WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 13, Issue 2, 445-457. Review Article ISSN 2277–7105

A NEW INNOVATION OF KERATIN BASED DRESSING IN SKIN WOUND HEALING AND TISSUE REGENERATION

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Article Received on
01 December 2023,

Revised on 22 Dec. 2023,
Accepted on 11 Jan. 2024

DOI: 10.20959/wjpr20242-31065

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ABSTRACT

Chronic wounds are a major issue that takes longer time than usual and is difficult to heal. Various potential dressing methods are studied on both healthy and unhealthy people to look over its potential and effectiveness to heal the wound in a short time. Anciently, traditional dressing was used. But in recent days, keratin is bringing out an evolutionary change in wound healing treatment. This development takes the help of natural materials to cover-up the surface of the wound to avoid direct exposure to atmosphere, that may be interactive to the wound, followed by any further infection, thus slowing down the healing process. Keratin is a versatile protein that activates the skin cells that stimulate the production of small peptides into the wound bed, which gradually facilitates healing and also used as tissue regeneration medicine. In this technique high sterility is maintained. A single pack is advised to use for a single patient to avoid any contamination. A proper packaging of the medicament should be overview during purchasing to keep away any kind of incompatibility or irritation among the patient and the medicaments. On the other hand, keratin is not found to show any adverse effect till date. So, it can be considered as one of the most convenient methods to get rid over wounds.

KEYWORDS: Keratinocytes, Peptide, Scheloprotein, tissue regeneration medicine, wound healing.

INTRODUCTION

Chronic wound can be defined as a severe lesion that do not get cured within a specific and an expected time. It takes longer time than usual to heal. Chronic wound is a worldwide disease and take a number of years to heal or even may not heal ever. Impaired wound is a common severe medical problem. Chronic wound can occur as a result of multiple factors including irregular circulation, nerval dysfunction, stiff body movements, poor respiration, hypertension, trauma or any genetic disorders. It is a long lasting and tenacious illness. Generally, these types of diseases cause severe pain but, in some cases, may not cause pain depending upon the site of illness and physical condition of the patient. These types of patients need to undergo proper treatment and care to avoid further infection. Treatments may include wound cleansing, dressing or surgical operations.[1]

A good healing is the one that undergo speedy recovery with cost effectiveness so that each and every one can afford at a minimal cost along with minimizing pain and burning sensation. Wounds show best recovery if kept dried.[2] So, it is always advisable to inhibit the mediation of water vapour between the environment and the wound surface. Whenever dressing is done, its suggested to make the processing even quicker to let the wound not exposed in free atmosphere for a longer period of time.[3]

Keratin is a non-dissolving, fibrous, multi-functioning protein structure with some specific physicochemical properties that makes up desquamation, also known as schleroprotein. Keratin is present in nails, hair, horn, beaks, claws and scales of skin that usually function as providing protection, haunting, beauty and self-defence.[4] Keratin is further divided into alpha and beta. Body enriched with keratin helps to strengthen nails, hair and make skin soft and smooth. Keratin is available in different forms and size as well from micro-scale to centimetre-scale. Keratin is mostly present in epidermis layer of specialized cells. Enrichment of keratin helps to make new scales on the skin.[5]

Keratin dressing is one of the most widely used treatment for chronic wound. Nowadays keratin is being used to cover and get rid over chronic wounds using different technologies. The basic fundamentals of keratin dressing are to release keratin peptides at the affected site, which facilitates the activation of keratinocytes over the affected site, inducing them to

accumulate new cells over the wound bed, thus healing the wound.[6] It is found to be less costly and more effective. Keratin treatment in chronic wound works only when the biochemical properties trigger out which accelerate the rate of healing even in severe condition.[7] By the help of keratin, formation of a matrix-like structure over the wound facilitates healing and enhance the efficacy towards cure. Keratin dressing formulation is available in different forms like foam, films or spray. Keratin gel or ointment is applied on dry wound generally. keratin-based products (a thick keratin gel (keragel®), a thin keratin gel (keragelT®), and a keratin matrix (keramatrix®), from the Replicine® range.[8]

Skin layers and wound healing strategy

Skin is known to be the largest organ of body consisting of follicle sac cavity gland. It helps in protection of body from external environment, touch active, release waster as sweat. Skin consists of a number of layers with different thickness and consistency. Skin is composed of three layers.

i) Epidermis (The top most layer that is responsible for touch sensation).

ii) Dermis.

iii) Hypodermis (Inner most layer where fats decompose).

