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Review

Gastropod Mucus: Interdisciplinary Perspectives on Biological Activities, Applications, and Strategic Priorities

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ABSTRACT: Terrestrial gastropod mucus exhibits multifunctional attributes, enabling diverse applications. This comprehensive review integrates insights across biomedicine, biotechnology, and intellectual property to elucidate the bioactivities, physicochemical properties, and ecological roles of snail and slug mucus. Following an overview of mucus functional roles in gastropods, promising applications are highlighted in wound healing, antimicrobials, biomaterials, and cosmetics, alongside key challenges. An analysis of global patent trends reveals surging innovation efforts to leverage gastropod mucus. Strategic priorities include bioprospecting natural diversity, optimizing stabilization systems, recombinant biosynthesis, and fostering collaboration to translate promising potentials sustainably into impactful technologies. Ultimately, harnessing the remarkable multifunctionality of gastropod mucus holds immense opportunities for transformative innovations in biomedicine, biotechnology, and beyond.

KEYWORDS: *gastropod mucus, slug, snail, biomaterial, biotechnology, biomedicine*

1. INTRODUCTION

Terrestrial gastropods, including snails and slugs (Figure 1), secrete mucus that serves integral roles in locomotion, environmental adhesion, innate immunity, and sensory reception.[1−4] The mucus exhibits a unique combination of physicochemical properties, including reversible gelation, mucoadhesivity, and viscoelasticity, that facilitate the gastropods' survival across diverse ecological niches.[5] Increasingly, researchers have sought to harness the useful attributes of gastropod mucus, spurring innovations in biomedicine, biotechnology, and cosmetics.

The rising global demand for natural products has further fuelled bioprospecting efforts to identify new sources of bioactive compounds and multifunctional biomaterials.[6] In this context, the complex composition and intrinsic bioactivities of terrestrial gastropod mucus present unique opportunities across diverse sectors. Recent omics profiling has revealed the mucus is abundant in glycoproteins, polysaccharides, peptides, lipids, and secondary metabolites with antioxidant, antimicrobial, anti-inflammatory, and wound healing properties.[7,8] The commercial success of snail mucus-based cosmetic products, with the global snail beauty product market valued at over 500 million USD in 2022,[9] has provided further impetus to translate the promising potential of gastropod mucus into impactful innovations for society.

This review integrates interdisciplinary insights into the molecular biology, physicochemical properties, ecological roles, and biotechnological promise of terrestrial gastropod mucus. Key topics addressed include comparative compositional analyses, structure−function relationships, antimicrobial activities, wound healing, biomaterial development, cosmeceutical innovations, and patent landscape analysis. Patent data provide valuable insights into emerging applications and regional research interests based on mucus-related patent filings and

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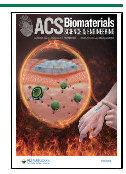

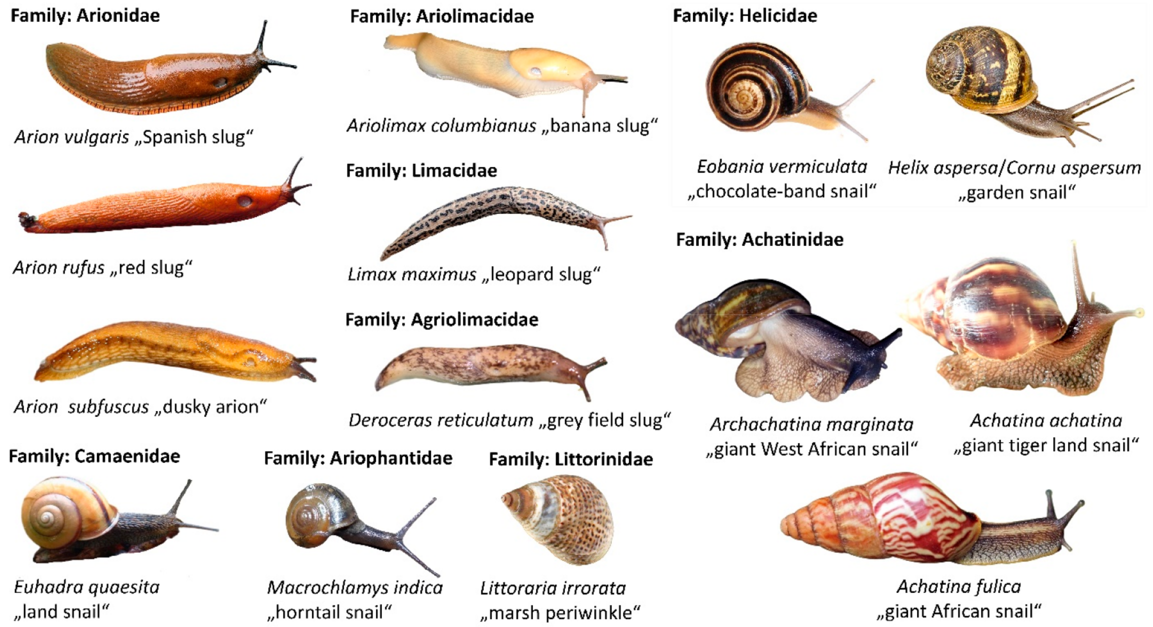

Figure 1. Prominent gastropod species in mucus research. Except for *Littoraria irrorata*, which belongs to the subclass Caenogastropoda (order Littorinimorpha), all species belong to the subclass Heterobranchia (order Stylommatophora).

grants. By synthesizing perspectives across diverse fields, including organismal biology, materials science, engineering, biomedicine, and intellectual property, this review elucidates critical research frontiers and strategic opportunities to harness the remarkable multifunctionality of gastropod mucus to create transformative innovations benefiting society.

2. COMPOSITION, PROPERTIES, AND BIOLOGICAL FUNCTIONS OF SNAIL AND SLUG MUCUS

Typically, terrestrial gastropods secrete diverse mucus types in response to varying stimuli. These are produced by several different single-cell glands located in the connective tissues.[3,10,11] Snail and slug mucus contains glycoproteins (mucins, lectins), polysaccharides (glycosaminoglycans), peptides, lipids, metal ions, and aromatic amino acids.[3,6,7,11,12] The major glycoproteins are heavily glycosylated mucins, with O-linked oligosaccharide chains making up 50−90% of their mass.[13] These are responsible for the gel-forming properties. Polysaccharide components include sulfated glycosaminoglycans like chondroitin sulfate. Smaller peptides and hydrophobic lipids are also present within the mucin network.[3,13,14] Variations in mucus biochemical properties such as lectin content, metal ions, and aromatic amino acids correlate with specialized adhesive functions adapted to diverse environments. Ions, oxidation cross-links, and lectin-carbohydrate interactions contribute to mucus gel stiffness and adhesion.[7,12,15] This composition allows mucus to exhibit properties such as reversible gelation, high viscosity, and self-healing (Figure 2).

Recent extensive proteomics research identified over 2800 peptides in the mucus of seven gastropod species (1218 were present in the mucus of all examined species), predicting numerous bioactive functions.[16] In *A. vulgaris*, numerous mucus-associated proteins, including many secreted C-type lectins, were identified.[17] Genomic analysis of *Achatina fulica* reconstructed metabolic pathways involved in mucus formation, providing insights into its biochemical origins.[14] The authors identified enzymes for glycosaminoglycan biosynthesis, including those producing keratan sulfate, heparan sulfate, acharan sulfate, and chondroitin sulfate found in the mucus. However, the specific mucin genes, protein structures, compositional differences accounting for functional diversity, and the exact functions of the different gland secretions remain unknown, and integrated multiomics approaches are needed to map genotype-phenotype relationships.

