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Biotechnology for Sustainable Materials

REVIEW

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Recent advances in preparation and biomedical applications of keratin based biomaterials

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Abstract

Keratin has gained increased curiosity from researchers in the last decade for its potential applications in preparation of biomaterials. Most emphasized properties of keratin as a candidate to manufacture biomaterials involves biodegradability, excellent biocompatibility, self – assembling capability, ability to support cell growth and proliferation, water absorption and easy availability as waste. Keratin based biomaterials in the form of fibres, scaffolds, films, hydrogels, nanoparticles are being explored for various biomedical applications including wound healing, drug delivery, oral tissue regeneration, study models as well as nerve regeneration. Methods opted for fabrication of these materials include electrospinning, cross-linking and solution casting among others. In order to improve antimicrobial properties and bioactivity of keratin biomaterials they could also be loaded with drug molecules, antibiotics, growth factors and other functional peptides. Keratin materials have the advantage of high loading capacity as well as controlled and prolonged release of drug, thus maximizing the availability at the target site. This current paper critically reviews the latest developments in the utilization of keratin-based biomaterials in the aforesaid fields.

Keywords Keratin, Biomaterials, Drug delivery, Wound healing, Tissue engineering, Nerve regeneration, Scaffolds, Hydrogels

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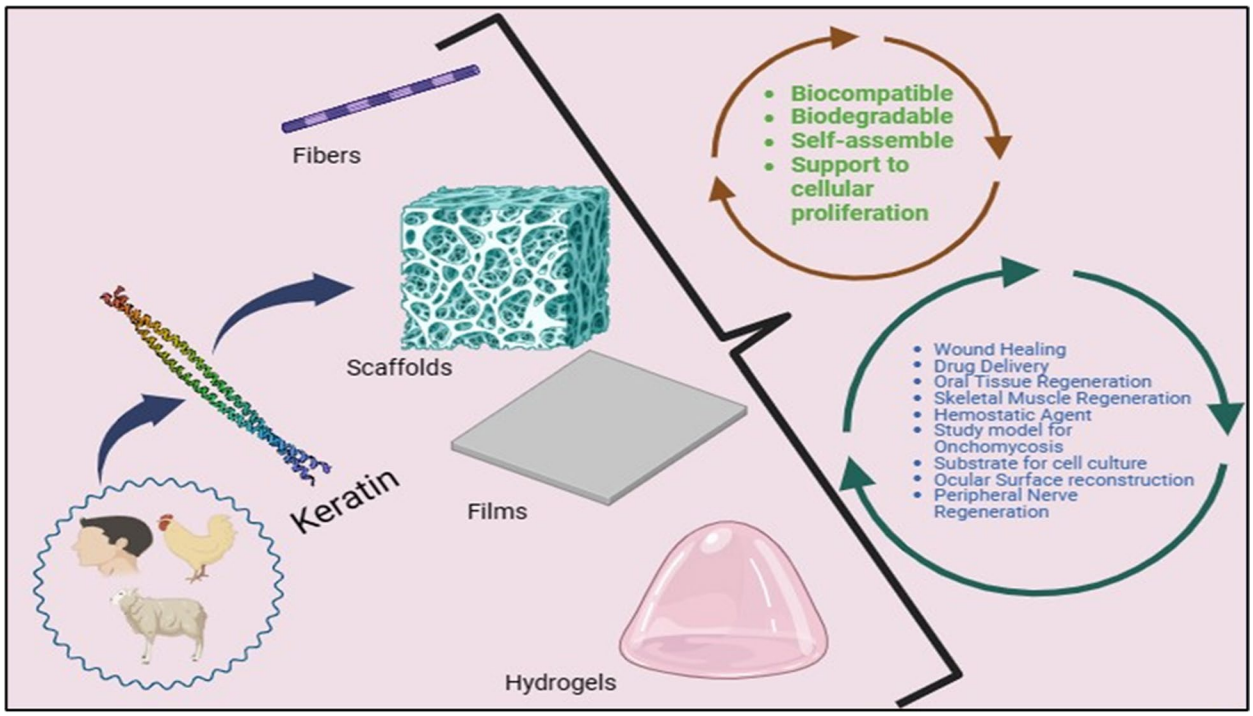
Graphical Abstract



Introduction

Due to advancements in technologies involving fabrication of biomaterials and their expanded utilizations in various medical applications, the research community in current era is focusing on using the raw materials being derived from livestock and agriculture [47, 85]. Such biomaterials are getting more attention because they tend to be sustainable as well as can deal with the problems of waste accumulation and efficient utilization. Thus, the "*Garbage In, Biomaterials Out* (GIBO)" concept focuses on the recycling of agricultural waste into biocompatible materials (Sah et al., 2022). Raw materials employed for such purposes involves, plant and animal proteins as well as carbohydrates among others [23, 94, 137]. Keratin based materials holds promising potential owing to their biological and physiochemical properties as well as availability as a cheap source in the form of waste [19, 92]. The keratin could be obtained from feathers, wool, hair, nails and horns and could be fabricated into variety of materials such as films, fibres, scaffolds, sponges and hydrogels [103]. Keratin waste including millions of tons of feathers accounts for a huge fraction among the waste generated worldwide per year [101, 111]. Thus, utilizing keratin waste for biomedical applications is of great interest. This review summarizes the structure, extraction strategies and various biomedical applications of keratin-based biomaterials. Although the review articles published until recently have highlighted the important physical and biochemical properties of keratin as well as their possible biomedical applications, the current article shall provide an exhaustive and updated information on the recent research and studies exploring various biomedical applications of keratin biomaterials including wound healing, drug delivery, oral tissue regeneration, nerve regeneration among others.

Structure, sources and properties of keratin

Keratin is an insoluble fibrous protein that makes up the cytoskeleton and epidermal structures in humans and animals including hair, horns, wool, feathers, claws and nails among others [53]. Based on the source, keratin presents variation in structure and properties but could be broadly classified as hard and soft keratin. The disulphide bridges between the cysteine molecules are mainly responsible for the stability and integrity of the protein structure in keratin. The hard keratins having more sulphur (cysteine) content and thus more disulphide linkages providing toughness to epidermal structures [33, 111]. Whereas the soft keratins have less sulphur content and is responsible for imparting elasticity to the epithelial

tissue [20]. The hard keratins from various sources have been mostly employed for the fabrications of biomaterials such as films, hydrogels, fibres and sponges [12, 13, 40, 86]. The polypeptide in keratin could be arranged either in α helix or β- fold. The α helical conformation results in good elasticity whereas the van der waals forces and hydrogen bonds in β- sheets are responsible for high tensile strength. The occurrence of α keratin is predominantly reported in hair, claws and hooves of mammals whereas that of β keratin is seen in feathers, scales and beaks of birds and reptiles. Based on their molecular weight and overall charge, keratins are classified as Type I (acidic and smaller) and Type II (basic-neutral and larger). Type I and Type II keratins interact with each other by forming heterodimers in the initial stage and then assembling into complete intermediate filaments (Fig. 1).

The inherent key properties of keratin that makes them usable in biomedical applications includes ability to self-assemble, biocompatibility, biodegradability and support to cellular proliferation [107, 139]. Reports are also available that shows the anti-bacterial and haemostatic property of keratin [60, 108, 131].

Keratin extraction methods

Multiple methods are available for the extraction of keratin from various sources. These extraction methods rely on breaking the disulphide bonds responsible for the stability of the protein structure. These extraction methods could be chemical, physical or biological. Major physical methods include high-pressure hydrolysis method, high-temperature hydrolysis method, high-pressure puffing method and extrusion method. Disadvantages of physical methods of keratin extraction includes destruction of primary structure of the protein as well as high energy input. The chemical extraction of keratin on the other hand can be done by oxidation methods, reduction methods or by acid–base treatments (Alahyaribeik et al. 2020). For the enzymatic isolation of keratin, keratinases from actinomycetes and fungi could be utilized. Reports are also available to extract keratin by using microwave irradiation, ionic liquids as well as steam explosion. Extraction methods of keratin from various sources employing different methods are summarized in Table 1.

Physical methods

Under physical methods of keratin extraction, high pressure and temperature during hydrolysis has been used. Although it is a convenient method but the extracted keratin is completely degraded into amino acids and peptides thus destroying the primary structure and rendering it unsuitable for biomaterial preparation [84]. Another disadvantage of high pressure or temperature hydrolysis is excess of power consumption. Alternate physical method for keratin extraction is steam explosion in which high pressure steam is enforced into a container with the raw materials. Steam explosion has been studied on wool degradation and it has been observed that almost 62% of wool degradation could be achieved by stem at higher temperatures of about 600 °C [114]. Higher rates of keratin decomposition could be achieved with increasing processing time, temperature and pressure [41].

Chemical methods

Acid–alkali treatment

Employing strong acids such as hydrochloric acid and sulphuric acid for the hydrolysis of keratin involves the treatment of keratinous waste for a given period of time, neutralization and further drying and purification to achieve final dried product [7, 12, 13]. The time employed for hydrolysis dominates the molecular weight composition of the extracted keratin, an increase in hydrolysis time results in lower molecular weight protein chains [87]. As a result of prolonged acid hydrolysis, certain amino acids such as tryptophan are degraded, moreover the leftover acid waste with is cumbersome to handle and dispose.

As far as use of alkali for the hydrolysis of keratin is concerned, the loss of amino acid is not observed [12, 13]. Treatment with alkali weakens the mechanical properties of keratin and thus renders it unsuitable for film formation [21]. Alkali such as $Ca(OH)_2$, KOH, NaOH have been studied for the hydrolysis of wool keratin. Combination of Acid and alkali for the hydrolysis of keratin have also been explored and found to be more effective [21, 30].

Oxidation

Oxidizing agents such as peracetic acid, performic acid, hydrogen peroxide, peroxyacetic acid, peroxyformic acid have found their use in keratin extraction. These compounds break the disulphide bonds to yield keratoses which predominantly have a crosslinked structure stabilized by noncovalent interactions and depict hygroscopic behaviour [132]. The keratoses are further subdivided into α- keratoses, β-keratoses and γ-keratoses based on their solubility in ammonia and their region of origin from the keratin tissue. α- keratoses could be which are derived from cortex region are soluble in ammonia and could be precipitated at acidic pH. β-keratoses, derived from cuticular region are insoluble in ammonia whereas γ-keratoses are soluble in ammonia but are not precipitated at acidic pH [132]. Disadvantages of oxidation method include loss of certain amino acids such as phenylalanine, tyrosine, tryptophan among others as well as long treatment times [86].

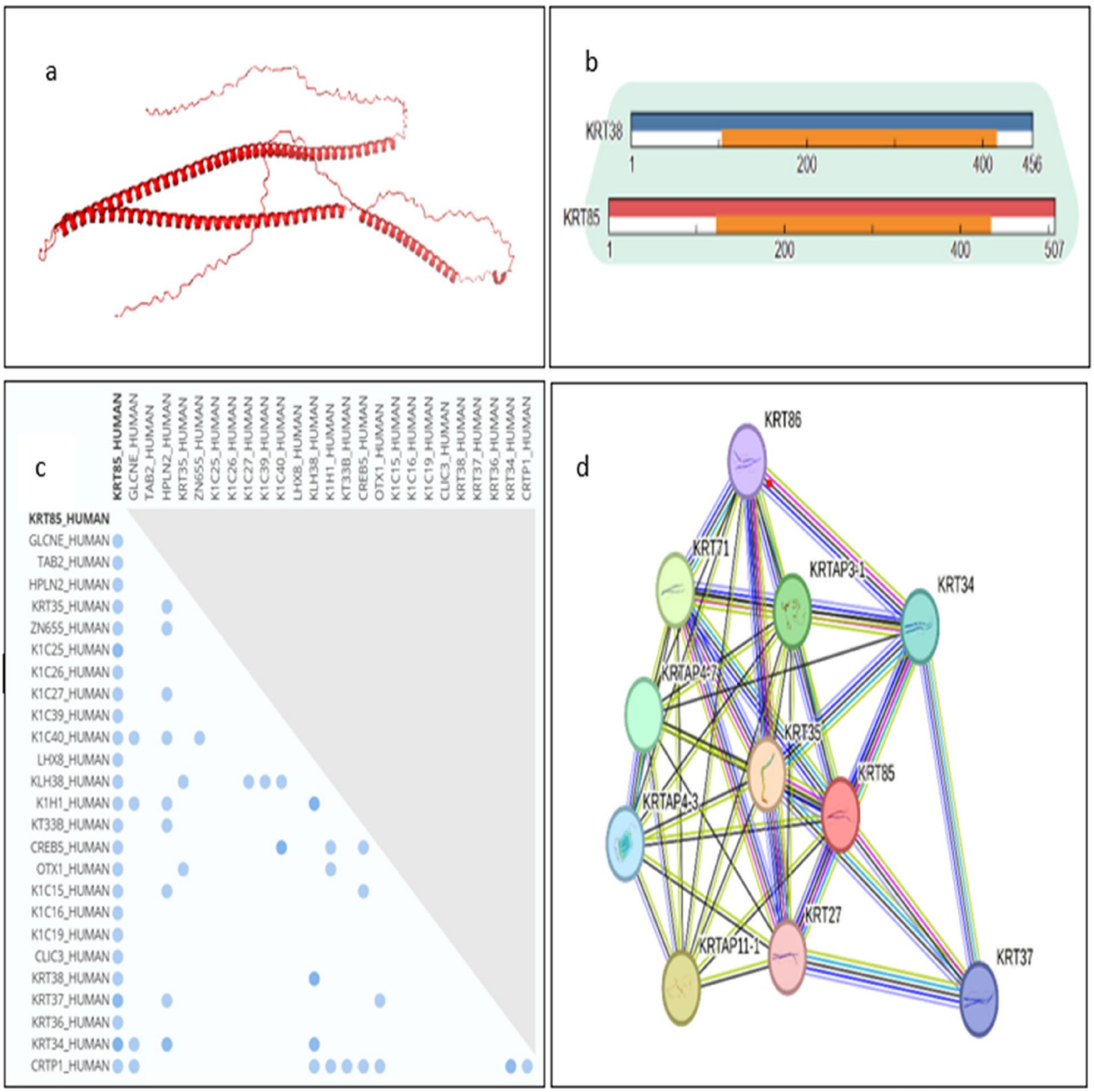


Fig. 1 Human hair keratins and their interactions. **a** Structure of KRT 85 derived from AlphaFold protein structure database. **b** Binary interaction of KRT85 with KRT38 drawn with IntAct database. **c** Binary interaction chart of KRT85 with 25 other proteins involving type 1 hair keratins and other proteins, retrieved from UniProt (ID P78386). **d** Network showing multiple interactions between different keratins and keratin associated proteins from *homo sapiens* involved in the formation of hair retrieved from STRING database

