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Testing toothpaste with cetyl pyridinium chloride and cymenol: Is it safe, effective, and what do patients think?

Submission date
09/07/2023

Recruitment status
No longer recruiting

Registration date
12/07/2023

Overall study status
Completed

Last Edited
04/06/2025

Condition category
Oral Health

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
There isn't much evidence on using cetylpyridinium chloride (CPC) toothpaste. So, it's important to test new toothpaste formulas that combine CPC with other germ-fighting ingredients. This study was done to see if a new toothpaste with CPC and cymenol is safe and well-tolerated. We also wanted to compare its effectiveness, impact on bacteria, and what patients thought of it, with a regular fluoride toothpaste that's already available.

Who can participate?
Adults over 18 years, with gingival inflammation

What does the study involve?
The study lasted for 6 weeks and involved four visits. The screening visit was the first visit where the researchers checked if the participants met the criteria to be included in the study. If they qualified and agreed to participate, they signed a form and then had the baseline visit scheduled or done on the same day.

During the baseline visit, the researchers recorded information about the participants' teeth, except for the wisdom teeth. They also collected samples from beneath the gums to test for bacteria. After this examination, no further treatment was given during the study. The participants were randomly assigned to one of two groups: the test group, which used a toothpaste called Bexident® Encías Uso Diario, containing CPC and cymenol as active ingredients, or the control group, which used Colgate Protection caries toothpaste containing fluoride and sodium monofluorophosphate as active ingredients.

The participants were given a manual toothbrush and instructed to brush their teeth three times a day for two minutes after meals. They were not given specific instructions on how to brush or floss, so they could follow their normal oral hygiene routine. The participants didn't know which toothpaste they were using, as the products were labeled with codes. They were also given instructions on how to use the assigned products and asked to fill out compliance forms and provide any feedback or report any issues they encountered.

During the visits at week 3 and week 6, the researchers recorded clinical data about the participants' teeth. At the week 6 visit, they collected another set of microbiological samples. The participants were asked if they experienced any adverse effects and were given a questionnaire to gather their opinions and perceptions about the product they used. At the last visit, all participants received professional cleaning of plaque from their teeth. The study coordinator collected the empty and unused toothpaste tubes from the participants.

What are the possible benefits and risks of participating?
Benefits. You may not get any medical benefit from participating in the research project.
Risk. All evaluations and interventions to be performed during the study are part of conventional and accepted protocols, with no associated risks.

Where is the study run from?
Isdin (Spain)

When is the study starting and how long is it expected to run for?
April 2021 to December 2022

Who is funding the study?
Complutense University of Madrid (Spain)

Who is the main contact?
Prof. David Herrera, davidher@ucm.es

Contact information

Type(s)
Principal Investigator

Contact name
Prof David Herrera

ORCID ID
https://orcid.org/0000-0002-5554-2777

Contact details
Plaza Ramón y Cajal s/n - Ciudad Universitaria
Madrid
Spain
28040
+34 913941907
davidher@ucm.es

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
49-290421

Study information

Scientific Title
Clinical evaluation of a toothpaste formulation including cetyl pyridinium chloride and cymenol: safety, clinical efficacy and microbiological impact and patient perception

Acronym
BexiPaste

Study objectives
Primary hypothesis: the tested formulation is safety, in terms of adverse events and tolerability, including microbiological safety.
Secondary hypothesis: the tested formulation may have (1) antiplaque and antigingivitis efficacy, as compared with a negative control toothpaste; (2) good results in terms of patient´s evaluation of the product, by means of patient-reported outcome measures (PROMs); and (3) a positive impact on the subgingival microbiome.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/04/2021, CEIm del Hospital Clínico San Carlos (Profesor Martín Lagos, s/n. - Puerta G - 4ª Norte, Madrid, 28040, Spain; +34 91 330 38 19; ceic.hcsc@salud.madrid.org), ref: 21/262.-EC_X

Study design
Pilot double-blind parallel randomized controlled 6-week clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Dental clinic

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied
Gingivitis

Interventions
Subjects were randomly assigned to one of the two groups: the test toothpaste (Bexident® Encías Uso Diario, ISDIN, Barcelona, Spain), with CPC and cymenol as active ingredients; and the control toothpaste (Colgate Protection caries toothpaste, Colgate-Palmolive España S.A., Madrid, Spain), with fluoride and sodium monofluorophosphate as active ingredients. Patients were asked to brush with a provided manual toothbrush (UltraThin ProGumCare®, OralB, Madrid, Spain), three times a day, for two minutes, after breakfast, lunch and dinner. Duration of treatment and follow up was the same, 6 weeks.
Subjects were identified through a unique trial number. Participants were randomly allocated to one of the two treatment groups (test toothpaste or control toothpaste). Randomization was performed using random numbers from a computer-generated list, in blocks of six patients by a researcher not involved in clinical evaluations. All subjects were blinded to their product assignment, and all researchers involved in patient recruitment or evaluation were also blinded.