The mucus can range from sticky or clear foamy secretions.[10,18,19] The versatile physicochemical properties of gastropod mucus enable it to serve several key biological functions intrinsic to survival strategies. The capacity to form gels provides hydration regulation and lubrication for efficient locomotion,[3,4] while interfacial adhesion enables environmental attachment and trail laying/following behaviors[2,20] (Figure 2). The mucus barrier traps microbes and particles and contains bioactive compounds that confer immune defense.[1,3] Variations in the rheological and biochemical properties of gastropod mucus across species reflect adaptations to their diverse ecological niches.[5]

Locomotion is facilitated by the lubricating effect of the gastropod mucus, secreted in a thin layer on the ventral surface of the foot (Figure 2). This allows close contact between the epithelia and substrate while reducing friction during muscular pedal waves that generate locomotor forces.[2,4,20] The mucus exhibits shear-thinning behavior, with viscosity decreasing under applied shear stress during movement. Rapid recovery of viscosity when strain is removed enables continuous gripping and release from the substrate.[4,20,21] The adhesive mucus has a higher protein content and specific "glue proteins", increasing gel strength and viscosity.[22] The mucus also provides a protective barrier against desiccation, mechanical damage, and pathogens.[1,3] The gel-like consistency cushions against physical impact, while the presence of lectins and glycoproteins facilitates trapping and clearance of microbes before tissue invasion can occur.

Additionally, gastropod mucus enables sensory reception and environmental interactions. Terrestrial gastropods leave mucus trails that facilitate navigation, aggregation, and mate-

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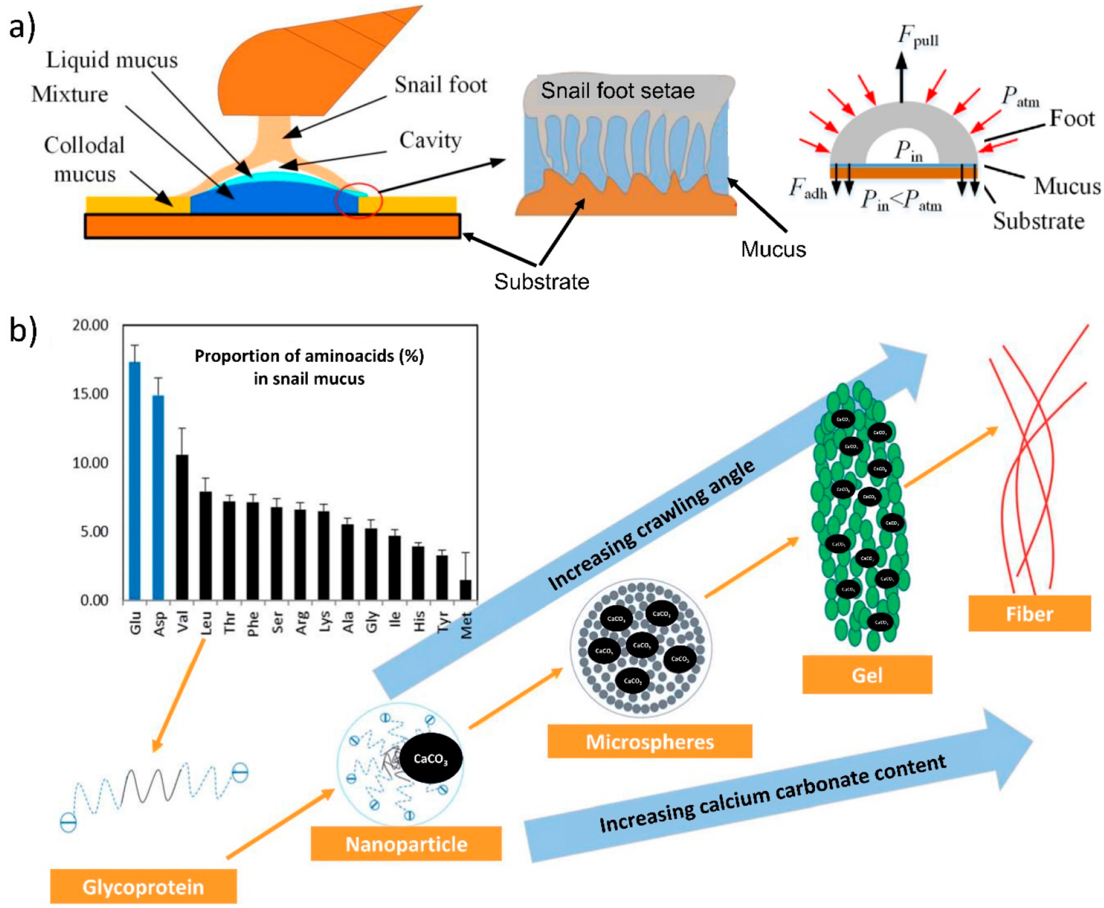

Figure 2. Snail mucus mechanics and its role in adhesion and locomotion. (a) Illustration of the contact interface of snails. Left: During locomotion (adhesion) to the substrate, the snail produces a colloidal mucus layer. Transparent "liquid mucus" can be extracted from the center of this colloidal layer. Beneath the liquid mucus, a combination of both types of mucus can be observed. Right: Schematic detailing the pulling process, emphasizing the resisting mechanisms when snails are pulled. Key forces involved: F_{adh} (adhesive force) and F_{pull} (pulling force). Experimental data reveal a pull-off force of approximately 22 times the snail's weight, with this force remaining consistent across varying substrate angles. The snail's flexible body augments work consumption through stretching and deformation during pulling, while a cavity with a negative pressure differential may form at the contact interface, aiding in resisting pull. This bioinspiration, notably the flexible body and the formation of a negative pressure cavity, is extrapolated as pivotal elements for the design of a bioinspired sucker. Adapted with permission from ref 81. Copyright 2021 Elsevier. (b) Structural transformation of snail mucus. Snail mucus changes structurally and compositionally, depending on the crawling angle. Predominantly composed of hydrophilic amino acids, such as glutamic and aspartic acids, the calcium content in this mucus increases during these structural transitions. This increase in calcium indicates that calcium carbonate leads to the agglomeration of nanoparticles. When the snail encounters inclined surfaces, more calcium carbonate facilitates the assembly of nanoparticles into larger microspheres, enhancing the viscosity of mucus. This increased viscosity aids in adhesive locomotion, especially on vertical surfaces. As the glycoprotein concentration in the mucus increases, it undergoes a transformation from intermicelle interactions to the formation of gels. When a snail is on an inverted plate, the mucus transforms from a gel-like state to a fiber. This adaptability suggests a unique adhesion strategy in gastropods, and the transition of mucus from a liquid to a fiber offers insights into potential adhesive and fiber designs. Adapted with permission from ref 87. Copyright 2018 The Royal Society of Chemistry.

finding.[4] Mucus may also allow gastropods to modulate plant biology through secreted bioactive compounds.[23,24] Some species use mucus directly for predator defense. Mucus from the red triangle slug contains adhesive proteins that immobilize predators,[25] while the mucus of *Deroceras reticulatum* deters predation by carabid beetles when stimulated.[26]

The trail mucus is considered to facilitate conspecific chemical communication, potentially involving pheromones,[27] and affect behavioral patterns.[28,29] Research on the mucus coating of love darts in the land snail *Euhadra quaesita* shows the ability of snail mucus to modulate reproductive physiology through bioactive factors that delay sexual arousal.[30] This functional diversity reflects the importance of mucus for gastropods across environments.

