ISRCTN13358268 https://doi.org/10.1186/ISRCTN13358268

Comparing the effects of two pain relievers on inflammation in healthy volunteers

Submission date
04/11/2024

Recruitment status
No longer recruiting

Registration date
18/12/2024

Overall study status
Completed

Last Edited
30/09/2025

Condition category
Other

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

Plain English summary of protocol
Background and study aims
This study aims to test a new type of pain reliever called NCX 701, which is designed to be easier on the stomach than regular acetaminophen (paracetamol). Researchers want to see if NCX 701 is effective and well-tolerated, and if it can reduce inflammation in a controlled setting.

Who can participate?
Healthy male volunteers aged 18-45 years can participate in this study.

What does the study involve?
Participants will be randomly assigned to receive either NCX 701, regular acetaminophen, or a placebo. They will take a single oral dose of the assigned treatment before being given a small amount of a substance (LPS) that causes mild inflammation. The study is double-blind, meaning neither the participants nor the researchers know who is receiving which treatment.

What are the possible benefits and risks of participating?
Participants may help in the development of a new, potentially safer pain reliever. Risks include possible side effects from the treatments and the mild inflammation caused by LPS.

Where is the study run from?
The study is conducted at the Medical University of Vienna (Austria)

When is the study starting and how long is it expected to run for?
June 2002 to January 2003.

Who is funding the study?
Not applicable (company does not exist any more)

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Effects of Acetaminophen and NO-Acetaminophen (NCX 701) in human endotoxemia: a randomized, placebo-controlled trial in healthy volunteers

Study objectives
For the human setting, the gastrointestinal-sparing effect of similar NO-derivations of aspirin was confirmed in several pharmacodynamic (PD) studies on inflammation and coagulation biomarkers. Enhanced potency and improved safety were attributed to multifactorial benefits of supplementing the NO-moiety to the parent compound, including anti-proliferative efficacy, endothelium protection, increased blood flow and COX- sparing besides the anti-inflammatory activity.
Based on these observations it seemed reasonable to test if a beneficial influence on the pharmacological activity might be obtained as well, if a NO-moiety is added to acetaminophen. It was anticipated that developing NO-acetaminophen (“NCX 701”) might open new perspectives in the treatment of pain.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 01/06/2002, Ethics Committee of the Medical University of Vienna (Borschkegasse, Vienna, 1090, Austria; +43 1 40 400 21 460; ethik-kom@meduniwien.ac.at), ref: not applicable

Study design
Placebo controlled randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Inflammatory status

Interventions
After giving written informed consent eligible subjects were hospitalized at the clinical site on day 0 and fed with 3 meals and water to control dietary nitrate intake until the following morning (day 1). On day 1, after overnight fasting, participants received their randomized treatment (1g NCX 701, 2 g NCX 701, 1g acetaminophen or placebo) orally after suspension in at least 180 mL of water. Intake of study medication was scheduled 60 minutes before lipopolysaccharide (LPS) infusion under the supervision of the clinical team. Volunteers were allowed to leave the study site eight hours after LPS infusion and were requested to return in the morning of the following day (day 2) for blood sampling for PD analysis and reporting of adverse events. One week after LPS infusion a final follow-up visit was scheduled for the morning of day 8. During this visit PD parameters were analysed again and adverse events were recorded once more.

Randomisation process by sealed envelope

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
NO-paracetamol (NCX-701)

Primary outcome(s)
1. Interleukin (IL)-6 is measured using high sensitivity enzyme immunoassays at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
2. Interleukin (IL)-8 is measured using high sensitivity enzyme immunoassays at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
3. Monocyte chemoattractant protein-1 (MCP-1) is measured using enzyme-immunoassay at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
4. Tumor necrosis factor-alpha (TNF-alpha) is measured using high sensitivity enzyme immunoassays at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
5. Soluble vascular cell adhesion protein-1 (VCAM-1) is measured using high sensitivity enzyme immunoassays at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2,

and day 8
6. Soluble E-selectin is measured using high sensitivity enzyme immunoassays at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8

Key secondary outcome(s))
1. Matrix metalloproteinase-2 (MMP-2) is measured using enzyme immune assays (R&D Systems) at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
2. Matrix metalloproteinase-9 (MMP-9) is measured using enzyme immune assays (R&D Systems) at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
3. White blood counts (WBC) are measured using a cell counter (Sysmex, Milton Keynes, UK) at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
4. Elastase is measured at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
5. Von Willebrand Factor (VWF) is measured using turbidometry with a commercial kit from Behring (Marburg, Germany) at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, 7 hours after LPS infusion, day 2, and day 8
6. Platelet counts are measured using a cell counter (Sysmex, Milton Keynes, UK) at baseline, 1 hour before LPS infusion, 2, 3, 4, 5, and 7 hours after LPS infusion, day 2, and day 8
7. ECG is measured every 15 minutes during the first 6 hours after endotoxin bolus infusion
8. Heart rate is measured every 15 minutes during the first 6 hours after endotoxin bolus infusion
9. Oxygen saturation is measured every 15 minutes during the first 6 hours after endotoxin bolus infusion
10. Lying blood pressure is measured every 15 minutes during the first 6 hours after endotoxin bolus infusion
11. Routine blood analysis is measured one week after endotoxin bolus infusion (day 8)
12. Occurrence of adverse events is monitored throughout the entire study period, including day 2 and day 8 follow-up visits

Completion date
01/01/2003

Eligibility

Key inclusion criteria
Healthy male volunteers aged 18-45 years

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
Male

Total final enrolment
40

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
01/08/2002

Date of final enrolment
01/10/2002

Locations

Countries of recruitment
Austria

Study participating centre
Medical University of Vienna
Währinger Gürtel 18-20
Vienna
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1090

Sponsor information

Organisation
Medical University of Vienna

ROR
https://ror.org/05n3x4p02

Funder(s)

Funder type
Other

Funder Name
Not applicable (company does not exist any more)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available due to data protection reasons and based on a previous agreement with the volunteers.

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		29/09/2025	30/09/2025	Yes	No
Participant information sheet	in German	13/05/2022	08/11/2024	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes