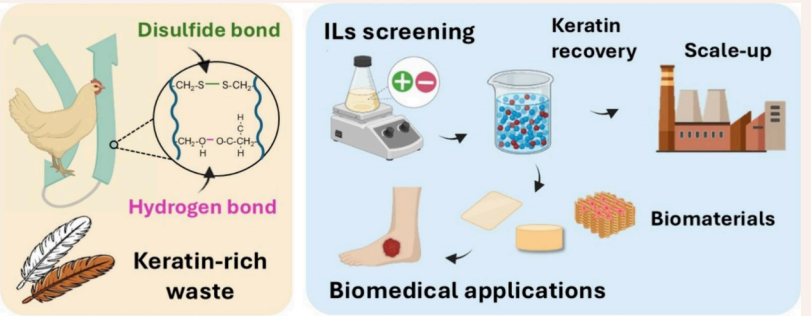
ACCOUNTS
—of materials research—

pubs.acs.org/amrcda
Article

Sustainable Recovery of Keratin from Chicken Feather Waste and Its Processing for Biomedical Applications

Cariny Polesca, Helena Passos, Jason P. Hallett, João A. P. Coutinho,* and Mara G. Freire*

Cite This: https://doi.org/10.1021/accountsmr.5c00368



CONSPECTUS: The global poultry industry has grown significantly in recent decades and is currently producing vast amounts of chicken feather waste, corresponding to around 7 wt % of the total weight of an adult chicken. This waste, which is typically incinerated or landfilled, poses both environmental and economic challenges, while being inconsistent with the principles of the circular economy. Chicken feathers are composed primarily of keratin (approximately 90 wt % on a dry weight basis), a natural protein with valuable properties, namely, anti-inflammatory and antioxidant activities, superior cytocompatibility, and ability to promote cellular migration. These characteristics make keratin an ideal candidate for various biomedical applications. However, traditional methods of recovering keratin from natural biomass are inefficient and costly and involve the use of toxic chemicals, limiting the broader use of this waste. In this Account, we discuss a sustainable and efficient process for keratin recovery and processing using ionic liquids. By employing acetate-based ionic liquids (80 wt % in water), we have developed a method that not only dissolves chicken feathers but also allows for high-yield keratin recovery. The developed process significantly reduces the need for harmful chemicals and energy-intensive steps traditionally associated with keratin recovery. Furthermore, the ionic liquids can be recovered and reused, which are important elements highlighted by our technoeconomic assessment. According to the process simulation, the minimum selling price for keratin is 22 $ per kg, based on a productivity of 350 tons of keratin per year, which is suitable for biomedical applications. The recovered keratin has been used to develop biocompatible films and hydrogels for wound healing, incorporated into biocomposites with melanin, cellulose, and chitin to enable tunable material properties, and integrated into advanced 3D printing technologies for tissue engineering applications. The produced keratin films exhibit remarkable properties, including strong antioxidant and anti-inflammatory effects and the potential to promote cell proliferation, thereby accelerating wound closure. Furthermore, the hydrogels produced with keratin and melanin presented outstanding UV-blocking capabilities (up to 99.9%), while the 3D printed scaffolds exhibited a dynamic shape-change over time, mediated by cellular traction forces, highlighting their potential for 4D printing toward innovative bioapplications. The work developed demonstrates the feasibility of transforming a largely untapped waste stream into high-value materials, contributing to both environmental sustainability and advancements in biomedical technologies. By offering a scalable and cost-effective method for keratin recovery, we aim to inspire future research in the development of keratin-based materials and the exploration of other waste-to-resource opportunities.

1. INTRODUCTION

The poultry-processing industry has experienced significant global growth driven by population increase, the high quality of poultry meat, known for its low-fat content, and its low price compared to other sources of animal protein. According to the Food and Agriculture Organization (FAO), global chicken production reached 123 million tons in 2022.[1] This expansion has been followed by the generation of significant amounts of chicken feather waste, corresponding to around 7 wt % of the total weight of an adult chicken.[2,3]

Received: December 17, 2025
Revised: April 1, 2026
Accepted: April 1, 2026

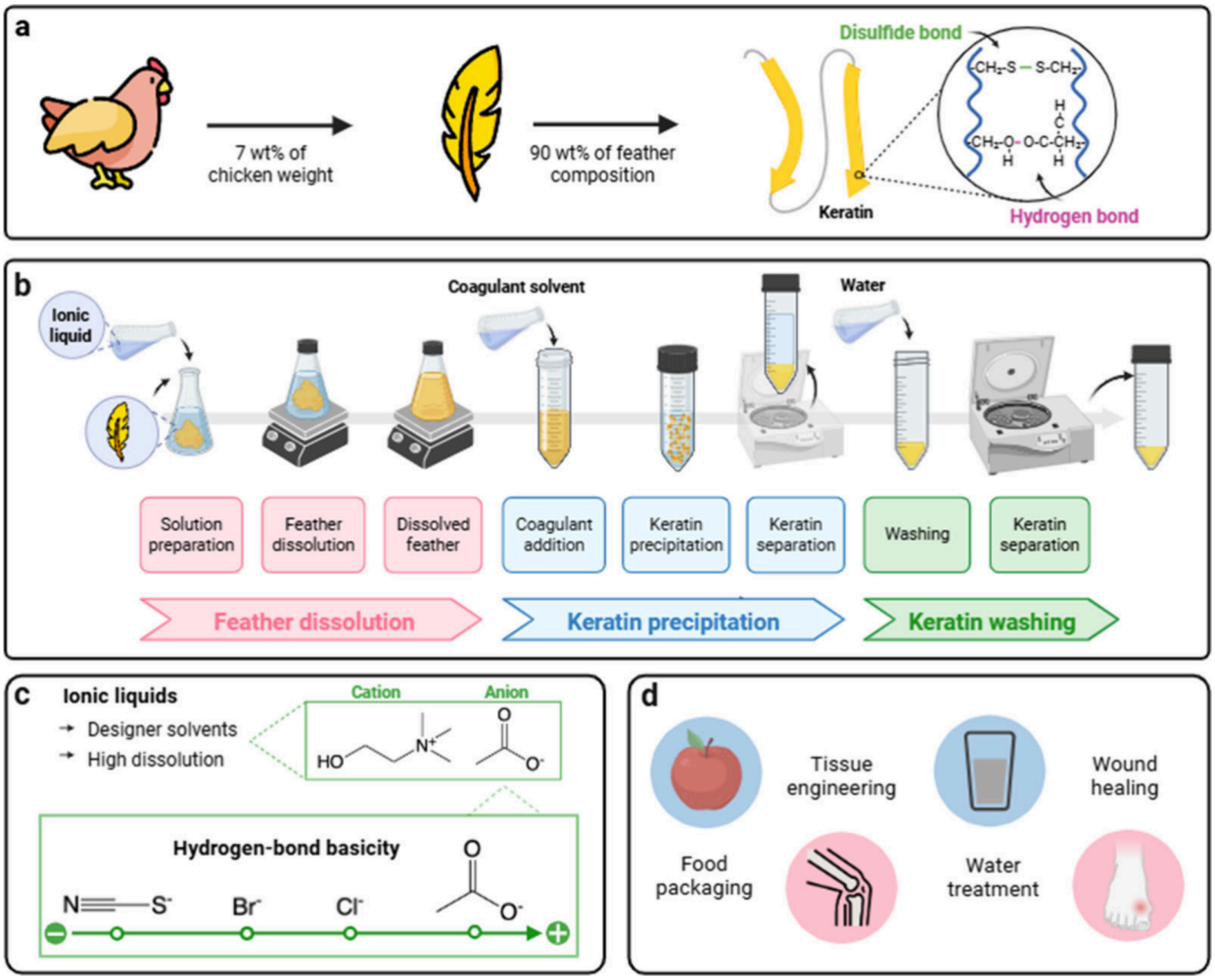


Figure 1. Overview of (a) chicken feather composition, (b) keratin recovery process using ILs, (c) properties of ILs, and (d) some keratin applications.