The highlighted properties like microbial protection, lubrication, and adhesion are critical for niche-specific adaptation.[3] However, structure−function relationships are limited. For instance, antimicrobial protection is attributed to lectins, enzymes, and cationic peptides,[14,16] but their relative contributions are unclear. Lubrication is proposed to involve proteoglycan hydration and fluid gel transitions,[14] but the molecular basis is unknown. The variation in mucus composition and rheology across species is not understood. Fundamental questions remain on how mucin sequences, glycosylation patterns, and intermolecular interactions define emergent material properties. Elucidating these relationships through multidisciplinary approaches is needed to provide guiding design principles for mucus-inspired biomaterials.

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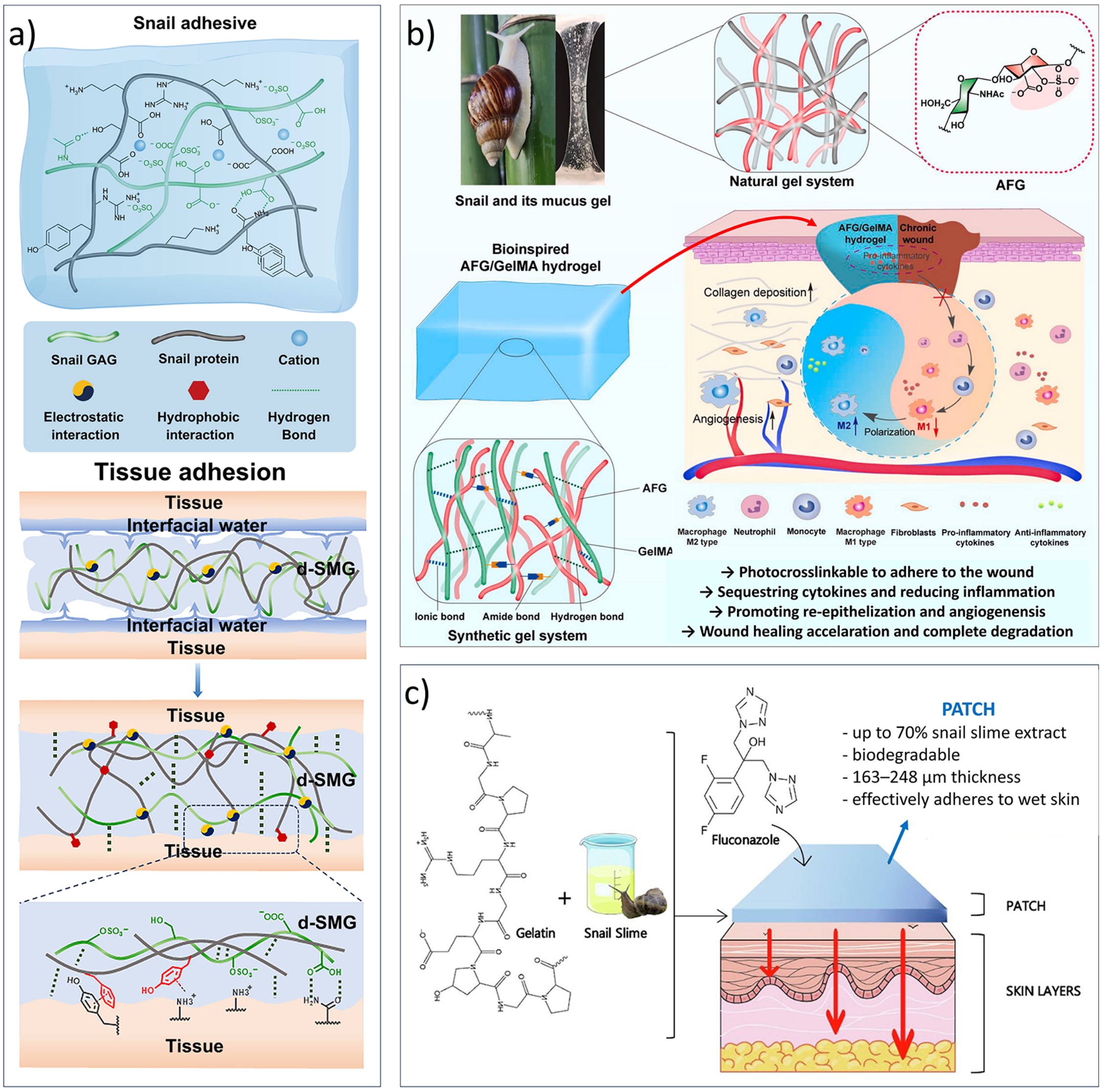

Figure 3. Snail mucus-derived innovations in wound healing and drug delivery. (a) Dried snail-mucus glue (d-SMG) mechanism in wound healing. Snail adhesive: The snail-mucus hydrogel has a double-network structure. Proteins form a 3D skeleton that binds with linear snail glycosaminoglycan (s-GAG), resulting in supramolecular entanglement. This is further reinforced by electrostatic interactions between positive amino or guanidine groups and negatively charged sulfate and carboxyl groups in s-GAG. Other bonds, such as hydrogen, π−π, and hydrophobic interactions, are prevalent due to the high presence of hydroxyl, aromatic, and aliphatic amino acids. Divalent cations (Ca^{2+} and Mg^{2+}) in the mucus modify gel elasticity via complexation and electrostatic interactions, resulting in a naturally resilient and cohesive snail adhesive. Tissue adhesion: On moist tissue surfaces, water blocks hydrogen bond receptors and donors, restricting interactions. The hydrophilic nature of sulfated GAG in d-SMG, attributed to its rich sulfates, carboxyl, and hydroxyl groups, effectively absorbs water. This removal of interface water facilitates supramolecular interactions, promoting tissue adhesion. Adapted with permission from ref 6. Copyright 2023 Springer Nature. (b) AFG/GelMA hydrogel for wound healing. This bioinspired hydrogel is formed by covalently linking the polyanionic snail glycosaminoglycan (AFG) with positively charged methacrylated gelatin (GelMA) polymers. Upon exposure to light, it undergoes *in situ* gelation directly at the wound site, establishing an array of covalent and noncovalent bonds that ensure rapid solidification. Mechanistically, the AFG within the hydrogel binds to inflammatory cytokines, inhibiting the TLR4/NF-κB signaling pathway. This results in an improved wound microenvironment by lowering inflammatory cytokine levels and fostering macrophage M2 polarization, which further supports epithelialization, angiogenesis, and collagen deposition. Adapted with permission from ref 41. Copyright 2023 Elsevier. (c) Gelatin and snail slime-based patches. Gelatin-based films demonstrate increased flexibility, stretchability, and adhesion with higher slime content and are proposed for cutaneous drug delivery. With Fluconazole as a model drug, snail slime also prevented drug recrystallization, enhancing skin permeation and film flexibility. Adapted with permission from ref 69. Copyright 2021 Elsevier.