Reduction

This is the most commonly used method of keratin extraction. Reducing agents used for breaking the disulphide linkages are β-mercaptoethanol and other thiols in combination with denaturing agents like urea and thiourea [54, 95]. Upon reduction in alkaline medium soluble protein known as kerateines are formed. Certain protocols also employ the use of sodium dodecyl sulphate and other surfactants along with reducing agents to increase the stability of the keratins in solution. This use of β-mercaptoethanol poses threat as it is toxic in nature thus sodium disulfite could be used as an alternate although it gives lesser yields. Urea in high concentrations disrupts the protein framework in keratin by hindering with the hydrophobic interactions and thus enhancing the action of reducing agents. The reducing

Table 1 Recent advances in extraction methods of keratin from various sources

Method	Source	Protein yield (%)	Properties of protein extract	Reference
Chemical methods				
Acid-Alkali Treatment	Wool	-	An average diameter of extracted keratin protein found was 25nm and length of less than 3 µm. These nanofibers constitute mainly α-helical proteins. Extracted keratin nanofibers have a uniform circular cross-section like morphology.	[19, 124]
	Chicken feathers	53.78%	White chicken feather keratin hydrolysate had pH 11.0, was soluble in nature with 1.0837 g/ml density while black chicken feather hydrolysate had pH 12.0, 1,0911 g/ml density and limited solubility. The isolated keratin possessed primary and secondary amine.	[97]
Oxidation	Tannery Sheep Hair	91.50%	Extracted keratin has molecular weight ranging from 3-15 kDa with amorphous structure and XRD peaks at 2Θ values 9.36° and 21.16° due to the presence of α-helix and β- sheet structures.	[76]
Reduction	Human hair	73%	Dialyzed protein consists mostly of alpha structural keratins.	[118]
	Chicken feathers	66.45%	Keratin proteins possessed semi-crystalline nature with rough surface morphology.	[4]
Ionic Liquid Treatment	Sheep wool	-	The regenerated keratins consisted of low sulphur keratins and fractions of matrix proteins, with improved thermal properties compared to raw wool.	[35]
	Wool, hair and chicken feather		1-Butyl-3-methylimidazolium chloride was used in one step process to composites of cellulose and keratin. Dtrongest bactericidal effects were recorded in feather composites.	[120]
Biological methods				
Enzymatic hydrolysis method	Chicken feather	76.20%	Protease enzyme was used in combination with alkali treatment. Maximum yield was obtained with 5%NaOH, 5% KOH and 2% protease concentration.	[3]
	Chicken feather	-	Feather meal produced by crude keratinase enzyme of *Bacillus pumilus* AR57 was rereported to be rich in essential amino acids. The isolated keratinase was found to be stable for 3 hours.	[49]
	Chicken feather	-	Keratinase from *Streptomyces netropsis* A-ICA and *Bacillus subtilis* ALICA showed optimum feather degrading abilities at pH values 7 and 7.5 at 25 and 30° C respectively.	[1]

Table 1 (continued)

Method	Source	Protein yield (%)	Properties of protein extract	Reference
Microbial treatment	Chicken feather	42.8	Keratin hydrolysates were clear and composed of peptides with molecular mass ranging from 800 to1079 D, suitable for application in cosmetics.	[130]
	Chicken feather	-	*Streptomyces griseoauran-tiacus* AD2 depicted highest keratinolytic activity followed by *Streptomyces albidoflavus* AN1 and *Streptomyces drozdowiczii* AD1.	[74]
Physical methods				
Microwave irradiation	Wool	-	Extracted keratin retained the pep-tide chain structure. Obtained wool keratin showed small particle size with low crystallinity (12.3%). This method disturbed the stabil-ity of the α-helix and the β-sheet structures resulting in random coil structures.	[28]
Steam explosion	Porcine hoof shell	-	Main components of the liquid protein fraction were short pep-tides (< 2 kDa, 84.72%) and amino acids (1.68 mg/mL), suitable as peptone substitute for fermen-tation culture.	[113]
Thermal hydrolysis or super-heated water extraction	Hog hair	70%	The amount of cystein reduced in the protein hydrolysate as the disulphide bond breaks at high temperature and sulphur is released as hydrogen sulfite. The original tertiary structure in alpha keratins and matrix proteins were reported to be lost after Thermal hydrolysis process (THP)	[121]

methods have been predominantly for keratin extraction with varied concentrations of urea and other components from sources such as feathers, hair, horns and hooves [54, 80].

Ionic liquid treatment

Ionic liquid are salts or cationic/ anionic compounds that exists as liquid at room temperature and possess strong solubilizing properties as they could disrupt the intermolecular hydrogen bonds present in the natural polymers [12, 13, 43]. These liquids have been studied for use in the extraction of keratin from chicken feather and wool. In comparison to acids and alkali, ionic liquids are eco-friendly, non- corrosive and non- flammable. Ionic liquids are often used in combination with chemicals such as sodium bisulfite that could break the disulphide linkages and also reduces the duration of the treatment. Ionic liquids such as BMIM + Cl- and 1-allyl-3-methylimidazolium chloride could be used to extract keratin at high temperatures of up to 130 °C [25] 19% yield of keratin from human hair have been reported with 1-allyl-3-methylimidazolium chloride [133, 135], and reduced solubility have been reported in BMIM + Cl- [112].

Biological/ enzymatic methods

Biological extraction or solubilization of keratin have been reported by the use of micro-organisms as well as purified enzymes. In comparison to chemical method of keratin extraction, biological methods are safer and results in lesser loss of amino acids along with being energy efficient method, as input of energy in the form of higher temperatures or pressure is not desired. But use of microorganisms and purified enzyme preparations make these methods costlier [52]. Bacillus isolated from poultry waste and soil, Amycolatopsis Chryseobacterium, Streptomyces, Staphylococcus, etc., are known to be keratin degrading [2, 5, 115, 116]. In addition to bacteria certain fungal species (Aspergillus flavus, Aphanoascus fulvesence, Microsporum gypseum) have also been studied for this purpose [7, 75]. Use of urea with microorganism have also been reported to achieve higher keratin yields.

Keratinases enzymes from Apergillus, Lysobacter, Bacillus, and Streptomyces genera could be used for keratin extraction [116]. Different molecular weight keratin fractions could be prepared depending upon the pH, temperature and exposure time [22].

Biomedical applications of keratin biomaterials

Wound healing

Wounds can arise from several factors such as severe injuries, major surgeries, diabetes, or vascular illnesses. Wound healing involves different types of cells such as fibroblasts cells, keratinocytes, various immune cells and vascular endothelial cells. Certain wounds do not heal in short time with normal clinical care and may bother the patients for months or even years. The accelerated healing in such challenging wounds could be achieved by application of biomaterials based on protein matrices. Collagen and keratin are the major components of the human skin that have gained interest in recent time to prepare biomaterials capable of accelerating healing in such chronic wounds. These biomaterials generally deliver materials such as growth factors, proteins or other molecules that could expediate the wound healing process. Keratin is present as filament in keratinocytes cells of the epidermal layer of the skin. Apart from providing mechanical strength, it also plays significant role in cell signalling. Keratins undergo post translational modifications and interact with various signalling proteins in order to perform the functions including cell migrations, adhesion and differentiation [104]. According to reports, keratin also plays a vital role in activation of keratinocytes that is an important step in normal wound healing process. Various types of keratin-based biomaterials employed for wound healing involves nanofibers, membranes, hydrogels, scaffolds and dressings. The keratin alone or in combination with polyurethane, PVA and cellulose have recently been reported to form these biomaterials. In a recent study, Ramey et al. [93] prepared human hair keratin matrices and explored their usage in wound healing in diabetic mice. Comparison of these keratin matrices was also made with amniotic membrane, bovine dermis and porcine decellularized small intestinal submucosa for wound healing purposes (Fig. 2). The authors reported these matrices to be thin with smooth and uniform surface morphology. Human epidermal (HEKa) keratinocytes when grown on keratin matrices showed upregulation of Interleukin 6 (IL-6) and Macrophage Inflammatory Protein-1 delta (MIP-1δ), that plays an important role in wound healing by modulating inflammatory response and promoting fibroblast migration. In vivo studies suggested that the wound size was smaller in mice that were treated with keratin matrices then those treated with amniotic membrane after 3, 4 and 5 weeks. Keratin based applications of biomaterial formation and utilization for wound healing has been summarized in Table 2.

Drug delivery

The term 'Drug delivery' defines the administration of any pharmaceutical compound to achieve therapeutic effect in humans or animals [38]. There are various techniques adopted by scientists to deliver these compounds effectively and safely to the target site in the body of human in correct concentration [29]. The aim of the drug delivery system is to enhance the efficacy, safety and bioavailability with minimized side effects to target tissue. This area covered many aspects including route of administration, targeted delivery, formulation technologies and biological barriers. The biocompatible nature of keratin has attracted researchers to exploit it in the applications involving designing of drug delivery systems [31].

Hydrogels and nanogels derived from proteins are lipophilic in nature but they do not dissolve in water instead they swell up after coming in contact with water. They have excessive drug loading capacity and are able to ameliorate cellular uptake efficiency [127]. Keratin biomaterials are loaded with drugs and used as a carrier because they act as a covering shield and protects encapsulated drugs from degradation in the physiological environment, before reaching the target site. Keratins also have the ability to bind effectively with various bioactive compounds, maximizing drug stability and providing controlled release [126, 149].

Keratin naturally possess cysteine-containing residues and ample of thiol groups, these sulfhydryl groups of keratins form a disulfide bond with a desired drug and use it as a carrier for selectively drug release under reducing circumstances. Additionally, it also possesses a lysine and arginine group that can be elicited by a known protease trypsin which is an essential enzyme generally augmented in tumor tissues [149]. Different biomaterials have been formed including nanogels (with hyaluronic acid and sodium alginate), hydrogels, nanofibers, microparticles, nano fibrous mats, nanotubes and nanoparticles like keratin/CHX NPs (keratin/chlorhexidine complex), by using various methods such as nanoprecipitation, self-assembly, de-solvation, iconic gelation and aggregation. Liu (2024) used keratin as an envelope of antitumor drug and used as a drug delivery agent in tumor chemotherapy.

Recent innovations in this area focus on smart drug delivery systems, biologics (i.e. monoclonal antibodies) and nanotechnology. Currently, these advancements are very crucial to treat any disease more effectively with minimizing side effects and improving patients' health. Recent advancements on the role of keratin in the drug delivery systems are summarized in Table 3.

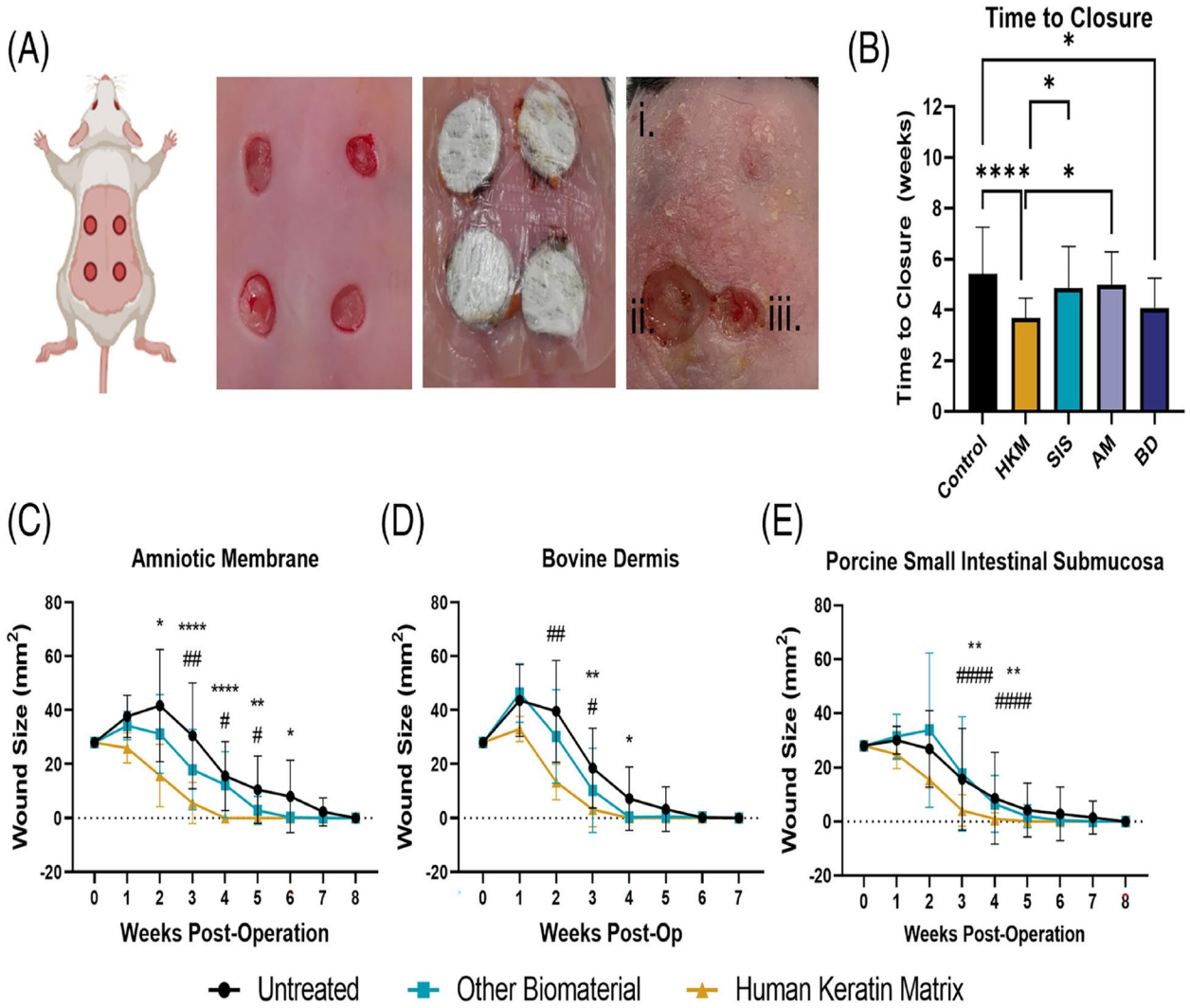


Fig. 2 Effect of various biomaterial wound care products on healing in vivo. **A** (left) Schematic showing four 6 mm diameter full thickness wounds on the backs of db/db mice that were treated with HKM, another biomaterial-based wound care product, or no treatment (control) in randomised locations. Image created with Biorender.com. Representative images of the four wounds at week 0 before application of treatment (middle-left), wounds treated and topped with secondary dressings (middle-right), and wounds after several weekly treatments (right), in this case HKM (i), control (ii), and bovine dermis (iii) at week 3 post-operation. **B** Bar graph showing average time to complete closure for each treatment applied. $^{*}p < 0.05$, $^{****}p < 0.0001$ by one-way ANOVA with Tukey's multiple comparisons. **C** Healing trajectories of wounds on mice treated with control (black circle, $n = 12$), amniotic membrane (blue square, $n = 12$), or HKM (gold triangle, $n = 12$). **D** Healing trajectories of wounds on mice treated with control (black circle, $n = 12$), bovine dermal collagen (blue square, $n = 12$), or HKM (gold triangle, $n = 12$). **E** Healing trajectories of wounds on mice treated with control (black circle, $n = 16$), porcine small intestinal submucosa (blue square, $n = 16$), or HKM (gold triangle, $n = 16$). Symbols indicate statistical significance of HKM compared to other treatments: $^{*}p < 0.05$ vs. control, $^{**}p < 0.01$ vs. control, $^{****}p < 0.0001$ vs. control, $^{\#}p < 0.05$ vs. corresponding comparative advanced wound care product, $^{\#\#}p < 0.01$ vs. corresponding comparative advanced wound care product, $^{\#\#\#\#}p < 0.0001$ vs. corresponding comparative advanced wound care product by two-way analysis of variance (ANOVA), paired by mouse, with Tukey's multiple comparisons at each timepoint [93]. Creative Commons Attribution License

