2026 IULTCS Young Leather Scientist Grant

Identification: YLSG_2026_applicantname

COMPLETE APPLICATION FORM (click application area)

☑ Basic Research ☐ Environmental/Sustainability ☐ Machinery/Testing

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By submitting this application, I commit to develop the project as outlined in the attached Research Project Plan and to complete a written report by February 28, 2027 with the following items:

1) Introduction
2) Materials and Methods
3) Results and Discussion
4) Conclusion
5) Suggestion for Future Work
6) References

2) Research Project Plan outline – Maximum 3 pages

Title: Strategy for stability enhancement of biological leather-making technology: Preparation of protease inhibitor and its application in bating process

Introduction:

Biological leather-making technology represents a pivotal direction driving the leather industry toward green and sustainable development [1]. This technology primarily involves treating animal hides with proteases to remove noncollagenous proteins while simultaneously loosening collagen fibers [2]. However, proteases, with molecular weights of 20-50 kDa, penetrate into the thick hide/leather (2-10 mm) slowly and tend to accumulate on the hide/leather surface, resulting in uneven spatial distribution, moreover, due to the high catalytic efficiency and low substrate specificity of proteases, collagen in the hide/leather surface layer undergoes prolonged longer enzymatic action compared to the inner layer, thereby leading to uneven hydrolysis (Fig.1) [3~5]. The obvious differences in enzymatic hydrolysis over time and space are highly prone to causing defects, such as grain damage and loose grain, in the finished leather, which severely diminish the quality and value of leather products and greatly hinder the industrial promotion and application of biological leather-making technology.

Our research team has effectively regulated the hydrolytic activity of proteases on the surface layer of hides by timely adding protease inhibitors during the bating process (Fig.1). This strategy successfully prevents excessive enzymatic hydrolysis of the hide surface and improves the hydrolytic uniformity in both the surface and inner layers of hides [6]. Scale-up experiments confirmed that the technical system is effective and feasible. However, the successful implementation and widespread application of this approach hinge on the appropriate selection of inhibitors. Although high temperatures, strong acids and bases, ultraviolet radiation, organic solvents, and heavy metals can inactivate proteases [7], their use simultaneously damages the protein-based hide/leather or poses environmental risks. In contrast, protein or peptide inhibitors offer advantages such as superior specificity and environmentally friendly. Nevertheless, the varieties of such inhibitors are limited, and they are primarily sourced from the pharmaceutical or food sectors, making them expensive and unable to meet the demands of large-scale industrial production [8]. Consequently, developing low-cost, efficient, and environmentally friendly protease inhibitors for leather-making is essential for advancing and promoting biological leather-making technology.

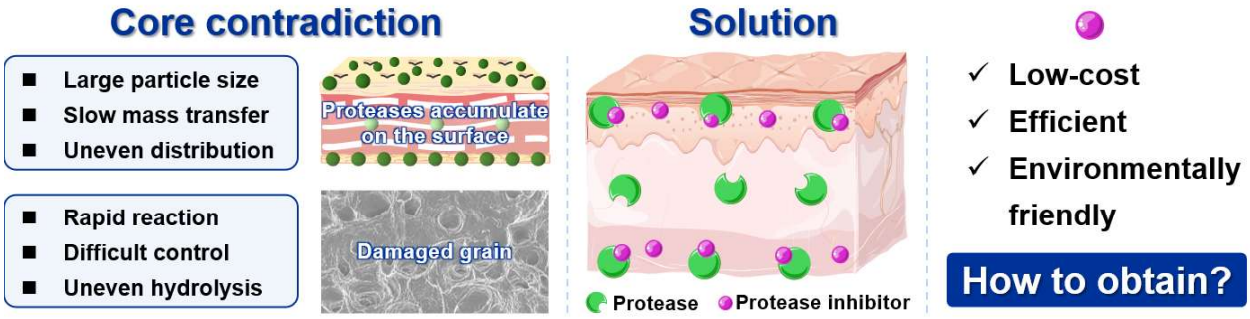

Fig.1. Schematic diagram of the core contradictions and solution of biological leather-making technology