Intervention Type
Supplement

Primary outcome measure
Safety and tolerability:
Each participant was interviewed regarding adverse events at each visit. Visual soft- and hard-tissue examinations of the oral cavity were performed at every visit to assess the safety of the products. Spontaneous reports of adverse events were also recorded.

Secondary outcome measures
Clinical outcome variables:
Two researchers trained and calibrated, and the results of the calibration trials were assessed by means of the Kappa test (Fleiss & Chilton, 1983). They were both blinded to the treatment assignment and to the data from previous visits, and performed all the examinations of 30 patients each.

Clinical examinations were performed in the following order:
1. The Gründemann index (GMSI) (Gründemann et al., 2000), modified by Koertge and Gunsolley (Koertge et al., 1993), in the upper and lower anterior teeth, buccal sites, by evaluating standardized clinical photographs.
2. The plaque index (PlI) of Quigley and Hein (Quigley & Hein, 1962), modified by Turesky et al. (Turesky et al., 1970), was assessed at six per tooth, using a revealing solution (Plac-Control®, Dentaid, Barcelona, Spain).
3. Bleeding on marginal probing (BOMP) (Lie et al., 1998; Van der Weijden et al., 1994), recording the presence or absence of bleeding within 30 seconds of probing on a 0-2 scale.
4. Bleeding on probing (BOP) (Ainamo & Bay, 1975) by dichotomous assessment of bleeding after gentle probing.

Microbiological outcomes:
Microbiological samples were collected at baseline and at week 6 in two sites, one in the upper jaw and one in the lower jaw, depending on the presence of bleeding at the baseline examination, but always at the same sites in both visits. Mesial of first molars (or alternatively, of the second molars or second premolars) was the preferred site for sampling. Sites were isolated with cotton rolls and gently dried with air. Two sterile paper points were consecutively inserted

(medium size, Maillefer, Ballaigues, Switzerland) in each site. Each paper point was inserted into the sulcus/pocket as deep as possible and left in place for 10 seconds. A unique sample, with the four paper points, was available for each patient and visit. The paper points were transferred to a cryo-vial with a DNA/RNA Shield™ reagent, which lyses the samples, inactivates pathogens (e. g., viruses and bacteria) and was/were compatible with the DNA extraction protocol. The vial was sent to the local laboratory for storage within 24 hours where it was kept at room temperature for three weeks. Then, the samples were sent by courier to Microomics SL, according to the recommendations for safe transport, where samples were processed (description of that process is described in a separate report).

Patient reported outcomes (PROMs):
All participants filled out a predefined questionnaire on the use and perception of the assigned products, during the visits after three and six weeks.

Overall study start date
21/04/2021

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. Over 18 years of age.
2. Systemically healthy, defined according to the criteria of the American Society of Anesthesiologists (ASA) (Doyle et al., 2021), as ASA type I or II (see also exclusion criteria).
3. Presence of at least three evaluable teeth in each quadrant.
4. Moderate gingival inflammation (≥ 40% bleeding on marginal probing, BOMP) (Van der Weijden et al., 1994) and Turesky plaque index ≥ 1.5 (Turesky et al., 1970). Likewise, the criteria of the World Workshop and the bleeding on probing (BOP) (Ainamo & Bay, 1975), and at least 10% of BOP (Chapple et al., 2015) were considered.
5. Absence of probing depths (PD) ≥ 5 mm,
6. No fixed orthodontic treatments or removable prostheses.
7. Brushed their teeth regularly (at least twice a day).

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
100 Years

Sex
Both

Target number of participants
60

Total final enrolment
55

Key exclusion criteria
1. Untreated or uncontrolled periodontitis.
2. Regularly users of mouthwashes during the month prior to the screening.
3. Antibiotics intake within the previous month.
4. Pregnant women.
5. Any chronic disease or medication that may influence gingival inflammation.
6. Conditions requiring antibiotic coverage.

Date of first enrolment
01/01/2022

Date of final enrolment
31/10/2022

Locations

Countries of recruitment
Spain

Study participating centre
Faculty of Odontology, Complutense University of Madrid
Plaza Ramón y Cajal s/n - Ciudad Universitaria
Madrid
Spain
28040

Sponsor information

Organisation
Isdin (Spain)

Sponsor details
Provençals 33
Barcelona
Spain
08019
+34 932 402 020
sylvie.gonzalez@isdin.com

Sponsor type
Industry

Website
http://www.isdin.com/en/

ROR
https://ror.org/04dg86p75

Funder(s)

Funder type
University/education

Funder Name
Universidad Complutense de Madrid

Alternative Name(s)
Complutense University of Madrid, UCM

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Spain

Results and Publications

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

Intention to publish date
31/12/2023

Individual participant data (IPD) sharing plan
Datasets can be available upon request (contact name: David Herrera, davidher@ucm.es)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Participant information sheet	in Spanish		11/07/2023	No	Yes
Results article		21/12/2023	27/12/2023	Yes	No
Results article		30/05/2025	04/06/2025	Yes	No