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Title: Fabrication of Dissolvable Microneedle Patches Loaded with α -Lactalbumin Nanomicelles for Transdermal Capsaicin Delivery and Adipose Tissue Reduction

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Author Questionnaire

1. We have marked your project as author-provided footage, meaning you film the video yourself and provide JoVE with the footage to edit. JoVE will not send the videographer. Please confirm that this is correct.

✓ Correct

2. Microscopy: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No**

3. Software: Does the part of your protocol being filmed include step-by-step descriptions of software usage? **No**

4. Proposed filming date: To help JoVE process and publish your video in a timely manner, please indicate the proposed date that your group will film here: **01/20/2026**

When you are ready to submit your video files, please contact our China Location Producer, [Yuan Yue](#).

Current Protocol Length

Number of Steps: 12

Number of Shots: 28

Introduction

INTRODUCTION:

~~What is the scope of your research? What questions are you trying to answer?~~

- 1.1. **Cheng Bao:** Our research involves the development of dissolvable microneedle patches to deliver capsaicin nanomicelles transdermally for adipose reduction.

- 1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera.

~~What are the most recent developments in your field of research?~~

- 1.2. **Jing Fu:** Recent developments in this field of research include rapid advances in microneedle-based transdermal delivery for painless, controlled metabolic regulation.

- 1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera.

NOTE to VO: Please record conclusion interview statements.

CONCLUSION:

~~What significant findings have you established in your field?~~

- 1.3. Significant findings established in this field include demonstrating an efficient, needle-free strategy for localized capsaicin delivery with reduced irritation and systemic exposure.

- 1.3.1. 3.6.1.

~~What research gap are you addressing with your protocol?~~

- 1.4. This protocol addresses the absence of simple, scalable methods combining enzymatic self-assembly with dissolvable microneedles for uniform drug loading.

- 1.4.1. 3.3.1.

~~What advantage does your protocol offer compared to other techniques?~~

- 1.5. This platform supports scalable transdermal delivery of hydrophobic molecules and may accelerate therapeutic development for obesity-related research.

- 1.5.1. *Figure 5*

Ethics Title Card

This research has been approved by the Science and Technology Ethics Review Committee of Ludong University (Approval No. LDU-IRB2025020011)

Protocol

2. Preparation of Alpha-Lactalbumin-Based Nanomicelles Encapsulating Capsaicin via Enzymatic Self-Assembly

Demonstrators: Jing Fu, Yuli Pan, Luna Li, Chunhui Rui

- 2.1. To begin, dissolve alpha lactalbumin in deionized water to a concentration of 6 milligrams per milliliter [1]. Adjust the pH to 7.4 [2], then use a magnetic stirrer to stir the solution at 8 to 28 g until the protein is completely dissolved [3].
 - 2.1.1. WIDE: Talent adding alpha lactalbumin powder to deionized water in a container.
 - 2.1.2. Talent adjusting the pH.
 - 2.1.3. Talent placing the solution on a magnetic stirrer until clear.
- 2.2. Now, add *Bacillus licheniformis* protease to the solution at an enzyme to substrate ratio of 1 to 100 [1]. Mix gently to ensure uniform distribution of the enzyme [2]. Incubate the mixture at 50 degrees Celsius for 30 minutes to generate amphiphilic peptides [3].
 - 2.2.1. Talent measuring and adding *Bacillus licheniformis* protease to the protein solution.
 - 2.2.2. Talent gently stirring the solution to mix the enzyme thoroughly.
 - 2.2.3. Talent placing the container into a heating device set to 50 degrees Celsius.
- 2.3. Heat the solution to 95 degrees Celsius for 5 minutes to terminate the enzymatic reaction [1]. After cooling the solution to room temperature, filter it through a 0.22-micrometer membrane [2].
 - 2.3.1. Talent placing the container into a heating device set to 95 degrees Celsius.
 - 2.3.2. Talent filtering the cooled solution through a 0.22 micrometer membrane filter.
- 2.4. Next, dissolve capsaicin in ethanol to a concentration of 1 milligram per milliliter [1]. Then add the capsaicin solution dropwise into the peptide solution under gentle stirring [2]. Continue stirring the mixture for 2 hours to allow self-assembly of nanomicelles [3].

