features [21–25]. Both mulberry and non-mulberry sericin is reported to have anti-oxidant, UV resistant, and anti-apoptotic properties [26–29]. Skin tissue needs these features ad they support the keratinocyte cell growth and regeneration. Sericin possesses these properties, making it an efficient biomaterial to be explored in this work area. For proper cell attachment and viability, it is required that the scaffolds exhibit properties of the natural extracellular matrix (ECM). This supports the proliferation, migration, and differentiation of the cells for specific tissue or organ. Sericin promotes the activation of collagen production and generates inadequate immune responses [30–32]. Skin tissue consists of three layers, i.e., the epidermis (outer), dermis (inner), and subcutaneous tissue (internal). The effective regeneration of the skin layers is needed for proper healing along with vascularization [33]. Combined effects of human keratinocytes and fibroblasts with allogeneic or xenogeneic decellularized dermis have been studied to understand the cell-cell interactions in vitro [34]. The graft materials must not be toxic, immunogenic or inflammatory and without any risk of transmissible disease. Sericin and its blends have potential pharmacological, biomedical, and biotechnological applications [21–24,29]. The highly hydrophilic nature of sericin is suggested to contribute to wound healing without showing any elevated immune response [31]. Sericin promotes the adhesion and growth of human skin cells (keratinocytes and fibroblasts), thus healing the wound [35], which is also tested clinically [36]. Due to the high hygroscopic nature of the sericin, it cannot be utilized alone and needs to be blended or cross-linked with other gel-forming ingredients to increase the matrix stability. Chitosan is an antibacterial biopolymer with prospects in wound repair [37,38]. Chitosan enhances the migration of polymorphonuclear leukocytes [39,40]. Chitosan and sericin are expected to be potential good natural raw materials for the suitable matrix to support the growth of skin tissue in vitro and/or in vivo with potential advantages like biocompatibility, chemical versatility, and controlled degradability.

Conclusion: In this article, we explained that the relevance and complications of burns are very dangerous. We also believe that new research is needed to treat burns. Scars that remain on the skin after a burn are also a problem. At the same time, we have presented the results of research and data on the substance sericin. In conclusion, in-depth studies on the use of sericin biomaterial in treating burns should be conducted. We hope that this article will contribute to this.

References

1. World Health Organization. September 2016. Archived from the original on 21 July 2017. Retrieved 1 August 2017.

2. Tintinalli, Judith E. (2010). Emergency Medicine: A Comprehensive Study Guide (Emergency Medicine (Tintinalli)). New York: McGraw-Hill Companies. pp. 1374–1386. ISBN 978-0-07-148480-0.

3. Granger J (January 2009). "An Evidence-Based Approach to Pediatric Burns". Pediatric Emergency Medicine Practice. 6 (1). Archived from the original on 17 October 2013.

4. Herndon D, ed. (2012). "Chapter 3: Epidemiological, Demographic, and Outcome Characteristics of Burn Injury". Total burn care (4th ed.). Edinburgh: Saunders. p. 23. ISBN 978-1-4377-2786-9.

5. King C, Henretig FM, King BR, Loiselle J, Ruddy RM, Wiley II JF, eds. (2008). Textbook of pediatric emergency procedures (2nd ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins. p. 1077. ISBN 978-0-7817-5386-9. Archived from the original on 22 May 2016.

6. Granger J (January 2009). "An Evidence-Based Approach to Pediatric Burns". Pediatric Emergency Medicine Practice. 6 (1). Archived from the original on 17 October 2013.

7. Brunicardi C (2010). "Chapter 8: Burns". Schwartz's principles of surgery (9th ed.). New York: McGraw-Hill, Medical Pub. Division. ISBN 978-0-07-154769-7.

8. Rojas Y, Finnerty CC, Radhakrishnan RS, Herndon DN (December 2012). "Burns: an update on current pharmacotherapy". Expert Opinion on Pharmacotherapy. 13 (17): 2485–94. doi:10.1517/14656566.2012.738195. PMC 3576016. PMID 23121414.

9. Juckett G, Hartman-Adams H (August 2009). "Management of keloids and hypertrophic scars". American Family Physician. 80 (3): 253–60. PMID 19621835.