Chicken feathers represent an underutilized biomass and are generally disposed of through incineration or landfilling.[2,3] Chicken feathers are composed of approximately 90 wt % of keratin (dry weight basis), whereas the remaining 10 wt % consist of fibers, ash, and fat.[3,4] Keratin is a fibrous structural protein with unique properties, including biocompatibility, low toxicity, and antioxidant and anti-inflammatory effects.[2,5,6] The presence of various reactive functional groups and essential amino acids in its structure[7] makes keratin highly promising for a wide range of applications, such as drug delivery,[8−10] tissue engineering,[11,12] food packaging,[13,14] water treatment,[15,16] animal feed,[17−19] and as fertilizer.[17,19,20]

Despite keratin's abundance and interest, its low solubility in water and most organic solvents, mainly due to the inter- and intramolecular disulfide bonds in the sulfur-containing amino acids of keratin, makes its recovery a challenge.[2] Various methods (e.g., oxidation, reduction, and alkaline and acid hydrolysis) have been proposed to address this issue (cf. Table S1 and a deeper discussion provided in the Supporting Information).[21−25] However, many of them involve high costs, lead to low protein yields, use hazardous and toxic solvents, or have long processing times, underscoring the necessity to identify more efficient and sustainable methods for keratin recovery.[3,26] To address these challenges, we considered alternative solvents, with ionic liquids (ILs) emerging as one of the most promising solutions. ILs consist of large organic cations and organic or inorganic anions and have lower melting temperatures than inorganic salts.[3,27−29]

In this context, our research in the field started by evaluating various ILs for feather dissolution, with acetate-based ILs showing significant potential due to their hydrogen bond acceptor properties.[2,3,28] Figure 1 summarizes the composition of chicken feathers and the chemical interactions of keratin (Figure 1a), the keratin recovery process developed using ILs (Figure 1b), IL's properties (Figure 1c), and some keratin applications (Figure 1d).

In this Account, we describe and discuss a sustainable process to valorize chicken feather waste, achieved using acetate-based ILs, enabling high-yield keratin recovery alongside solvent recovery and reuse. The recovered keratin was used to create biocompatible films and hydrogels for wound healing, incorporated into biocomposites with melanin, cellulose, and chitin to create materials with tunable properties, and integrated into advanced 3D printing technologies. Overall, this Account emphasizes the valorization of chicken feathers using ILs for the development of advanced keratin-based materials.

2. FEATHER VALORIZATION USING IONIC LIQUIDS

In 2005, 1-butyl-3-methylimidazolium chloride ($[C_4C_1im]Cl$) was first described to be able to dissolve wool and regenerate keratin, representing a breakthrough in keratin recovery methods.[30] Since then, ILs have shown their excellent capability

https://doi.org/10.1021/accountsmr.5c00368
Acc. Mater. Res. XXXX, XXX, XXX−XXX

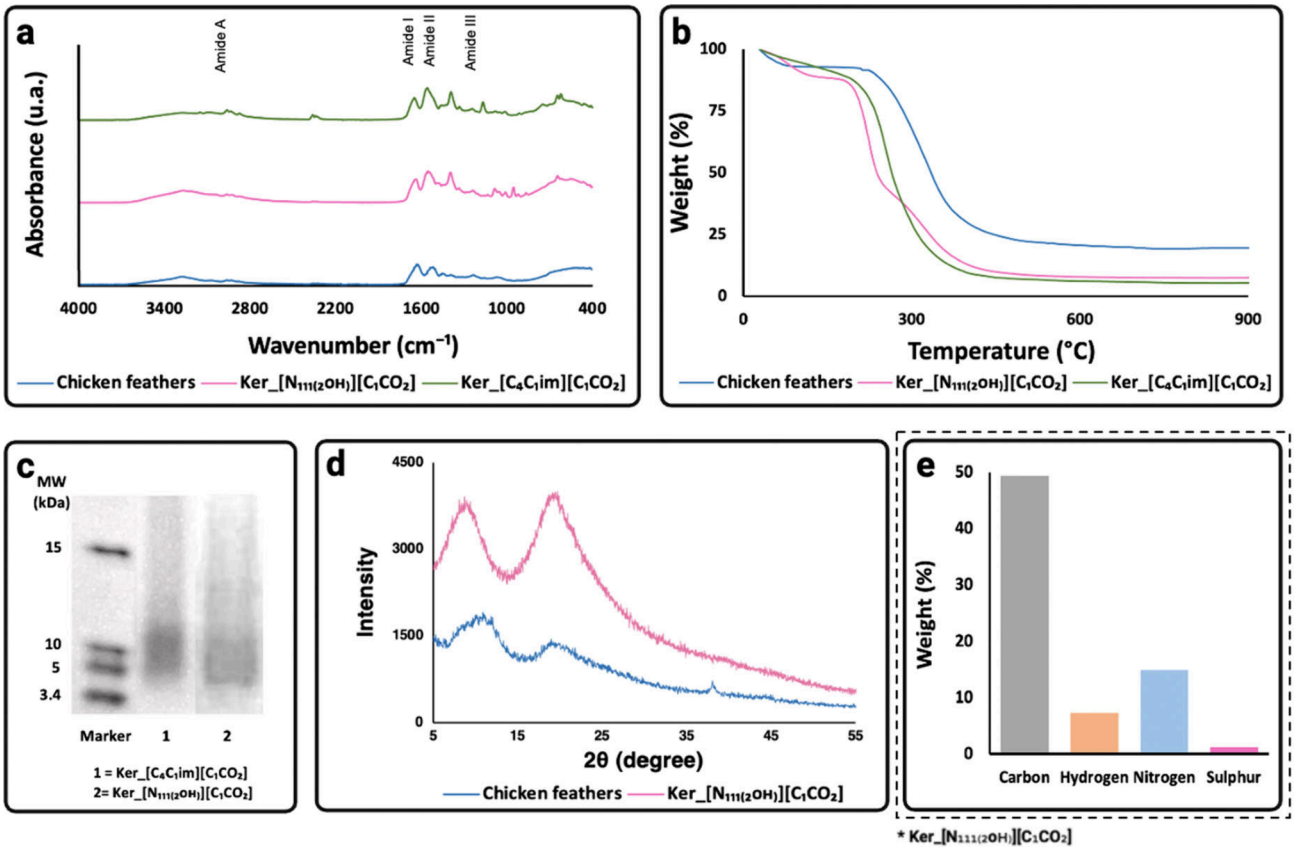


Figure 2. Structural and thermal characterization of chicken feathers and keratin recovered using acetate-based ILs. (a) FTIR spectra confirming the structure maintenance of the samples, (b) TGA profiles showing thermal stability, (c) SDS-PAGE analysis indicating the molecular weight distribution, (d) X-ray diffraction reflecting structural organization, and (e) elemental analysis. Ker_$[C_4C_1im][C_1CO_2]$ and Ker_$[N_{111(2OH)}][C_1CO_2]$ corresponds to keratin recovered using $[C_4C_1im][C_1CO_2]$ and $[N_{111(2OH)}][C_1CO_2]$, respectively. *Reproduced from Polesca et al.*[2,3] *with permission from the Royal Society of Chemistry.*

to cleave disulfide bonds (S−S) in keratin, overcoming the solubility limitations of traditional solvents. Zhang et al.[31] demonstrated through molecular dynamic simulation that S−S bonds are reduced to H_2S during the dissolution process and that the IL's ability to dissolve keratin is proportional to its disulfide bond-cleaving capability. Their results also indicated that changing the IL anions and cations may significantly impact the efficiency of disulfide bond cleavage.[31] Additionally, the hydrophobic (e.g., alanine and valine) and hydrogen-bond donor amino acids (e.g., glutamic acid and serine) of keratin can establish noncovalent (hydrogen bonding)[2,32] with the ILs, enabling the dissolution of keratin.

2.1. Understanding the Ability of Ionic Liquids to Dissolve Keratin

The high diversity of ILs and the complexity of keratin (which lacks regular repeating units) make identification of an efficient, low-cost, and low-toxicity IL a challenge. To illustrate this, Qin et al.[27] investigated 143 ILs and three model compounds to predict the dissolving ability of ILs for human hair. The authors observed that despite the influence of both cations and anions, the anions play a critical role in the dissolution process. According to their results, the ILs with acetate and diethylphosphate anions have the strongest dissolving ability due to their high hydrogen bonding acceptor ability.[27]

Based on these results, we started by investigating seven ILs, namely, 1-ethyl-3-methylimidazolium chloride ($[C_2C_1im]Cl$), 1-ethyl-3-methylimidazolium acetate ($[C_2C_1im][C_1CO_2]$), $[C_4C_1im]Cl$, 1-butyl-3-methylimidazolium acetate ($[C_4C_1im][C_1CO_2]$), 1-butyl-3-methylimidazolium bromide ($[C_4C_1im]$-Br), 1-butyl-3-methylimidazolium thiocyanate ($[C_4C_1im]$-[SCN]), and 1-butyl-1-methylpyrrolidinium chloride ($[C_4C_1pyrr]Cl$), for chicken feather dissolution. The dissolution assay was carried out at 100 °C for 4 h in a solid:liquid (feathers:solvent) ratio of 1:20 w/w. Most ILs tested failed to achieve complete feather dissolution, except for the acetate-based ILs, whose effectiveness is attributed to the high ability of the acetate anion to cleave S−S and its strong hydrogen bond acceptor properties.[2,31]