In summary, gastropod mucus exhibits functional diversity in its physicochemical properties and bioactive compounds. Glycoproteins and reversible gelation facilitate locomotion, adhesion, and protective barriers. Variations in composition relate to ecological niche adaptations and specialized adhesion. While recent research reveals intriguing details about mucus gland origins, composition, and biological roles, much remains unknown regarding mucin diversity, cross-linking, and structure−function relationships.

3. MULTIFUNCTIONAL BIOMATERIAL WITH DIVERSE BIOMEDICAL AND COSMETIC APPLICATIONS

Wound Healing and Tissue Repair. Gastropod mucus and its components have shown promise in accelerating wound

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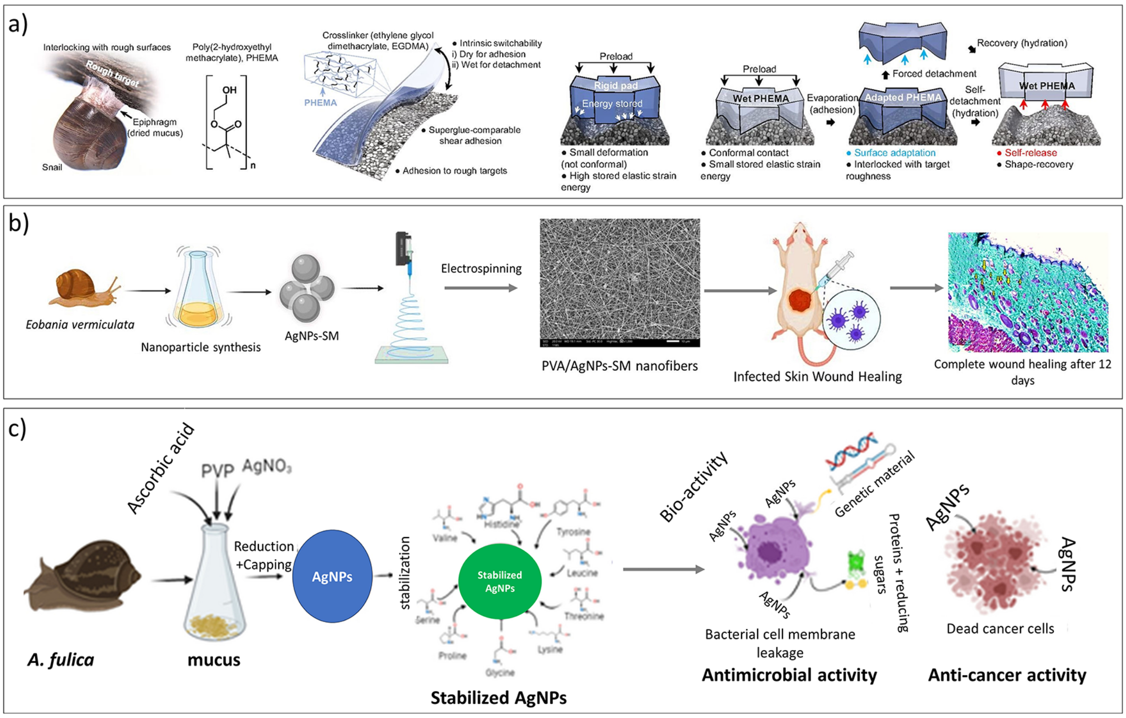

Figure 4. Bioinspired applications of snail mucus in nanotechnology and adhesion. (a) PHEMA hydrogel superglues. An overview of the epiphragm in snails, where dried mucus aids in adhering to uneven surfaces. Depicted are the chemical structure of PHEMA and its advantages in surpassing the challenges of liquid and dry adhesives. Challenges faced by solid adhesives with a high modulus when adhering to rough surfaces are illustrated. The proposed adhesion method using PHEMA gel showcases shape adaptability in a wet state, solidifying upon drying for optimized adhesion. Post drying, the hydrogel retains its deformed shape even under force (blue arrows). However, upon hydration, it reverts to its initial shape, enabling its easy detachment from the substrate (red arrows). Adapted with permission from ref 79. Copyright 2019 National Academy of Sciences. (b) PVA nanofibers loaded with silver nanoparticles (Ag-NPs) synthesized using snail mucus (reducing and stabilizing agents) for wound healing applications. Adapted with permission from ref 41. Copyright 2022 MDPI. (c) Green synthesis of silver nanoparticles employing snail mucus. The mucus's rich content of proteins and amino acids not only drove the nanoparticle synthesis but also emphasized its role in biostabilization and controlled the reduction of silver nitrate to silver particles. The process is marked by its ecofriendliness, simplicity, and scalability. Resulting nanoparticles exhibited potent antibacterial, antifungal, and anticancer activities. Adapted with permission from ref 82. Copyright 2021 Springer Nature.

closure (Figure 3a). Topical application of snail mucus extracts and gel promoted early re-epithelialization and accelerated the healing of second-degree burns in burnt mouse skin, likely attributable to antioxidant, antimicrobial, moisturizing, and anti-inflammatory properties.[31,32] The mucus components likely contributed to its ability to accelerate the proliferative and remodeling phases of burn wound healing. Spray-dried snail mucus powder displayed properties favorable for wound healing applications, including high protein content, antioxidant effects, and interactions with wound components *in vitro*.[33] In a rat model, topical application of snail mucus gel was shown to modulate the inflammatory process during wound healing by increasing the number of polymorphonuclear leukocytes in the early inflammatory phase.[34] The snail mucus gel stimulated the release of chemotactic factors to recruit inflammatory cells necessary for the clearance of debris and tissue regeneration.

A rat skin wound model showed that topical application of *A. fulica* snail mucus gel enhanced angiogenesis during wound healing in a concentration-dependent manner.[35] This proangiogenic effect is likely due to the ability of glycosaminoglycans and other compounds in snail mucus to bind and stabilize angiogenic growth factors. The ability to promote angiogenesis highlights the potential of incorporating snail mucus into regenerative medicine and tissue engineering applications, where vascularization is key to ensuring the engraftment and survival of engineered tissues.

While high concentrations of *A. fulica* mucus exhibited increased cytotoxicity against BHK-21 fibroblast cells *in vitro*, lower doses demonstrated the ability to promote fibroblast proliferation, suggesting the snail mucus contains bioactive factors that can stimulate cell growth.[36] However. These preliminary results indicated that the mucus may have concentration-dependent cytotoxic and proliferative effects.

An ophthalmic lubricating solution containing snail mucus extract exhibited regenerative effects on corneal cells and tissues.[37] Testing in a dry eye disease model further showed anti-inflammatory effects. Dental pulp stem cells cultured with the mucus of *A. fulica* showed increased mineralization and expression of bone differentiation markers, suggesting applications in dental and bone repair.[38] Encapsulation of *Helix aspersa* mucus extracts in liposomes created a stable delivery system that enhanced wound healing in preliminary studies, presenting opportunities for cell-based therapies.[39]

Nanofibers composed of poly(vinyl alcohol), silver nanoparticles, and *Eobania vermiculata* snail mucus exhibited homogeneous morphology and controlled silver release suitable for wound dressing applications[40] (Figure 4b). *In vivo* testing showed that the nanofiber dressings reduced bacterial growth and enhanced tissue regeneration in infected rat skin wounds. This highlights opportunities for snail mucus-

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based nanomaterials in therapeutic tissue engineering. The AFG/GelMA hydrogel, modeled after the natural adhesive qualities of snail mucus, offers a promising solution for treating chronic diabetic wounds[41] (Figure 3b). Preliminary evidence from animal studies suggests that gastropod mucus may accelerate wound healing through antioxidant and anti-inflammatory effects. However, further clinical testing is required to confirm whether these benefits translate to human wounds.