10. Medically reviewed by Modern Weng, do: Written by April Khan and Matthew Solan. https://www.healthline.com/health/burns#outlook. Updated on March 7, 2019.

11. Sapru, S., Das, S., Mandal, M., Ghosh, A. K., & Kundu, S. C. (2019). Nonmulberry silk protein sericin blend hydrogels for skin tissue regeneration - in vitro and in vivo. International Journal of Biological Macromolecules. doi:10.1016/j.ijbiomac.2019.06.121.

12. Nielson CB, Duethman NC, Howard JM, Moncure M, Wood JG. Burns: pathophysiology of systemic complications and current management. J Burn Care Res 2017;38:e469–81, doi: http://dx.doi.org/10.1097/BCR.0000000000000355.

13. Rowan MP, Cancio LC, Elster EA, Burmeister DM, Rose LF, Natesan S, et al. Burn wound healing and treatment: review and advancements. Crit Care 2015;19:243, doi:http://dx.doi. org/10.1186/s13054-015-0961-2.

14. Committee IPG. ISBI practice guidelines for burn care. Burns 2016;42:953–1021, doi:http://dx.doi.org/10.1016/j. burns.2016.05.013.

15. Wang Y, Beekman J, Hew J, Jackson S, Issler-Fisher AC, ParungaoR, et al. Burninjury: challenges andadvances inburn wound healing, infection, pain and scarring. Adv Drug Deliv Rev 2018;123:3–17, doi:http://dx.doi.org/10.1016/j. addr.2017.09.018.

16. Vigani A, Culler CA. Systemic and local management of burn wounds. Vet Clin North Am Small Anim Pract 2017;47:1149–63, doi:http://dx.doi.org/10.1016/j.cvsm.2017.06.003.

17. Orgill DP. Excision and skin grafting of thermal burns. N Engl J Med 2009;360:893–901, doi:http://dx.doi.org/10.1056/ NEJMct0804451.

18. Finnerty CC, Jeschke MG, Branski LK, Barret JP, Dziewulski P, Herndon DN. Hypertrophic scarring: the greatest unmet challenge after burn injury. Lancet (London England) 2016;388:1427–36, doi:http://dx.doi.org/10.1016/S0140-6736 (16)31406-4.

19. Foubert, P., Liu, M., Anderson, S., Rajoria, R., Gutierrez, D., Zafra, D., … Fraser, J. K. (2018). Preclinical assessment of safety and efficacy of intravenous delivery of autologous adipose-derived regenerative cells (ADRCs) in the treatment of severe thermal burns using a porcine model. Burns. doi:10.1016/j.burns.2018.05.006.

20. Siavashani, A. Z., Mohammadi, J., Rottmar, M., Senturk, B., Nourmohammadi, J., Sadeghi, B., … Maniura-Weber, K. (2020). Silk fibroin/sericin 3D sponges: The effect of sericin on structural and biological properties of fibroin. International Journal of Biological Macromolecules. doi:10.1016/j.ijbiomac.2020.02.316.

21. S.C. Kundu, B.C. Dash, R. Dash, D.L. Kaplan, Natural protective glue protein, sericin bioengineered by silkworms: potential for biomedical and biotechnological applications, Prog. Polym. Sci. 33 (10) (2008) 998–1012.

22. R.I. Kunz, R.M. Brancalhao, L.F. Ribeiro, M.R. Natali, Silkworm sericin: properties and biomedical applications, Biomed. Res. Int. 2016 (2016) 8175701.

23. T.T. Cao, Y.Q. Zhang, Processing and characterization of silk sericin from Bombyx mori and its application in biomaterials and biomedicines, Mat Sci Eng C-Mater 61 (2016) 940–952. Fig. 7. Histological (Masson's trichrome) and immunohistochemical analysis (CD 31) of in the skin tissue obtained four weeks post-implantation of the designed sericin based hydrogels showing the formation of blood vessels. Scale bar represents 1000 μm (CD31) and 500 μm (for the magnified images). Black arrows represent the blood vessels. 552 S. Sapru et al. / International Journal of Biological Macromolecules 137 (2019) 545–55.

24. L. Lamboni, M. Gauthier, G. Yang, Q. Wang, Silk sericin: a versatile material for tissue engineering and drug delivery, Biotechnol. Adv. 33 (8) (2015) 1855–1867.