After identification of the most effective ILs ($[C_4C_1im][C_1CO_2]$ and $[C_2C_1im][C_1CO_2]$) and considering their similar performance, subsequent studies were carried out with $[C_4C_1im][C_1CO_2]$. For this, we investigated the impact of IL concentration using pure $[C_4C_1im][C_1CO_2]$ and its aqueous solutions at 80 and 60 wt %. The results revealed that adding up to 20 wt % of water reduced viscosity, accelerating mass transfer and facilitating feather dissolution. However, increasing the water concentration to 40 wt % hindered dissolution due to competition with hydrogen bonds necessary for the dissolution process.[2]

Despite the effective dissolution achieved by imidazolium-based ILs, environmental and economic concerns prompted us to further explore the use of other ILs with lower toxicity and higher biocompatibility.[3] Considering the efficacy of the acetate anion, we explored the use of cholinium acetate ($[N_{111(2OH)}]$-

https://doi.org/10.1021/accountsmr.5c00368
Acc. Mater. Res. XXXX, XXX, XXX−XXX

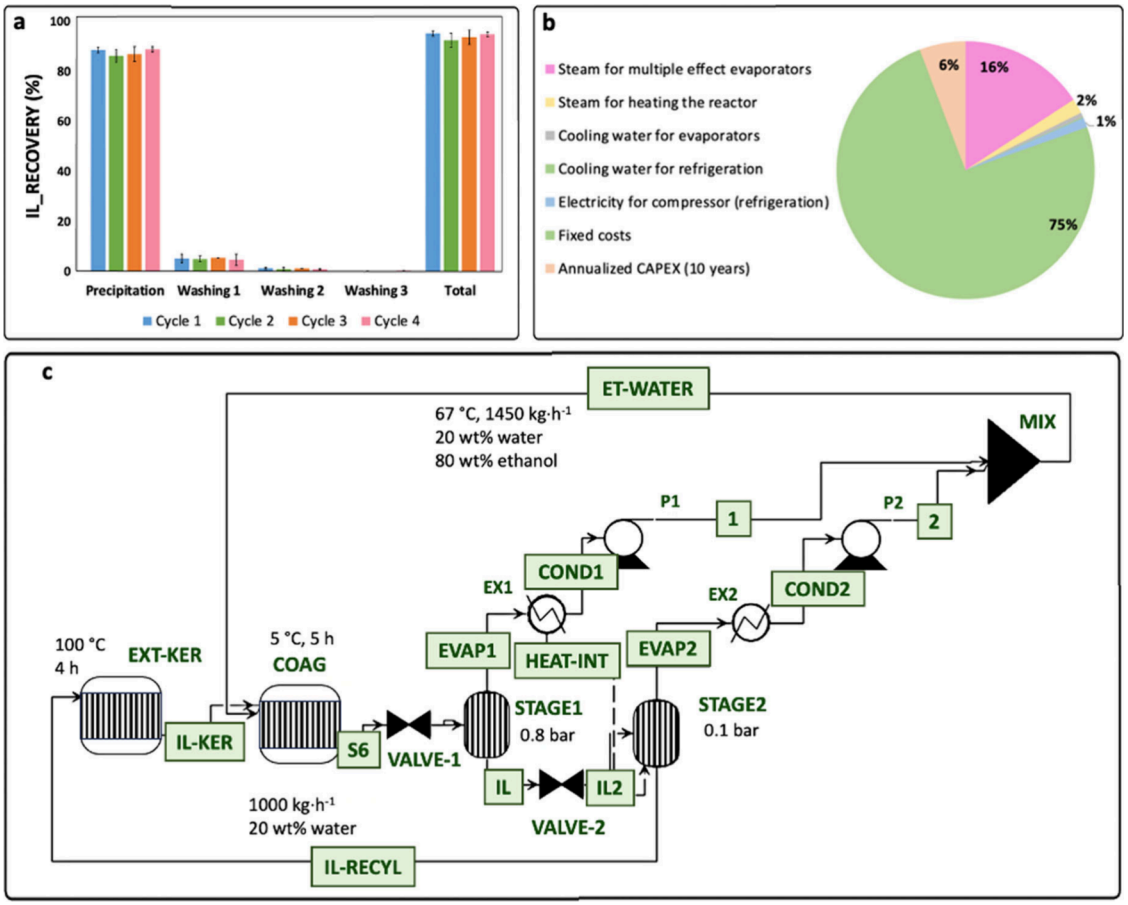


Figure 3. Assessment of process scalability and economic feasibility of the IL-based keratin recovery process: (a) IL recovery and reuse efficiency over 4 cycles, (b) cost contributions for keratin production, and (c) process flow diagram illustrating key operational steps. Abbreviations: EXT-KER = mixer for chicken feather dissolution, IL-KER = chicken feather dissolved in IL, COAG = mixer used for keratin precipitation, EVAP = evaporator used to remove the volatile solvent, COND = condenser, IL-RECYL = recovered IL, HEAT-INT = heating integration, MIX = mixer used to prepare the coagulant in an adequate concentration, and ET-WATER = coagulant (ethanol−water). *Reproduced from Polesca et al.*[3] *with permission from the Royal Society of Chemistry.*

$[C_1CO_2]$) for feather dissolution.[3] Using the same conditions as before,[2] complete feather dissolution was reached.[3]

2.2. Keratin Recovery Optimization

An additional advantage of using ILs is the simplicity of the protein recovery process, which avoids methods such as dialysis and the use of acids for isoelectric point adjustments. Instead, an inexpensive coagulant solvent, such as water or ethanol, may lead to efficient keratin precipitation from the IL solution due to the preferential solvation of the IL by the antisolvent.[2]

We initially investigated the dissolution of feathers using $[C_4C_1im][C_1CO_2]$ and evaluated the keratin precipitation process by testing various coagulant solvents including water, ethanol, water−ethanol mixtures, and acetone. We investigated these coagulants at different solution: coagulant ratio (1:1 w/w to 1:5 w/w), temperatures (−20 to 25 °C), and times (1 to 24 h). The results demonstrated that ethanol and water, following this order, were more effective than acetone in maximizing keratin recovery. Temperature variations did not significantly affect the results, while the time was important for water but not for ethanol. Overall, these variables significantly influenced the keratin recovery yield, emphasizing the need for further optimization.[2]

In this context and aiming to optimize keratin precipitation after feather dissolution with $[N_{111(2OH)}][C_1CO_2]$, we applied response surface methodology (RSM). Diverse variables were evaluated, including coagulant type (different ethanol concentrations in water), solution: coagulant ratio (from 1:12.5 to 1:1.08 w/w), and time (from 0.64 to 7.36 h). Optimal conditions for keratin recovery were found to be 20.25 wt % of ethanol in water, 5 h, and a solution: coagulant ratio of 1:1.45 w/w, resulting in a keratin recovery yield of (93 ± 4) wt %.[3]

2.3. Keratin Characterization

Keratin samples were characterized by Fourier transform infrared attenuated total reflectance (FTIR-ATR), thermogravimetric analysis (TGA), sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), elemental analysis, and X-ray diffraction (Figure 2), confirming preservation of the properties of feather-derived keratin samples.[2,3] Detailed discussion of the characterization results is provided in the Supporting Information.

3. KERATIN RECOVERY AT AN INDUSTRIAL SCALE

Recent efforts toward sustainable industrial processing focus on reducing toxic solvents use, minimizing hazardous waste generation, and streamlining processing time and costs.[33] In this context, we investigated the recovery and reuse of $[N_{111(2OH)}][C_1CO_2]$ as a crucial step toward process scale-up.[3]

