ISRCTN10262904 https://doi.org/10.1186/ISRCTN10262904

Testing whether an herbal product can reduce gum inflammation when used alongside standard periodontal treatment

Submission date 23/01/2026	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 20/02/2026	**Overall study status** Completed	[X] Statistical analysis plan [_] Results
Last Edited 20/02/2026	**Condition category** Oral Health	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Control (SRP) group- patients with periodontitis who received SRP treatment - by ultrasonic scaler Woodpecker and curettage with curettage of periodontal pockets for five consecutive days. The experimental group - patients with periodontitis who received local phytotherapy after causal periodontal therapy.

Who can participate?
Adults who are systemically healthy and diagnosed with moderate periodontitis (Stage II, Grade A) may participate. Participants must have at least 24 natural teeth and radiographic evidence of periodontal bone loss. Individuals who smoke, consume alcohol, have systemic diseases (such as diabetes or immune disorders), or are undergoing systemic drug therapies affecting the gums are not eligible.

What does the study involve?
Participants are randomly assigned to one of two groups. One group receives standard SRP therapy only, while the other receives SRP plus a topical application of the polyherbal phytopreparation. Treatment is performed over five consecutive days. Clinical examinations are carried out before treatment and one month later. Gingival cell samples are collected for microscopic analysis.

What are the possible benefits and risks of participating?
Participants may experience improvement in gingival inflammation and periodontal health. No side effects were observed during the study period. However, mild local reactions are possible, as with any topical dental treatment.

Where is the study run from?
The study is conducted at the Clinic of Dentistry, Faculty of Medicine, University of Niš, Serbia.

When is the study starting and how long is it expected to run for?
Each participant is involved in the study for approximately one month, including treatment and follow-up. The exact start date 18/10/2020, and it is expected to run for four years.

Who is funding the study?
This work was supported by the Ministry of Education, Science, and Technological Development of the Republic of Serbia. The funders had no role in the design of the study; the collection, analysis, or interpretation of data; the writing of the manuscript; or the decision to publish the results.

Who is the main contact?
The study is conducted under the supervision of the Clinic of Dentistry, Faculty of Medicine, University of Niš, Serbia. Principal investigator was dr Milica Petrović, Assistant Professor (milica.petrovic@medfak.ni.ac.rs)

Contact information

Type(s)
Principal investigator

Contact name
Prof Milica Petrović

ORCID ID
https://orcid.org/0000-0001-6564-5131

Contact details
Cara Dušana 28/7
Niš
Serbia
18000
+381 642373966
milica.petrovic@medfak.ni.ac.rs

Type(s)
Scientific

Contact name
Prof Bojana Miladinović

ORCID ID
https://orcid.org/0000-0003-2880-6519

Contact details
Blagoja Parovića 16
18000
Serbia
18000
+381 691045097
bojana.miladinovic@medfak.ni.ac.rs

Type(s)
Public

Contact name
Prof Dušanka Kitić

ORCID ID
https://orcid.org/0000-0001-8551-274X

Contact details
Timočka 11
Niš
Serbia
18000
+381 62328036
dusanka.kitic@medfak.ni.ac.rs

Type(s)
Principal investigator

Contact name
Prof Ljiljana Kesić

ORCID ID
https://orcid.org/0000-0003-0463-3246

Contact details
Železničkih Kolonija 3a
Niš
Serbia
18000
+381 642373966
kesic.ljiljanaa@gmail.com

Additional identifiers

Study information

Scientific Title
Efficacy of a topical polyherbal phytopreparation as an adjunct to scaling and root planing therapy in patients with periodontitis: a randomized controlled clinical study

Acronym
PHYTO-PERIO Trial

Study objectives
The primary objective of this randomized controlled clinical study was to evaluate the clinical efficacy of a topical polyherbal phytopreparation (Tinctura paradentoica®, https://www.mocbilja.rs/proizvod/kapi-za-jacanje-desni/) as an adjunct to scaling and root planing (SRP) in patients with stage II, grade A periodontitis, by assessing changes in gingival inflammation

(gingival index) and periodontal pocket depth. Secondary objectives included evaluation of cytomorphometric changes in gingival epithelial cells following treatment and exploration of potential mechanistic support using HPLC-guided in silico molecular docking (COX-1/COX-2) and ADME/Tox profiling.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 23/07/2020, Ethics Committee of Faculty of medicine, University of Niš (Dr Zoran Djindjić Ave 81, Niš, 18000, Serbia; +381 184226644; pravna.sluzba@medfak.ni.ac.rs), ref: 12-6422-2/7

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Active

Assignment
Parallel

Purpose
Supportive care, Treatment

Study type(s)

Health condition(s) or problem(s) studied
The efficacy of a polyherbal phytopreparation as an adjunctive therapy to scaling and root planing in patients with periodontitis.

Interventions
This study is designed as a randomized controlled clinical trial including 80 adults diagnosed with stage II, grade A periodontitis. After baseline assessment, participants are randomly allocated in a 1:1 ratio into two groups using computer-generated randomization with equal block sizes. Allocation concealment is ensured by sequentially numbered, opaque, sealed envelopes prepared by an independent examiner not involved in enrollment or outcome assessment. Participants and the recruiting investigator remain blinded to group assignment.

Control group(SRP): Participants receive causal periodontal therapy consisting of ultrasonic scaling, root planing, polishing and curettage of periodontal pockets performed over five consecutive days (SRP using an ultrasonic scaler and Gracey curettes). Standardized oral hygiene instructions are provided.