25. S.C. Kundu, B. Kundu, S. Talukdar, S. Bano, S. Nayak, J. Kundu, B.B. Mandal, N. Bhardwaj, M. Botlagunta, B.C. Dash, C. Acharya, A.K. Ghosh, Invited review nonmulberry silk biopolymers, Biopolymers 97 (6) (2012) 455–467.

26. J.P. Kumar, B.B. Mandal, Antioxidant potential of mulberry and non-mulberry silk sericin and its implications in biomedicine, Free Radical Bio Med 108 (2017) 803–818.

27. R. Dash, C. Acharya, P.C. Bindu, S.C. Kundu, Antioxidant potential of silk protein sericin against hydrogen peroxide-induced oxidative stress in skin fibroblasts, BMB Rep. 41 (3) (2008) 236–241.

28. R. Dash, M. Mandal, S.K. Ghosh, S.C. Kundu, Silk sericin protein of tropical tasar silkworm inhibits UVB-induced apoptosis in human skin keratinocytes, Mol. Cell. Biochem. 311 (1–2) (2008) 111–119.

29. Y.Q. Zhang, Applications of natural silk protein sericin in biomaterials, Biotechnol. Adv. 20 (2) (2002) 91–100.

30. P. Aramwit, S. Kanokpanont, T. Nakpheng, T. Srichana, The effect of sericin from various extraction methods on cell viability and collagen production, Int. J. Mol. Sci. 11 (5) (2010) 2200–2211.

31. P. Aramwit, S. Kanokpanont, W. De-Eknamkul, T. Srichana, Monitoring of inflammatory mediators induced by silk sericin, J. Biosci. Bioeng. 107 (5) (2009) 556–561.

32. Z. Jiao, Y. Song, Y. Jin, C. Zhang, D. Peng, Z. Chen, P. Chang, S.C. Kundu, G. Wang, Z. Wang, L. Wang, In vivo characterizations of the immune properties of sericin: an ancient material with emerging value in biomedical applications, Macromol. Biosci. 17 (12) (2017).

33. S. MacNeil, Biomaterials for tissue engineering of skin, Mater. Today 11 (5) (2008) 26–35.

34. C.A. Harrison, M.J. Heaton, C.M. Layton, S. Mac Neil, Use of an in vitro model of tissueengineered human skin to study keratinocyte attachment

and migration in the process of reepithelialization, Wound Repair Regen. 14 (2) (2006) 203–209.

35. T. Siritientong, J. Ratanavaraporn, T. Srichana, P. Aramwit, Preliminary characterization of genipin-cross-linked silk sericin/poly(vinyl alcohol) films as twodimensional wound dressings for the healing of superficial wounds, Biomed. Res. Int. 2013 (2013), 904314 13.

36. T. Siritientong, A. Angspatt, J. Ratanavaraporn, P. Aramwit, Clinical potential of a silk sericin-releasing bioactive wound dressing for the treatment of split-thickness skin graft donor sites, Pharm. Res. 31 (1) (2014) 104–116.

37. K. Mizuno, K. Yamamura, K. Yano, T. Osada, S. Saeki, N. Takimoto, T. Sakurai, Y. Nimura, Effect of chitosan film containing basic fibroblast growth factor on wound healing in genetically diabetic mice, J. Biomed. Mater. Res. A 64A (1) (2003) 177–181.

38. H. Liu, C.Y. Wang, C. Li, Y.G. Qin, Z.H. Wang, F. Yang, Z.H. Li, J.C. Wang, A functional chitosan-based hydrogel as a wound dressing and drug delivery system in the treatment of wound healing, RSC Adv. 8 (14) (2018) 7533–7549.

39. S. Kim, Competitive biological activities of chitosan and its derivatives: antimicrobial, antioxidant, anticancer, and anti-inflammatory activities, Int J Polym Sci (2018), 1708172 13.

40. Y. Usami, Y. Okamoto, S. Minami, A. Matsuhashi, N.H. Kumazawa, S. Tanioka, Y. Shigemasa, Chitin and chitosan induce migration of bovine polymorphonuclear cells, J. Vet. Med. Sci. 56 (4) (1994) 761–762.