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Evaluation of the effects of azithromycin and platelet-rich fibrin on wound healing after surgical removal of mandibular third molars

Submission date 20/05/2026	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [X] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 22/05/2026	**Overall study status** Completed	
Last Edited 01/07/2026	**Condition category** Oral Health	

Plain English summary of protocol
Not provided at time of registration

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Study information

Scientific Title
Cytomorphometric, immunological, and clinical analysis of the effects of azithromycin and platelet-rich fibrin on postoperative wound healing following surgical extraction of impacted mandibular third molars

Acronym
APRIM Study

Study objectives
This study was conducted to evaluate the influence of azithromycin and platelet-rich fibrin (PRF) on postoperative inflammatory parameters and healing outcomes after extraction of impacted mandibular third molars, relative to routine treatment, by means of cytomorphometric, immunohistochemical, and clinical evaluations.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 20/02/2024, Ethics committe, Medical Faculty, University of Niš (Blv. Dr Zorana Đinđića 81, Niš, 18000, Serbia; +381184226644; info@medfak.ni.ac.rs), ref: 12/1760-1/2-5

2. Approved 19/01/2024, Ethics committee, Clinics Of Dentistry Niš (Blv. Dr Zorana Đinđića 52, Niš, 18000, Serbia; +381184226216; stomatolog_nis@kzsnis.rs), ref: 14/1-2023-3/EO

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Active

Assignment
Crossover

Purpose
Health services research, Supportive care, Treatment

Study type(s)

Health condition(s) or problem(s) studied
Surgical extraction of impacted mandibular third molar

Interventions
Participants were randomly allocated into three study groups using computer-generated randomisation. Group assignments were placed in sequentially numbered, sealed opaque envelopes, which were opened at the time of intervention allocation.

Intervention description
Control group:
Participants received standard postoperative therapy consisting of oral amoxicillin 500 mg every 8 hours for 5 days following surgical extraction of vertically impacted mandibular third molars (standard protocol).

PRF group:
Following extraction and socket debridement, platelet-rich fibrin (PRF) prepared from autologous venous blood was placed into the extraction socket. Participants additionally received standard postoperative oral amoxicillin therapy (500 mg every 8 hours for 5 days).

PRF + azithromycin group:
Participants received a single prophylactic oral dose of azithromycin (1 g) one day before surgery. Following extraction and socket debridement, PRF prepared from autologous venous blood was placed into the extraction socket. Standard postoperative oral amoxicillin therapy (500 mg every 8 hours for 5 days) was also administered.

PRF preparation protocol:
Twenty millilitres of venous blood were collected into sterile tubes without anticoagulant and centrifuged at 1300 rpm (200 × g) for 14 minutes using a fixed-angle rotor centrifuge. The PRF clot was isolated and placed into the extraction socket within 15 minutes after centrifugation.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Cytomorphometric changes (area, IntDen, AR, StdDev, Min, Max, Perim, Circ, FeretX, FeretY, and roundness) measured using exfoliative cytology with Papanicolaou staining and ImageJ morphometric analysis at baseline and postoperative day 7

2. Immunologic observation in cervical fluid samples measured using an ELISA at preoperative and postoperative

3. Microbiological findings measured using PCR analysis at preoperative and postoperative

Key secondary outcome(s)

1. Postoperative pain measured using a Visual Analogue Scale (VAS) at postoperative days 3 and 7

2. Postoperative edema, assessed via standardized facial reference point distances (tragus–gonion and tragus–oral commissure) measured using manual linear measurements with a flexible measuring tape at baseline and postoperative day 7

3. Wound healing measured using the Landry Healing Index at postoperative days 3, 7, and 14

Completion date
03/02/2026

Eligibility

Key inclusion criteria
Vertically impacted third molars that are radiographically diagnosed according to Winter’s classification

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
All

Total final enrolment
124

Key exclusion criteria
1. Allergies to penicillin or lidocaine
2. Chronic systemic diseases
3. Cystic lesions
4. Infections around the impacted third molar, odontomas, or syndromes affecting the orofacial region

Date of first enrolment
03/04/2024

Date of final enrolment
29/09/2025

Locations

Countries of recruitment
Serbia

Sponsor information

Organisation
Medical Faculty, University of Niš

Funder(s)

Funder type

Funder Name
University of Niš

Alternative Name(s)
Univerzitet u Nišu, Универзитет у Нишу, University of Nis, University of Niš

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

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?
Results article		21/06/2026	01/07/2026	Yes	No
Other files			21/05/2026	No	No
Statistical Analysis Plan			21/05/2026	No	No