https://doi.org/10.1021/accountsmr.5c00368
Acc. Mater. Res. XXXX, XXX, XXX−XXX

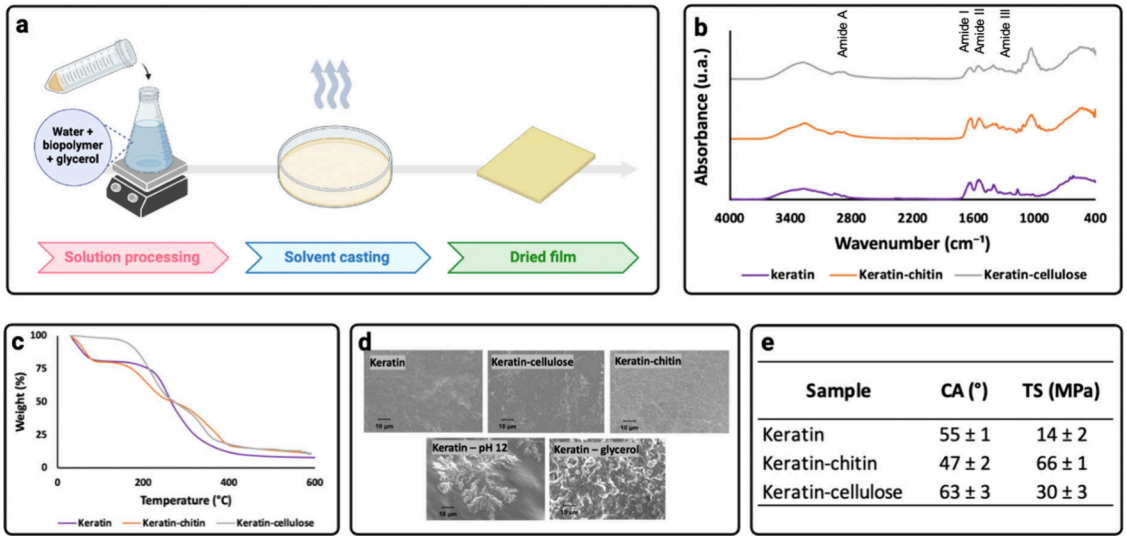


Figure 4. Processing and characterization of keratin-based films. (a) Schematic illustration of keratin-based film processing, (b) FTIR spectra confirming the preservation of the structure of the compounds in the films, (c) TGA profiles assessing the thermal stability, (d) SEM images for surface morphology analysis, and (e) contact angle (CA) and tensile strength (TS) analysis demonstrating the influence of processing conditions on film properties. *Reproduced from Polesca et al.*[16] *with permission from the Royal Society of Chemistry.*

IL recovery was evaluated over four cycles (Figure 3a), indicating that reused IL did not impact the keratin recovery efficiency. A recovery of ∼ 88% of the IL from the precipitation step was achieved, followed by ∼ 6% IL recovery from the washing steps. The integrity of the recovered IL was confirmed by ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR), revealing that no solvent degradation occurs under the conditions used.[3] In a similar context, Nakasu et al.[34] reported ≥ 97% $[N_{111(2OH)}][C_1CO_2]$ recovery over six cycles during the recovery of protein and chitin from squid pen, with no signs of contamination by NMR spectra.[34] Overall, although solvent performance remained high, it is essential to investigate long-term solvent stability across multiple cycles and to characterize the recovered IL and protein. From an environmental perspective, potential IL losses must be carefully considered. While cholinium-based ILs have been reported to exhibit lower toxicity and higher biodegradability than imidazolium-based ILs,[35] incomplete recovery or formation of degradation products may still pose environmental risks. Therefore, maintaining high IL recovery efficiency, solvent chemical stability, and protein quality across cycles while conducting a comprehensive evaluation of IL ecotoxicity and biodegradability is essential to fully validate the long-term sustainability of this process.

A techno-economic assessment was carried out,[3] aiming to understand the key cost-effective limitations in keratin recovery using $[N_{111(2OH)}][C_1CO_2]$. Further details are provided in the Supporting Information. The process flow diagram is presented in Figure 3c, and the results of the contributions of the different factors affecting the process cost are reported in Figure 3b.

The process simulation estimated a CO_2 emission of approximately 4.04 kg of CO_2 per kg of keratin, mainly due to the unavailability of heat sources in the process compared to other biomass-based approaches. However, considering the renewable raw material used, the product will not produce excess CO_2 at the end of its life cycle. The minimum selling price was estimated to be 22 $ per kg, based on a productivity of 350 tons of keratin per year, which is suitable for specialty applications such as personal care and biomedical.[3] Although no commercial keratin production from chicken feathers currently exists for direct comparison, the estimated cost is competitive with hydrolyzed keratin powder (30−50 $ per kg, cosmetic grade, CAS 69430-36-0).[36]

While $[N_{111(2OH)}][C_1CO_2]$ can be easily synthesized via an acid−base reaction, its recovery significantly influences operating costs. Steam demand to regenerate the IL and capital investment represents major cost drivers. Therefore, alternative IL recovery strategies, such as membrane-based separation, can further enhance the sustainable character of the process and decrease the keratin price.[37]

4. KERATIN-BASED MATERIALS

Keratin-based materials have attracted increasing interest for biomedical, food packaging, and environmental applications. Despite their potential, some challenges remain to achieve cost-effective production and to produce versatile keratin-based materials. To address these issues, we explored various conditions for preparing keratin-based materials with adjustable properties.

We first produced keratin films using keratin recovered from three acetate-based ILs ($[C_4C_1im][C_1CO_2]$, $[C_2C_1im][C_1CO_2]$, and $[N_{111(2OH)}][C_1CO_2]$) and different processing conditions, including variations in keratin concentration, pH, and addition of glycerol as a plasticizer. Thereafter, biocomposites were prepared by blending keratin with cellulose and chitin, two abundant biopolymers with good mechanical properties.[16] A schematic illustration of keratin-based film preparation, as well as the film's characterization, is provided in Figure 4. Detailed discussion of the characterization results is provided in the Supporting Information. Overall, the findings confirm that the properties of keratin-based films can be adjusted by varying the processing conditions according to the desired final application. Notably, keratin-chitin materials have a high potential to pioneer a new field of sustainable and high-performance biomaterials that can offer tunable mechanical properties.

4.1. Keratin-Based Materials for Biomedical Applications

In recent years, natural polymers have gained significant attention in the biomedical field due to their abundance, biocompatibility, biodegradability, low toxicity, and biological properties.[2,5,6] Keratin stands out in this field due to its unique structure, which includes both hydrophilic and hydrophobic domains.[38] Additionally, keratin exhibits enhanced cytocompatibility and promotes cellular migration and differentiation.[39] To explore the potential of keratin for biomedical applications,

https://doi.org/10.1021/accountsmr.5c00368
Acc. Mater. Res. XXXX, XXX, XXX−XXX

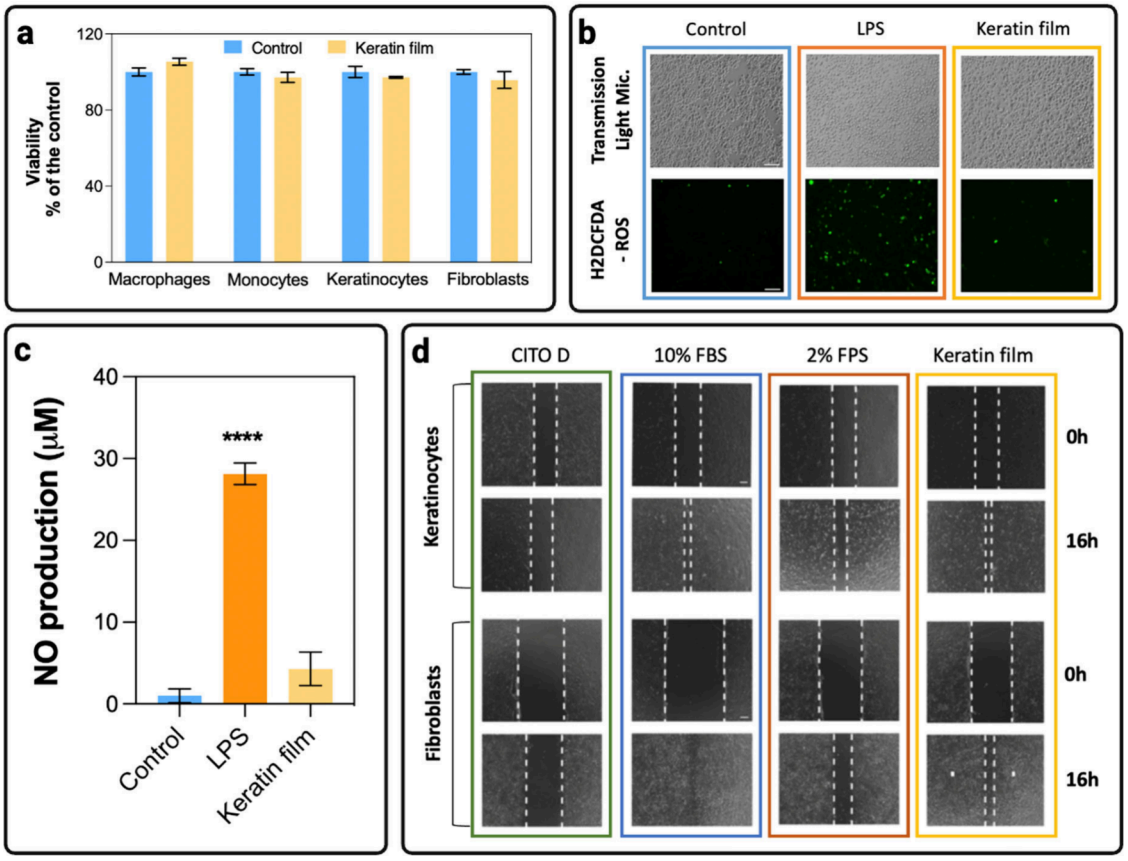


Figure 5. *In vitro* biological evaluation of keratin-based film for wound healing application: (a) *in vitro* cytotoxicity assays demonstrating cell viability, (b) oxidative stress evaluation, (c) NO production as an indicator of inflammatory response, and (d) *in vitro* wound healing assay assessing cell migration. Statistical analysis was performed using ordinary one-way ANOVA tests, ****$p < 0.0001$. *Reproduced from Polesca et al.*[2] *with permission from the Royal Society of Chemistry.*