The maximum critical keratins involved in wound recuperation are krt16/krt17-krt6. All through the first hours after wounding, krt16/krt17-krt6 is being extraordinarily expressed, on the price of krt10-krt1, which makes it less difficult to promote proliferation over differentiation.[9] Its miles believed that krt6 is wanted to aid the stableness of krt16, which in vivo creates krt6/krt16 heteropolymers.[10] On top of that, krt6 directly interacts with src kinase, lowering its pastime, which weakens mobile migration in wounded skin. Migrating cells missing krt6a/krt6b proteins confirmed drastically reduced cell-cellular adhesion, normally leaving gaps between cells. In comparison, healthy cells from the manipulate organization made prepared systems after cell migration.[11]

Keratin-17 (krt-17) is responsible for keratinocyte proliferation. Krt-17 null keratinocytes are smaller, have reduced velocity of protein translation associated with reduced mtor/akt signal, which has a direct effect on keratinocytes proliferation.[12] Every other function of krt-17 is to support the phosphorylation of stat3 and the transportation of this protein to the cellular nucleus. This will increase translation of d1 cyclin this is important for the right proliferation of keratinocytes.[13] Antimicrobial efficacy is one of the maximum essential requirements for current scaffolds for wound care, tissue engineering, and biomedical applications as an

entire.[14] It should be noted that keratin itself famous antimicrobial hobby, even though it isn't always awesome as compared to the hobby of silver nanoparticles, it's far significant. Regardless of the supply of keratin (hair, fur, or feathers), the materials show off antimicrobial properties which can be better via the addition of antimicrobial materials or tablets (e.g., mupirocin).[15] Konop et al.[16,17] confirmed that insoluble fraction of keratin scaffolds alone or with the addition of silver nanoparticles show off antimicrobial residences against s. Aureus and e. Coli in vitro. Furthermore, they do no longer study the sign of bacterial infection in keratin-handled wounds in diabetic mice. Further, every other group confirmed that keratin biomaterial alone or mixed with antibacterial marketers possess antimicrobial residences.[18]

Advantages keratin based dressing in skin wound healing

Keratin substances have been significantly used in tissue engineering and regenerative medicine owing to their organic function, structural aid, extremely good biocompatibility, and favourable biodegradability traits. Accordingly, those homes permit scientists to create a brand-new sort of wound dressing that could beautify the recuperation system in particular in persistent non restoration wounds.[19] It should be mentioned that keratins are worried in intracellular signalling pathways, e.g., protection from stress, apoptosis, and wound recuperation.[20] The physicochemical and organic houses of various biomaterials, we are able to create a brand-new material that can be used for biomedical packages, consisting of wound dressing or drug transport systems. Wounds are healed by various techniques depending upon the patients age, physical condition and pre-medical cases. Numerous in vitro research on one of kind cellular traces were shown that keratin biomaterials are biocompatible and assist cell growth Additionally, they possess a hydrophilic surface, which is absent in many artificial polymers Keratins may additionally have ability as conduit fillers due to the fact they are cheaper, easy to use, inherently bioactive and biocompatible.[21] Similarly, keratins extracted by way of an oxidation technique may be separated into different fractions of alpha-, beta-, and gamma- keratin consistent with their solubility and are suitable for fabricating the biomedical gels, that have the capability to comply directly to the irregularly fashioned disorder in a minimally invasive manner. Because of this, the maximum used keratin shape as a conduit filler for nerve tissue engineering is kos.[22] Keratins own many essential functions suitable for wound dressing together with gel-forming potential upon absorption of wound exudates, precise water absorptivity, best water vapor transmission charge, nontoxicity and biodegradability. Furthermore, keratin derivatives aren't liable to speedy proteolytic

breakdown, hence they can engage with the proteolytic wound surroundings to facilitate the recuperation method.[23]

