FINAL SCRIPT: APPROVED FOR FILMING

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Title: Oromucosal as an Alternative Method for Administration of *Cannabis* Products in Rodents

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Author Questionnaire

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

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

3. **Filming location:** Will the filming need to take place in multiple locations? **NO**

Current Protocol Length
Number of Steps: 6
Number of Shots: 16

Introduction

Videographer: Obtain headshots for all authors available at the filming location.

1.1. **Deborah da Costa Rodrigues:** Our research develops an innovative, stress-reducing oromucosal method for administering cannabis extracts to rats. We aim to enhance animal welfare in long-term studies and assess the neurochemical effects of these treatments.

1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.2.1*
NOTE: Clip: _0001 = Scene: 1.1.1 - Take: 1 (BAD), Clip: _0002 = Scene: 1.1.1 - Take: 2 (GOOD)

What are the current experimental challenges?

1.2. **Deborah da Costa Rodrigues:** A major challenge is minimizing animal stress during drug administration, particularly in long-term studies. Traditional methods like gavage can induce significant distress and affect translational relevance.

1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.3.1*

What research gap are you addressing with your protocol?

1.3. **Yolanda Paes-Colli:** We address the need for a non-invasive, stress-free method for long-term oral drug administration in rodents, better mimicking clinical practices and preserving animal welfare for reliable behavioral studies.

1.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.5.1*

What advantage does your protocol offer compared to other techniques?

1.4. **Deborah da Costa Rodrigues:** It is a quick and simple method that only requires animal handling training. It improves compliance for long-term studies, aligning preclinical methods with clinical applications.

1.4.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 3.3.1*

What research questions will your laboratory focus on in the future?

1.5. **Yolanda Paes-Colli:** We will continue exploring the long-term effects of phytocannabinoids in neurological disorders using this refined administration method. This approach allows for more ethical and reliable preclinical research.

1.5.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.6.1*

Videographer: Obtain headshots for all authors available at the filming location.

Testimonial Questions (OPTIONAL):

How do you think publishing with JoVE will enhance the visibility and impact of your research?

1.6. **Yolanda Paes-Colli:** JoVE's video format is ideal for showcasing our non-invasive drug administration protocol, enhancing its reproducibility globally. This visual clarity will increase the adoption of humane research methods and broaden the impact of our neurochemical findings in long-term cannabinoid studies.

1.6.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.6.1*

Authors: Could you please also deliver the above statement in Portuguese?

Videographer: Please film the testimonial in both English and Portuguese

Ethics Title Card

This research has been approved by the Ethics Committee on the Use of Animals in Research (CEUA) of the Center of Health Sciences (CCS) at the Federal University of Rio de Janeiro

Protocol

2. Administration of the *Cannabis* Extract to the Rat

Demonstrator: Deborah da Costa Rodrigues

2.1. To begin, position a small container on the weighing scale **[1]** and place each rat individually in the container **[2]**. Wait until the weight stabilizes **[3]** and record the weight in grams **[4]**.
- 2.1.1. WIDE: Talent placing a small container on the weighing scale.
- 2.1.2. Talent placing the animal in the container.
- 2.1.3. Shot of the scale display reading stabilizing.
- 2.1.4. Talent writing down the weight in a book.

2.2. Now, remove the animal from the scale **[1]** and calculate the dosage of *Cannabis* extract to be administered using the formula for each animal **[2-TXT]**.
- 2.2.1. Talent removing the rat gently from the scale.
- 2.2.2. Talent working on a computer to calculate the dosages. **TXT: Dose (mg) = [Weight (g) x CBD concentration (mg/kg)]/1,000** NOTE: Clip: _0021 = Scene: 2.2.2 - Take: 1, Clip: _0022 = Scene: 2.2.2 – Take: 2

2.3. Take each animal individually from its cage at the time of administration to prevent disturbances **[1]**. Using a micropipette, draw the specific dosage of *Cannabis* extract calculated for that animal **[2]**.
- 2.3.1. Talent removing a single rat from its group cage.
- 2.3.2. Talent drawing the required volume of *Cannabis* extract using a micropipette.

2.4. To immobilize the animal, gently pull the skin behind its neck backward **[1]** and hold it until its tail no longer touches the bedding **[2]**. If the animal becomes agitated, gently swing the elevated animal to calm it down **[3]**.
- 2.4.1. Talent gently pulling the skin behind the rat's neck to hold it.
- 2.4.2. Shot of the tail off the bedding.
- 2.4.3. Talent performing a gentle swinging motion to calm an agitated rat.