Composite hydrogels fabricated from snail mucus blended with chitosan demonstrate tunable degradation and cytocompatibility, along with enlarged pore size and swelling capacity compared to pure chitosan films.[42−44] Human chondrocyte assays reveal that mucus-chitosan hydrogels support cartilage cell viability and differentiation through the release of stimulatory glycosaminoglycans and metabolites.[45] Novel gradient chitosan scaffolds with bioactive *H. aspersa* mucus and slime extract also show potential for osteochondral tissue regeneration, significantly increasing the synthesis of extracellular matrix components for tissue regeneration and biomineralization in osteoblast and cartilage model cell lines.[46] Moreover, the hydrogels serve as bioactive scaffolds for human osteoblasts, enhancing alkaline phosphatase activity and osteogenic markers.[44] A double-network hydrogel composed of snail glycosaminoglycan and methacrylated gelatin showed promise for diabetic wound healing applications based on its tissue adhesive properties and ability to modulate inflammation.[41]

The ability to release osteoinductive small molecules while supporting bone and cartilage growth highlights the potential of these injectable matrices as acellular constructs for bone grafts or implants. However, the therapeutic potential of these mucus-chitosan hydrogels remains preliminary pending more rigorous *in vivo* evaluation and clinical validation of safety, efficacy, and advantage over existing options for bone and cartilage repair applications.

Medical Glues and Sealants. The innate bioadhesive properties of gastropod mucus (Figure 2a, b) have enabled the development of novel medical glues. A bulk adhesive matrix formulated from snail mucus showed rapid gelation on contact with tissue, excellent hemostatic activity, and the ability to markedly accelerate re-epithelialization, collagen remodeling, and angiogenesis in a rat wound model.[6] The regenerative effects were attributed to glycosaminoglycans within the mucus. Though the application potential of this mucus-based glue includes wound closure, dental sealants, and surgical repair, where it might hold advantages over synthetic options, extensive clinical testing in humans remains necessary to validate the efficacy, safety, and comparative benefits of these experimental gastropod mucus medical adhesives over existing approved products.

Antimicrobials. Gastropod mucus contains an array of antimicrobial proteins and peptides with potential as new antibiotics against resistant bacteria.[47,48] Novel proteins isolated from *Cornu aspersum* mucus display potent activity against *Pseudomonas aeruginosa*, including multidrug-resistant isolates.[49] *H. aspersa* mucus proteins were shown to inhibit *Staphylococcus aureus* and *P. aeruginosa*.[50] Other studies have analyzed the antimicrobial properties of mucus isolated from land snail species such as *Archachatina marginata*, *Achatina achatina*, and *A. fulica*.[51,52] Mucus extracts from *A. marginata* showed the strongest antibacterial effects against both Gram-positive and Gram-negative bacteria, with particular potency against *Bacillus subtilis*.[51] Purified mucus fractions from *A. fulica* also exhibited antimicrobial, antibiofilm, and antivirulence activities against *S. aureus* strains.[52] A high molecular weight fraction containing hemocyanin-derived peptides had inhibitory effects on *S. aureus* growth, biofilm formation, and virulence factors. Together, these findings provide evidence that bioactive components within snail mucus, such as protective proteins and peptides, may have therapeutic potential as new antibiotics or antivirulence agents against drug-resistant microbes.

The cysteine-rich antimicrobial peptide Mytimacin-AF isolated from *A. fulica* mucus showed potent antimicrobial activity against a wide range of bacteria (with the strongest antimicrobial activity against *S. aureus*) and the fungus *Candida albicans*.[53] Further chemical analyses identified antimicrobial metabolites, including glycosaminoglycans, achasin, acharan sulfate, and beta-agglutinin, exhibiting potent antibacterial effects against *Enterococcus foecalis*, one of the bacteria responsible for causing periodontitis.[54] Bioactive compounds extracted from *H. aspersa* soft tissue demonstrated strong antifungal effects against *C. albicans*, *Aspergillus flavus*, and *Aspergillus brasiliensis*.[55] Liquid chromatography−mass spectrometry identified metabolites, including flavonoids, fatty acids, and steroids, as antifungal agents within the snail extracts.

These studies reveal mucus as a promising source of new antimicrobial agents. However, elucidating the specific molecular effectors and mechanisms of action against pathogens remains an open research front. Future directions include high-resolution proteomics and transcriptomics profiling of mucus from poorly studied gastropod species, integrated with bioassays against drug-resistant microbes. There is also a need to move beyond descriptive studies and employ genetic or biochemical approaches to validate the proposed antimicrobial molecules and modes of action within the mucus. Harnessing the antimicrobial potential of gastropod mucus requires a transition from broad surveys to deeper mechanistic understanding.

Anti-Cancer Effects. Unexpected anticancer effects have been observed for specific mucus fractions, which selectively induce apoptosis in triple-negative breast cancer cells while sparing normal breast epithelium cells.[56] In xenograft models, the mucus enhanced chemotherapy-induced apoptosis by suppressing survival signaling and activating cell death pathways. Antimelanogenic and antitumor effects against melanoma cells have also been demonstrated.[57] Extracts from lyophilized *H. aspersa* mucus decreased the viability of Caco-2 colorectal cancer cells,[58] while mucin from *Ereminia desertorum* snail mucus displayed antioxidant effects and upregulated antioxidant and tumor suppressor genes in colon and liver cancer cell lines, suggesting its potential as a natural source of therapeutic compounds against liver and colon cancers.[59] Additionally, extracellular vesicles derived from *Arion vulgaris* mucus were successfully loaded with the chemotherapy drug doxorubicin. Using *in vitro* internalization assays, it was demonstrated that these vesicles can penetrate human glioblastoma cells,[60] highlighting opportunities for targeted cancer therapy.

While initial studies report promising anticancer effects *in vitro* and in xenograft models, extensive clinical evaluation is required to validate the therapeutic potential and safety of mucus-derived compounds and extracellular vesicles for applications in human cancers.

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Other Therapeutic Applications. Gastropod mucus exhibits a range of other intrinsic therapeutic bioactivities. *H. aspersa* agglutinin specifically binds metastatic cancer cell markers, suggesting applications for improving cancer diagnostic techniques.[61] *A. maginata* and *H. aspera* mucus demonstrated gastroprotective effects as antiulcer agent.[62,63] The antidiabetic potential of snail mucin was demonstrated by the dose-dependent reduction in blood glucose levels observed in diabetic mice treated with a combination of whole *Costus afer* (ginger lily) flowers and snail mucus.[64]

In a mouse model of lupus nephritis, oral administration of mucus from *A. fulica* significantly reduced the renal histological activity index compared to control mice.[65] The highest mucus dose in combination with methylprednisolone showed the maximum decrease in the activity index, suggesting a potential adjuvant therapeutic effect.