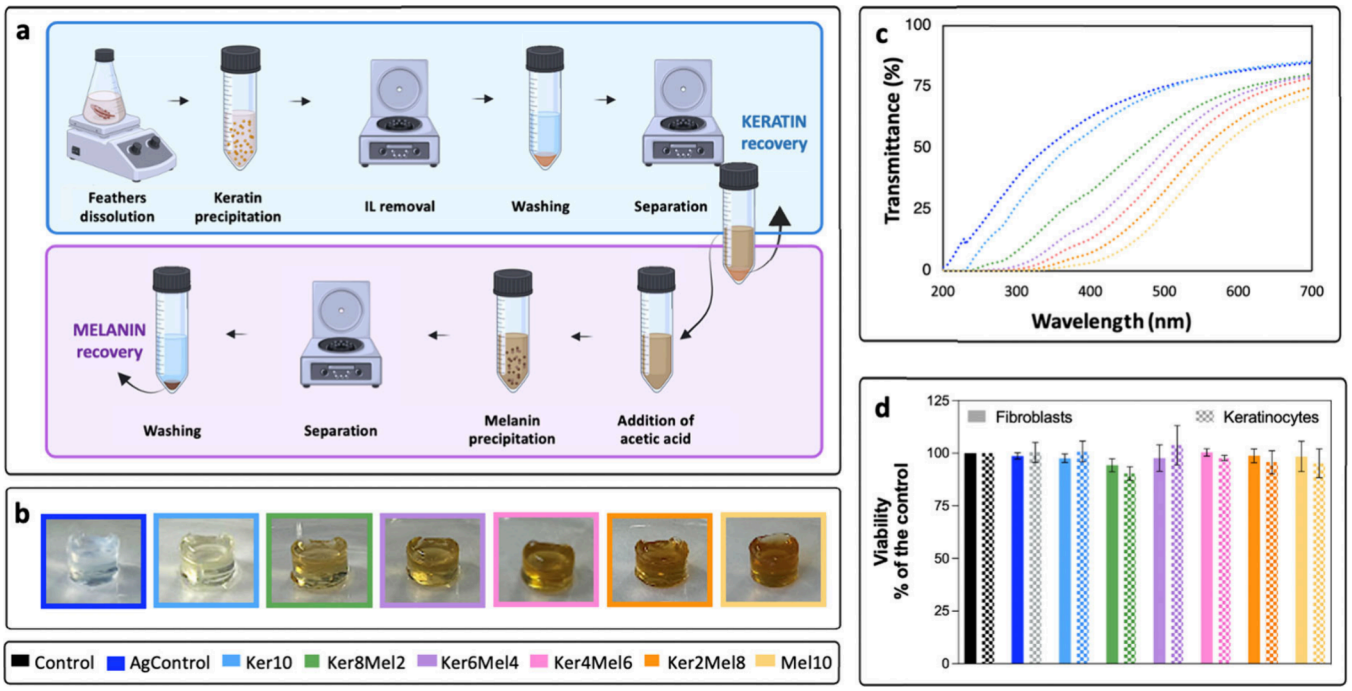


Figure 6. Integrated recovery of keratin and melanin from brown chicken feathers and functional evaluation of keratin-melanin hydrogels for biomedical applications. (a) Schematic representation of brown chicken feathers valorization using ILs, (b) digital photos of the prepared hydrogels, (c) UV-blocking evaluation on a range of 200 to 700 nm demonstrating enhanced UV-blocking capability with increasing melanin content in the hydrogels, and (d) evaluation of hydrogels' cell viability *in vitro*, confirming cytocompatibility.

https://doi.org/10.1021/accountsmr.5c00368
Acc. Mater. Res. XXXX, XXX, XXX−XXX

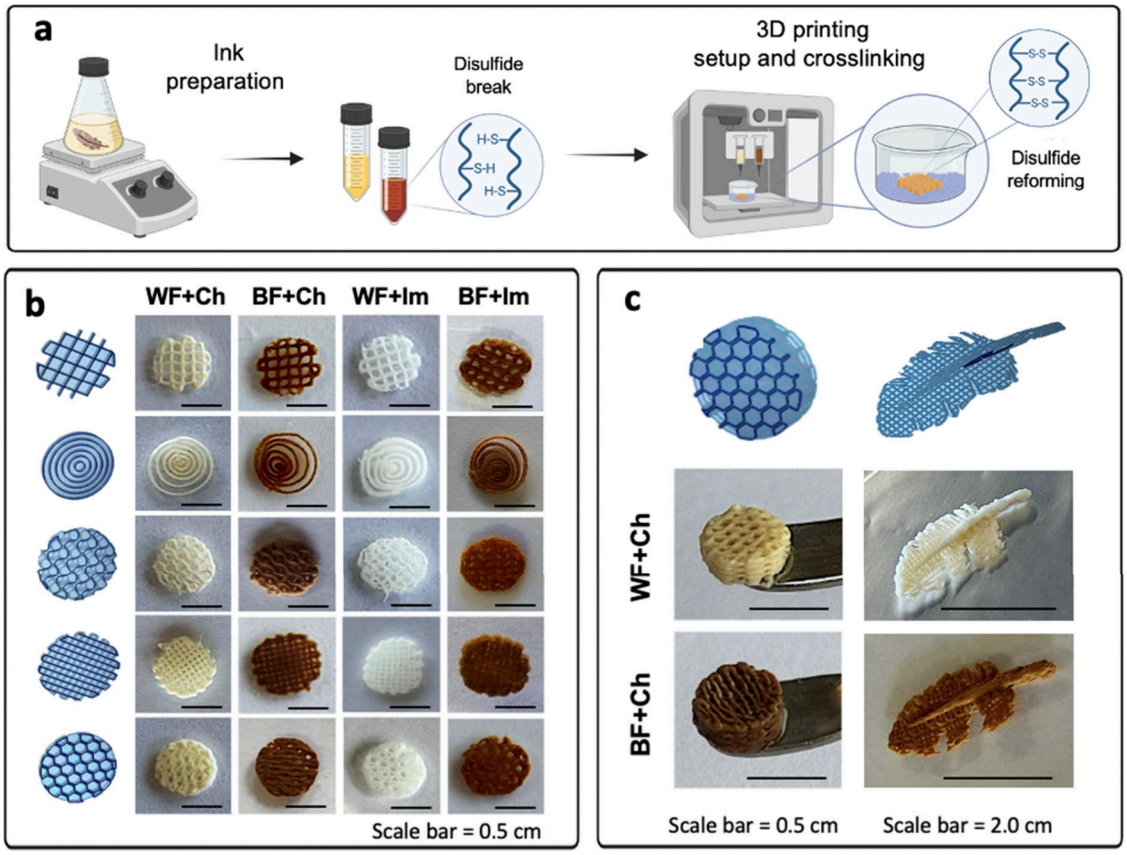


Figure 7. Fabrication and printability assessment of IL-dissolved keratin scaffolds via 3D printing. (a) Schematic illustration of the process used to produce IL-dissolved keratin scaffolds, (b) printability evaluation using cylinder geometries with 4 layers (10 mm × 1 mm), (c) 12 layers (10 mm × 3 mm), and a more complex geometry with 14 layers (30 mm × 12 mm). Abbreviations: Ch = cholinium acetate, Im = 1-ethyl-3-methylimidazolium acetate, BF = brown feathers, and WF = while feathers. *Adapted with permission from Polesca et al..*[42] *Copyright 2026 American Chemical Society.*