Keratin based biomaterials used in wound healing

In current years, the use of recent keratin-based wound dressings represents a unique method to wound control in medical practice. Keratin based totally biomaterials have an intrinsic capacity to self -assembly, biocompatibility, biodegradation and support mobile proliferation. This belonging of self-meeting has been investigated appreciably at each the nanoscale and macro scale stages, and it allows them to polymerize into porous scaffolds.[24] Over the last three decades, many investigations have been carried out to manufacture new keratin-based totally biomaterials within the shape of movies, sponges, fibers, gels and scaffolds. The most usually used strategies for keratin film manufacturing are solvent casting approach, compress moulding, thermal pressing, electrospinning and layer via layer (lbl) deposition.[25] Amongst all the biodegradable herbal polymers "keratin-based substances "revolutionized the sphere of present-day biomaterials due to their distinct homes like biodegradability, biocompatibility and mechanical durability. The use of numerous natural and artificial substances in the shape of film, gel, scaffold, or nano-debris may be very not unusual to hold therapeutic marketers to the focused website to prevent infection and beautify the restoration technique.[26]

It was shown by Sierpinski et al. and Apel et al. that hydrogels based on keratin were neuroinductive and could promote regeneration in a mouse model of peripheral nerve damage. Through the induction of cellular proliferation and migration as well as the upregulation of particular gene expression necessary for crucial neural activities, human hair keratins improved the in vitro activity of Schwann cells. As a neuro-inductive temporary matrix that facilitated axon regeneration and enhanced functional recovery over sensory nerve autografts, keratin gel-filled conduits were applied to a mouse model of tibial nerve damage.[27]

Fujii et al. reported a quick casting technique and showed how hair keratins may be used to produce protein films. The viability of adding bioactive compounds like alkaline phosphatase to keratin films for controlled-release uses was also demonstrated by this research. But the films were not very flexible or strong.[28]

Tachibana et al. used calcium phosphate to hybridise keratin sponges. By encasing hydroxyapatite particles in the keratin carboxy-sponges or chemically bonding calcium and

phosphate ions, two varieties of calcium phosphate composite sponges were created. Based on the expression pattern of alkaline phosphatase, both hybridised materials facilitated osteoblast culture and changed the differentiation pattern of the cells. Additionally, keratin carboxy-sponges have been functionalized with bone morphogenetic protein-2 (BMP-2), which has been demonstrated to localise the differentiation of pre-osteoblasts cultured with the construct and to interact closely inside the keratin sponge. The fact that no appreciable quantity of BMP-2 seeped out and that the effects were contained inside the modified keratin sponge is indicated by the lack of differentiation in cells outside of the BMP-2-loaded construct.[29]

Table 1: Natural Polymer Used to Formulate Keratin Based Dressing.