Oral tissue regeneration

Keratin have found a place in various ways pertaining to the production and utilization of biomaterials applicable in oral tissue or bone regeneration. A post operative infection in dentine region, damage to alveolar bone, wound healing and degeneration in pulp dentine are some of the scenarios exploiting remarkable biological properties of keratin to form bio composite materials. Wound repair in oral cavities takes 2–10 days to heal and it requires processes such as epithelial cell migration, proliferation and cell plasticity. Trans-differentiation of epithelial cell resulting from persistent inflammation is

Table 2 Wound healing applications of keratin and keratin-based biomaterials

Composition	Keratin source	Biomaterial type	Properties and function	References
PVA and Keratin	Sheep Wool	Asymmetric Nanofibers-Membranes	Top layer is made up of cross-linked PVA nanofibers and bottom layer is composed of wool keratins and PVA. Keratin/PVA asymmetric membranes displayed improved cell adhesion in in vitro experiments.	[102]
Silk-wool-Tannic acid	Sheep Wool	Hydrogel	These hydrogels possessed porous structure that could support cell growth and proliferation. The hydrogel demonstrates in situ gelation, recyclability, moldability, elasticity (G'>100 kPa), adhesiveness, self-healing properties, 3D printability, antibacterial activity, antioxidant properties, and biocompatibility.	[48]
Bacterial cellulose and keratin	Human hair	Scaffolds	The scaffolds do not show any toxicity to cells under cytocompatibility tests. These scaffolds were grafted on dorsal region of rabbit over a burned wound and displayed the potential of regeneration at the wound site.	[91]
Keratin-derived powder containing silver nanoparticles	Mouse fur	Wound dressing	These keratin dressings were found to be biocompatible in diabetic mice model, it increased the rate of wound closure and epithelization after a period of 5 and 8 days. The wounds treated with these dressings mostly showed the presence of macrophages whereas the untreated mice wounds were had a greater number of neutrophiles. Presence of macrophages favours healing and tissue regeneration.	[57]
Keratin fibres supplemented with 0.1% sodium butyrate	Rat fur	Wound dressing	These dressings have heterogenous structure and the butyrate was released slowly into the wounds. These dressings are non-toxic and promotes proliferation of cells in diabetic rats. The treated wounds also showed increased mRNA expression of keratin 16 and 17.	[59]
Reduced keratin, hyperbranched polymer and MnO2 nanoparticles	Human hair	Composite hydrogel	These hydrogels displayed antibacterial properties against gram positive and gram-negative bacteria. The composite hydrogel also scavenged ROS and protected L929 cells from oxidative stress.	[67]
Keratose (KO) and Kerateine (KN)	Human hair	LL-37 encapsulated hydrogel dressings	Sustained release of LL-37 from the keratin hydrogel was obtained by these hydrogels that resulted in improved wound healing by increase in fibroblast proliferation in full thickness rat wounds. Enhanced cell adhesion and migration was also reported. L-KO25:KN75 is capable of eradicating both Gram-negative and Gram-positive bacteria after 18 h. mRNA expression of VEGF (Vascular endothelial growth factor) and IL-6 (Interleukin-6) was also enhanced in treated groups.	[50]

Table 2 (continued)

Composition	Keratin source	Biomaterial type	Properties and function	References
Poly(L-lactate-caprolactone) copolymer (PLCL) and keratin	Human hair	Bilayer hydrogel wound dressing loaded with fibroblast growth factor (FGF-2)	This material possessed good porosity with water absorption of 874.09%. Elastic modulus - about 44kPa. Biocompatible and Biodegradable. In vivo - promoted re-epithelialization, collagen deposition, skin appendages (hair follicles) regeneration, micro angiogenesis construction, and adipose-derived stem cells (ADSCs) recruitment	[151]
Keratin and biphalin	Mouse fur	ber-dressing	These dressings increased proliferation in NIH/3T3 cell lines. Slow biphalin release from the dressing onto wound in experimental diabetic mice resulted in increasing expression level of mTOR, and p-AKT 72 at 72h. Acceleration in would healing is reported on days 5 and 15.	[99]
Keratin	Human Hair	Keratin Matrices	Degradation resistant, contained more than 99% keratin. Human epidermal keratinocytes grown in contact with these matrices showed increased expression of epidermal growth factor. Also, increased of cytokines was observed in these cells.	[93]
Keratin	Sheep Wool	Hydrolysates	These hydrolysates possess favourable cytotoxicity profile and displays anti - inflammatory properties in endothelial cells.	[83]
Keratin	Human hair	Hydrogel loaded with Human Platelet Lysate	Hydrogel formed with 15% keratin were stable and supported cell growth without cytotoxicity for 3 days under in vitro conditions	[153]
Keratin and casomorphin	Mouse fur	Wound Dressing	Wounds showed reepithelization quicker with these dressings. The dressing stimulated macrophages infiltration, which favours tissue remodelling and regeneration.	[58]
Keratin	Human hair	Ulcer-adhesive Hydrogel	These hydrogels increased the rate of ethanol-induced gastric ulcer healing by stopping the bleeding, preventing the epithelium cells from gastric acid damage, suppressing inflammation and promoting re-epithelization in rat .	[18]
Keratin	Human hair	Hydrogel	Keratin hydrogels treated irradiated wounds showed an increased rate of closure in comparison to untreated group in rats.	[16]
S-nitrosated keratin and polyurethane	Human hair	biocomposite mats/ dressings	The bio composite mats released NO for 72 hrs and possessed cytocompatibility and antibacterial activity. These mats promoted wound healing.	[26]
Keratin and PVA	Human hair	Scaffolds	The scaffolds loaded gentamycin sulphate (GS) as a model drug were prepared with Keratin and PVA by using alginate dialdehyde as crosslinking agent. These scaffolds promoted wound healing and demonstrated biocompatibility with NIH 3T3 fibroblast cells.	[79]

Table 2 (continued)

Composition	Keratin source	Biomaterial type	Properties and function	References
Keratin, cysteine and glucose oxidase (GOD)	Chicken feather	Hydrogel	GOD catalysed oxidation shortened the gelation time to almost 3 mins in a full thickness wound bed in in mice and improved the mechanical strength of the keratin hydrogel. Deferoxamine-loaded hydrogels also accelerated the wound healing in diabetic rats.	[17]
Polyacrylonitrile (PAN) and Keratin	Chicken feathers	Nanofiber mats	The electrospun PAN/Keratin mats had smooth surface and increased porosity with 0.05% keratin concentration. The mats demonstrated antibacterial properties against Pseudomonas aeruginosa and Staphylococcus aureus.	[108]
Sulfobetaine and Keratin	Human Hair	Hydrogel Dressing	Chlorhexidine (CHX) loaded hydrogels displayed cytocompatibility, antioxidant property as well as antibacterial activity. The CHX was released in wound microenvironments.	[109]
Keratin, Sodium Alginate and zinc oxide nanoparticles (ZnO NPs)	Goat hoof	Wound dressing	Zinc oxide nanoparticles (ZnO NPs) using C. roseus (leaf part) imparts good antibacterial activity, increases swelling of the dressing mats. These mats exhibited biocompatibility with NIH 3T3 fibroblast cells with accelerated wound healing.	[106]
Keratin	Human hair	Human keratin matrices (HKM)	HKM were composed of greater than 99% human keratin (Fig.2). Adult human epidermal keratinocytes (HEKa) cultured in contact with HKM depicted enhanced expression of Epidermal Growth Factor (EGF) and increased release of cytokines. In vivo studies in mice suggested accelerated wound closure with HKM in comparison to amniotic membrane (AM), bovine dermis (BD), or porcine decellularized small intestinal submucosa (SIS)	[93]

Table 3 Application of keratin based biomaterials in drug delivery systems

Composition	Keratin source	Biomaterial type	Properties and function	References
Tragacanth gum and keratin	Chicken feather	Nanogel	Nanogels with cinnamon as herbal extract and enclosed by cotton fabrics depicted antibacterial activity against both gram +ve and gram -ve bacteria. Nanogels were reported to be biocompatible. Release of cinnamon extract is reported to be concentration dependent and follows first order kinetics.	[73]
Chitosan and keratin	Chicken feather	Hydrogels	Hydrogels with keratin chitosan ratio of 3/2 displayed most efficient controlled release of two drugs viz. Rhodamine B (RB) and Bovine Serum Albumin (BSA). At 27 °C and 7.4 pH, a maximum cumulative release of 81.7% and 31.2% for RB and BSA respectively was recorded. Approximately, the attainment of equilibrium was achieved after 8 hours for RB and 44 hours for BSA.	[143]
Poly butylene succinate (PBS) and keratin	Wool, hair and nails	Nanofibers	Electrospun nanofiber mats formed with PBS and keratin by using hexafluoro isopropanol as blending solvent showed increased release rate of Rhodamine B with increase in concentration of keratin. The blend solutions of Keratin/PBS displayed non-Newtonian behaviour, with 70/30 and 30/70 ones possessing thinner mean diameter in nanofibers owing to better orientation of polymer chains under shear stress. Electrospun mats with higher PBS content had improved thermal and mechanical properties.	[44]
Lipids and keratin microparticles	Porcupine quills	Microparticles	Produced microparticles showed 29.83% antioxidant activity. Lipid coating of keratin microparticles increased antibacterial activity for about 55% against *E. coli* and *Staphylococcus aureus*. Lipid-loaded erythromycin further improved the antibacterial properties once carried on surface of keratin microparticles.	[68]
Keratin and polybutylene succinate (PBS)	Wool	Nanofibrous mats	Ker-PBS 50-50 electrospun nanofibrous mats loaded with 23 wt.% of diclofenac released 165.2±38.3 and 307.8±24.4 µg/cm2 after 6 and 8h respectively.	[45]
KAPs (keratin-associated proteins) and KIFs (keratin intermediate filaments)	Human hair	Keratin nanoparticles	The current study revealed that KAPs/KIFs ratios directly act upon properties and structures of keratin nanoparticles. the authors observed that higher concentration of KAPs offers higher repulsive force between particles and minimizing their aggregation potential. Reversely, increase amount of KIFs offers weak repulsive force and smaller particle size and able to maximize theophylline release.	[63]
Keratin/chitosan/glucosamine sulfate (KRT/CS/GLS)		Multi-walled carbon nanotubes (MWCNTs)	Produced composites have amorphous nature with high thermal decomposition temperature of 420 °C. MTT assay revealed maximum concentration of MWCNT-GLS/CS/KRT nanocomposites showed 83% cell viability in RAW 264.7 cells.	[117]

Table 3 (continued)

Composition	Keratin source	Biomaterial type	Properties and function	References
Alginate, chitosan, and tripolyphosphate (TPP)	Chicken feathers	Microparticles	Encapsulation efficiency of 69.24% was recorded for amoxicillin in keratin and TPP microparticles with a gradual release of up to 96% in 6 hours' time. In comparison to pure amoxicillin the drug loaded microparticles depicted increased antibacterial activity against both E. coli and S. aureus because of controlled and prolonged drug release.	[147]
β-cyclodextrin (β-CD), keratin (K), Insulin (IN) and dialdehyde glucan (DG)	Human hair	Nanoparticles	Keratin based (β-CD-K-IN-DG) NPs had high drug loading capacity (32.81%), high encapsulation efficiency of 98.52% and has the ability to protect insulin from enzymatic and acid degradation. NPs assisted in prolonging the residence time and controlled release of insulin leading to a maximum oral bioavailability of 12.27% and high hypoglycaemic effect in type 1 diabetic rats.	[134]
Xanthan/gelatin (XG) and keratin/xanthan/gelatin (KXG)		Hydrogels	Hydrogels produced by crosslinking of xanthan, gelatin with glycerol in different ratios and loaded with vitamin C. Addition of keratin with xanthan, gelatin, glycerol (1:1:2) gave water vapour transmission at the rate 4523 ± 133 g m−2 d−1, improved L929 fibroblast viability and maximized protein release. Vitamin C increased collagen synthesis in L929 fibroblasts and was released for 100 hours showing inhibition of bacterial growth.	[24]

called type 2 EMT (Epithelial-Mesenchymal Transition). Vimentin is the biomarker for Type 2 EMT, which indicated that keratin induces EMT in the oral keratinocytes and enhances migration of cells. Thus, human hair keratin could serve as an excellent material to form biomaterials with varied properties and functions. Moreover, the alveolar bone that provides support to the tooth may undergo loss and degeneration as a result of various factors. In order to replace the lost tooth, dental implants need proper dimensions of this alveolar bone with required surface area for implantation. With damaged alveolar edge, the success of implants could be reduced. Keratin biomaterials among others have been reported to promote regeneration of alveolar bone. Another area involves utilization of stem cells including Dental pulp-derived stem cells (DPSCs) to generate pulp-dentine like tissue. Collagen and keratin have been used in form of scaffolds to induce differentiation in DPSCs through cell homing and providing binding sites [110]. Keratin composite membranes could also be employed to release antibacterial agents at a control rate in order to prevent postoperative infections. Latest researches exploring the potential use of keratin biomaterial for various dental applications are summarized in Table 4. In a notable study by Feroz & Dias [34], Scaffolds were prepared from sheep wool keratin, hydroxyapatite and hydroxypropyl methylcellulose which depicted cytocompatibility with osteoblast cells and could be employed for alveolar bone regeneration (Figs. 3 and 4).