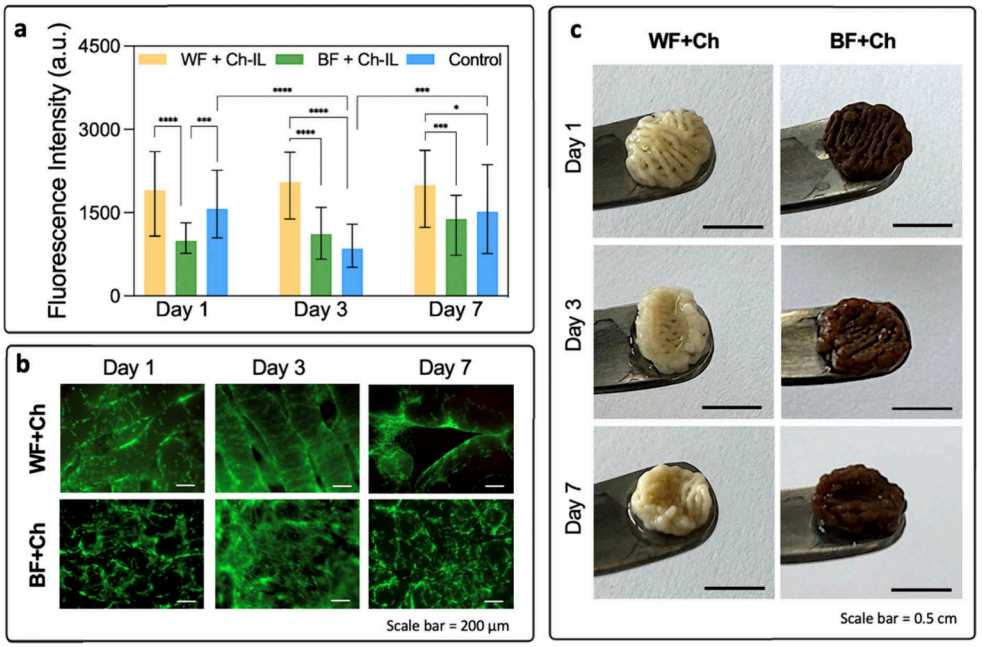


Figure 8. *In vitro* biological performance of IL-dissolved keratin scaffolds. The cytocompatibility and cell−material interactions of the scaffolds were evaluated using hASCs over 1, 3, and 7 days of culture. (a) Metabolic activity assay demonstrated by AlamarBlue, (b) live/dead fluorescent staining microscope images of the scaffolds, and (c) digital photos of the scaffolds showing a dynamic shape-changing over time mediated by cellular traction forces. Statistical analysis was performed using ordinary one-way ANOVA tests, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$. Abbreviations: Ch = cholinium acetate, BF = brown feathers, and WF = while feathers. *Adapted with permission from Polesca et al..*[42] *Copyright 2026 American Chemical Society.*

https://doi.org/10.1021/accountsmr.5c00368
Acc. Mater. Res. XXXX, XXX, XXX−XXX

Table 1. Applications of Keratin Across Multiple Fields

Field	Application	Benefits	ref.
Biomedical	Wound healing, tissue engineering, drug delivery	Biocompatibility, supports cellular adhesion and proliferation	2,6,8,10,11,24
Water treatment	Removal of contaminants (e.g., heavy metals and dyes)	Effective contaminant removal, eco-friendly material	15,16
Food packaging	Biobased films	Barrier properties, reduces the use of synthetic plastics	13,14
Human consumption	Novel dietary protein	Essential amino acids, *in vitro* and *in vivo* low cytotoxicity and high digestibility	23,43
Agriculture	Fertilizers and animal feed	Sustainable farming, essential nutrients	17,18,20
Textile industry	Yarn production and manufacture of technical textile	Appropriate properties (e.g., low density, durability) and eco-friendly	4,44

we first developed pure keratin films and conducted a series of biological tests to validate their suitability for wound healing (Figure 5).

We initially evaluated the biosafety testing of these films by conducting cytotoxicity assays (Figure 5a) using macrophages, monocytes, keratinocytes, and fibroblasts. No significant effects on cell viability were observed, confirming the absence of toxicity under the conditions addressed and the safety of the IL-based process.[2] Further assessments of the keratin film's properties demonstrated antioxidant and anti-inflammatory effects (Figures 5b and 5c), with reduced reactive oxygen species (ROS) production and inhibition of NO production without compromising cell viability.[2]

The wound-healing potential of keratin films was assessed *in vitro* (Figure 5d) using keratinocytes (principal cells of the epidermis) and fibroblasts (responsible cells for making the extracellular matrix). The films promoted cell proliferation and accelerated wound healing after 16 h. This effect is attributed to the interaction between keratin and cells, facilitated by specific amino acid sequences such as RGD (arginine-glycine-aspartic acid), LDV (leucine-aspartic acid-valine), LDS (leucine-aspartic acid-serine), and EDS (glutamic acid-serine), which promote cellular attachment, migration, and proliferation.[2,40] Overall, keratin films are efficient and less invasive than conventional wound closure methods, such as gauze (which is produced synthetically and can create secondary injury when peeling off).[6] Nevertheless, despite promising results, more research is necessary in this field, mainly *in vivo* assays.

In alignment with the biorefinery concept, our group has expanded the focus of this research to include the simultaneous recovery of keratin and melanin (a natural pigment with high photoprotective and antioxidant capacities) from brown chicken feathers (Figure 6a).[41] Following dissolution with $[N_{111(2OH)}][C_1CO_2]$ (80 wt % in water), selective precipitation steps enabled sequential recovery of keratin (using water or ethanol as coagulant solvent) and melanin (using acetic acid).[41]

By using agarose (a biocompatible polysaccharide with a high ability to form physically cross-linked hydrogels in aqueous dispersion) and varying ratios of keratin and melanin, hydrogels were designed to mimic the diverse tones of human skin, exhibiting tunable colors (Figure 6b) and enhanced UV-blocking capabilities (up to 99.9%) (Figure 6c). Aiming to use the hydrogels for biomedical applications, cell viability assays were performed (Figure 6d), confirming the hydrogels' capacity to support cell growth, further highlighting their promise in the field.[41]

Using the results from the work described above, we have then pioneered an innovative approach to produce keratin scaffolds using IL-dissolved keratin as an ink for 3D printing (Figure 7a).[42] We investigated two ILs, $[C_2C_1im][C_1CO_2]$ and $[N_{111(2OH)}][C_1CO_2]$, due to their proven efficacy in dissolving chicken feathers,[2,3] and aimed to explore further how these ILs influence the scaffold's formation and properties. Both brown feathers and white feathers were employed to assess their valorization and potential application in the biomedical field. Using a carbonate-bicarbonate microparticle support bath, we successfully printed initial structures (4 layers, 10 mm × 1 mm) with diverse geometries and high structural integrity (Figure 7b). Notably, when printing a 12-layer model (10 mm × 3 mm), only the scaffolds produced with $[N_{111(2OH)}][C_1CO_2]$ exhibited satisfactory results (Figure 7c), likely due to its higher viscosity compared to $[C_2C_1im]$-$[C_1CO_2]$. Moreover, a more complex structure with 14 layers (30 mm × 12 mm) was printed using $[N_{111(2OH)}][C_1CO_2]$, demonstrating its superior performance.[42]

After demonstrating the effectiveness in producing scaffolds from $[N_{111(2OH)}][C_1CO_2]$-dissolved keratin, the biosafety of these structures was evaluated by AlamarBlue metabolic activity assays (Figure 8a) and live/dead cell viability assays (Figure 8b), using human adipose-derived stem cells (hASCs). All structures proved to be biocompatible, promoting cellular adhesion and proliferation, underscoring keratin's potential for biomedical application.[39] Remarkably, the scaffolds exhibited a dynamic shape-changing over time mediated by cellular traction forces, demonstrating their 4D printing potential (Figure 8c). This work led to a direct and innovative method to produce keratin biomaterials via 3D printing, overcoming the limited solubility of keratin and the long-time processing.[42] While the *in vitro* results are promising, the absence of *in vivo* data and long-term safety evaluation still remains a critical barrier to clinical translation, and therefore need to be addressed.

4.2. Expanding the Potential of Keratin Applications

Keratin is a versatile protein with applications in multiple fields. In water treatment, keratin has demonstrated the potential to adsorb heavy metals and dyes, addressing the need for sustainable environmental solutions.[15,16] In the field of food packaging, keratin's natural barrier properties make it a promising material, reducing the use of synthetic plastics.[13,14] Additionally, keratin's nutrient-rich composition supports its use as a fertilizer[17,19,20] and in animal feed.[17−19] A summary of keratin's applications is presented in Table 1.

5. CONCLUSION AND PERSPECTIVES

In this Account, we presented an integrated IL-based strategy for keratin recovery from feathers and its valorization into advanced materials for biomedical applications. Acetate-based ILs, particularly $[N_{111(2OH)}][C_1CO_2]$, enabled high-yield keratin recovery while overcoming some concerns related to toxicity, cost, and synthesis complexity. The process integrates solvent recovery and reuse, supported by experimental optimization and techno-economic assessment, underscoring the potential industrial application.