Serial no.	Composition	Application	Reference
1	Keratin dialysate (aqueous) with alkaline keratin dialysate	Wound restoration of corneal epithelial turned into discovered in vitro	Tachibana A et al.[30]
2	Photo active keratin derived films	Photodynamic remedy, wound recovery, tissue engineering	Peplow PV et al.[31]
3	Keratin film crosslinked by transglutaminase (tg)	Drug shipping, enhance stability in artificial gastric juice environment	Aluigi A et al.[32]
4	Keratin film	These films continuously launch loaded rhodamine b for 12 h	Varesano A et al.[33]
5	Keratin, chitosan/gelatine 1:1:2 (w/w)	Soft tissue engineering	Zoccola M et al.[34]
6	Keratin -chitosan	Wound dressing material	Katoh K et al.[35]
7	Pla/chitosan/keratin composites	Allows attachment and proliferation of osteoblast	Wrzesniewska-Tosik K et al.[36]
8	Keratin/poly (vinyl alcohol) composite	Nanofibres with excessive optical transmittance	Sierpinski P et al.[37]
9	Keratin wound dressing	As hemostatic material	Apel PJ et al.[38]
10	Keratin gel	The drug release rate was 97% at ph 8.4 for 24 h	Noishiki Y et al.[39]
11	Keratin gel	Act as a substrate for cellular attachment and proliferation, transport of healing agents	Vasconcelos A et al.[40]
12	Keratin hydrogel	Pupal tissue regeneration	Tonin C et al.[41]
13	Keratin hydrogel	Fibroblasts culturing	Zoccola M et al.[42]
14	Keratin hydrogel	Dressing material for diabetic wound	Fujii T et al.[43]
15	Keratin based therapeutic dermal patches	Wound healing	Katoh K et al.[44]
16	Keratin/poly (vinyl alcohol) nanofibers	Tissue engineering	Tachibana A et al.[45]

Keratin in tissue engineering

The goal of tissue engineering (TE) is to repair or enhance sick or damaged tissues by assembling the right cells and growth signalling molecules onto biomaterial scaffolds. The process of further modifying such biomaterials to improve or impart a biological function and/or stimulus—whether transient or permanent—while maintaining their biological compatibility is known as biofunctionalization. For instance, titanium implants utilised in bone prostheses have good mechanical stability and biocompatibility, but they don't have any osteogenic (stimulating) properties that would enhance their eventual integration into bone. Thus, one important field of study has been the immobilisation of natural and synthetic biopolymers for the purpose of bio functionalizing implant surfaces. Since the 16th century, keratin—a fibrous protein that is easily found in hair, nails, wool, feathers, horn, and hooves—has been utilised as a biomaterial for haemostasis and wound healing.[46] Simultaneously, formal tissue engineering research first showed its promise as a covering for vascular grafts in the early 1980s.

Keratin is mostly classified as hard or soft based on its physical and chemical characteristics, especially its sulphur content. Hard keratin is found in wool, hair, nails, horns, and other tissues, while soft keratin is located in the stratum corneum of the skin and has a lower sulphur concentration (<3% wt). About 82% of wool is made up of keratinous proteins, which have a high cysteine concentration, 17% is made up of non-keratinous material, which has a low cysteine content, and 1% is made up of non-proteinaceous materials including waxy lipids and polysaccharides. A rich and pure source of intermediate filament proteins (IFPs), wool with up to 95% keratin by weight can be used in biomaterials applications that offer mechanical support or in applications which require for controlling cellular activities (e.g., migration, adhesion, proliferation etc.).

Although wool keratin will be the main topic of this study, human hair keratin has been extensively used in tissue engineering and regeneration, including haemostatic agents, wound healing, and peripheral nerve regeneration. Both types of keratins have comparable qualities. Promising outcomes were seen in wound healing and drug delivery applications when a scaffold composed of human hair keratin and polyvinyl alcohol (PVA) was created utilising the cross-linker alginate dialdehyde in combination with antibiotics such as gentamicin sulphate. In a rat sciatic nerve model, a porous human hair keratin sponge also encouraged peripheral nerve regeneration. A new scaffold with osteo-inductive potential for bone tissue

creation was demonstrated. It was composed of human hair keratin, collagen from jellyfish, and hydroxyapatite generated from eggshells. Bacterial growth was significantly inhibited by an antibacterial wound dressing made from human hair keratin, carboxymethylcellulose (CMC), and clindamycin. Additionally, the composite material promoted fibroblast cell adhesion and proliferation and produced clindamycin with regulated release. The self-assembly and polymerization properties of hair keratin, like those of wool keratin, enable the creation of diverse morphologies, including films, sponges, and hydrogels, which may have wider uses in tissue regeneration.