Tissue engineering

Tissue engineering comes to safeguard in situations where conventional medicine systems render to be incompetent, such as failure of function or loss of a particular tissue or organ. Success of tissue engineering relies on the fabrications of scaffolds or other forms of biomaterials that could effectively replace the original tissue/ organ. Various biomaterials being explored for in this regard involves nanoparticles, nanofibers, films and hydrogels [37, 69–71, 100]. Hydrogels are most commonly being employed for tissue engineering because they could most effectively bio-mimic as well as can be designed into variety of different structures according to specific needs [6]. Owing to their three-dimensional cross-linked network and hydrophilic characteristics, hydrogels have the ability to absorb and retain large amounts of biological fluids [72]. Disulfide bonds in the keratin structure provide it with high mechanical strength, moreover it its non- immunogenicity makes it a suitable candidate for tissue engineering. The amino acid sequences of keratins are known to interact with integrins such as glutamic acid-aspartic acid-serine (EDS), and

Table 4 Advances in the use of keratin biomaterial for oral tissue regeneration

Composition	Keratin source	Biomaterial type	Properties and function	References
PEG-g-keratin	Human Hair	Powder	Keratin has the potential to enhance monolayer wound healing using HOKs (human oral keratinocytes). PEGylated keratin treatment has demonstrated no toxicity to periodontal fibroblasts or dental keratinocytes.	[56]
PLGA and keratin	Wool	Ornidazole loaded membrane	These membranes inhibited growth of Porphyromonas gingivalis, Fusobacterium nucleatum and Peptostreptococcus anaerobius. Also promoted growth of human periodontal ligament fibroblasts.	[150]
Mineralized keratin	Nano keratin	Nanoparticles	Cultivation of DPSCs with mineralized keratin resulted in more extracellular matrix proteins interaction with culture interface. The number of cells also increased.	[15]
keratin/hydroxyapatite (HA)/ hydroxypropyl methylcellulose (HPMC)	Sheep wool	Scaffold	The scaffold has highly porous interconnected structure with average pore size of 108.36nm. These scaffolds also possessed cytocompatibility with osteoblast cells, having ability to regenerate alveolar bone. (Fig. 3, 4)	[34]
Keratin and Fibrinogen	Human Hair	Injectable Hydrogels	Depict cytocompatibility with human gingiva fibroblasts (HGF) cells. Free flow of biological fluids, cell migration and growth were also absorbed inside these hydrogels.	[51]
keratin/hydroxyapatite	Wool	Keratin/hydroxyapatite (keratin/HA) scaffold	Osteocalcin or Bone Gla Protein was detected in the Saos-2 cells cultured on these scaffolds, moreover these cells could be seen adhering, migrating and proliferating in the scaffolds.	[36]
Keratin and Titanium	Wool	Keratin coated titanium surface	Solution casting gave a thick covering of titanium while molecular grafting resulted in discontinuous coating of titanium.	[96]

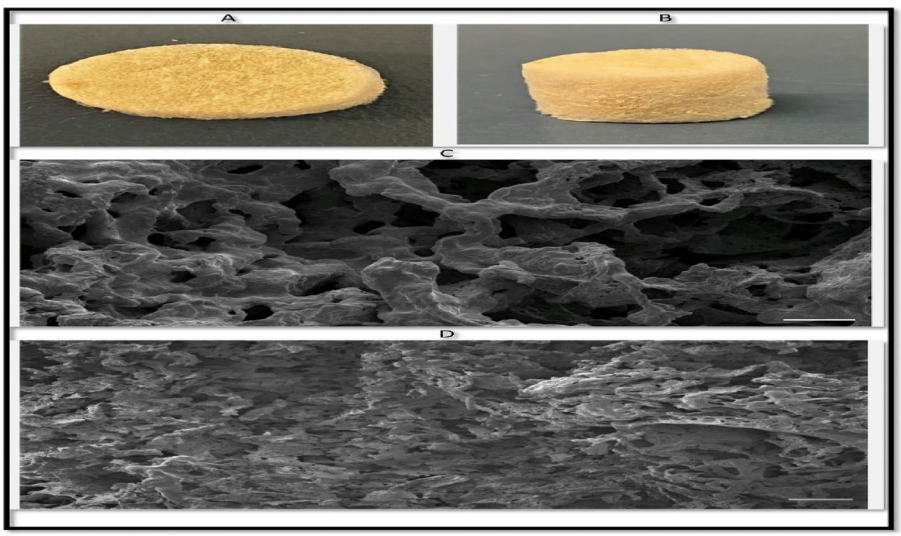


Fig. 3 General Appearance of Keratin/HA/HMPMC scaffolds (diameter: 15 mm, height: 5 mm) (**A** & **B**), SEM micrographs of Pure keratin scaffolds (**C**) and Keratin/HA/MPMC scaffolds (**D**). (Size bars in Fig. 4 C & D represents 100 µm). Feroz & Dias [34]; Creative Commons CC-BY-NC-ND

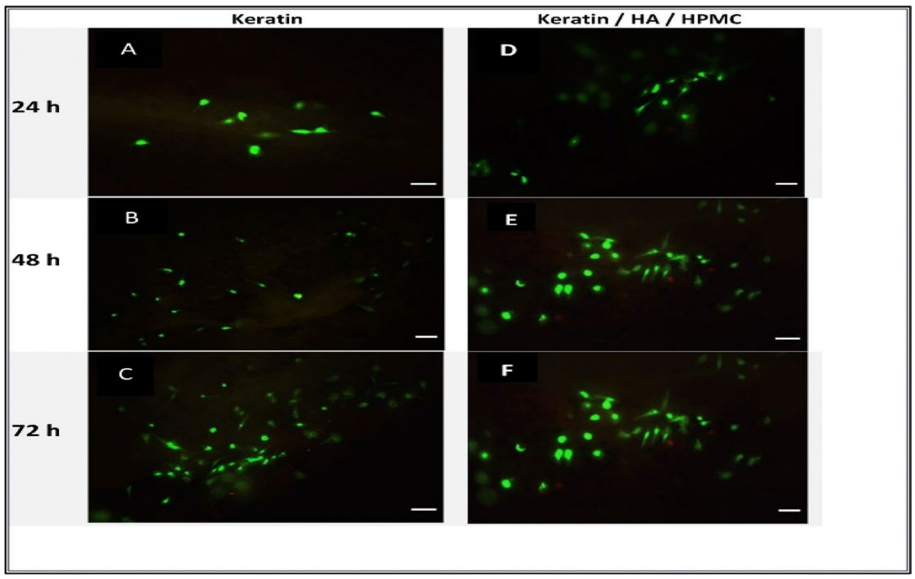


Fig. 4 Fluorescence images of keratin (**A**, **B**, **C**) and keratin/HA/HPMC scaffolds (**D**, **E**, **F**) seeded with Saos-2 cells after live/dead viability assay. Images shows Saos-2 cell viability at 24 h, 48 h & 72 h. Bar = 100 µm. [34], Creative Commons CC-BY-NC-ND

leucine-aspartic acid-valine (LDV) and others [129]. One more advantage of using keratin for generation of tissue engineering biomaterial is that the animal cells mostly do not contain the keratinase enzymes so the in vivo breakdown of this protein like other does not occurs. The generation of keratin-based hydrogels generally requires a cross-linking agent such as transglutaminase, dialdehyde, formaldehyde, glutaraldehyde, ethylene glycol diglycidyl ether [10, 27, 82, 123, 142].

Application of keratin biomaterial is being studied for the regeneration of skin tissue regeneration, vascular tissue regeneration and skeletal muscles regeneration specifically volumetric muscle loss (VML). Minor injuries as a result of exercise or strain in skeleton muscle could be repaired by the intrinsic mechanism of self – repair involving multiple cell signalling events, but major muscle loss following a trauma or surgical intervention results in disturbances in signalling cascade leading to long term loss of structure and function [89]. Use of allografts, muscle flaps are adopted for volumetric muscle loss treatment but has their own drawbacks. Keratin based scaffolds and other biomaterials constructs are being designed and studied for the purpose of restoring functional loss in VML as well as other tissue engineering applications (Table 5).

Peripheral nerve regeneration

Peripheral nervous system (PNS) helps the body to feel sensations and move the muscles. PNS works as a bridge between central nervous system and various tissues or organs [138]. The fundamental units of nervous system i.e. neurons are made up of bundles of axons which forms the peripheral nerves. The types of injuries that can affect the PNS includes neuropraxia, axonotmesis, or neurotmesis. Although the PNS has the capacity to self-repair, but in cases of delayed treatment, severe injury or an injury larger then 3 cm leads to incomplete repair and loss in functionality [64]. In order to regenerate the damaged peripheral nerve, various nerve tissue grafts are being studied including autografts, allografts and xenografts, among which autografts are considered to be the most efficient. Nevertheless, there are certain limitations to nerve grafts including limited availability, surgical complications, immune rejection and diameter mismatch between the donor and recipient nerve to name a few [136]. More recent alternative to nerve grafts includes the artificial nerve conduits made up of biological polymers. Nerve conduits help to fill the nerve gap resulting from nerve injury by guiding the axon regeneration and thus improving the efficiency of the clinical treatment. Different nerve conduits with added functionality of drug and growth factor delivery, capacity to support cell proliferation as well as conductivity with design specific to the particular function are being developed [62, 140, 141]. Similarly other types of biomaterials including membranes have found potential use in regeneration of PNS injuries.

The chitosan/keratin biomimetic composite membrane prepared by [11] depicted potential for angiogenesis and nerve repair efficiency [55]. Fabricated tubular nanofibers with keratin extracted from chicken feather and PVA by using electrospinning, to be used as nerve conduits.

Table 5 Tissue engineering applications of keratin-based biomaterials

Composition	Keratin source	Biomaterial type	Properties and function	Applications	References
Keratin and fibrinogen	Human hair	Hydrogels	Suitable for controlled protein delivery.	Skin tissue regeneration	[78]
PCL (poly(ε-caprolactone) and keratin	-	Mats	These mats accelerated the migration and growth of human vein endothelial cells and displayed excellent blood compatibility with antibacterial properties in rabbit study models.	Vascular tissue regeneration.	[77]
Collagen and keratin	Human hair	Hydrogel	Co-transplantation of C2C12 cells with the combination of Collagen and keratin can promote myogenesis in muscle injury sites. The generation of de novo muscle fibres in biceps femoris of mice was observed that received the combination of cells and hydrogels after 15 days.	Skeletal muscles regeneration	[81]
Keratin and gelatin	Human hair	Scaffolds	These scaffolds accelerated myogenesis with significant expression of myogenin mRNA and enhanced myotube development.	Skeletal muscles regeneration	[122]
γ-PGA and keratin	Human hair	Electrospun nanofibrous scaffolds (ENS)	The cells can grow and stick to the ENS in in-vitro studies. The mouse fibroblasts cells could also grow and proliferate on these scaffolds.	Tissue engineering	[46]

Table 5 (continued)

Composition	Keratin source	Biomaterial type	Properties and function	Applications	References
Phosphobetainized keratin (PK) and poly(ε-caprolactone) (PCL)	Human hair	Nanofibrous mats	Biocomposite mats selectively enhanced adhesion, migration, and growth of endothelial cells while suppressed proliferation of smooth muscle cells in the presence of glutathione (GSH) and GSNO due to the catalytic generation of NO. These mats exhibited good blood anticoagulant activity by reducing platelet adhesion, prolonging blood clotting time, and inhibiting hemolysis.	Vascular tissue engineering	[61]
Keratin and chitosan	Human hair	Hydrogels	The cell viability of more than 80% was observed in hydrogels prepared with varied concentrations of chitosan, KAP and KIFs . These hydrogels showed negligible cytotoxicity against the L929 fibroblasts cells.	Tissue engineering	[65]
Polylactic acid (PLA), keratin and chitosan	Human hair and chicken feathers' barbs	Scaffolds	PLA-Keratin feathers scaffolds at 0.5 wt.% showed the best cell growth.	Tissue engineering	[98]
Gelatin and Keratin	Poultry feathers	Scaffolds	MC3T3-E1 pre-osteoblastic cells could proliferate and grow within the scaffolds. Cells grown on electrospun biomaterial showed less stress than the one grown on casted films.	Tissue engineering	[88]

Table 5 (continued)

Composition	Keratin source	Biomaterial type	Properties and function	Applications	References
Poly (lactic-co-glycolic acid) (PLGA)/wool keratin	Wool	Electrospun membrane	Sustained release of basic fibroblast growth factor (bFGF) from bFGF-loaded PLGA/wool keratin composite membranes can be maintained for 28 d. These membrane loaded with bFGF promoted adhesion, proliferation and osteogenic differentiation of human periodontal ligament fibroblasts (hPLDFs).	Tissue engineering	[148]
Fibroin and Keratin and vanillin	Human hair	Spongy scaffolds	Vanillin-loaded scaffolds presented a clear zone of inhibition against both *E. coli* and *S. aureus* in a dose dependent manner.	Tissue engineering	[145]
Polyhydroxybutyrate (PHB) and keratin	Chicken feather	Scaffolds	PHB scaffolds with up to 20% keratin had better mechanical properties with increased cell attachment and proliferation than scaffolds composed of PHB alone.	Tissue engineering	[146]

These nanofibers had diameter ranging from 170 to 234 nm. The authors also reported a decrease in diameter of the nanofiber with increase in concentration of keratin [39] reported that the human hair keratin can promote the extension of axon in Dorsal root ganglion neurons in vivo. The authors prepared a keratin sponge and also suggested that these could enhance the cell adhesion, proliferation, migration and secretion of neurotrophic factors by Schwann cells in vitro [144] studied spinal cord injury (SCI) in rat models and reported that keratin biomaterials can induce polarization of macrophages and promote functional recovery.

Promoting macrophages to move towards M2 anti-inflammatory phenotype is regarded as a target to treat the SCI [152] studied the anti-inflammatory activities of 17 human hair keratins, the authors have found that recombinant keratins 33A and 35 demonstrated superior anti- inflammatory properties. The authors also established the role of recombinant keratin 33A in nerve regeneration and increasing M2 polarization by working with rat T9 spinal cord lateral hemisection model and utilizing keratin nanofibers.

Qin et al. [90] used activated Schwann cells with human hair keratin to prepare nerve grafts. The nerve grafts thus produced, promoted the nerve conduction function as well as motor function in rats with sciatic nerve injury due to increased expression of nerve growth factors, thus could be applicable in healing peripheral nerve injuries. In yet another more recent research [119], Explored the potential of curcumin to promote peripheral nerve regeneration. The researchers exploited the properties of keratin/ chitosan hydrogel to effectively deliver the curcumin to the target site in appropriate concentration. The hydrogels were found to be capable of delivering the curcumin for 10 days in vitro. In rat studies also, the hydrogel was found to be capable of enhancing nerve regeneration (Fig. 5).