2.5. Now, insert the micropipette tip into the inner cheek of the immobilized rat **[1]** and dispense the *Cannabis* extract slowly, ensuring that the animal swallows it **[2]**.
- 2.5.1. Talent placing the micropipette tip into the inner cheek of the rat.
  NOTE: Clip: _0030 = Scene: 2.5.1 + 2.5.2 - Take: 1 (the authors decided to film both scenes in a single shot.)
  Clip: _0031 = Scene: 2.5.1 + 2.5.2 - Take: 2
  Clip: _0032 = Scene: 2.5.1 + 2.5.2 - Take: 3

2.5.2. Talent dispensing the extract.

2.6. Finally, release the rat **[1]** and return it to its cage group **[2]**.

2.6.1. Talent releasing the rat carefully from hands.

2.6.2. Talent placing the rat into its group cage.

Results

3. Results

3.1. Administration of 3 milligrams per kilogram per day of cannabidiol-enriched *Cannabis* extract via the oro-mucosal route did not significantly affect body weight gain **[1]**, urine output **[2]**, or food and water intake in rats over the treatment period **[3]**.

3.1.1. LAB MEDIA: Figure 1 A

3.1.2. LAB MEDIA: Figure 1 D

3.1.3. LAB MEDIA: Figure 1 B C

3.2. Rats treated with the extract exhibited normal locomotor activity in the open field test, with total distance traveled comparable to controls, indicating no distress or motor deficits **[1]**.

3.2.1. LAB MEDIA: Figure 2A.

3.3. Synaptic protein analysis showed a nearly 30 percent reduction in GFAP *(G-F-A-P)* levels in the hippocampus, suggesting reduced astrogliosis **[1]**, along with a 29 percent decrease in GluA1 *(Glu-A-One)* **[2]** and a 42 percent increase in PSD95 *(P-S-D-Ninety-Five)* levels, indicating modulation of synaptic plasticity **[3]** without affecting GluN1 *(Glu-N-One)* or cannabinoid receptors **[4]**.

3.3.1. LAB MEDIA: Figure 3D *Video editor: Highlight the bar for extract group*.

3.3.2. LAB MEDIA: Figure 3E *Video editor: Highlight the bar for extract group*

3.3.3. LAB MEDIA: Figure 3G *Video editor: Highlight the bar for extract group*

3.3.4. LAB MEDIA: Figure 3F and H *Video editor: Highlight the bar for extract group*

1. **cannabidiol**
   Pronunciation link: https://dictionary.cambridge.org/us/pronunciation/english/cannabidiol (Cambridge Dictionary)
   IPA: /ˌkæn.ə.bɪˈdaɪ.ɑːl/ (Cambridge Dictionary)
   Phonetic Spelling: *kan-uh-bih-DYE-ohl*

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2. **dosage**
   IPA: /ˈdoʊ.sɪdʒ/
   Phonetic Spelling: *DOH-sij*

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3. **micropipette**
   Pronunciation link: https://dictionary.cambridge.org/dictionary/english/micropipette (Cambridge Dictionary) *(though Cambridge gives pronunciations for many technical words; micropipette is standard)*
   IPA: /ˌmaɪ.kroʊ.pɪˈpɛt/
   Phonetic Spelling: *MY-kroh-pih-PET*

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4. **oro-mucosal**
   IPA: /ˌɔːr.oʊ məˈkyoʊzəl/
   Phonetic Spelling: *OR-oh mu-KOH-zuhl*

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5. **astrogliosis**
   IPA: /ˌæs.troʊ.gliˈoʊ.sɪs/
   Phonetic Spelling: *AS-troh-glya-OHsis*

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6. **synaptic**
   Pronunciation link: https://dictionary.cambridge.org/dictionary/english/synaptic (Cambridge Dictionary) *(general dictionary of English)*
   IPA: /sɪˈnæp.tɪk/
   Phonetic Spelling: *si-NAP-tik*

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7. **plasticity**
   IPA: /plæsˈtɪs.ə.ti/
   Phonetic Spelling: *plas-TIS-uh-tee*

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8. **locomotor**
   IPA: /ˌloʊ.kəˈmoʊ.tər/
   Phonetic Spelling: *loh-kuh-MOH-ter*

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9. **restraint**
   IPA: /rɪˈstreɪnt/
   Phonetic Spelling: *ri-STRAYNT*

10. **visual analogue scale** (usually abbreviated “VAS”)
    - **visual**: IPA: /ˈvɪʒ.u.əl/ — *VIZH-oo-uhl*
    - **analogue**: IPA: /ˈæn.ə.lɑːg/ — *AN-uh-log*
    - **scale**: IPA: /skeɪl/ — *skayl*