ISRCTN48573608 https://doi.org/10.1186/ISRCTN48573608

Curly kale relieves inflammation after tooth extraction

Submission date	Recruitment status	[_] Prospectively registered
28/02/2024	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
18/03/2024	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
18/03/2024	Oral Health	[_] Record updated in last year

Plain English summary of protocol
Background and study aims
Curly kale is an edible vegetable that has biological and nutraceutical properties. Interestingly, among chemical compositions, anthocyanins are active ingredients which present analgesic and anti-inflammatory activities. This study aims to compare the effectiveness of a water extract of kale leaves with ibuprofen in reducing pain and inflammation in patients after lower third molar extraction.

Who can participate?
Patients aged 18-25 years old with impacted left and right lower mandibular third molars

What does the study involve?
Each participant will be asked to take the encapsulated kale extract or ibuprofen and vice versa for 7 days. Pain and inflammation indicators will be assessed daily for 7 days after each molar extraction.

What are the possible benefits and risks of participating?
Participants may benefit from consuming an anthocyanin-rich kale supplement as it will relieve pain, inhibit inflammation, and avoid adverse effects of Non-steroidal anti-inflammatory drugs (NSAIDs) in patients after lower third molar extraction and consumption of ibuprofen. Participants may be at risk if they are allergic to plant-derived products.

Where is the study run from?
The study protocol has been approved by the ethical committee of the Faculty of Dentistry, Chiang Mai University, and the trial will be conducted at the Oral and Maxillofacial Surgery Clinic, Faculty of Dentistry, Chiang Mai University

When is the study starting and how long is it expected to run for?
December 2022 to March 2023

Who is funding the study?
This work will be performed under the Residency Training Program in Oral and Maxillofacial Surgery, Faculty of Dentistry, Chiang Mai University, Chiang Mai, Thailand, consumable chemicals and reagents was partially supported by the Royal Project Foundation, Chiang Mai.

Who is the main contact?
Dr. Vuttinun Chatupos, D.D.S., vuttinunch@yahoo.co.th, vuttinun.ch@cmu.ac.th

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Ni known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
65/2565

Study information

Scientific Title
A randomized controlled study comparing anti-inflammatory effect between ibuprofen and curly kale (Brassica oleracea var. sabellica) extract in patients after extraction of impacted lower mandibular third molars

Study objectives
Curly kale leaves which are abundant with flavonoids (e.g. anthocyanins) exert strong anti-inflammatory and wound healing effects on the tooth extraction wound.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 16/12/2022, Human Experimentation Committee, Faculty of Dentistry (Chiang Mai University, Chiang Mai, 50200, Thailand; +66 5394451; anak.ia@cmu.ac.th), ref: 12/12/2565

Study design
Split-mouth randomized single-center clinical trial

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Dental clinic

Study type(s)
Efficacy

Participant information sheet
See outputs table

Health condition(s) or problem(s) studied
Patients after surgical removal of impacted mandibular third molar

Interventions
In this split-mouth randomized single-center clinical trial, patients (n = 20, aged 18-25 years) following surgical removal of two impacted mandibular third molar (1 month apart) will be asked to take ibuprofen and encapsulated kale extract for 7 days. Patients are randomised using the Block randomization method

For the interventional study, the same surgeon performed all the surgery at our institution (S.N., T.S., A.K.). Volunteers received anesthetic blockade of the inferior alveolar nerve and lingual nerve block of the surgical site with 1.8 mL of the anesthetic solution (Septanest® SP, Septodont, France) containing 4% articaine and 1:100,000-dilution epinephrine. Three minutes after this injection, every volunteer received an additional injection of 0.9 mL of the same

anesthetic solution into the buccal mucosa of the surgical area to guarantee hemostasis and complete anesthesia of the region. Immediately after this injection, the lower third molar surgery commenced via a standard protocol.

For postoperative pain management, participants were informed to take the kale extract capsule (500 mg anthocyanin equivalent) and an ibuprofen tablet (400 mg size, Probufen-400, Advanced Pharmaceutical Manufacturing Company Limited, Bangkok, Thailand) after the extraction of impacted mandibular third molar or vice versa every 6 hours for 7 days. In addition, 500 mg amoxicillin (SANOMOX - G 500, SEVEN STARS PHARMA, Thailand) was prescribed 4 times daily for 5 days. If needed or VAS > 5, analgesic medication by 500 mg acetaminophen (Tylenol, OLIC Limited Company, Thailand) was available for all volunteers throughout the study.

The subjects were instructed to assess their pain level using the VAS scoring tool and collect their saliva for analysis of -amylase activity, MMP9 and TGF-2 concentrations.

Intervention Type
Procedure/Surgery

Primary outcome measure
The following primary outcome measures were assessed in saliva specimens collected before tooth extraction and on days 3 and 7 after tooth extraction:
1. Alpha-amylase activity measured using a colorimetric method
2. MMP9 concentrations measured using sandwich-type ELISA kits
3. TGF-1 concentrations measured using sandwich-type ELISA kits

Secondary outcome measures
Pain was measured using a visual analogue scale (VAS) every day for 7 days

Overall study start date
01/11/2022

Completion date
31/05/2023

Eligibility

Key inclusion criteria
1. Healthy according to the American Society of Anesthesiologists (ASA) criteria: Level I and II
2. Male and female
3. 18-25 years old
4. Had left and right lower mandibular third molars impacted

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
25 Years

Sex
Both

Target number of participants
20

Total final enrolment
20

Key exclusion criteria
1. History of ibuprofen sensitivity
2. Painful of mandibular third molar or maxillofacial area before operation
3. Taken an analgesic drug for one week before surgical removal of impacted mandibular third molar
4. Psychiatric
5. Non-compliance on recording pain and symptoms after operation
6. Unable to revisit for the next follow-up

Date of first enrolment
04/01/2023

Date of final enrolment
30/03/2023

Locations

Countries of recruitment
Thailand

Study participating centre
Oral and Maxillofacial Surgery Clinic, Faculty of Dentistry, Chiang Mai University
Suthep Road, Tambol Suthep, Amphur Muang
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Sponsor information

Organisation
Chiang Mai University

Sponsor details

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Sponsor type
University/education

Website
https://www.cmu.ac.th/

ROR
https://ror.org/05m2fqn25

Funder(s)

Funder type
Research organisation

Funder Name
Royal Project Foundation

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Thailand

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
05/04/2024

Individual participant data (IPD) sharing plan

The datasets generated during and/or analyzed during the current study will be available upon request from Dr. Vuttinun Chatupos, D.D.S., vuttinunch@yahoo.co.th

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	English		18/03/2024	No	Yes
Participant information sheet	Thai		18/03/2024	No	Yes
Protocol file			18/03/2024	No	No