Our extensive research on collagen hydrolysis by proteases has revealed that collagen enzymatic hydrolysates contain components that inhibit enzymatic catalytic activity. Drawing inspiration from this phenomenon, the hydrolysis of hide collagen using typical leather-making proteases is likely to yield potent inhibitors. In this research, cowhide or sheepskin waste (offcuts from raw hide or limed hide) are utilized as raw materials. The target peptides with protease inhibitory activity will be efficiently screened out via molecular

simulation technology. Peptide-based protease inhibitors with low-cost and environmentally friendly will be prepared through targeted enzymatic hydrolysis and enzyme-membrane coupling technology. Furthermore, the intrinsic relationship between inhibitor application parameters and the spatiotemporal distribution characteristics of enzyme activity during the bating process will be investigated systematically. The intelligent decision-making model for the bating process will be constructed. The research results will offer theoretical guidance and technical support for overcoming technological bottlenecks and facilitating the widespread industrial application of biological leather-making technology.

Objectives:

- Develop green, low-cost methods for preparing protease inhibitors, and reveal their generation mechanisms and inhibitory characteristics.
- Ascertain the effect of timely inhibition of surface proteases on the spatiotemporal enzyme activity distribution and leather properties, and build an intelligent decision-making model for the bating process.

Methods:

The research content includes four aspects (Fig. 2):

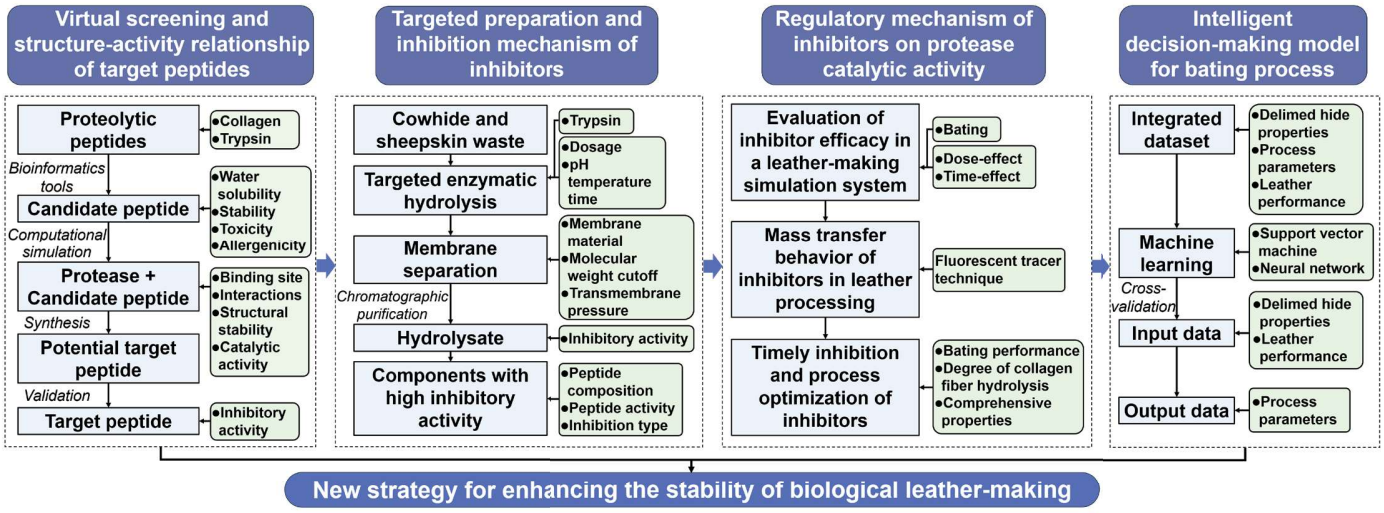

Fig.2. Research plan

- Virtual screening and structure-activity relationship study of target peptides

Bioinformatics tools are utilized to predict peptide sequences derived from collagen hydrolysis by trypsin, and candidate peptides exhibiting good water solubility and stability, non-toxicity, and non-allergenicity are screened systematically. Subsequently, binding sites and interaction mechanisms of candidate peptides with trypsin, and changes in structural stability and catalytic activity of trypsin–peptide complexes are predicted using Schrödinger molecular docking and GROMACS molecular dynamics simulations software are utilized to predict. Potential target peptides capable of altering enzyme molecular conformation or affecting active sites are identified and then synthesized via Fmoc solid-phase synthesis method. Inhibitory effects of the potential target peptides on trypsin are evaluated using enzymatic experiments, yielding target peptides with good inhibitory activity. Ultimately, the structure-activity relationship between the structural features and inhibitory activity of the target peptides is elucidated.