Recovered keratin was used to develop biomaterials, including films, hydrogels, and 3D-printed scaffolds, with processing conditions presenting a dominant effect on their properties. These biomaterials exhibited antioxidant and anti-inflammatory properties, as evidenced by *in vitro* tests, with keratin:melanin hydrogels presenting enhanced UV-blocking capability. Notably, 3D-printed keratin scaffolds promoted remarkable cell adhesion and proliferation, and their dynamic shape-changing properties over time, mediated by cellular stimuli, further suggest the potential for 4D printing applications.

Despite these advances, several challenges remain. Extending the developed IL-based strategy to other keratin-rich wastes will be essential to assessing feedstock versatility and economic performance. In addition, life cycle assessment (LCA) studies are required to assess potential environmental impacts throughout keratin recovery processes. Furthermore, investigat-

https://doi.org/10.1021/accountsmr.5c00368
Acc. Mater. Res. XXXX, XXX, XXX−XXX

ing the impact of different acetate-based ILs on keratin's primary structure is essential for defining amino acid composition and understanding the sequences critical for medical applications. Importantly, the absence of *in vivo* validation, long-term biocompatibility data, and immune response remains a critical limitation for clinical translation. Future research is necessary to fully evaluate biocompatibility and biodegradation behavior, immune response, and safety to attest to the efficacy of keratin-based materials. By addressing these points we can then significantly enhance the potential of keratin-based materials and ensure their sustainable integration into modern practices.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/accountsmr.5c00368.

Extended Introduction and discussion sections and Table 1, as follows: **Table S1.** Common methods proposed for keratin recovery and their most relevant characteristics (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

João A. P. Coutinho − *CICECO - Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal;* orcid.org/0000-0002-3841-743X; Email: jcoutinho@ua.pt

Mara G. Freire − *CICECO - Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal;* orcid.org/0000-0001-8895-0614; Email: maragfreire@ua.pt

Authors

Cariny Polesca − *CICECO - Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal; Department of Chemical Engineering, Imperial College London, London SW7 2AZ, United Kingdom;* orcid.org/0000-0002-1214-9043

Helena Passos − *LSRE-LCM, ALiCE, Faculty of Engineering, University of Porto, 4200-465 Porto, Portugal;* orcid.org/0000-0002-0573-093X

Jason P. Hallett − *Department of Chemical Engineering, Imperial College London, London SW7 2AZ, United Kingdom;* orcid.org/0000-0003-3431-2371

Complete contact information is available at: https://pubs.acs.org/10.1021/accountsmr.5c00368

Notes

The authors declare no competing financial interest.

Biographies

Cariny Polesca is a Research Associate in the Department of Chemical Engineering at Imperial College London. She earned her PhD in Chemical Engineering from the University of Aveiro (Portugal) in 2025 and received her MSc degree in Chemical Engineering from the Federal University of Viçosa (Brazil) in 2020. Her research interests include waste valorization using ionic liquids for the processing of advanced biomaterials for biomedical applications.

Helena Passos is an Assistant Professor in the Department of Chemical and Biological Engineering at the Faculty of Engineering, University of Porto. She earned her PhD in Chemical Engineering from the University of Aveiro in 2017. Currently, she leads a research team at LSRE-LCM and ALiCE, the largest Portuguese Associate Laboratory in the area of Chemical Engineering, focusing on waste recycling and valorization through the application of alternative solvents and innovative extraction and separation processes.

Jason P. Hallett is Professor of Sustainable Chemical Technology and holds a Royal Academy of Engineering Chair in Emerging Technologies within the Dept. of Chemical Engineering, Imperial College London. His research focuses on the development of emerging sustainable technologies, with 9 spin−out companies translating the group's research into commercial practice.

João A. P. Coutinho is Full Professor at the Chemistry Department of University of Aveiro, Portugal where he is director of CICECO, one of the leading European Laboratories in Materials Science. He leads a multidisciplinary research team that focuses on the development of green solvents and novel separation processes for biorefinery and circular economy. Currently he strives to apply biobased solvents, DES and ionic liquids to these processes and attempts to better understand their physical-chemical behavior.

Mara G. Freire graduated in Chemistry and completed her PhD in Chemical Engineering. Freire is Full Professor at the Chemistry Department of University of Aveiro, and Vice-Director of CICECO. She is member of the European Academy of Sciences and of the Lisbon Academy of Sciences. Freire is a Subject Chair of the Content Selection Advisory Board (CSAB) from Scopus. Her scientific interests comprise the development of more sustainable manufacturing and processing platforms for biological materials.

■ ACKNOWLEDGMENTS

This work was developed within the scope of the project CICECO−Aveiro Institute of Materials, UID/50011 & LA/P/0006/2020 (DOI 10.54499/LA/P/0006/2020), financed by national funds through the FCT/MCTES (PIDDAC). This work was financially supported by Fundação para a Ciência e a Tecnologia, I.P. /MCTES through national funds: LSRE-LCM, UID/50020/2025; and ALiCE, LA/P/0045/2020 (DOI: 10.54499/LA/P/0045/2020). C. Polesca acknowledges FCT − Fundação para a Ciência e a Tecnologia for the PhD grant with the reference UI/BD/151282/2021 (DOI 10.54499/UI/BD/151282/2021).

■ REFERENCES

(1) *Food and Agriculture Organization of the United Nations.* FAO. https://www.fao.org/faostat/en/#data/QCL (accessed 2024-07-14).

(2) Polesca, C.; Passos, H.; Neves, B. M.; Coutinho, J. A. P.; Freire, M. G. Valorization of Chicken Feathers Using Aqueous Solutions of Ionic Liquids. *Green Chem.* **2023**, *25*, 1424−1434.

(3) Polesca, C.; Al Ghatta, A.; Passos, H.; Coutinho, J. A. P.; Hallett, J. P.; Freire, M. G. Sustainable Keratin Recovery Process Using a Bio-Based Ionic Liquid Aqueous Solution and Its Techno-Economic Assessment. *Green Chem.* **2023**, *25*, 3995−4003.

(4) Tesfaye, T.; Sithole, B.; Ramjugernath, D. Valorisation of Chicken Feather Barbs: Utilisation in Yarn Production and Technical Textile Applications. *Sustain. Chem. Pharm.* **2018**, *8*, 38−49.

(5) Zhang, J.; Li, Y.; Li, J.; Zhao, Z.; Liu, X.; Li, Z.; Han, Y.; Hu, J.; Chen, A. Isolation and Characterization of Biofunctional Keratin Particles Extracted from Wool Wastes. *Powder Technol.* **2013**, *246*, 356−362.

(6) Rajabi, M.; Ali, A.; McConnell, M.; Cabral, J. Keratinous Materials: Structures and Functions in Biomedical Applications. *Materials Science and Engineering C* **2020**, *110*, 110612.