Ocular surface reconstruction

Ocular surface reconstruction means repairing the eye's tissue such as cornea, conjunctiva and limbus and restoring the vision of eyes. Ocular surface reconstruction often become necessary in case of damage caused by various factors including trauma, infections, chemical

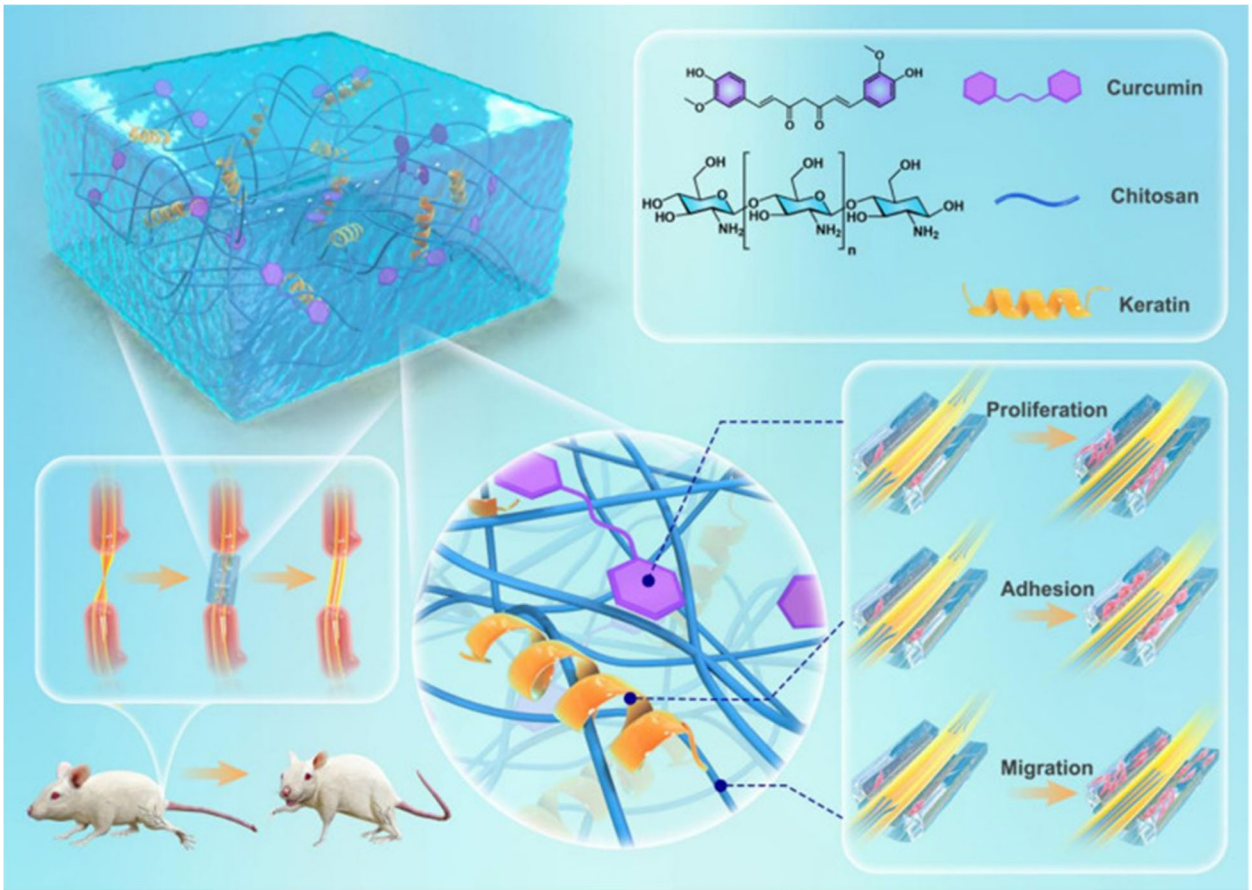


Fig. 5 Schematic diagram of keratin chitosan hydrogel synthesis process loaded with curcumin, cell adhesion in complex hydrogel, complex hydrogel promotes repair of peripheral nerve injury. Sun et al., (2023); Creative Commons CC-BY

burns, surgical complications and autoimmune diseases. The ultimate objective of this technique is reconstructing vision, alleviating pain and prevention from further damage. As already stated, keratin is known for its biocompatibility, biodegradability and ability to promote cell proliferation, cell division and cell adhesion it has now gained attention of researchers in the application of ocular surface reconstruction. This can be achieved by creating scaffolds, membranes and fibrous mats to repair and regenerate ocular surface tissue. Keratin-based biomaterials provide a supportive structure to promote cell proliferation and cell migration of corneal and conjunctival epithelial cells. These materials have mechanical properties which are similar to the native ocular surface and facilitate in healing and integration. Owing to its anti-inflammatory effect, keratin can provide a more conducive environment for tissue healing and reduce inflammation in the ocular surface. The research on the exploitation of keratin for ocular surface reconstruction is still evolving with ongoing studies exploring its full potential and optimizing the application processes. However, current results are promising and indicate that keratin and keratin-based biomaterials could become an ideal tool for ocular surface reconstruction. Generally amniotic membrane is applied as an alternative substitute during ocular surface reconstruction. Additionally, dexamethasone eye-drop is continuously required to supress inflammation and fast recovery rate after surgery.

Schwab & Reichl [105] successfully developed keratin films incorporated with dexamethasone drug. They used different concentrations of dexamethasone, and their findings suggest that prepared films with moderate dexamethasone gives satisfactory positive results as they influenced the biochemical properties and transparency of the films whereas highly loaded films showed exact similar result to those of amniotic membranes. The authors also compared these films with amniotic membranes and found that developed films could be a promising alternative to be used in ocular surface reconstruction [9]. Also compared keratin films with amniotic membranes by using ofloxacin and dexamethasone eye-drop externally on the regular intervals instead of incorporating in the membrane. The experiments involved use of amniotic membranes and keratin films separately in white rabbits and recorded the results after a period of 10 days. The eyes of rabbits treated with keratin films were reported to be completely healed without any neovascularization and those treated with amniotic membranes showed neovascularization on seventh day however, it recovered on tenth day.

Haemostatic agent

In case of any injury or cut, the loss of blood from the body is stopped by the formation of blood clot. The sequence of regulated events leading to the formation of blood clot is known as hemostasis and the agents that participate in hemostasis are called hemostatic agents. In case of a major bleeding or accidental situations, hemostasis may not be efficient enough and that could even lead to the death of the patient. Advance and new hemostatic technologies are continuously being developed to tackle uncontrolled hemorrhage in an emergency, battlefield and surgical conditions. Hemostasis involves activation of signaling pathways to clot the blood, including platelets and other proteins like fibrinogen and thrombin.

Although, many hemostatic agents, adhesives, and sealants are available in the market. But developing an ideal hemostatic agent with multiple properties such as effective and immediate management of bleeding, biodegradability, biocompatibility, appropriate mechanical properties, strong adhesion property, antibacterial activity, easily manageable in wet and dynamic conditions and many more still remains a huge leap. Keeping these conditions in mind, researchers have used keratin as a hemostatic agent because it is a versatile compound that has all these characteristics. Keratin activates platelets and other important proteins directly as it promotes platelet adhesion and aggregation. It can be used to produce physical scaffolds that supports the formation of blood clot. Scaffolds trap blood platelets and RBCs which contribute to the formation of a stable clot and can efficiently seal the injury and stop bleeding. Keratin can be isolated from different source material and processed into various forms such as sponges, powders and films which can be applied to wounds and on an injury directly. These materials enhance hemostasis as they can absorb blood immediately, aggregate clotting factors and provide a suitable environment for clot formation.

Goudarzi et al. [42] successfully developed keratin crosslinked sponges with the help of glutaraldehyde by utilizing freeze-drying technique. They performed experiments on human foreskin fibroblasts cells and suggested that developed sponges were able to absorb 91% of water and had good cell viability resulting into blood clotting and major liquid absorption. The authors also observed that prepared sponges were capable to be used in haemostasis [32]. Used freeze-gelation method to prepare composite scaffolds of methylene blue-loaded keratin and alginate. Developed composite scaffolds could absorb over 1600% liquid effectively, had good biodegradability, high biocompatibility and well interconnected pores. The researchers concluded that composite scaffolds of keratin and alginate work synergistically on wound and significantly minimizes haemostasis time. They also reported that the drug loaded into developed scaffolds prevent infection by absorbing wound

secretions and increase burst release at the early stages of wound recovery.

Chen et al. [14] worked on keratin polymers (high and low molecular weight keratins) i. e. KIFs and KAPs. They used a combination of both proteins in different ratios to precipitate fibrinogen and reported that equal amount of KIFs and KAPs participate in haemostasis as it yielded highest accumulation of fibrinogen protein [136]. Utilized a novel approach viz. recombinant synthesis for maximizing the performance of keratin in haemostasis. They adopted those α- helical keratin sequences which are responsible for haemostatic activities and noticed that amino acids found on N-terminal of α- helices (such as Tyr, Phe and Gln) residues are very important in fibrin polymerization. The researchers also mutated the Cystine to Serine residues on α-helices and found a positive results in haemostasis. High efficiency keratin biomaterials could be produced by exploring such strategies with improved potential over gelatin sponges. In another study from [140, 141] also reported that keratin/chitosan sponges with porosity 90.12 ± 2.17% have potential to work as haemostatic agent [66]. Successfully developed KAPs nanoparticles from KAPs fragments extracted from human hairs and used these KAPNPs as haemostatic agent. Their researchers reported that KAPNPs have great potential, good biocompatibility and minimum clotting time.

Miscellaneous

Valkov et al. [128] prepared keratin films from human hair with structural similarity to human nail plate. The authors reported that the keratin films could be used as a model for studying onychomycosis. Also after infecting the dermatophytic fungi *Trichophyton rubrum,* the growth was observed on the surface of the film and the fungi was also able to penetrate inside the films [125] studied the use of chicken feather keratin as a template to produce silver nanoparticles (AgNP) and gold nanoparticles (AuNP). The AuNP and AgNP had spherical shape and a reported diameter of 3-13 nm and 4- 20 nm respectively. The authors proposed the use of synthesized nanoparticles for controlling growth of *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* as well as potential urease inhibitor. Keratin materials are also being explored as a substrate or coating material for in vitro culturing of cells [8] utilized keratin from goat hair to prepare biomaterial and use it as coating material for in vitro culturing of mesenchymal stem cells (MSC's) and primary goat fibroblast cells. The authors reported that the keratin biomaterials hold promising suitability in the area of cell-based tissue engineering and wound healing owing to their biocompatibility.

Conclusion

Keratin from variety of waste sources such as chicken feather, human hair are being utilized for the fabrication of biomaterials and have gained immense interest in various biomedical applications. Interesting physical and biological properties of keratin makes it a suitable candidate for applications such as skin tissue engineering, treating volumetric muscle loss, drug delivery and bone tissue regeneration among others. The use of hydrogels, scaffolds made up of keratin alone or loaded with either growth factors or drug molecules is an emerging option to handle and cure chronic wounds. In a similar fashion, the nanogels, nanoparticles, microfibers based on keratin have also been found to be effective in drug delivery systems that are biocompatible and show prolonged drug delivery in addition to growth promoting capabilities for different human cell lines. For oral tissue regeneration as well, keratin biomaterials have been found to be non-toxic for periodontal fibroblasts or dental keratinocytes as well as have also shown growth promotion for human periodontal ligament fibroblasts among others. At present multiple roles of keratin in tissue engineering and haemostasis are being established and more research could be focused on the detailed role of keratin in these areas.

Future perspectives

Various biomaterials in the form of films, hydrogels, nanoparticles have been utilized and put to diverse biomedical applications. Apart from being a cheap raw material keratin biomaterial have also been found to be biocompatible and biodegradable. Still fraction of keratin based biomaterials in commercial market and actual use in medical field is very less. The major challenges for keratin biomaterials could be summarized into inconsistent source material, complex extraction and purification methods, scalability and structural stability under varied physiological conditions such as pH, moisture and temperature. Detailed studies pertaining to molecular interactions and regarding the mechanical properties of these materials need to be taken up in order to overcome the aforesaid challenges.

Research needs to be focused on the behaviour of the keratin biomaterials with varied concentrations of different keratin components such as keratose, keratein, α keratin, β keratin and γ keratin under diverse physiological conditions as well as their cellular interactions and attachment profiles. Knowledge from these studies would be a great leap towards success in keratin based biomaterials production and application. Further endeavours could be made to fabricate customised biomaterials for specific biomedical roles and additional validation of the usage of keratin-based biomaterials needs to be done in large animal models.

Abbreviations

ADSC	Adipose-derived stem cells
AgNP	Silver nanoparticles
AM	Amniotic membrane
ANOVA	Analysis of variance
AuNP	Gold nanoparticles
BD	Bovine dermis
bFGF	Basic fibroblast growth factor
BSA	Bovine Serum Albumin
C.roseus	Catharanthus roseus
CHX	Chlorhexidine
CS	Chitosan
D	Dalton
DPSCs	Dental pulp-derived stem cells
EDS	Glutamic acid-aspartic acid-serine
EGF	Epidermal Growth Factor
EMT	Epithelial-Mesenchymal Transition
ENS	Electrospun nanofibrous scaffolds
FGF	Fibroblast growth factor
GIBO	Garbage In, Biomaterials Out
GLS	Glucosamine sulfate
GOD	Glucose oxidase
GS	Gentamycin sulphate
GSH	Glutathione
HA	Hydroxyapatite
HEKa	Human epidermal keratinocytes
HGF	Human gingiva fibroblasts
HKM	Human keratin matrices
HOK	Human oral keratinocytes
hPLDFs	Human periodontal ligament fibroblasts
HPMC	Hydroxypropyl methylcellulose
IL-6	Interleukin-6
KAPNPs	Keratin associated proteins nanoparticles
KAPs	Keratin associated proteins
kDa	Kilo Dalton
KIFs	Keratin intermediate filaments
KN	Kerateine
KO	Keratose
KOH	Potassium hydroxide
KRT	Keratin
KXG	Keratin/xanthan/gelatin
LDV	Leucine-aspartic acid-valine
MIP-1δ	Macrophage Inflammatory Protein-1 delta
MnO2	Manganese dioxide
MRNA	Messenger ribosomal nucleic acid
MSC's	Mesenchymal stem cells
mTOR	Mammalian target of rapamycin
MWCNTs	Multi-walled carbon nanotubes
NaOH	Sodium hydroxide
NPs	Nanoparticles
p-AKT 72	Phosphorylated serine/threonine protein kinase
PAN	Polyacrylonitrile
PBS	Poly butylene succinate
PCL	poly(ε-caprolactone)
PEG	Poly ethylene glycol
PHB	Polyhydroxybutyrate
PK	Phosphobetainized keratin
PLCL	Poly(L-lactate-caprolactone) copolymer
PLCL	Poly(L-lactate-caprolactone) copolymer
PLGA	Poly Lactic-co-Glycolic Acid
PNS	Peripheral nervous system
PVA	Polyvinyl alcohol
RB	Rhodomine B
RBCs	Red blood cells
ROS	Reactive oxygen species
SCI	Spinal cord injury
SIS	Small intestinal submucosa
THP	Thermal hydrolysis process
TPP	Tripolyphosphate
VEGF	Vascular endothelial growth factor
VML	Volumetric muscle loss
XG	xanthan/gelatin
XRD	X- ray diffraction
ZnO NPs	Zinc oxide nanoparticles
β-CD-K-IN-DG	β-cyclodextrin-keratin- insulin- dialdehyde glucan

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Authors' contributions
AS: Conceptualization, data collection, manuscript preparation GS: Conceptualization and review RM: Data collection and manuscript preparation.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