- Targeted preparation and inhibition mechanism study of protease inhibitors

Cowhide or sheepskin waste undergoes targeted hydrolysis with trypsin. Enzymatic hydrolysis parameters (pH, temperature, time, enzyme dosage) and membrane separation parameters (membrane material, molecular weight cut-off, transmembrane pressure) are systematically optimized to prepare hydrolysates matching the molecular weight of the virtually screened target peptides. Hydrolysates exhibiting inhibitory activity are multi-stage purified, and their peptide compositions are identified using ultra-high-resolution mass spectrometry. The experimental findings are validated against the virtual screening of target peptides. Subsequently, the inhibitory activity and type of each peptide are determined, providing insight into the molecular mechanisms underlying their inhibitory effects.

- Study on the spatiotemporal regulation of enzyme activity by inhibitors during bating

The dose-effect and time-effect relationships of the inhibitors on collagen hydrolysis by trypsin are investigated within a simulated bating system (pH 8-9, 30-35°C). Effects of inhibitor addition dosage and timing, among other parameters, on the bating performance of the delimed hides, the extent of collagen fiber hydrolysis, and the overall performance of the finished leather are investigated by fluorescence tracer technology, basing on the research results of the penetration kinetics of trypsin during the bating process (prior work by our research group). Finally, the rational combinations of inhibitor types and application parameters are obtained.

- Development of an intelligent decision-making model for the bating process

Experimental datasets, encompassing delimed hide properties (thickness, porosity), bating process parameters, and finished leather performance, are integrated. Model architectures with demonstrated non-linear mapping capabilities are screened and trained by using machine learning algorithms (support vector machines and neural networks). A predictive model is developed through cross-validation and hyperparameter optimization. This model takes delimed hide properties and finished leather performance as inputs to predict optimal bating process parameters (including temperature, pH, time, protease dosage and activity, and inhibitor dosage and addition time), thereby achieving a data-intelligence-driven process decision-making.

Hypothesis/Expected Results:

Low-cost, efficient trypsin inhibitors can be obtained from cowhide or sheepskin waste through computational screening, targeted enzymatic hydrolysis, and biochemical validation. These inhibitors can effectively mitigate the damage to surface collagen by enzymes during the bating process, thereby enhancing leather quality and providing theoretical and data support for the intelligent decision-making in leather processes.

Research benefit for the local or global leather industry (one sentence only):

This research will offer an economical, efficient, and sustainable solution for quality enhancement and process control in the bating process, thus promoting the green transformation and intelligent upgrading of the leather industry.

Literature:

[1] Shi, B., Chen, K.F., Wang, Q., et al., 2023. **Strategic Study of CAE** 25(1), 167-177.
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[3] Zeng, Y.H., Yang, Q., Wang, Y.N., et al., 2016. **J. Am. Leather Chem. As.** 111, 345-353.
[4] Song, Y., Wu, S.Q., Yang, Q., et al., 2019. **J. Leather Sci. Eng.** 1, 4.
[5] Gao, M.C., Song, J.Z., Zhang, X., et al., 2023. **Collagen and Leather** 5, 9.
[6] Chen, T.Y., Zeng, Y.H., Shi, B., 2023. **J. Am. Leather Chem. As.** 118, 245-252.
[7] Sujitha, P., Shanthi, C., 2023. **J. Clean. Prod.** 425, 138915.
[8] Cotabarren, J., Lufrano, D., Parisi, M.G., et al., 2020. **Plant Sci.** 292, 110398.