AWARD NUMBER: W81XWH-22-1-0838

TITLE: A Novel Non-Opioid Topical Therapy for Chronic Musculoskeletal Pain

PRINCIPAL INVESTIGATOR: Rachael Rzasa Lynn MD

CONTRACTING ORGANIZATION: University of Colorado Denver, Aurora, CO

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The goal of this study is to learn more about the analgesic effects of state-regulated topical cannabinoid products (creams, lotions, salves, etc) and to determine if these topical products are absorbed systemically and can be detected in blood samples. Given that cannabinoid products cannot be brought onto campus, this observational study design utilizes a Mobile Pharmacology Laboratory that will go to study participants' homes to collect data and blood samples. We hypothesize that topical cannabinoids will improve chronic musculoskeletal pain via local tissue interaction, with minimal systemic absorption and no effects on cognition or psychomotor performance. All local regulatory approvals are in place and the Mobile Pharmacology Laboratory is fully equipped and is ready for study visits. However, enrollment has not yet begun due to OHRO request for FDA consultation regarding the potential need for an investigational new drug application and ongoing communication with FDA regarding this issue.

15. SUBJECT TERMS
Chronic pain, cannabinoids, non-opioid treatment, analgesia, joint pain, musculoskeletal pain, topical

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

The goal of this study is to learn more about the analgesic efficacy of state-regulated topical cannabinoid products (creams, lotions, salves, etc) and to determine if these topical products are absorbed systemically and can be detected in blood samples. Given that cannabinoid products cannot be brought onto campus, this observational study design utilizes a Mobile Pharmacology Laboratory that will go to study participants' homes to collect data and blood samples. We hypothesize that topical cannabinoids will improve chronic musculoskeletal pain via local tissue interaction, with minimal systemic absorption and no effects on cognition or psychomotor performance.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Chronic pain, cannabinoids, non-opioid treatment, analgesia, joint pain, musculoskeletal pain, topical

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Finalize Protocol: Refine eligibility criteria; finalize statistical analysis plan; finalize study documents (months 1-3; completed on 11/04/2022)

Protocol Submission and Registration:
Submit protocol to Scientific Advisory and Review Committee (SARC) – omitted as unnecessary
Submit protocol to IRB – IRB approval obtained 11/22/2022
CU OnCore clinical research management system – Completed 7/2023
Submission to OHRO – completed Q2 on 01/01/2023
REDCap database completed 12/04/2022
MyCap mobile database completed 12/04/2022
NIH clinicaltrials.gov registration approved 06/2023 (NCT05908552)

Hiring of Study Staff:
Two study staff research assistants were identified and hired with a start date of 04/01/2023
Study staff have completed all training 07/2023

Obtain cargo van for mobile pharmacology laboratory:
Cargo van purchased 01/05/2023
Van uplift completed Q3 on 03/15/2023
All supplies for the mobile pharmacology laboratory have been purchased 5/2023

Obtain supplies for research office:
Purchase of office supplies complete 5/2023

Develop and distribute recruitment materials:

Recruitment materials finalized and approved by local IRB (11/22/22, revisions approved 3/23/23)
Recruitment website on hold for now, as we already have an adequate number of interested individuals waiting to be screened (06/2023). Will move forward with paid website if numbers start to decrease.
Veteran and military spouse groups for recruitment identified (04/2023)

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Study personnel have completed all training, which fulfills Major Task 2, Subtask 2.

NIH clinicaltrials.gov registration completed, which is part of Subtask 3, Major Task 1. OnCore has been completed, fulfilling all of Major Task 1 except OHRO approval.

We have acquired all of the office supplies and all supplies for the Mobile Pharmacology Lab. We have not yet received OHRO approval, which was anticipated in Q2. Please see Section 4 for more details.

We identified local veteran and military spouse groups, including the local VA, the Buckley Space Force Base Family Readiness Center, and Buckley Spouse Groups on Facebook. At this time we have decided not to build a professionally developed website, as we have already identified potential participants through screening in other clinical studies. This fulfills Subtask 1 of Major Task 4.

What opportunities for training and professional development has the project provided?

If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and

individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We hope to have OHRO approval and begin recruitment and conducting study visits in the next quarter.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report

5. CHANGES/PROBLEMS: *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

We have not yet obtained OHRO approval as expected. Upon their initial review of our documents, OHRO asked us to consult with the FDA on whether an Investigational New Drug (IND) application is required. We have been in communication with the FDA since February, and heard from them in late July that they determined that our protocol as written would need an IND. This was intended and designed to be an observational study rather than a clinical trial so this determination was unexpected.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Upon receiving the IND determination from the FDA, we consulted with our local university IND office and our DoD science officer and made changes to the protocol taking into consideration the feedback from the FDA. We have since contacted the FDA to determine how to move forward with this revised protocol. However, as of 9/29/2023 we have not received instructions for next steps.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Expenditures were lower than anticipated for several reasons: study staff were hired later than originally estimated, enrollment has not begun, and microsampling devices no longer need to be purchased. Protocol changes to eliminate any form of prescriptive instruction to study participants have obviated the opportunity for timed blood samples immediately following first use of the participant's chosen topical product. As the protocol is now written, participants will notify our study team once they have begun using their chosen topical cannabinoid product and the Mobile Pharmacology Laboratory will return after that to obtain venous blood samples rather than providing home microsampling devices.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. **PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report

  Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report

- **Website(s) or other Internet site(s)**
List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

https://medschool.cuanschutz.edu/orthopedics/research/labs/lindley-lab

Dr. Lindley's laboratory website will be used to disseminate results when available.

- **Technologies or techniques**
Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report

- **Inventions, patent applications, and/or licenses**
Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report

- **Other Products**
Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention,

diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name: *Rachael Rzasa Lynn*
Project Role: *Partnering PI*
Researcher Identifier (e.g. ORCID ID): *0000-0002-7035-0140*
Nearest person month worked: *2*
Contribution to Project: *Dr. Rzasa Lynn has performed work on protocol development, document preparation and submission for regulatory approval, personnel recruitment, equipment acquisition (cargo van)*

Name: *Mark Steinke*
Project Role: *Study Staff*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *5*
Contribution to Project: *Mr. Steinke helped with ordering study supplies, preparing subject materials, submission of regulatory documents and identifying potential participants.*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Concluded Other Support:
Title: Observational Approaches to the Influence of Cannabis and its Constituent Cannabinoids on Pain, Inflammation, and Cognition
Time Commitments: 0.6 calendar
Supporting Agency: NCCIH R01 AT 0095421
Performance period: 10/01/2017 - 09/30/2022

New Other Support:
Title: Cannabinoids and Traumatic Brain Injury: A Randomized, Placebo Controlled Trial
Time Commitments: 0.6 calendar
Supporting Agency: Institute of Cannabis Research. ICR-23-001
Performance Period: 10/01/2022 - 09/30/2025
Overlap: none

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)
- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc.,*

available to project staff);

- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ebrap.org/eBRAP/public/index.htm*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil/Pages/Resources.aspx) should be updated and submitted with attachments.*

9. APPENDICES:

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.