Fractions of mucus serum (seromucous) from *A. fulica* showed immunomodulatory effects when tested in combination with chitosan *in vitro*.[66] The seromucous and chitosan fractions significantly increased lymphocyte proliferation and optimized levels of cytokines such as IFN-gamma and IL-4. A mixture of the two showed synergistic effects, indicating the potential of *A. fulica* seromucous as a bioimmunomodulator, including as a possible adjuvant to tuberculosis therapy. However, further research is needed to isolate and characterize the specific immunologically active compounds.

Acharan sulfate, a heparin-like sulfated polysaccharide purified from *A. fulica* mucus, presents a promising alternative to heparin with the capacity to inhibit the binding of SARS-CoV-2 spike protein to the ACE2 receptor.[67] Small bioactive molecules like polyphenols also impart anti-inflammatory, antioxidant, and immunomodulatory effects.[8,68]

Films made from gelatin combined with snail slime were introduced as innovative biodegradable patches with intrinsic bioadhesive properties, ideal for cutaneous drug delivery[69] (Figure 3c).

Additionally, mucus granules secreted by the slug *Ariolimax columbianus* could be rapidly triggered to release their contents by extracellular ATP at micromolar levels.[70] Understanding this mechanism could provide principles for the engineering of on-demand mucus delivery vehicles. For example, packaging drugs into mucus granules with tuned ATP sensitivity could enable triggered release at injury sites, where ATP is elevated.

This array of bioactivities provides early evidence of the potential of mucus components in medicines, but substantial clinical research remains necessary to confirm the efficacy, safety, and advantages of gastropod-mucus-derived compounds as nutraceuticals, pharmaceuticals, or diagnostics in humans.

Cosmetic and Skincare Applications. The high-water content and hygroscopic glycosaminoglycans enable gastropod mucus to provide hydrating effects on the skin. Extracts increased skin hydration and reduced trans-epidermal water loss in animal studies,[71] likely attributable to their moisturizing physical properties. Some bioactive compounds in gastropod mucus also exhibit antioxidant activities, including certain peptides and polyphenols.[5,72] In canine skin cell models, secretion filtrate from snail mucus reduced the production of inflammatory mediators implicated in atopic dermatitis, including cytokines like IL-6, IL-8, and IL-17A.[73] These anti-inflammatory effects suggest the potential for snail mucus components as natural therapeutic agents for inflammatory skin conditions in veterinary species.

Mucus obtained from *A. fulica* exhibited antioxidant activity as well as anti-inflammatory effects *in vivo* in a chicken model,[74] topical application of the snail mucus gel reduced carrageenan-induced paw edema.

In vitro studies demonstrate that gastropod mucus can protect human skin cells and tissue models from oxidative damage induced by UV radiation or environmental pollutants.[8]

Beyond hydration and antioxidant properties, gastropod mucus may modulate skin cell physiology. Mucus derived from *Limax maximus* and *Arion rufus* decreased metabolic activity and proliferation in human keratinocytes,[75] indicating potential for products promoting healthy skin cell turnover. *In vitro* studies illustrated that antioxidant-rich edible flower waste extracts amplify the cytoprotective effects of snail mucus against UVB-induced damage in keratinocytes, as evidenced by enhanced antioxidant activity, reduced glutathione content, ROS, and lipid peroxidation levels, thereby suggesting potential cosmeceutical applications for flower waste.[72]

Finally, most mollusc mucus demonstrates broad-spectrum antimicrobial and anti-inflammatory properties,[50,76,77] conferring preservative effects against contaminants in cosmetics. However, antimicrobial efficacy varies widely between species and individuals. Isolating and standardizing the specific microbicidal components would enable their incorporation into cosmetic formulations.

Despite the commercial success of snail mucus in available skin care products (the snail beauty market offers cell renewal, antiacne, antiaging, and antiwrinkle creams, shampoos, and similar products valued at over 500 million USD in 2022), critical assessment reveals that the evidence base for cosmetic efficacy remains limited. Most research has evaluated antioxidant, antimicrobial, and anti-inflammatory effects using *in vitro* assays or animal models, while *in vivo* and clinical studies in humans are scarce.

4. POTENTIAL APPLICATIONS OF GASTROPOD MUCUS IN BIOTECHNOLOGY

Adhesives. Gastropod mucus possesses a unique combination of properties that present diverse opportunities across the various fields of biotechnology. A key promising and well-studied attribute is the adhesive nature of the mucus. Gastropod mucus enables snails and slugs to strongly attach to surfaces even under wet conditions, owing to the mucus' ability to rapidly transition from a viscous liquid to a solid gel upon contact[2,78] (Figure 2). For instance, the mucus of the snail *Macrochlamys indica* can adhere glass slides together with a force of up to 9 kPa in an alkaline environment.[78] This wet adhesion results from transient cross-links that enable rapid gelation upon secretion. The amphiphilic nature and pH-responsiveness of the mucus facilitate this rapid transition from liquid to gel. For decades, researchers have aimed to develop synthetic underwater adhesives that mimic natural biological glue.

Inspired by the snail's epiphragm (sealing of the aperture of the shell against desiccation), a novel hydrogel-based, reversible, superglue-like adhesive with strong, reversible adhesion (up to 892 N cm^{-2}) to both smooth and uneven surfaces was designed.[79] This intrinsically reversible "superglue" easily conformed to surfaces when hydrated and solidified upon drying, similarly to snail behavior, promising scalability and practical application (Figure 4a).

Gastropod-inspired adhesives may find diverse applications as eco-friendly antifouling ship coatings, repair glues for wet

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environments, and biocompatible surgical sealants.[80] The adhesive properties arise in part from specific proteins present in the mucus. The adhesive mucus of marsh periwinkle snails, *Littorina irrorata,* contains unique proteins not found in nonadhesive trail mucus.[22] These "glue proteins" constitute a substantial portion of the adhesive mucus and significantly increase the stiffness and viscosity of polymer gels when added, even at low concentrations.[80]

The gel-stiffening properties of gastropod mucus largely arise from transient cross-links mediated by specific glycoproteins. Removal of calcium and transition metals like zinc and iron causes substantial decreases in mucus gel stiffness and elasticity,[12,15] revealing metal coordination interactions are key for modulating the material properties. Iron binds adhesive proteins like the 15 kDa glue protein in *Arion subfuscus* mucus,[15] identifying molecular targets for controlling cross-links. Calcium ions also facilitate polymer interactions by charge balancing, presenting opportunities to optimize scaffold ionic composition,[12] enabling tuning of stiffness through oxidative treatments. By elucidating the molecular factors underlying useful rheological properties, these insights facilitate the rational design of mucus-inspired biomaterials. Further research into isolating and engineering these proteins could enable the development of strong and reversible natural adhesives.

Bioinspired Grippers. Biomechanical research elucidated the response mechanisms of snails to pulling forces during locomotion[81] (Figure 2a). Experiments measuring the pull-off force showed that snails can resist up to 22 times their body weight, enabled by the flexible foot stretching to store elastic energy and a cavity forming under the foot during pulling. The cavity allows for the maintenance of a negative pressure differential even on rough surfaces, enhancing temporary adhesion. These insights provide principles for designing bioinspired suckers utilizing soft deformable membranes and cavities, which could enable adaptable gripping across diverse surfaces and objects compared with conventional rigid vacuum cups. Further engineering of the durability and adhesion strength of such suckers could enable applications in automated handling and manufacturing.