- 2.4.1. Talent dissolving capsaicin in ethanol in a separate container.
- 2.4.2. Talent adding the capsaicin solution dropwise into the peptide solution while stirring gently.
- 2.4.3. Talent leaving the solution on a magnetic stirrer.
- 2.5. To remove free capsaicin, dialyze the mixture against deionized water for 12 hours [1-TXT]. Then freeze-dry the prepared alpha lactalbumin nanomicelles [2].
 - 2.5.1. Talent transferring the mixture into dialysis tubing. **TXT: Replace water every 4 h**
 - 2.5.2. Talent placing the sample into a freeze dryer.

3. Fabrication and In Vitro Evaluation of Dissolvable Microneedle Patches Loaded with Capsaicin Nanomicelles

Demonstrator: Jing Fu, Chunhui Rui

- 3.1. To fabricate dissolvable microneedle patches, dissolve hyaluronic acid and polyvinyl alcohol in deionized water at 60 degrees Celsius [1-TXT]. Stir until the solution becomes clear [2]. Then, mix the cooled solution with the capsaicin-loaded nanomicelles at a ratio of 4 to 1 [3].
 - 3.1.1. Talent adding hyaluronic acid and polyvinyl alcohol to heated deionized water. **TXT: Hyaluronic Acid: 5% w/v; Polyvinyl Alcohol: 5% w/v**
 - 3.1.2. Talent stirring the solution until it appears clear and homogeneous.
 - 3.1.3. Talent combining the polymer solution with nanomicelles and mixing thoroughly.
- 3.2. Next, degas the mixture under vacuum in a desiccator connected to a vacuum pump at approximately minus 80 kilopascals for 10 minutes [1].
 - 3.2.1. Talent placing the mixture into a desiccator and applying vacuum.
- 3.3. Load 200 microliters of the degassed mixture into polydimethylsiloxane molds [1] containing a 10 by 10 microneedle array with a height of 600 micrometers [2]. Then centrifuge the molds at 1800 *g* at room temperature for 10 minutes to ensure complete filling of the microneedle cavities [3].
 - 3.3.1. Talent pipetting the mixture into the microneedle molds.
 - 3.3.2. Shot of the mold with microneedle arrays.

- 3.3.3. Talent placing the molds into a centrifuge.

- 3.4. After filling and centrifuging the molds again, dry them under vacuum at approximately minus 80 kilopascals at room temperature for 12 hours [1]. Then carefully peel the microneedle patches from the molds [2].
 - 3.4.1. Talent placing the molds into a vacuum chamber for drying.
 - 3.4.2. Talent gently removing the microneedle patches from the molds.

- 3.5. To perform the in vivo insertion and dissolution test, apply a depilatory cream to the mouse inguinal region [1], then wipe and clean the skin [2].
 - 3.5.1. Talent applying depilatory cream onto the inguinal region of the mouse.
 - 3.5.2. Shot of the skin being wiped clean.

- 3.6. Place the microneedle patch onto the skin above the inguinal fat pad and press firmly for 30 seconds [1-TXT]. After 30 minutes, remove the patch [2] and inspect microneedle dissolution [3]
 - 3.6.1. Talent applying the microneedle patch onto the skin with firm pressure. **TXT: Maintain contact between the patch and skin for 30 min**
 - 3.6.2. Shot of the patch being removed.
 - 3.6.3. Talent inspecting for microneedle dissolution.

Results

4. Results

- 4.1. Transmission electron microscopy showed uniformly dispersed, spherical α -lactalbumin nanomicelles [1]. Capsaicin loading increased the mean diameter from approximately 22 nanometers to 30 nanometers [2].

4.1.1. LAB MEDIA: Figure 1A.

4.1.2. LAB MEDIA: Figure 1B. *Video editor: Highlight the bar chart labeled “SNS-Cap”*

- 4.2. Confocal laser scanning microscopy showed rapid uptake of Cy3(*psy-three*)-labeled nanomicelles by 3T3-L1 (*Three-T-Three-L-One*) preadipocytes within 2 hours [1]. BODIPY (*bod-ee-pee*) staining indicated that M(Cap) (*M-Cap*) significantly reduced intracellular lipid droplet accumulation [2].