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References

1. Abdelmoteleb, A., Gonzalez-Mendoza, D., Tzintzun-Camacho, O., Grimaldo-Juárez, O., Mendez-Trujillo, V., Moreno-Cruz, C., ... & Roumia, A. F. (2023). Keratinases from Streptomyces netropsis and Bacillus subtilis and their potential use in the chicken feather degrading. Fermentation, 9(2):96. https://doi.org/10.3390/fermentation9020096.
2. Adelere, I. A., & Lateef, A. (2019). Degradation of keratin biomass by different microorganisms. Keratin as a Protein Biopolymer: Extraction from Waste Biomass and Applications, 123–162. https://doi.org/10.1007/978-3-030-02901-2_5
3. Akter N, Chakma S, Fatema K, Azad AK, Jaman Chowdhury M, Mia AS, M. Alkali enzymatic extraction of keratin protein from chicken feather waste in Bangladesh. Iran J Energy Environ. 2019;10(4):235–41. https://doi.org/10.5829/ijee.2019.10.04.02.
4. Amin S, Abbas M, Javed H, Asghar Z, Ghani N, Shaheen S, Yousaf HS, et al. Extraction of keratin from chicken feathers and its application in the treatment of contaminated water: an eco-friendly approach. Br Arch Biol Technol. 2024;67:e24220892. https://doi.org/10.1590/1678-4324-2024220892
5. Anbesaw MS. Bioconversion of keratin wastes using keratinolytic microorganisms to generate value-added Products. Int J Biomater. 2022;2022(1):2048031. https://doi.org/10.1155/2022/2048031.
6. Bakhtiary N, Liu C, Ghorbani F. Bioactive inks development for osteochondral tissue engineering: a mini-review. Gels. 2021;7(4):274. https://doi.org/10.3390/gels7040274.
7. Banasaz S, Ferraro V. Keratin from Animal By-Products: Structure, Characterization, Extraction and Application—A Review. Polymers. 2024;16(14):1999. https://doi.org/10.3390/polym16141999.
8. Bhat, H. F., Amin, N., Nasir, Z., Nazir, S., Bhat, Z. F., Malik, A. A., ... & Abdi, G. (2024). Keratin as an effective coating material for in vitro stem cell culture, induced differentiation and wound healing assays. Heliyon. https://doi.org/10.1016/j.heliyon.2024.e27197
9. Borrelli M, Witt J, Roth M, Reichl S, Bradenbrink P, Schoppe M, Geerling G, et al. Keratin films for ocular surface reconstruction: wound healing in an in-vivo model. Exp Eye Res. 2023;227:109356. https://doi.org/10.1016/j.exer.2022.109356

10. Cao G, Rong MZ, Zhang MQ. Continuous high-content keratin fibers with balanced properties derived from wool waste. ACS Sustain Chem Eng. 2020;8(49):18148–56. https://doi.org/10.1021/acssuschemeng.0c06530.
11. Carvalho CR, Costa JB, Costa L, Silva-Correia J, Moay ZK, Ng KW, Oliveira JM, et al. Enhanced performance of chitosan/keratin membranes with potential application in peripheral nerve repair. Biomater Sci. 2019;7(12):5451–66. https://doi.org/10.1039/C9BM01098J.
12. Chen H, Gao S, Li Y, Xu HJ, Li W, Wang J, Zhang Y. Valorization of livestock keratin waste: application in agricultural fields. Int J Environ Res Public Health. 2022;19(11):6681. https://doi.org/10.3390/ijerph19116681.
13. Chen L, Meng R, Qing R, Li W, Wang Z, Hou Y, Hao S, et al. Bioinspired robust keratin hydrogels for biomedical applications. Nano Lett. 2022;22(22):8835–44. https://doi.org/10.1021/acs.nanolett.2c02530.
14. Chen WC, Hsieh NC, Huang MC, Yang KC, Yu J, Wei Y. An in vitro analysis of the hemostatic efficacy of fibrinogen precipitation with varied keratin fraction compositions. Int J Biol Macromol. 2023;243:125255. https://doi.org/10.1016/j.ijbiomac.2023.125255.
15. Chen WY, Li X, Feng Y, Lin S, Peng L, Huang D. M-keratin nanomaterials create a mineralized micro-circumstance to promote proliferation and differentiation of DPSCs. J Mater Sci - Mater Med. 2020;31:1–13. https://doi.org/10.1007/s10856-020-06465-8.
16. Chen X, Zhai D, Wang B, Hao S, Song J, Peng Z. Hair keratin promotes wound healing in rats with combined radiation-wound injury. J Mater Sci - Mater Med. 2020;31:1–9. https://doi.org/10.1007/s10856-020-06365-x(b).
17. Chen Y, Li Y, Yang X, Cao Z, Nie H, Bian Y, Yang G. Glucose-triggered in situ forming keratin hydrogel for the treatment of diabetic wounds. Acta Biomater. 2021;125:208–18. https://doi.org/10.1016/j.actbio.2021.02.035.
18. Cheng Z, Qing R, Hao S, Ding Y, Yin H, Zha G, Wang B, et al. Fabrication of ulcer-adhesive oral keratin hydrogel for gastric ulcer healing in a rat. Regen Biomater. 2021;8(2):rbab008. https://doi.org/10.1093/rb/rbab008.
19. Chilakamarry CR, Mahmood S, Saffe SNBM, Bin Arifin MA, Gupta A, Sikkandar MY, et al. Extraction and application of keratin from natural resources: a review. 3 Biotech. 2021;11(5):220. https://doi.org/10.1007/s13205-021-02734-7.
20. Davari N, Bakhtiary N, Khajehmohammadi M, Sarkari S, Tolabi H, Ghorbani F, Ghalandari B. Protein-based hydrogels: promising materials for tissue engineering. Polymers. 2022;14(5):986. https://doi.org/10.3390/polym14050986.
21. Dąbrowska M, Sommer A, Sinkiewicz I, Taraszkiewicz A, Staroszczyk H. An optimal designed experiment for the alkaline hydrolysis of feather keratin. Environ Sci Pollut Res. 2022;29(16):24145–54. https://doi.org/10.1007/s11356-021-17649-2.
22. Das, S., Das, A., Das, N., Nath, T., Langthasa, M., Pandey, P., ... & Pandey, P. (2024). Harnessing the potential of microbial keratinases for bioconversion of keratin waste. Environmental Science and Pollution Research, 1–30. https://doi.org/10.1007/s11356-024-34233-6
23. Del Olmo JA, Pérez-Álvarez L, Martínez VS, Cid SB, Ruiz-Rubio L, González RP, Alonso JM, et al. Multifunctional antibacterial chitosan-based hydrogel coatings on Ti6Al4V biomaterial for biomedical implant applications. Int J Biol Macromol. 2023;231:123328. https://doi.org/10.1016/j.ijbiomac.2023.123328
24. Demir GC, Erdemli Ö, Keskin D, Tezcaner A. Xanthan-gelatin and xanthan-gelatin-keratin wound dressings for local delivery of Vitamin C. Int J Pharm. 2022;614:121436. https://doi.org/10.1016/j.ijpharm.2021.121436.
25. Deng L, Yue W, Zhang L, Guo Y, Xie H, Zheng Q, Chen P, et al. Biobased protic ionic liquids as sustainable solvents for wool keratin/cellulose simultaneous dissolution: solution properties and composited membrane preparation. ACS Sustain Chem Eng. 2022;10(6):2158–68. https://doi.org/10.1021/acssuschemeng.1c07662.
26. Dou J, Yang R, Jin X, Li P, Han X, Wang L, Yuan J, et al. Nitric oxide-releasing polyurethane/S-nitrosated keratin mats for accelerating wound healing. Regen Biomater. 2022;9:rbac006. https://doi.org/10.1093/rb/rbac006.
27. Dou Y, Zhang L, Zhang B, He M, Shi W, Yang S, Yin G, et al. Preparation and characterization of edible dialdehyde carboxymethyl cellulose crosslinked feather keratin films for food packaging. Polymers. 2020;12(1):158. https://doi.org/10.3390/polym12010158.
28. Du W, Zhang L, Zhang C, Cao J, Wang D, Li H, Zeng J, et al. Green and highly efficient wool keratin extraction by microwave induction method. Front Mater. 2022;8:789081. https://doi.org/10.3389/fmats.2021.789081
29. Ezike, T. C., Okpala, U. S., Onoja, U. L., Nwike, C. P., Ezeako, E. C., Okpara, O. J., ... & Nwanguma, B. C. (2023). Advances in drug delivery systems, challenges and future directions. Heliyon, 9(6). https://doi.org/10.1016/j.heliyon.2023.e17488
30. Fagbemi OD, Sithole B, Tesfaye T. Optimization of keratin protein extraction from waste chicken feathers using hybrid pre-treatment techniques. Sustain Chem Pharm. 2020;17:100267. https://doi.org/10.1016/j.scp.2020.100267
31. Fazal T, Murtaza BN, Shah M, Iqbal S, Rehman MU, Jaber F, Ibrahium HA, et al. Recent developments in natural biopolymer based drug delivery systems. RSC Advances. 2023;13(33):23087–121. https://doi.org/10.1039/D3RA03369D.
32. Feng CC, Lu WF, Liu YC, Liu TH, Chen YC, Chien HW, Yu J, et al. A hemostatic keratin/alginate hydrogel scaffold with methylene blue mediated antimicrobial photodynamic therapy. J Mater Chem B. 2022;10(25):4878–88. https://doi.org/10.1039/D2TB00898J.
33. Feroz S, Muhammad N, Ratnayake J, Dias G. Keratin based materials for biomedical applications. Bioact Mater. 2020;5:496–509. https://doi.org/10.1016/j.bioactmat.2020.04.007.
34. Feroz, S., & Dias, G. (2021). Hydroxypropylmethyl cellulose (HPMC) crosslinked keratin/hydroxyapatite (HA) scaffold fabrication, characterization and in vitro biocompatibility assessment as a bone graft for alveolar bone regeneration. Heliyon, 7(11). https://doi.org/10.1016/j.heliyon.2021.e08294
35. Feroz S, Muhammad N, Dias G, Alsaiari MA. Extraction of keratin from sheep wool fibres using aqueous ionic liquids assisted probe sonication technology. J Mol Liq. 2022;350:118595. https://doi.org/10.1016/j.molliq.2022.118595.
36. Feroz, S., Muhammad, N., Ullah, R., Nishan, U., Cathro, P., & Dias, G. (2023). Mechanical properties, and in vitro biocompatibility assessment of biomimetic dual layered keratin/hydroxyapatite scaffolds. Frontiers in Bioengineering and Biotechnology, 11. https://doi.org/10.3389/fbioe.2023.1304147
37. Frone AN, Panaitescu DM, Nicolae CA, Gabor AR, Trusca R, Casarica A, Salageanu A, et al. Bacterial cellulose sponges obtained with green cross-linkers for tissue engineering. Mater Sci Eng: C. 2020;110:110740. https://doi.org/10.1016/j.msec.2020.110740
38. Fuhrmann G. Drug delivery as a sustainable avenue to future therapies. J Control Release. 2023;354:746–54. https://doi.org/10.1016/j.jconrel.2023.01.045.
39. Gao J, Zhang L, Wei Y, Chen T, Ji X, Ye K, Hu J, et al. Human hair keratins promote the regeneration of peripheral nerves in a rat sciatic nerve crush model. J Mater Sci: Mater Med. 2019;30:1–13. https://doi.org/10.1007/s10856-019-6283-1.
40. Ghafari F, Karbasi S, Eslaminejad MB, Sayahpour FA, Kalantari N. Biological evaluation and osteogenic potential of polyhydroxybutyrate-keratin/Al2O3 electrospun nanocomposite scaffold: a novel bone regeneration construct. Int J Biol Macromol. 2023;242:124602. https://doi.org/10.1016/j.ijbiomac.2023.124602.
41. Giteru SG, Ramsey DH, Hou Y, Cong L, Mohan A, Bekhit AEDA. Wool keratin as a novel alternative protein: a comprehensive review of extraction, purification, nutrition, safety, and food applications. Comprehensive reviews in food science and food safety. 2023;22(1):643–87. https://doi.org/10.1111/1541-4337.13087.
42. Goudarzi G, Dadashian F, Vatanara A, Sepehrizadeh Z. Optimization of keratin sponge preparation conditions for hemostatic application using Response Surface Methodology (RSM). J Polym Environ. 2024;32(3):1135–49. https://doi.org/10.1007/s10924-023-03020-8.
43. Gough CR, Rivera-Galletti A, Cowan DA, Salas-De La Cruz D, Hu X. Protein and polysaccharide-based fiber materials generated from ionic liquids: a review. Molecules. 2020;25(15):3362. https://doi.org/10.3390/molecules25153362.
44. Guidotti G, Soccio M, Bondi E, Posati T, Sotgiu G, Zamboni R, Aluigi A, et al. Effects of the blending ratio on the design of keratin/poly (butylene succinate) nanofibers for drug delivery applications. Biomolecules. 2021;11(8):1194. https://doi.org/10.3390/biom11081194.