Green Nanoparticle Synthesis. Gastropod mucus also provides a medium for the green synthesis of nanoparticles, eliminating harsh chemical reducing agents[82] (Figure 4c). Mucus from the snail *A. fulica* produced silver nanoparticles, with the mucus biomolecules acting as capping and reducing agents to generate biocompatible nanoparticles. These mucus-silver composites exhibited potent antibacterial effects against *Escherichia coli* and antifungal effects against *Aspergillus fumigatus*.[82] Using purified snail slime from *H. aspersa*, biogenic silver nanoparticles were greenly synthesized, exhibiting substantial antibacterial properties and remarkable stability, even after aqueous redispersion.[83]

In another study, gold nanoparticles synthesized using *H. aspersa* mucus had an average diameter of 14 ± 6 nm.[84] High-resolution mass spectrometry identified peptides and amino acids from the mucus bound to the nanoparticle surfaces. Gold nanoparticles greenly synthesized using snail slime demonstrated dose-dependent antioxidant, skin-lightening, and sunscreen properties without any observed cytotoxicity, suggesting the potential for their use and further tuning in diverse cosmetic and biomedical applications.[85]

Analysis of *H. aspersa* mucus used for Au nanoparticle synthesis revealed increased levels of nitrogen- and sulfur-containing metabolites compared to pure mucus, based on untargeted high-resolution mass spectrometry.[86] The elevated presence of compounds such as peptides, amino acids, and polyphenols suggests they likely contribute to the green synthesis and stabilization of nanoparticles. Profiling both natural and nanoparticle-containing mucus provided insights into the metabolites involved in the nanoparticle interactions.

The stabilizing and biocompatible properties of gastropod mucus provide advantages for green nanotechnology over conventional methods.

Snail Mucus-Inspired Nanomaterials. Intriguing research by Zhong and colleagues revealed new insights into the dynamic self-assembly behavior of snail mucus nanostructures during locomotion, demonstrating that the mucus transforms from dispersed nanoparticles on horizontal surfaces into interconnected fiber networks when the snail crawls inverted up smooth vertical surfaces[87] (Figure 2b). This structural reorganization was enabled by changes in the secretion of glycoproteins and calcium carbonate levels as the crawling angle increased. Most significantly, the authors leveraged these natural self-assembly principles to engineer novel biomimetic mucus fibers with favorable elasticity and extensibility. This provided a new, biologically inspired material based on harnessing the innate properties of snail mucus.

Further advancing these mucus biomimicry approaches, recent materials science research demonstrated the ability to recreate the fibrous architecture of snail mucus through electrospinning techniques[88] (Figure 4b). By optimizing processing parameters, nanofibers were produced with diameters tunable from 200 to 700 nm that mirrored the fibrous networks in natural snail mucus. Spectroscopic analysis confirmed the fibers contained characteristic protein and sugar components of snail mucus. This nanoengineering strategy establishes modular principles for fabricating mucus-inspired biomaterials with wide-ranging potential in regenerative medicine. However, rigorous *in vitro* cytotoxicity screening and *in vivo* evaluation in tissue models are still required to comprehensively assess the viability as implantable scaffolds.

Overall, these recent studies reveal promising new techniques to replicate the favorable properties of snail mucus, paving the way for innovative bioinspired materials and nanotechnologies. Further research on mechanistic mucus characterization, self-assembly modeling, and scalable manufacturing will be key to fully unlocking the potential.

Potential Applications in Plant Biotechnology. Extracellular vesicles derived from the mucus of *A. vulgaris* demonstrated the ability to be loaded with agents and internalized by plant cells under *in vitro* conditions. These findings open up intriguing possibilities for their use in pest management strategies and broader applications within the field of plant biotechnology.[60]

Realizing the promising biotechnological potential of gastropod mucus requires moving beyond speculative possibilities to critically evaluate its technical viability based on current research. For instance, developing mucus-based medical adhesives demands greater detail on methods for the isolation and engineering of adhesive proteins like those studied in *Arion subfuscus*[6] and marsh periwinkle mucus.[22] Analysis of binding forces, gelation kinetics, tissue compatibility, and safety is needed to assess the feasibility of surgical sealants or wound glues. Regarding green nanoparticle synthesis, important challenges include optimizing reaction

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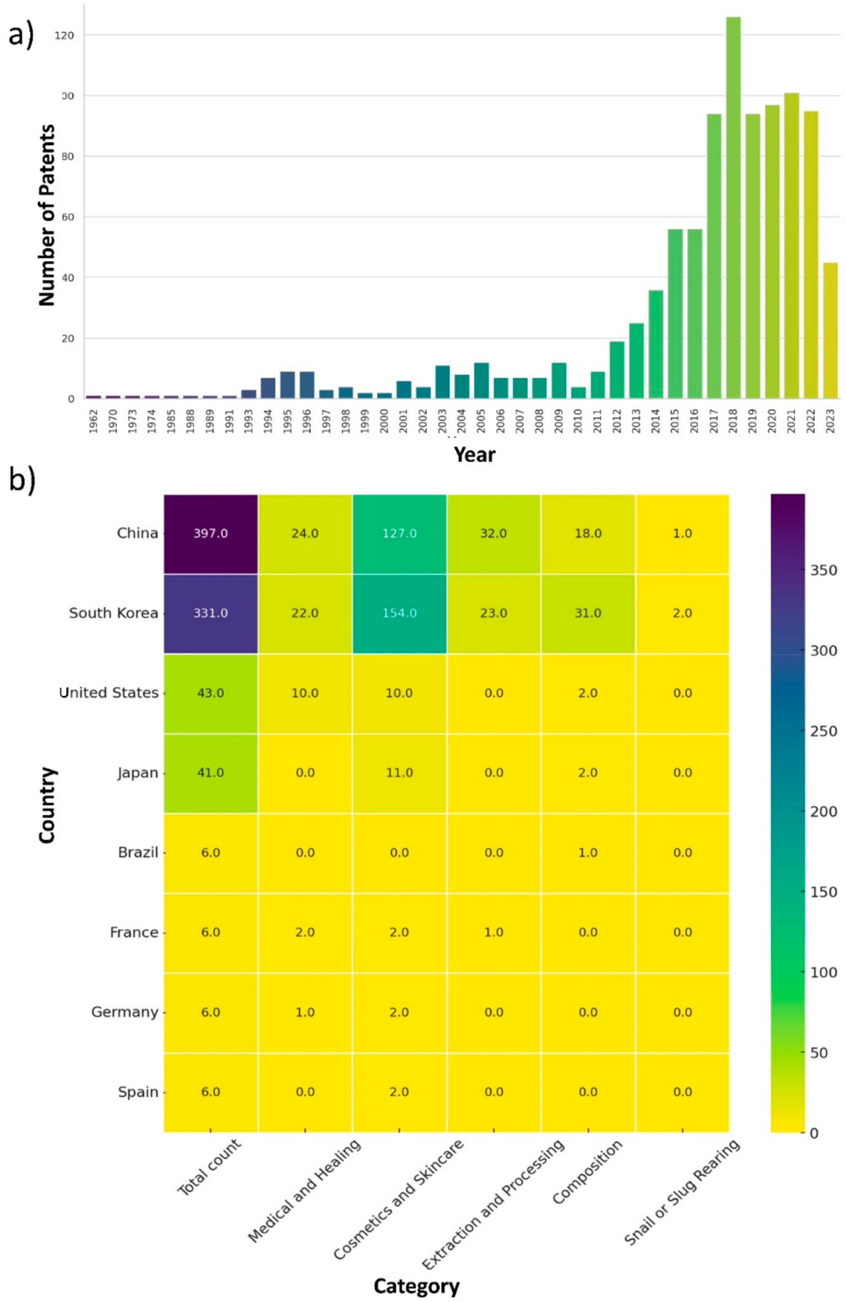