(7) Peydayesh, M.; Bagnani, M.; Soon, W. L.; Mezzenga, R. Turning Food Protein Waste into Sustainable Technologies. *Chem. Rev.* **2023**, *123* (5), 2112−2154.
(8) Ferroni, C.; Varchi, G. Keratin-Based Nanoparticles as Drug Delivery Carriers. *Applied Sciences (Switzerland)* **2021**, *11* (20), 9417.
(9) Liu, P.; Wu, Q.; Li, Y.; Li, P.; Yuan, J.; Meng, X.; Xiao, Y. DOX-Conjugated Keratin Nanoparticles for PH-Sensitive Drug Delivery. *Colloids Surf. B Biointerfaces* **2019**, *181*, 1012−1018.
(10) Zhang, H.; Liu, P. One-Pot Synthesis of Chicken-Feather-Keratin-Based Prodrug Nanoparticles with High Drug Content for Tumor Intracellular DOX Delivery. *Langmuir* **2019**, *35* (24), 8007−8014.
(11) Kang, H. J.; Ko, N.; Oh, S. J.; An, S. Y.; Hwang, Y. S.; Kim, S. Y. Injectable Human Hair Keratin-Fibrinogen Hydrogels for Engineering 3d Microenvironments to Accelerate Oral Tissue Regeneration. *Int. J. Mol. Sci.* **2021**, *22* (24), 13269.
(12) Hartrianti, P.; Nguyen, L. T. H.; Johanes, J.; Chou, S. M.; Zhu, P.; Tan, N. S.; Tang, M. B. Y.; Ng, K. W. Fabrication and Characterization of a Novel Crosslinked Human Keratin-Alginate Sponge. *J. Tissue Eng. Regen. Med.* **2017**, *11* (9), 2590−2602.
(13) Asgher, M.; Qamar, S. A.; Bilal, M.; Iqbal, H. M. N. Bio-Based Active Food Packaging Materials: Sustainable Alternative to Conventional Petrochemical-Based Packaging Materials. *Food Research International* **2020**, *137*, 109625.
(14) Wei, L.; Zhu, S.; Yang, H.; Liao, Z.; Gong, Z.; Zhao, W.; Li, Y.; Gu, J.; Wei, Z.; Yang, J. Keratin-Based Composite Bioactive Films and Their Preservative Effects on Cherry Tomato. *Molecules* **2022**, *27* (19), 6331.
(15) Peiravi-Rivash, O.; Mashreghi, M.; Baigenzhenov, O.; Hosseini-Bandegharaei, A. Producing Bacterial Nano-Cellulose and Keratin from Wastes to Synthesize Keratin/Cellulose Nanobiocomposite for Removal of Dyes and Heavy Metal Ions from Waters and Wastewaters. *Colloids Surf. A Physicochem. Eng. Asp.* **2023**, *656*, 130355.
(16) Polesca, C.; Passos, H.; Nakasu, P.; Coutinho, J. A. P.; Freire, M. G.; Hallett, J. P. Ionic-Liquid-Processed Keratin-Based Biocomposite Films with Cellulose and Chitin for Sustainable Dye Removal. *RSC Sustainability* **2024**, *2*, 2239−2248.
(17) Chen, H.; Gao, S.; Li, Y.; Xu, H. J.; 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.
(18) Van Heugten, E.; Van Kempen, T. A. T. G. Growth Performance, Carcass Characteristics, Nutrient Digestibility and Fecal Odorous Compounds in Growing-Finishing Pigs Fed Diets Containing Hydrolyzed Feather Meal 1. *J. Anim. Sci.* **2002**, *80*, 171−178.
(19) Banasaz, S.; Ferraro, V. Keratin from Animal By-Products: Structure, Characterization, Extraction and Application—A Review. *Polymers (Basel).* **2024**, *16* (14), 1999.
(20) Gurav, R. G.; Jadhav, J. P. A Novel Source of Biofertilizer from Feather Biomass for Banana Cultivation. *Environmental Science and Pollution Research* **2013**, *20* (7), 4532−4539.
(21) Alahyaribeik, S.; Ullah, A. Methods of Keratin Extraction from Poultry Feathers and Their Effects on Antioxidant Activity of Extracted Keratin. *Int. J. Biol. Macromol.* **2020**, *148*, 449−456.
(22) Agarwal, V.; Panicker, A. G.; Indrakumar, S.; Chatterjee, K. Comparative Study of Keratin Extraction from Human Hair. *Int. J. Biol. Macromol.* **2019**, *133*, 382−390.
(23) Giteru, S. G.; Ramsey, D. H.; Hou, Y.; Cong, L.; Mohan, A.; Bekhit, A. E. D. A. Wool Keratin as a Novel Alternative Protein: A Comprehensive Review of Extraction, Purification, Nutrition, Safety, and Food Applications. *Compr. Rev. Food Sci. Food Saf.* **2023**, *22* (1), 643−687.
(24) Su, C.; Gong, J. S.; Ye, J. P.; He, J. M.; Li, R. Y.; Jiang, M.; Geng, Y.; Zhang, Y.; Chen, J. H.; Xu, Z. H.; Shi, J. S. Enzymatic Extraction of Bioactive and Self-Assembling Wool Keratin for Biomedical Applications. *Macromol. Biosci.* **2020**, *20* (9). DOI: 10.1002/mabi.202000073.
(25) 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.
(26) Muir, V. G.; Burdick, J. A. Chemically Modified Biopolymers for the Formation of Biomedical Hydrogels. *Chem. Rev.* **2021**, *121* (18), 10908−10949.
(27) Qin, C.; Gao, H.; Liu, X.; Li, X.; Xie, Y.; Bai, Y.; Nie, Y. The Dissolution of Human Hair Using Ionic Liquids through COSMO-RS Predication and Experimental Verification. *J. Mol. Liq.* **2022**, *349*, 118094.
(28) Liu, X.; Nie, Y.; Liu, Y.; Zhang, S.; Skov, A. L. Screening of Ionic Liquids for Keratin Dissolution by Means of COSMO-RS and Experimental Verification. *ACS Sustain. Chem. Eng.* **2018**, *6* (12), 17314−17322.
(29) Bharmoria, P.; Tietze, A. A.; Mondal, D.; Kang, T. S.; Kumar, A.; Freire, M. G. Do Ionic Liquids Exhibit the Required Characteristics to Dissolve, Extract, Stabilize, and Purify Proteins? Past-Present-Future Assessment. *Chem. Rev.* **2024**, *124* (6), 3037−3084.
(30) Xie, H.; Li, S.; Zhang, S. Ionic Liquids as Novel Solvents for the Dissolution and Blending of Wool Keratin Fibers. *Green Chem.* **2005**, *7* (8), 606−608.
(31) Zhang, Z.; Nie, Y.; Zhang, Q.; Liu, X.; Tu, W.; Zhang, X.; Zhang, S. Quantitative Change in Disulfide Bonds and Microstructure Variation of Regenerated Wool Keratin from Various Ionic Liquids. *ACS Sustain. Chem. Eng.* **2017**, *5* (3), 2614−2622.
(32) Montazerian, H.; Sampath, R. R.; Annabi, N.; Khademhosseini, A.; Weiss, P. S. Polyphenolic Gelatin-Based Bioadhesives. *Acc. Mater. Res.* **2023**, *4* (7), 627−640.
(33) Radoiu, M.; Mello, A. Technical Advances, Barriers, and Solutions in Microwave—Assisted Technology for Industrial Processing. *Chem. Eng. Res. Des.* **2022**, *181*, 331−342.
(34) Nakasu, P. Y. S.; Piccoli, V.; Ovejero-Pérez, A.; Kumar, P.; Al Ghatta, A.; Melanie, S.; Polesca, C.; Martinez, L.; Hallett, J. P. Fractionation of Squid Pens with Ionic Liquids−An Upgraded β-Chitin and Shellfish Protein Production. *ACS Sustain. Chem. Eng.* **2025**, *13* (7), 2649−2660.
(35) Costa, S. P. F.; Azevedo, A. M. O.; Pinto, P. C. A. G.; Saraiva, M. L. M. F. S. Environmental Impact of Ionic Liquids: Recent Advances in (Eco)Toxicology and (Bio)Degradability. *ChemSusChem* **2017**, *10* (11), 2321−2347.
(36) Keratin Price Mnaufactures & Suppliers. Made-in-China. 2024. https://www.made-in-china.com/products-search/hot-china-products/99_Keratin_Price.html.
(37) Sosa, F. H. B.; Carvalho, P. J.; Coutinho, J. A. P. Recovery of Ionic Liquids from Aqueous Solutions Using Membrane Technology. *Sep. Purif. Technol.* **2023**, *322*, 124341.
(38) Mi, X.; Xu, H.; Yang, Y. Submicron Amino Acid Particles Reinforced 100% Keratin Biomedical Films with Enhanced Wet Properties via Interfacial Strengthening. *Colloids Surf. B Biointerfaces* **2019**, *177*, 33−40.
(39) Zuniga, K.; Ghousifam, N.; Sansalone, J.; Senecal, K.; Van Dyke, M.; Rylander, M. N. Keratin Promotes Differentiation of Keratinocytes Seeded on Collagen/Keratin Hydrogels. *Bioengineering* **2022**, *9* (10), 559.
(40) Ranjit, E.; Hamlet, S.; George, R.; Sharma, A.; Love, R. M. Biofunctional Approaches of Wool-Based Keratin for Tissue Engineering. *Journal of Science: Advanced Materials and Devices* **2022**, *7* (1), 100398.
(41) Polesca, C. Valorisation of Chicken Feathers Using Ionic Liquids and Biomaterial Production for Biomedical Applications, Thesis, University of Aveiro, Aveiro, 2025. https://ria.ua.pt/ (accessed 2026-03-31).
(42) Polesca, C.; Sobreiro-Almeida, R.; Passos, H.; Coutinho, J. A. P.; Hallett, J. P.; Mano, J. F.; Freire, M. G. Engineered from Waste: Ionic Liquid Processing of Keratin for 3D Printing Biomedical Scaffolds. *ACS Mater. Lett.* **2025**, *7*, 3370−3379.
(43) Dias, G. J.; Haththotuwa, T. N.; Rowlands, D. S.; Gram, M.; Bekhit, A. E. D. A. Wool Keratin - A Novel Dietary Protein Source: Nutritional Value and Toxicological Assessment. *Food Chem.* **2022**, *383*, 132436.
(44) Ni, R.; Cheng, M.; Meng, J.; Hu, W.; Ke, Q.; Zhao, Y. Edible Pullulan Enhanced Water-Soluble Keratin with Improved Sizing

Performance for Sustainable Textile Industry. *Int. J. Biol. Macromol.* **2023**, *238*, 124066.

https://doi.org/10.1021/accountsmr.5c00368
Acc. Mater. Res. XXXX, XXX, XXX−XXX