Experimental group (SRP + phytotherapy): Participants receive the same SRP protocol and oral hygiene instructions as the control arm, followed by topical subgingival application of the polyherbal phytopreparation Tinctura paradentoica®. The intervention is administered locally using a sterile syringe with a 23-gauge needle (110° angulation). A dose of 0.1 mL per periodontal pocket is applied subgingivally under cotton roll isolation for 2 minutes per quadrant, according to the study protocol.

Clinical outcomes (gingival index and periodontal pocket depth) are assessed at baseline and at one month after therapy initiation by a single calibrated examiner blinded to treatment allocation. Cytomorphometric analysis of gingival epithelial cells is performed using exfoliative cytology samples collected at baseline and at one month. In addition, the study includes an exploratory HPLC-guided in silico analysis (molecular docking to COX-1/COX-2 and ADME/Tox profiling of identified phenolic constituents) to support mechanistic plausibility.

Intervention Type
Supplement

Primary outcome(s)
1. Gingival inflammation, Gingival Index (GI) measured using the Löe and Silness Gingival Index at baseline (pre-treatment), five days and 1 month after therapy initiation

Key secondary outcome(s))
1. Periodontal pocket depth (PPD, mm) at baseline (pre-treatment) and 1 month after therapy initiation. measured using a manual WHO periodontal probe at baseline (pre-treatment) and 1 month after therapy initiation

2. Nuclear area (μm²) measured using cytomorphometric analysis of exfoliative gingival epithelial cells (light microscopy/image analysis) at baseline and 1 month after therapy initiation

3. Nuclear perimeter (μm) measured using cytomorphometric analysis of exfoliative gingival epithelial cells (light microscopy/image analysis) at baseline and 1 month after therapy initiation

4. Ferret’s diameter (μm) measured using cytomorphometric analysis of exfoliative gingival epithelial cells (light microscopy/image analysis) at baseline and 1 month after therapy initiation

5. Integrated optical density (IntDen) measured using densitometric cytomorphometric analysis of exfoliative gingival epithelial cells (image analysis software) at baseline and 1 month after therapy initiation

6. Binding affinity to COX-2 measured using molecular docking (in silico docking score) at in silico analysis performed after identification of phytochemicals by HPLC-DAD

7. Binding affinity to COX-1 measured using molecular docking (in silico docking score) at in silico analysisperformed after identification of phytochemicals by HPLC-DAD

8. ADME profile measured using in silico pharmacokinetic prediction (SwissADME or equivalent ADME prediction tool) at in silico analysis performed after identification of phytochemicals by HPLC-DAD

9. Toxicological profile measured using in silico toxicity prediction (ProTox-II or equivalent toxicity prediction tool) at in silico analysis performed after identification of phytochemicals by HPLC-DAD

Completion date
18/10/2024

Eligibility

Key inclusion criteria
1. Adults aged 18 to 65 years.
2. Individuals diagnosed with periodontitis based on medical history and clinical evaluation.
3. Presence of at least 24 natural teeth.
4. Radiographic evidence of bone loss.
5. Periodontal status determined using the 2018 classification of periodontal diseases and conditions.
6. Diagnosis of periodontitis confirmed by either interdental clinical attachment loss at two or more nonadjacent teeth, or buccal/oral clinical attachment loss of 3 mm or more together with periodontal pocket depth of 3 mm or more at two or more teeth.
7. Individuals not meeting the above diagnostic criteria were considered periodontally healthy and therefore not included.

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Total final enrolment
98

Key exclusion criteria
1. A history of alcohol consumption
2. Tobacco use in any form (past or present)
3. A medical history of anemia
4. Diabetes
5. Hepatitis
6. Tuberculosis
7. AIDS
8. Leukemia
9. Other systemic or hormonal disorders linked to gingival manifestations
10. Those who were undergoing or had previously undergone treatment with systemic hormonal therapy, contraceptive usage, corticosteroids, immunosuppressants, radiation therapy, or chemotherapy before the study started

Date of first enrolment
18/10/2020

Date of final enrolment
18/08/2024

Locations

Countries of recruitment
Serbia

Study participating centre
Dentistry Clinic, Department of Oral medicine and periodontology, Faculty of Medicine, University of Niš
Bulevar Dr Zorana Djindjica 52
Niš
Serbia
18000

Study participating centre
Pathology Center of the Clinical Center Niš
Bulevar Dr Zorana Djindjica 48
Niš
Serbia
18000

Study participating centre
Faculty of Medicine, Department of Pharmacy University of Niš
Bulevar Dr Zorana Djindjica 81
Niš
Serbia
18000

Sponsor information

Organisation
University of Niš - Faculty of Medicine

Funder(s)

Funder type

Funder Name
Ministarstvo Prosvete, Nauke i Tehnološkog Razvoja

Alternative Name(s)
Ministry of Education, Science and Technological Development of the Republic of Serbia, Ministry of Education, Science and Technological Development, Министарство просвете, науке и технолошког развоја, Ministarstvo Prosvete, Nauke i Tehnološkog Razvoja Republike Srbije, MPNTR, MEST

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Serbia

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other files	Participant flow diagram		26/01/2026	No	No
Other files	Informed Consent Form		28/01/2026	No	No
Other files	Schedule of Enrolment, Interventions, and Assessments		28/01/2026	No	No
Participant information sheet			28/01/2026	No	Yes
Protocol file			28/01/2026	No	No
Statistical Analysis Plan			28/01/2026	No	No