45. Guidotti G, Soccio M, Posati T, Sotgiu G, Tiboni M, Barbalinardo M, Aluigi A, et al. Regenerated wool keratin-polybutylene succinate nanofibrous mats for drug delivery and cells culture. Polymer Degrad Stab. 2020;179:109272. https://doi.org/10.1016/j.polymdegradstab.2020.109272
46. Hao, M., Liu, Y., Chen, Z., Hu, X., Zhang, T., Zhu, X., ... & Yang, B. (2022). Cross-linked gamma polyglutamic acid/human hair keratin electrospun nanofibrous scaffolds with excellent biocompatibility and biodegradability. Polymers, 14(24), 5505. https://doi.org/10.3390/polym14245505
47. Hobbi P, Okoro OV, Nie L, Shavandi A. Fabrication of bioactive polyphenolic biomaterials for bone tissue engineering. Materials Today Sustainability. 2023;24: 100541. https://doi.org/10.1016/j.mtsust.2023.100541.
48. Jafari, H., Ghaffari-Bohlouli, P., Alishahi, M., Davani, F., Daneshi, S. S., Heidari, R., ... & Shavandi, A. (2023). Tissue adhesive hydrogel based on upcycled proteins and plant polyphenols for enhanced wound healing. Materials Today Chemistry, 33, 101722. https://doi.org/10.1016/j.mtchem.2023.101722
49. Jagadeesan Y, Meenakshisundaram S, Saravanan V, Balaiah A. Sustainable production, biochemical and molecular characterization of thermo-and-solvent stable alkaline serine keratinase from novel Bacillus pumilus AR57 for promising poultry solid waste management. Int J Biol Macromol. 2020;163:135–46. https://doi.org/10.1016/j.ijbiomac.2020.06.219.
50. Jelodari S, Daemi H, Mohammadi P, Verdi J, Al-Awady J, M., Ai, J., & Azami, M. Assessment of the efficacy of an LL-37-encapsulated keratin hydrogel for the treatment of full-thickness wounds. ACS Applied Biomaterials. 2023;6(6):2122–36. https://doi.org/10.1021/acsabm.2c01068.
51. Kang HJ, Ko N, Oh SJ, An SY, Hwang YS, Kim SY. Injectable human hair keratin–fibrinogen hydrogels for engineering 3d microenvironments to accelerate oral tissue regeneration. Int J Mol Sci. 2021;22(24):13269. https://doi.org/10.3390/ijms222413269.
52. Kaur M, Bhari R, Singh RS. Chicken feather waste-derived protein hydrolysate as a potential biostimulant for cultivation of mung beans. Biologia. 2021;76:1807–15. https://doi.org/10.1007/s11756-021-00724-x.
53. Khodaei D, Álvarez C, Mullen AM. Biodegradable packaging materials from animal processing co-products and wastes: An overview. Polymers. 2021;13(15):2561. https://doi.org/10.3390/polym13152561.
54. Khumalo M, Sithole B, Tesfaye T. Valorisation of waste chicken feathers: optimisation of keratin extraction from waste chicken feathers by sodium bisulphite, sodium dodecyl sulphate and urea. J Environ Manage. 2020;262:110329. https://doi.org/10.1016/j.jenvman.2020.110329.
55. Khumalo M, Sithole B, Tesfaye T, Lekha P. Valorization of waste chicken feathers: fabrication and characterization of novel keratin nanofiber conduits for potential application in peripheral nerve regeneration. J Nanomater. 2022;2022(1):7080278. https://doi.org/10.1155/2022/7080278.
56. Kim SY. Development of hair keratin protein to accelerate oral mucosal regeneration. 치위생과학회지. 2023;23(4):369–77. https://doi.org/10.17135/jdhs.2023.23.4.369.
57. Konop M, Czuwara J, Kłodzińska E, Laskowska AK, Sulejczak D, Damps T, Rudnicka L, et al. Evaluation of keratin biomaterial containing silver nanoparticles as a potential wound dressing in full-thickness skin wound model in diabetic mice. J Tissue Eng Regen Med. 2020;14(2):334–46. https://doi.org/10.1002/term.2998.
58. Konop M, Laskowska AK, Rybka M, Kłodzińska E, Sulejczak D, Schwartz RA, Czuwara J. Keratin scaffolds containing casomorphin stimulate macrophage infiltration and accelerate full-thickness cutaneous wound healing in diabetic mice. Molecules. 2021;26(9):2554. https://doi.org/10.3390/molecules26092554.
59. Konop M, Rybka M, Szudzik M, Mazurek Ł, Laskowska AK, Sulejczak D, Czuwara J, et al. Keratin-butyrate scaffolds promote skin wound healing in diabetic rats through down-regulation of IL-1β and Up-regulation of keratins 16 and 17. J Nat Fibers. 2023;20(1):2136325. https://doi.org/10.1080/15440478.2022.2136325.
60. Lei T, Fan J, Wang Y, Cao F, Yang Q, Tian F, Liu Y, et al. The fabrication and evaluation of silver nanoparticle-based keratin scaffolds. J Biomater Appl. 2023;37(6):1071–85. https://doi.org/10.1177/08853282221150685.
61. Li P, Wang Y, Jin X, Dou J, Han X, Wan X, Shen J, et al. Catalytic generation of nitric oxide from poly (ε-caprolactone)/phosphobetainized keratin mats for a vascular tissue engineering scaffold. Langmuir. 2020;36(16):4396–404. https://doi.org/10.1021/acs.langmuir.0c00579.
62. Liu K, Yan L, Li R, Song Z, Ding J, Liu B, Chen X. 3D printed personalized nerve guide conduits for precision repair of peripheral nerve defects. Adv Sci. 2022;9(12):2103875. https://doi.org/10.1002/advs.202103875.
63. Liu, L. R., Huang, M. C., Lee, Z. J., & Wei, Y. (2023). Rational design of keratin nanoparticles utilizing diverse hair protein fractions for controlled drug release. Journal of the Taiwan Institute of Chemical Engineers, 105240. https://doi.org/10.1016/j.jtice.2023.105240
64. Lopes B, Sousa P, Alvites R, Branquinho M, Sousa AC, Mendonça C, Maurício AC, et al. Peripheral nerve injury treatments and advances: one health perspective. Int J Mol Sci. 2022;23(2):918. https://doi.org/10.3390/ijms23020918.
65. Lu TY, Huang WC, Chen Y, Baskaran N, Yua JS, Wei Y. Effect of varied hair protein fractions on the gel properties of keratin/chitosan hydrogels for the use in tissue engineering. Colloids Surf B. 2020;195:111258. https://doi.org/10.1016/j.colsurfb.2020.111258.
66. Lu WF, Lu TY, Liu YC, Liu TH, Feng CC, Lin CW, Yu J, et al. Keratin-associated protein nanoparticles as hemostatic agents. ACS Appl Nano Mater. 2021;4(11):12798–806. https://doi.org/10.1021/acsanm.1c03558.
67. Lu Y, Ye W, Kang W, Wang S, Zhu Z, Chen X, Li J. Wound-healing material with antibacterial and antioxidant functions, constructed using keratin, hyperbranched polymers, and MnO2. ACS Appl Mater Interfaces. 2023;15(25):29841–53. https://doi.org/10.1021/acsami.3c03237.
68. Majeed Z, Farhat H, Ahmad B, Iqbal A, Mahnashi MH, Alqarni AO, Momenah AM, et al. Process optimization, antioxidant, antibacterial, and drug adjuvant properties of bioactive keratin microparticles derived from porcupine (Hystrix indica) quills. PeerJ. 2023;11:e15653. https://doi.org/10.7717/peerj.15653
69. Mamidi N, Velasco Delgadillo RM, Barrera EV. Covalently functionalized carbon nano-onions integrated gelatin methacryloyl nanocomposite hydrogel containing γ-cyclodextrin as drug carrier for high-performance pH-triggered drug release. Pharmaceuticals. 2021;14(4):291. https://doi.org/10.3390/ph14040291.
70. Mamidi N, Delgadillo RMV. Design, fabrication and drug release potential of dual stimuli-responsive composite hydrogel nanoparticle interfaces. Colloids Surf, B. 2021;204:111819.
71. Mamidi N, Zuníga AE, Villela-Castrejón J. Engineering and evaluation of forcespun functionalized carbon nano-onions reinforced poly (ε-caprolactone) composite nanofibers for pH-responsive drug release. Mater Sci Eng C. 2020;112:110928. https://doi.org/10.1016/j.msec.2020.110928.
72. Mancha Sánchez E, Gómez-Blanco JC, López Nieto E, Casado JG, Macías-García A, Díaz Díez MA, Pagador JB, et al. Hydrogels for bioprinting: a systematic review of hydrogels synthesis, bioprinting parameters, and bioprinted structures behavior. Front Bioeng Biotechnol. 2020;8:776. https://doi.org/10.3389/fbioe.2020.00776.
73. Mansouri Shirazi N, Eslahi N, Gholipour-Kanani A. Production and characterization of keratin/tragacanth gum nanohydrogels for drug delivery in medical textiles. Front Mater. 2021;8:720385. https://doi.org/10.3389/fmats.2021.720385.
74. Martín-González D, Bordel S, Santos-Beneit F. Characterization of the keratinolytic activity of three Streptomyces strains and impact of their co-cultivation on this activity. Microorganisms. 2023;11(5):1109. https://doi.org/10.3390/microorganisms11051109.
75. Masood S, Hussain A, Javid A, Bukahri SM, Ali W, Ali S, Sattar S, et al. Fungal decomposition of chicken-feather waste in submerged and solid-state fermentation. Br J Biol. 2021;83:e246389.
76. Mengistu A, Angassa K, Tessema I. Optimization of keratin hydrolysate extraction from tannery sheep hair waste. Int J Chem Eng. 2023;2023:1–18. https://doi.org/10.1155/2023/9293505.
77. Miao C, Du J, Dou J, Wang C, Wang L, Yuan J, Yin M, et al. Facile fabrication of copper-incorporating poly (ε-caprolactone)/keratin mats for tissue-engineered vascular grafts with the potential of catalytic nitric oxide generation. J Mater Chem B. 2022;10(32):6158–70. https://doi.org/10.1039/D2TB01031C.
78. Min SJ, Lee JS, Nah H, Moon HJ, Lee SJ, Kang HJ, Heo DN, et al. Degradable and tunable keratin-fibrinogen hydrogel as controlled release system for skin tissue regeneration. J Bionic Eng. 2023;20(3):1049–59. https://doi.org/10.1007/s42235-022-00317-7.
79. Mohamed JMM, Alqahtani A, Al Fatease A, Alqahtani T, Khan BA, Ashmitha B, Vijaya R. Human hair keratin composite scaffold: characterisation and biocompatibility study on NIH 3T3 fibroblast cells.

Pharmaceuticals. 2021;14(8):781. https://doi.org/10.3390/ph14080781.
80. Mykhaliuk VV, Havryliak VV. Obtaining human hair keratin-based films and their characteristics. Biol Stud. 2021;15:27–36. https://doi.org/10.30970/sbi.1501.643.
81. Namjoo AR, Hassani A, Amini H, Nazaryabrbekoh F, Saghati S, Saadatlou MAE, Rahbarghazi R, et al. Multiprotein collagen/keratin hydrogel promoted myogenesis and angiogenesis of injured skeletal muscles in a mouse model. BMC Biotechnology. 2024;24(1):23. https://doi.org/10.1186/s12896-024-00847-4.
82. Nuutinen EM, Virtanen T, Lantto R, Vähä-Nissi M, Jääskeläinen AS. Ductile keratin films from deep eutectic solvent-fractionated feathers. RSC Adv. 2021;11(44):27512–22. https://doi.org/10.1039/D1RA05123G.
83. Olariu L, Dumitriu BG, Gaidau C, Stanca M, Tanase LM, Ene MD, Tablet C, et al. Bioactive low molecular weight keratin hydrolysates for improving skin wound healing. Polymers. 2022;14(6):1125. https://doi.org/10.3390/polym14061125.
84. Ossai IC, Hamid FS, Hassan A. Valorisation of keratinous wastes: a sustainable approach towards a circular economy. Waste Manage. 2022;151:81–104. https://doi.org/10.1016/j.wasman.2022.07.021.
85. Panda, J., Mishra, A. K., Mohanta, Y. K., Patowary, K., Rauta, P. R., & Mishra, B. (2024). Exploring Biopolymer for Food and Pharmaceuticals Application in the Circular Bioeconomy: An Agro-Food Waste-to-Wealth Approach. Waste and Biomass Valorization, 1–31. https://doi.org/10.1007/s12649-024-02452-0
86. Perța-Crișan S, Ursachi CȘ, Gavrilaș S, Oancea F, Munteanu FD. Closing the loop with keratin-rich fibrous materials. Polymers. 2021;13(11):1896. https://doi.org/10.3390/polym13111896.
87. Peydayesh M, Bagnani M, Soon WL, Mezzenga R. Turning food protein waste into sustainable technologies. Chem Rev. 2022;123(5):2112–54. https://doi.org/10.1021/acs.chemrev.2c00236.
88. Pulidori E, Micalizzi S, Koutsomarkos N, Bramanti E, Tinè MR, Vozzi G, Duce C, et al. Analysis of gelatin secondary structure in gelatin/keratin-based biomaterials. J Mol Struct. 2023;1279:134984. https://doi.org/10.1016/j.molstruc.2023.134984
89. Purslow PP. The structure and role of intramuscular connective tissue in muscle function. Front Physiol. 2020;11:519145. https://doi.org/10.3389/fphys.2020.00495.
90. Qin HJ, Li H, Chen JZ, Zhang KR, Zhao XQ, Qin JQ, Yang J, et al. Artificial nerve graft constructed by coculture of activated Schwann cells and human hair keratin for repair of peripheral nerve defects. Neural Regen Res. 2023;18(5):1118–23. https://doi.org/10.4103/1673-5374.355817.
91. Radu CD, Verestiuc L, Ulea E, Lipsa FD, Vulpe V, Munteanu C, Istrate B, et al. Evaluation of keratin/bacterial cellulose based scaffolds as potential burned wound dressing. Appl Sci. 2021;11(5):1995. https://doi.org/10.3390/app11051995.
92. Rajabi M, Ali A, McConnell M, Cabral J. Keratinous materials: Structures and functions in biomedical applications. Mater Sci Eng, C. 2020;110:110612. https://doi.org/10.1016/j.msec.2019.110612.
93. Ramey-Ward AN, Walthall HP, Smith S, Barrows TH. Human keratin matrices promote wound healing by modulating skin cell expression of cytokines and growth factors. Wound Repair and Regeneration. 2024. https://doi.org/10.1111/wrr.13137.
94. Rangappa SM, Siengchin S, Parameswaranpillai J, Jawaid M, Ozbakkaloglu T. Lignocellulosic fiber reinforced composites: Progress, performance, properties, applications, and future perspectives. Polym Compos. 2022;43(2):645–91. https://doi.org/10.1002/pc.26413.
95. Ranjit E, Hamlet S, George R, Sharma A, Love RM. Biofunctional approaches of wool-based keratin for tissue engineering. J Sci: Adv Mater Devices. 2022;7(1):100398. https://doi.org/10.1016/j.jsamd.2021.10.001.
96. Ranjit E, Hamlet S, Love RM. Keratin coated titanium as an aid to osseointegration: physicochemical and mechanical properties. Surf Coat Technol. 2023;462:129457.
97. Riyanto, Yusmiati, N. Cahyandaru, Isolation and characterization of keratin from chicken feathers. In: In AIP Conference Proceedings, vol. 2229, no. 1, AIP Publishing, 2020: p. 030038. https://doi.org/10.1063/5.0002792
98. Rojas-Martínez LE, Flores-Hernandez CG, López-Marín LM, Martinez-Hernandez AL, Thorat SB, Vasquez CR, Velasco-Santos C, et al. 3D printing of PLA composites scaffolds reinforced with keratin and chitosan: effect of geometry and structure. Eur Polymer J. 2020;141:110088. https://doi.org/10.1016/j.eurpolymj.2020.110088
99. Rybka M, Mazurek Ł, Czuwara J, Laskowska A, Szudzik M, Ruszczak Z, Konop M, et al. Biomedical potential of keratin-biphalin wound dressing in diabetic mice: in vitro and in vivo studies. J Nat Fibers. 2024;21(1):2287647. https://doi.org/10.1080/15440478.2023.2287647.
100. Sahranavard M, Zamanian A, Ghorbani F, Shahrezaee MH. A critical review on three dimensional-printed chitosan hydrogels for development of tissue engineering. Bioprinting. 2020;17:e00063. https://doi.org/10.1016/j.bprint.2019.e00063.
101. Said, M. I. (2020, April). Potential development of poultry feather waste resources as raw material in industry: A review. In *IOP Conference Series: Earth and Environmental Science* (Vol. 492, No. 1, p. 012089). IOP Publishing. https://doi.org/10.1088/1755-1315/492/1/012089
102. Sanchez Ramirez DO, Cruz-Maya I, Vineis C, Tonetti C, Varesano A, Guarino V. Design of asymmetric nanofibers-membranes based on polyvinyl alcohol and wool-keratin for wound healing applications. J Funct Biomater. 2021;12(4):76. https://doi.org/10.3390/jfb12040076.
103. Sarma A. Biological importance and pharmaceutical significance of keratin: a review. Int J Biol Macromol. 2022;219:395–413. https://doi.org/10.1016/j.ijbiomac.2022.08.002.
104. Schiller T, Scheibel T. Bioinspired and biomimetic protein-based fibers and their applications. Commun Mater. 2024;5(1):56. https://doi.org/10.1038/s43246-024-00488-2.
105. Schwab R, Reichl S. Dexamethasone-loaded keratin films for ocular surface reconstruction. J Mater Sci - Mater Med. 2022;33(3):29. https://doi.org/10.1007/s10856-021-06638-z.
106. Sellappan LK, Manoharan S. Fabrication of bioinspired keratin/sodium alginate based biopolymeric mat loaded with herbal drug and green synthesized zinc oxide nanoparticles as a dual drug antimicrobial wound dressing. Int J Biol Macromol. 2024;259: 129162. https://doi.org/10.1016/j.ijbiomac.2023.129162.
107. Senthilkumar N, Chowdhury S, Sanpui P. Extraction of keratin from keratinous wastes: current status and future directions. J Mater Cycles Waste Manage. 2023;25(1):1–16. https://doi.org/10.1007/s10163-022-01492-9.
108. Serag E, El-Aziz AMA, El-Maghraby A, Taha NA. Electrospun non-wovens potential wound dressing material based on polyacrylonitrile/chicken feathers keratin nanofiber. Sci Rep. 2022;12(1):15460. https://doi.org/10.1038/s41598-022-19390-3.
109. Shang Y, Wang P, Wan X, Wang L, Liu X, Yuan J, Shen J, et al. Chlorhexidine-loaded polysulfobetaine/keratin hydrogels with antioxidant and antibacterial activity for infected wound healing. Int J Biol Macromol. 2023;242:124754. https://doi.org/10.1016/j.ijbiomac.2023.124754
110. Sharma LA, Ramesh N, Sharma A, Ratnayake JT, Love RM, Alavi SE, Dias GJ, et al. In vitro effects of wool-derived keratin on human dental pulp-derived stem cells for endodontic applications. Br J Oral Maxillofac Surg. 2023;61(9):617–22. https://doi.org/10.1016/j.bjoms.2023.08.240.
111. Sharma S, Rostamabadi H, Gupta S, Nadda AK, Kharazmi MS, Jafari SM. Nano/micro-formulations of keratin in biocomposites, wound healing and drug delivery systems; recent advances in biomedical applications. Eur Polymer J. 2022;180:111614. https://doi.org/10.1016/j.eurpolymj.2022.111614.
112. Shavandi A, Jafari H, Zago E, Hobbi P, Nie L, De Laet N. A sustainable solvent based on lactic acid and l-cysteine for the regeneration of keratin from waste wool. Green Chem. 2021;23(3):1171–4. https://doi.org/10.1039/D0GC04314A.
113. Shen Q, Wang H, Zhang C, Qin X, Jia W, Xu X, Zheng Q, et al. Liquefaction of porcine hoof shell to prepare peptone substitute by instant catapult steam explosion. J Biosci Bioeng. 2020;129(4):467–75. https://doi.org/10.1016/j.jbiosc.2019.09.019.
114. Shen Q, Ma Y, Qin X, Guo Y, Zhang C. Steam explosion as a green method to treat animal waste: a mini-review. Process Saf Environ Prot. 2023. https://doi.org/10.1016/j.psep.2023.11.012.
115. Shestakova A, Timorshina S, Osmolovskiy A. Biodegradation of keratin-rich husbandry waste as a path to sustainable agriculture. Sustainability. 2021;13(16):8691. https://doi.org/10.3390/su13168691.
116. Siddiqui M, Vimal A, Bhargava P. Biological degradation of keratin by microbial keratinase for effective waste management and potent

