ISRCTN16727861 https://doi.org/10.1186/ISRCTN16727861

The beneficial effect on gingivitis of a food supplement based on botanical extracts

Submission date 03/08/2023	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 09/08/2023	**Overall study status** Completed	
Last Edited 28/03/2024	**Condition category** Oral Health	

Plain English summary of protocol

Background and study aims

Gingivitis is a common and mild form of gum disease (periodontal disease) that causes irritation, redness, and swelling (inflammation) of the portion of the gum around the base of the teeth. It is important to take gingivitis seriously and treat it promptly as it can lead to much more serious gum diseases, such as periodontitis, up to the loss of teeth.

It is also believed that chronic inflammation of the gingiva (gums) is associated with certain systemic diseases such as respiratory diseases, diabetes, coronary artery disease, stroke, and rheumatoid arthritis. Research suggests that the bacteria responsible for periodontitis may enter the bloodstream through the gum tissue, possibly affecting the heart, lungs, and other parts of the body, but further studies are needed to confirm this link.

Gingivitis is, therefore, an inflammatory condition of the gum tissue, most commonly caused by a bacterial infection. Unlike periodontitis, there is no loss of gum tissue adhesion to the tooth and therefore no migration of the junction epithelium.

Gingivitis rarely generates spontaneous bleeding and is commonly painless, so many patients do not recognize the disease. For this reason, indices for the diagnosis of gingivitis are commonly accepted that use the "bleeding on probing" tests, that is, the use of a probe, a toothbrush, or floss to assess possible bleeding of the gingiva following slight stimulation.

Microorganisms most strongly associated with gingivitis include Streptococcus, Fusobacterium, Actinomyces, Veillonella e Treponema, Bacteroides, Capnocytophaga, and Eikenella species.

The classic and radical treatment for periodontal disease consists of the removal of dental plaque and tartar from the teeth, as the main causative agents of periodontal disease, and the administration of antibiotics. However, bacteria on the tooth surface cannot be removed completely by mechanical procedures, and the use of long-term antibiotics carries the risk of promoting the development of antibiotic resistance and inducing the occurrence of side effects. For this reason, the development of alternative therapies has increasingly attracted the attention of researchers in recent years.

Therefore, two botanical varieties have been selected, Scutellaria lateriflora L. and Cistus x incanus L., which have obtained promising results in previous investigations, are commonly used in the formulation of food supplements, and which have been included in a supplement in the form of chewing gum to ensure that the extracts remain as much as possible in contact with the chewing apparatus.

The aim of this study is to evaluate the effectiveness of the use of a food supplement, in

chewing gum form, based on extracts of Scutellaria lateriflora L. and Cistus x incanus L., in improving the symptoms associated with gingivitis, and consequently, the quality of life of the individual, avoiding, at the same time, the possible progression of this condition in periodontitis.

Who can participate?
People aged 18-70 years who have gingivitis

What does the study involve?
Participants will be randomly allocated to consume a food supplement, in a chewing gum form, based on two botanical extracts, or a placebo, for 90 days.

What are the possible benefits and risks of participating?
No risks are foreseen. An improvement in the clinical and symptomatologic picture of gingivitis of the subjects randomized in the food supplement group is hypothesized. However, no benefit may be achieved.

Where is the study run from?
Comegen, Naples (Italy)

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

Who is funding the study?
Epo Srl. (Italy)

Who is the main contact?
1. Prof. Maria Daglia (scientific) maria.daglia@unina.it
2. Dr. Alessandra Baldi (public) alessandra.baldi.alimenti@gmail.com

Contact information

Type(s)
Public

Contact name
Dr Alessandra Baldi

ORCID ID
https://orcid.org/0000-0002-2877-9445

Contact details
Viale delle Medaglie d'Oro 305
Rome
Italy
00136
+39 (0)3483854114
alessandra.baldi.alimenti@gmail.com

Type(s)
Scientific

Contact name
Prof Maria Daglia

ORCID ID
https://orcid.org/0000-0002-4870-7713

Contact details
Via Domenico Montesano, 49
Naples
Italy
800016
+39 (0)3398177623
maria.daglia@unina.it

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
PLANORAL22_01

Study information

Scientific Title
Study on the efficacy of a food supplement, in the form of chewing gum, based on extracts of Scutellaria lateriflora L. and Cistus x incanus L., in adults who have gingivitis as a risk factor for periodontitis, on the symptoms associated with this condition: placebo-controlled, single-centre clinical study, randomized, in parallel groups, double-blind

Acronym
PLANORAL22

Study objectives
The aim of this study was to evaluate the effectiveness of the use of a food supplement, in chewing gum form, based on Scutellaria lateriflora L. and Cistus x incanus L extracts., in improving the symptoms associated with gingivitis, and consequently, the quality of life of the individual, avoiding, at the same time, the possible progression of this condition in periodontitis.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/02/2023, Ethics Committee of ASL Napoli1 CENTRO (Via Comunale del Principe, 13 /A, Naples, 80145, Italy; + 39 (0)812544495; comitatoetico@aslnapoli1centro.it), ref: 73

Study design
Interventional monocentric randomized parallel double-blind placebo-controlled clinical trial

Primary study design

Interventional

Study type(s)
Prevention, Quality of life

Health condition(s) or problem(s) studied
Preventing periodontitis in individuals with symptomatic gingivitis

Interventions
Participants will consume a food supplement, in chewing gum form, based on Scutellaria lateriflora L. and Cistus x incanus L. extracts, or a placebo, for 90 days, based on the randomization group.