4.2.1. LAB MEDIA: Figure 2A. *Video editor: Highlight the merged image*

4.2.2. LAB MEDIA: Figure 2B. *Video editor: Highlight the “M(Cap)” panel*

- 4.3. Western blot and qPCR analysis showed that M(Cap) treatment downregulated PPAR γ (*P-P-A-R-Gamma*) and C/EBP α (*C-E-B-P-Alpha*) [1], while upregulating TRPV1 (*T-R-P-V-One*), UCP1 (*U-C-P-One*), and Cyt (*sight*) C expression [2].

4.3.1. LAB MEDIA: Figure 2C and 2D. *Video editor: Highlight the PPAR γ and C/EBP α bands and bars in the “M(Cap)” group.*

4.3.2. LAB MEDIA: Figure 2C and 2D. *Video editor: Highlight the TRPV1, UCP1, and Cyt C bands and bars in the “M(Cap)” group.*

- 4.4. Transmission electron microscopy confirmed increased mitochondrial numbers and reduced lipid droplet size in M(Cap)-treated adipocytes [1].

4.4.1. LAB MEDIA: Figure 2E. *Video editor: Highlight the “M(Cap)” panel*

- 4.5. Scanning electron microscopy confirmed well-defined pyramidal microneedles [1]. Confocal laser scanning microscopy showed that Cy5-labeled M(Cap) was evenly distributed throughout the microneedle matrix [2].

4.5.1. LAB MEDIA: Figure 3A.

4.5.2. LAB MEDIA: Figure 3B.

4.6. Microneedles dissolved completely within 30 minutes after insertion into murine abdominal skin [1], creating distinct microchannels through the stratum corneum [2].

4.6.1. LAB MEDIA: Figure 4A. *Video editor: Highlight the post-insertion image (right-most photos) showing the flattened microneedles and patch imprint on skin.*

4.6.2. LAB MEDIA: Figure 4B. *Video editor: Highlight the bottom H&E-stained section showing visible microchannels labeled "Microneedle patch".*

4.7. In vitro release testing showed pH-responsive behavior, with approximately 98% capsaicin release at pH 6.5 [1] and 78% at pH 7.4 after 50 minutes [2].

4.7.1. LAB MEDIA: Figure 4C. *Video editor: Please highlight the purple curve*

4.7.2. LAB MEDIA: Figure 4C. *Video editor: Please highlight the green curve*

1. Alpha-lactalbumin

Pronunciation link: <https://www.merriam-webster.com/dictionary/alpha-lactalbumin>