industrial applications. Curr Protein Pept Sci. 2021;22(4):304–12. https://doi.org/10.2174/1389203722666210215151952.
117. Srinivasan V, Palanisamy P. Design and development of keratin/chitosan/glucosamine sulfate composite loaded MWCNT intended for osteoarthritis drug delivery. Biomed Mater. 2023;18(4):045021. https://doi.org/10.1088/1748-605X/acd6c9.
118. Suarato G, Contardi M, Perotto G, Jose'A HG, Fiorentini F, Ceseracciu L, Athanassiou A, et al. From fabric to tissue: recovered wool keratin/polyvinylpyrrolidone biocomposite fibers as artificial scaffold platform. Mater Sci Eng, C. 2020;116:111151. https://doi.org/10.1016/j.msec.2020.111151.
119. Sun, X., Huang, X., Liang, Q., Wang, N., Zheng, X., Zhang, Q., & Yu, D. (2024). Curcumin-loaded keratin-chitosan hydrogels for enhanced peripheral nerve regeneration. *International Journal of Biological Macromolecules*, 132448. https://doi.org/10.1016/j.ijbiomac.2024.132448
120. Tran CD, Prosenc F, Franko M, Benzi G. Synthesis, structure and antimicrobial property of green composites from cellulose, wool, hair and chicken feather. Carbohyd Polym. 2016;151:1269–76. https://doi.org/10.1016/j.carbpol.2016.06.021.
121. Tasaki K. A novel thermal hydrolysis process for extraction of keratin from hog hair for commercial applications. Waste Manage. 2020;104:33–41. https://doi.org/10.1016/j.wasman.2019.12.042.
122. Thilagam R, Mubeena S, Punnose AM, Gnanamani A. Fibrous protein composite scaffolds (3D) for tissue regeneration: an in vitro study on skeletal muscle regeneration. Colloids Surf B. 2022;217:112656. https://doi.org/10.1016/j.colsurfb.2022.112656.
123. Tinoco A, Rodrigues RM, Machado R, Pereira RN, Cavaco-Paulo A, Ribeiro A. Ohmic heating as an innovative approach for the production of keratin films. Int J Biol Macromol. 2020;150:671–80. https://doi.org/10.1016/j.ijbiomac.2020.02.122.
124. Tissera ND, Wijesena RN, Ludowyke N, Priyadarshana G, Dahanayake D, de Silva RM, de Silva KN. Keratin protein nanofibers from merino wool yarn: a top-down approach for the disintegration of hierarchical wool architecture to extract α-keratin protein nanofibers. RSC Adv. 2024;14(10):6793–804. https://doi.org/10.1039/D3RA07063H.
125. Ullah, R., Hameed, A., Azam, A., Aziz, T., Farhan, & Qiao, S. (2022). Facile synthesis of silver and gold nanoparticles using chicken feather extract as template and their biological applications. *Biomass Conversion and Biorefinery*, 1–9. https://doi.org/10.1007/s13399-022-03447-4
126. Varanko A, Saha S, Chilkoti A. Recent trends in protein and peptide-based biomaterials for advanced drug delivery. Adv Drug Deliv Rev. 2020;156:133–87. https://doi.org/10.1016/j.addr.2020.08.008.
127. Vardaxi A, Kafetzi M, Pispas S. Polymeric nanostructures containing proteins and peptides for pharmaceutical applications. Polymers. 2022;14(4):777.
128. Valkov A, Zinigrad M, Sobolev A, Nisnevitch M. Keratin biomembranes as a model for studying onychomycosis. Int J Mol Sci. 2020;21(10):3512. https://doi.org/10.3390/ijms21103512.
129. Vasile C, Pamfil D, Stoleru E, Baican M. New developments in medical applications of hybrid hydrogels containing natural polymers. Molecules. 2020;25(7):1539. https://doi.org/10.3390/molecules25071539.
130. Villa ALV, Aragão MRS, Dos Santos EP, Mazotto AM, Zingali RB, De Souza EP, Vermelho AB. Feather keratin hydrolysates obtained from microbial keratinases: effect on hair fiber. BMC Biotechnol. 2013;13:1–11. https://doi.org/10.1186/1472-6750-13-15.
131. Vineis C, Maya IC, Mowafi S, Varesano A, Ramírez DS, Abou Taleb M, El-Sayed H, et al. Synergistic effect of sericin and keratin in gelatin based nanofibers for in vitro applications. Int J Biol Macromol. 2021;190:375–81. https://doi.org/10.1016/j.ijbiomac.2021.09.007.
132. Vineis, C., Varesano, A., Varchi, G., & Aluigi, A. (2019). Extraction and characterization of keratin from different biomasses. Keratin as a Protein Biopolymer: Extraction from Waste Biomass and Applications, 35–76. https://doi.org/10.1007/978-3-030-02901-2_3
133. Wang J, Gao H, Qin C, Zhao Z, Yuan H, Wei J, Nie Y. Experimental and theoretical study on the extraction of keratin from human hair using protic ionic liquids. J Mol Liq. 2022;368:120626. https://doi.org/10.1016/j.molliq.2022.120626.
134. Wang, Y., Song, W., Xue, S., Gao, B., Zhang, Y., & Zhang, G. (2024). Keratin-based Nanoparticles for Oral Delivery of Insulin. https://doi.org/10.21203/rs.3.rs-3807836/v1
135. Wang Y, Xu Y, Zhang Z, He Y, Hou Z, Zhao Z, Hao S, et al. Rational design of high-performance keratin-based hemostatic agents. Adv Healthc Mater. 2022;1(15):2200290. https://doi.org/10.1002/adhm.202200290.
136. Wang Y, Zhang Y, Li X, Zhang Q. The progress of biomaterials in peripheral nerve repair and regeneration. J Neurorestoratol. 2020;8(4):252–69. https://doi.org/10.26599/JNR.2020.9040022.
137. Wu S, Dong T, Li Y, Sun M, Qi Y, Liu J, Duan B, et al. State-of-the-art review of advanced electrospun nanofiber yarn-based textiles for biomedical applications. Appl Mater Today. 2022;27:101473. https://doi.org/10.1016/j.apmt.2022.101473
138. Xue W, Shi W, Kong Y, Kuss M, Duan B. Anisotropic scaffolds for peripheral nerve and spinal cord regeneration. Bioactiv Mater. 2021;6(11):4141–60. https://doi.org/10.1016/j.bioactmat.2021.04.019.
139. Yalçın D, Top A. Novel biopolymer-based hydrogels obtained through crosslinking of keratose proteins using tetrakis (hydroxymethyl) phosphonium chloride. Iran Polym J. 2022;31(9):1057–67. https://doi.org/10.1007/s13726-022-01058-4.
140. Yan RR, Xue D, Su C, Xu Y, Gong JS, Liu YL, Shi JS, et al. A keratin/chitosan sponge with excellent hemostatic performance for uncontrolled bleeding. Colloids Surf B: Biointerfaces. 2022;218:112770. https://doi.org/10.1016/j.colsurfb.2022.112770
141. Yan Y, Yao R, Zhao J, Chen K, Duan L, Wang T, Li G, et al. Implantable nerve guidance conduits: material combinations, multi-functional strategies and advanced engineering innovations. Bioactiv Mater. 2022;11:57–76. https://doi.org/10.1016/j.bioactmat.2021.09.030.
142. Ye JP, Gong JS, Su C, Liu YG, Jiang M, Pan H, Shi JS, et al. Fabrication and characterization of high molecular keratin based nanofibrous membranes for wound healing. Colloids Surf B: Biointerfaces. 2020;194:111158. https://doi.org/10.1016/j.colsurfb.2020.111158
143. Yin X, Du M, Sun Z, Zhu H, Xu P, Wang H. Solid-waste-based keratin/chitosan hydrogel for controlling drug release in vitro. Eur Polymer J. 2023;199:112451. https://doi.org/10.1016/j.eurpolymj.2023.112451.
144. Zabarsky ZK, Dean GM, Luo TD, Marquez-Lara A, Jinnah AH, Van Dyke M, Smith TL. Keratin Biomaterials Improve Functional Recovery in a Rat Spinal Cord Injury Model. Spine. 2021;46(16):1055–62. https://doi.org/10.1097/BRS.0000000000003993.
145. Zakeri-Siavashani A, Chamanara M, Nassireslami E, Shiri M, Hoseini-Ahmadabadi M, Paknejad B. Three-dimensional spongy fibroin scaffolds containing keratin/vanillin particles as an antibacterial skin tissue engineering scaffold. Int J Polym Mater Polym Biomater. 2022;71(3):220–31. https://doi.org/10.1080/00914037.2020.1817021.
146. Zarei M, Tanideh N, Zare S, Aslani FS, Koohi-Hosseinabadi O, Rowshanghias A, Muthuraj R, et al. Electrospun poly (3-hydroxybutyrate)/chicken feather-derived keratin scaffolds: fabrication, in vitro and in vivo biocompatibility evaluation. J Biomater Appl. 2020;34(6):741–52. https://doi.org/10.1177/0885328219873090.
147. Zemljič, L. F., Tušek, L., Mešl, A., Plohl, O., Čolnik, M., & Škerget, M. (2024). Feathered Innovation: Transforming Recycled Keratin into Bioactive Micro/Nanoparticles for Advanced Drug Delivery Systems. https://doi.org/10.21203/rs.3.rs-4406149/v1
148. Zhang H, Ma H, Zhang R, Wang K, Liu J. Construction and characterization of antibacterial PLGA/wool keratin/ornidazole composite membranes for periodontal guided tissue regeneration. J Biomater Appl. 2020;34(9):1267–81. https://doi.org/10.1177/0885328220901396.
149. Zhang H, Su F, Ma X, Zhao G. Brief introduction of keratin and its biological application, especially in drug delivery. Emerg Mater. 2021;4(5):1225–42. https://doi.org/10.1007/s42247-021-00216-3.
150. Zhang H, Wang K, Gao T, Zhang R, Cai Z, Liu J, Zhang W, et al. Controlled release of bFGF loaded into electrospun core–shell fibrous membranes for use in guided tissue regeneration. Biomed Mater. 2020;15(3):035021.
151. Zhang M, Xu S, Du C, Wang R, Han C, Che Y, Zhao W, et al. Novel PLCL nanofibrous/keratin hydrogel bilayer wound dressing for skin wound repair. Colloids Surf B: Bio interfaces. 2023;222:113119. https://doi.org/10.1016/j.colsurfb.2022.113119

152. Zhong W, Shi D, Zhou J, Yang Y, Wang B, Sun X, Xia H, et al. Role of trichocytic keratins in anti-neuroinflammatory effects after spinal cord injury. Adv Funct Mater. 2023;33(23):2212870. https://doi.org/10.1002/adfm.202212870.
153. Zuniga K, Isaac A, Christy S, Wrice N, Mangum L, Natesan S, Kowalczewski C, et al. Characterization of a human platelet lysate-loaded keratin hydrogel for wound healing applications in vitro. Int J Mol Sci. 2022;23(8):4100. https://doi.org/10.3390/ijms23084100.

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