Antimicrobial properties of keratin

Since infection is a major concern in tissue engineering, the perfect biomaterial should also have strong antibacterial capabilities. The literature has reported on keratin products that have minimal antibacterial properties. It has been demonstrated that keratin's secondary structure and place of origin are related to its antibacterial properties. Compared to wool-derived keratin, which has a larger alpha-helix and a more organised structure, feather-based keratin demonstrated stronger antibacterial activity. According to Ferraris et al., keratin nanofibers placed on titanium with a 0.1–0.2 μm nanogroove had modest bacteriostatic action but no discernible decrease in bacterial adhesion.

Similar to this, another research altered wool fibres by adding metal cations (silver, Ag+, and copper, Cu2+) and treating them with chemicals, tannic acid (TA) and ethylenediaminetetraacetic (EDTA) dianhydride. The microbiological growth of Escherichia coli and Corynebacterium spp. was significantly inhibited by Ag+ doped wool, which also showed a low degree of metal release, indicating good metal complex stability. However, when Cu2+ was added to wool, the outcome was the reverse. Similarly, it was discovered that Ag+ and silver nanoparticles were effective against gram-positive and gram-negative bacteria, fungi, and microbes when they were treated with wool.[42]

Nevertheless, compared to the same composite in film form, electrospun keratin/cellulose chlorinated composite demonstrated increased efficacy against E. coli and S. aureus bacteria. antibacterial properties of decreased wool fibers, cuticle, and cortical cells, it was found that the former showed a 33% decrease in bacterial growth, while the latter two showed a greater decrease of 66% and 100%, respectively. The immobilisation of wool fabric with lysozyme using glutaraldehyde demonstrated a bacteriostatic effect against S. aureus. The antibacterial properties of wool keratin were also demonstrated against vancomycin-resistant Enterococcus

faecalis (VREF) and Escherichia coli as well as Methicillin-resistant S. aureus (MRSA) when combined with cellulose. Keratin-chitosan-tricalcium phosphate (KCTPs) bio-composite was created in different research, and it was shown to be an effective antibacterial against E. faecalis and Streptococcus mutans, making it a potential biomaterial for regenerative endodontic treatment. An antibacterial impact based on chitosan content was demonstrated by the observed decrease in bacterial growth in the keratin and chitosan composite compared to a cellulose or keratin film.[40]

DISCUSSION

Keratin being easily available and cost-effective protein molecule, is being used in a wider range nowadays worldwide in medical field. As chronic wound is a severe case it may be responsible for inflammation with pain. Keratin is having a large number of benefits such as providing a definite structure to the skin, as keratin is present in the uppermost layer (Epithelial layer), it also helps in providing protection when an external molecule tries to enter our body by nourishing epithelial tissue, control its growth and maintain the flexibility of skin too. Keratin plays a very important role in each and every step of wound healing from prevention of blood loss to formation of new layer of cells. Our body hair is somehow responsible for providing protection against external hazard. The areas having hair follicle are healed more rapidly as compared to the portion not having hair follicle. Keratin helps in the growth of these body hair and strengthen them to protect the body part. Use of keratin dressing is though high but it also has some highlighted factors that needs to be considered before proceeding. These factors include age, physical condition like any chronic illness, immunosuppressing, chemotherapy or radiation or nutritional insufficiency.

CONCLUSION

Traditional dressing using cotton, bandages, gauges work on the principle of cleaning the wound and thus minimizing the chances of prevention of infection. Traditional dressing also has many negative aspects such that it needs frequent change, sometimes it may be painful to remove the dressing material if it gets glued to the wound. Keeping in mind the disadvantages of traditional dressing, use of keratin dressing is increasing day by day. Although, further researches are needed to study to know more about the mechanism of healing by keratin to develop multiple layers of new cells and overcome wounds.

ACKNOWLEDGEMENT

I would like to express my special thanks to the support of School of pharmacy, The Neotia University, Sarisa, Diamond Harbour Road, South 24 Parganas, West Bengal – 743368, India.

CONFLICTS OF INTEREST

I declare that there are no potential conflicts of interest.

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