The randomization sequence will be generated by a statistician using STATA 16 software (Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC) and the randomization list will be kept hidden. The participants will be assigned to each of the two treatment groups (food supplement or placebo) casually and by simple randomization (1:1 allocation ratio). The randomization code will consist of a three-digit number as indicated in the respective Case Report Form (CRF).

In the clinical study, 60 participants will be enrolled and divided into two groups (30 for each group):
Group 1: food supplement containing botanical extracts
Group 2: placebo

Participants will undergo five visits (screening visit, baseline = t0; after 30 days of treatment = t1; after 60 days of treatment = t2; after 90 days of treatment = t3) in an outpatient setting. After each clinical visit, all data are filled in the CRF by physicians.

During the screening visit, subjects will undergo the following investigation to understand if they meet the study participation requirements:
1. Administration of questionnaire OH-15
2. Assessment of eligibility by applying inclusion and exclusion criteria

Subsequently, all enrolled subjects will undergo the following:
At t0 (baseline) evaluation of the gingival health indices QGBI and MGI, filling in the questionnaire OH-15, execution of the VAS, administered by the clinical investigators, and filling out the questionnaire CGI-S by the experimental doctor.
At t1, t2, and t3 (30 days, 60 days, and 90 days from the start of treatment) evaluation of the gingival health indices QGBI and MGI, compilation of the OH-15 questionnaire, and of the VAS, administered by the experimental physician and filling in the CGI-S and CGI-I questionnaire (only at t3) by the experimenter.
At t0 and t3 (baseline and 90 days from the start of treatment) saliva samples were collected to analyze the oral microbiota using Next Generation Sequencing technology.

Intervention Type
Supplement

Primary outcome(s)
1. Gum health assessed using the Quantitative Gingival Bleeding Index (QGBI) at t0 (baseline), t1 (30 days of treatment), t2 (60 days of treatments), t3 (90 days of treatments)

2. Symptoms of discomfort at the level of the oral cavity in the 7 days prior to completion, assessed using Oral Health 15 items (OH-15) at t0 (baseline), t1 (30 days of treatment), t2 (60 days of treatments), t3 (90 days of treatments)

Key secondary outcome(s))
1. Oral microbiota composition assessed using next-generation sequencing (NGS) on saliva samples at t0 (baseline) and t3 (90 days of treatment). Ribosomal RNA 16 s (16s rRNA) analysis of oral microbial species and strains, through PCR.
2. Pain assessed using the Visual Analogue Scale (VAS) at t0 (baseline), t1 (30 days of treatment), t2 (60 days of treatments), t3 (90 days of treatments)
3. General oral health condition assessed using the Clinical Global Impression Scale for Severity of Illness (CGI-S) at t0 (baseline), t1 (30 days of treatment), t2 (60 days of treatments), t3 (90 days of treatments)
4. General condition of gingivitis assessed using the Clinical Global Impression Scale for Improvement (CGI-I) at t0 (baseline), t1 (30 days of treatment), t2 (60 days of treatments), t3 (90 days of treatments)

Completion date
11/10/2023

Eligibility

Key inclusion criteria
1. Aged 18-70 years of both sexes
2. Able to understand and sign informed consent
3. Have symptomatic gingivitis
4. Absence of diagnosed periodontitis or loss of teeth caused by periodontal disease
5. Cut-off value for QGBI index score ≥1
6. Cut-off value for MGI index score ≥1
7. Score >2 on the question "Did you have gum bleeding problems?" in completing the questionnaire OH-15
8. At least 20 teeth for people older than 60 years

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
70 years

Sex
All

Total final enrolment
60

Key exclusion criteria
1. Aged <18 and >70 years
2. Have a medical history or condition that could affect the subject's safety or negatively impact the validity of the study results
3. Pregnant or breastfeeding women
4. Cognitive impairments which could hinder the response to questionnaires
5. History of allergy to ingredients contained in the study treatments (dietary supplement and placebo)
6. Suffering from periodontitis
7. Suffering from pathologies of the oral cavity (tongue cancer, glossitis, dry mouth)
8. Have undergone dental cleaning or scaling within 2 months of enrollment
9. Have undergone antibiotic therapy within 2 months of enrollment
10. Current use or in the week preceding the recruitment of prescription or over-the-counter drugs, which may affect inflammatory levels (NSAIDs and others)
11. History of addiction or abuse of drugs, drugs, or alcohol
12. Heavy smokers (> 10 cigarettes/day)
13. Genetic-metabolic diseases
14. Diabetes
15. Rheumatic disorders
16. Neuropsychiatric/neurologic disorders

Date of first enrolment
07/07/2023

Date of final enrolment
11/07/2023

Locations

Countries of recruitment
Italy

Study participating centre
Comegen
Viale Maria Bakunin 41
Naples
Italy
80126

Sponsor information

Organisation

Epo S.r.l.

Funder(s)

Funder type
Industry

Funder Name
Epo S.r.l.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the subsequent results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		16/03/2024	28/03/2024	Yes	No