Figure 5. Patent trends and applications in snail mucus research. (a) Bar graph representing the total number of patents related to snail mucus for individual years. (b) Heatmap representing a detailed overview of the number of patents related to snail mucus across the main application categories for countries that have issued more than five patents in this field.

conditions for reproducibility, increasing production, and preventing nanoparticle aggregation. While initial studies demonstrate snail mucus can be used for the green synthesis of silver and gold nanoparticles,[82−85] data on real-world stability, cost analysis, and cytotoxicity testing remain preliminary. Proposed applications in on-demand drug delivery also lack key details about delivery vehicle fabrication, mucus loading efficiency, release kinetics, and *in vivo* biocompatibility.

Significant research is still needed to translate these innovative possibilities into viable technologies. Strategic priorities should include the isolation and engineering of adhesive mucus proteins, scalable production and prevention of nanoparticle aggregation, and comprehensive evaluation of drug delivery vehicle fabrication and performance. A solution-oriented path can guide the strategic advancement of mucus-based biotechnologies by identifying key gaps between conceptual potential and current technical capabilities.

5. GASTROPOD MUCUS PATENT LANDSCAPE REVEALS RISING INNOVATIONS ACROSS SECTORS

Analysis of the global patent landscape, specifically the Google Patents database (patents.google.com), which contains over 200 million records, provides insights into emerging applications and innovation trends for natural compounds such as gastropod mucus. A targeted search strategy utilizing gastropod mucus-related keywords generated a highly relevant data set of at minimum 978 mucus-related patents.

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Examination of the patent landscape timeline (Figure 5a) reveals a marked increase in patent issuances starting in 2015, suggesting rapidly expanding global research and innovation efforts to leverage gastropod mucus. Peak patent activity was seen in 2018 and 2021, with more than 100 new patents granted each year. Although patent numbers appear to decline post-2021, this more likely stems from patent approval lags rather than slowing research activity.

Earlier patents focused predominantly on pharmaceutical applications, including mucus proteins for wound healing in the 1970s (DE-1813154-A1, FR-2146909-A1). Recent patents display increasing diversity, spanning from various cosmetics and skincare applications (CN-113262183-B, KR-102491996-B1), biomedical uses such as laser-assisted wound treatments (US-2023211173-A1) to industrial applications, including fermented mucus extraction (KR-102505942-B1). This broadening patent landscape aligns with the multifunctional bioactive properties of gastropod mucus highlighted in this review.

Distribution analysis of the patents (Figure 5b) reveals several striking trends. The majority of patents are held by China and South Korea, together accounting for over 75% of total patents. This predominance is most pronounced for cosmetics and skincare, likely indicative of strong commercial interest in these countries. After the Asia-Pacific leaders, the United States, Japan, and Brazil also demonstrate significant patent activity, albeit an order of magnitude lower.

The substantial commercial success of snail mucus-based cosmetic products, with the global snail beauty product market valued at over 500 million USD in 2022,[9] provides further impetus to build upon the promising potential of gastropod mucus highlighted in the patent record. The dominant patent activity around cosmetics and skincare applications, especially in Asia-Pacific countries, mirrors the surging commercial interest in bringing snail-muscus-based formulations to market. Realizing the diverse bioactive properties and emerging applications captured in the patent data represents an opportunity to translate academic insights into transformative innovations that meet the needs of society across industries. The cosmetics sector serves as a launching point to demonstrate real-world viability and drive broader adoption. Continued patent monitoring and strategic intellectual property management will be crucial to sustaining an innovation ecosystem that transforms gastropod mucus from a traditional remedy into next-generation products worldwide.

In summary, analysis of patent trends provides insights into accelerating research and commercial interest in gastropod mucus applications across materials science, cosmetics, and biomedicine. The substantial patent activity from China and South Korea underscores the potential to build upon traditional medicine knowledge to spur new innovations. Ongoing monitoring of patent data grants the opportunity to identify emerging applications and strategic opportunities to harness gastropod mucus' vast potential into transformative products worldwide.

6. OPPORTUNITIES AND FUTURE DIRECTIONS

This review synthesizes the diverse biological activities and physicochemical properties that enable multifaceted applications of terrestrial gastropod mucus across biomedicine, biotechnology, and cosmetics. However, fully realizing this promising potential necessitates strategic innovation to overcome the key challenges.

Sourcing adequate mucus quantities remains a constraint, yet expanding sustainable gastropod culture and engineering mucus-secreting cell bioreactors could provide scalable production. Elucidating compositional variability via omics profiling of diverse species and implementing standardization methods can improve quality control and formulation reproducibility. Effective stabilization systems and advanced delivery platforms are required to maintain bioactivity during processing, storage, and administration. Comprehensive preclinical development and rigorous clinical testing must demonstrate safety, efficacy, and advantages over conventional approaches to gain regulatory and consumer acceptance.

Nonetheless, abundant opportunities exist to strategically advance the field. Bioprospecting the vast gastropod diversity offers an expansive natural compound library for therapeutic discovery. Genomic elucidation of biosynthetic pathways can enable recombinant production of the desired mucus components. Optimization of bioreactor culture systems and the application of green chemistry principles provide paths to sustainable sourcing. Harnessing polymers, nanoparticles, and innovative scaffolds to protect and deliver mucus bioactives may overcome formulation challenges. Fostering collaborations among academics, clinicians, industry groups, and regulatory bodies can synergistically progress technologies from promise to societal impact.

Taken together, leveraging the multifunctionality of gastropod mucus holds immense potential to create transformative innovations, addressing unmet needs across many sectors. A solutions-focused approach grounded in bench-to-bedside translation can propel gastropod mucus from its rich history into its future realization as a multifaceted biomaterial advancing human health and biotechnology.

7. CONCLUSIONS

In conclusion, this comprehensive review integrates interdisciplinary perspectives on the diverse biological activities, physicochemical properties, and ecological roles of terrestrial gastropod mucus that enable its promising multifaceted applications. The analysis of global patent trends provides valuable insights into accelerating research and commercial interest in leveraging gastropod mucus across sectors. However, fully realizing the potential of gastropod mucus requires overcoming key challenges in sustainable production, variability, stabilization for storage, and rigorous translation through preclinical and clinical testing. Abundant strategic opportunities exist to advance the field through bioprospecting natural diversity, optimization of recombinant synthesis methods, engineering innovative mucus-based biomaterials, and fostering collaborations among researchers, clinicians, regulators, and industry. With persistence and ingenuity, the remarkable multifunctionality of gastropod mucus holds immense potential for transformative, sustainable technologies meeting unmet needs in diverse sectors, including biomedicine, biotechnology, cosmetics, and beyond.

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Notes

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