IPA: /ˌæl.fə.lækˈtæl.bjə.mɪn/

Phonetic Spelling: al·fuh lak·tal·byuh·min

2. Deionized

Pronunciation link: <https://www.merriam-webster.com/dictionary/deionized>

IPA: /diˈaɪ.ə.naɪzd/

Phonetic Spelling: dee·eye·uh·nyzd

3. Protease

Pronunciation link: <https://www.merriam-webster.com/dictionary/protease>

IPA: /ˈproʊ.ti.ɛs/

Phonetic Spelling: proh·tee·ays

4. Amphiphilic

Pronunciation link: <https://www.merriam-webster.com/dictionary/amphiphilic>

IPA: /ˌæm.fəˈfɪl.ɪk/

Phonetic Spelling: am·fuh·fil·ik

5. Enzymatic

Pronunciation link: <https://www.merriam-webster.com/dictionary/enzymatic>

IPA: /ˌen.zəˈmæt.ɪk/

Phonetic Spelling: en·zye·mat·ik

6. Capsaicin

Pronunciation link: <https://www.merriam-webster.com/dictionary/capsaicin>

IPA: /ˈkæp.seɪ.ɪ.sɪn/

Phonetic Spelling: kap·say·uh·sin

7. Nanomicelles
Pronunciation link: <https://www.merriam-webster.com/dictionary/micelle>
IPA: /ˌnaɪ.noʊ.miˈsɛlz/
Phonetic Spelling: nye·noh·mih·selz
8. Dialyze
Pronunciation link: <https://www.merriam-webster.com/dictionary/dialyze>
IPA: /ˈdaɪ.əˌlaɪz/
Phonetic Spelling: dye·uh·lyze
9. Hyaluronic
Pronunciation link: <https://www.merriam-webster.com/dictionary/hyaluronic>
IPA: /ˌhaɪ.ə.ləˈrɑː.nɪk/
Phonetic Spelling: hye·uh·luh·ron·ik
10. Polyvinyl
Pronunciation link: <https://www.merriam-webster.com/dictionary/polyvinyl>
IPA: /ˌpɑː.liˈvaɪ.nəl/
Phonetic Spelling: pah·lee·vye·nul
11. Desiccator
Pronunciation link: <https://www.merriam-webster.com/dictionary/desiccator>
IPA: /ˈdɛs.əˌkeɪ.tər/
Phonetic Spelling: des·uh·kay·ter
12. Polydimethylsiloxane
Pronunciation link: <https://www.howtopronounce.com/polydimethylsiloxane>
IPA: /ˌpɑː.li.daɪ.mɛθ.əl.sɪˈlɑːk.seɪn/
Phonetic Spelling: pah·lee·dye·meth·uhl si·lok·sayn
13. Microneedle
Pronunciation link: <https://www.merriam-webster.com/dictionary/microneedle>
IPA: /ˈmaɪ.kroʊ.niː.dəl/
Phonetic Spelling: mye·kroh·nee·duhl
14. Microliters
Pronunciation link: <https://www.merriam-webster.com/dictionary/microliter>
IPA: /ˈmaɪ.kroʊ.liː.təz/
Phonetic Spelling: mye·kroh·lee·terz
15. Micrometers
Pronunciation link: <https://www.merriam-webster.com/dictionary/micrometer>
IPA: /maɪˈkrɑː.mə.təz/
Phonetic Spelling: mye·krah·muh·terz
16. Depilatory
Pronunciation link: <https://www.merriam-webster.com/dictionary/depilatory>
IPA: /dɪˈpɪl.əˌtɔːr.i/
Phonetic Spelling: dih·pil·uh·tor·ee
17. Inguinal
Pronunciation link: <https://www.merriam-webster.com/dictionary/inguinal>
IPA: /ˈɪŋ.gwə.nəl/
Phonetic Spelling: ing·gwuh·nul
18. Confocal
Pronunciation link: <https://www.merriam-webster.com/dictionary/confocal>

IPA: /kən'foʊ.kəl/

Phonetic Spelling: kun·foh·kuhl

19. Preadipocytes

Pronunciation link: <https://www.howtopronounce.com/preadipocyte>

IPA: /,pri:.ə'dɪp.ə'saɪts/

Phonetic Spelling: pree·uh·dip·uh·sytes

20. Intracellular

Pronunciation link: <https://www.merriam-webster.com/dictionary/intracellular>

IPA: /,ɪn.trə'sel.jə.lə/

Phonetic Spelling: in·truh·sel·yuh·ler

21. Adipocytes

Pronunciation link: <https://www.merriam-webster.com/dictionary/adipocyte>

IPA: /'æd.ɪ.poʊ'saɪts/

Phonetic Spelling: ad·uh·poh·sytes

22. Mitochondrial

Pronunciation link: <https://www.merriam-webster.com/dictionary/mitochondrial>

IPA: /,maɪ.tʃə'kɔːn.dri.əl/

Phonetic Spelling: mye·tuh·kon·dree·uhl

23. Pyramidal

Pronunciation link: <https://www.merriam-webster.com/dictionary/pyramidal>

IPA: /pɪ'ræm.ə.dəl/

Phonetic Spelling: pih·ram·uh·duhl

24. Murine

Pronunciation link: <https://www.merriam-webster.com/dictionary/murine>

IPA: /'mjʊr.aɪn/

Phonetic Spelling: myoor·ine

25. Stratum corneum

Pronunciation link: <https://www.merriam-webster.com/dictionary/stratum%20corneum>

IPA: /'streɪ.tʃəm 'kɔːr.ni.əm/

Phonetic Spelling: stray·tuhm kor·nee·um