# A study to investigate the pharmacodynamics, safety and tolerability of cutaneous capsaicin in healthy adult subjects.

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-To investigate the feasibility, applicability, safety, tolerability, and reproducibility of addition of the capsaicin-heat model and the thermal grill to the existing nociceptive pain test battery in healthy subjects.-To investigate the feasibility...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Peripheral neuropathies |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON37233

**Source**
ToetsingOnline

**Brief title**
Development of a nociceptive test battery - capsaicin models

### Condition

- Peripheral neuropathies

**Synonym**
Small fibre neuropathy

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Centre for Human Drug Research

**Source(s) of monetary or material Support:** Astellas Pharma,Internal

## Intervention

**Keyword:** Allodynia, Hyperalgesia, Pain

## Outcome measures

### Primary outcome

Baseline demographics & personality

Immunogenicity

Pharmacodynamics Leg

-Intra-epidermal nerve fibre density [IENFD]

-Quantitative sensory testing [QST] (Leg PD)

-Videothermography [VT] (Leg PD)

-Laser Doppler blood flow [LDBF]

Pharmacodynamics Back

-Heat-Capsaicin-Warmth Model (Back PD)

### Secondary outcome

Pharmacodynamics PainCart

- Nociceptive Pain Tasks

Potential for pain an discomfort associated with skin biopsies, pain tests and capsaicin applications. No benefit to the individual is expected.

# Study description

### Background summary

Local application of low-dose (0.075%) capsaicin can be used during early drug development of analgesics to evaluate a compound*s anti-hyperalgesic/anti-allodynic potential. Patches of high-dose capsacin (8%) were recently approved for the treatment of localized peripheral neurpathic pain. As they have been shown to cause intra-epidermal denervation, application of 8% capsaicin can also be used as a model of nerve regeneration in healthy subjects. It is not known if the acute capsaicin reaction (erythema, hyperalgesia, allodynia) is related to the level of subsequent loss of intra-epidermal nerve fibres. Furthermore, it is known that there are relationships between immunogenicity and capsaicin/pain sensitivity; this will be explored in greater detail.

The thermal grill is a pain paradigm that has been reported to be useful as a model in early phase drug development and sensitive to drugs used for the treatment of neuropathic pain.

The aim of this study is to validate these methodologies within the context of CHDR and to investigate relationships between acute capsaicin reactions and loss of intra-epidermal nerve fibers.

### Study objective

-To investigate the feasibility, applicability, safety, tolerability, and reproducibility of addition of the capsaicin-heat model and the thermal grill to the existing nociceptive pain test battery in healthy subjects.
-To investigate the feasibility, applicability, safety, tolerability, and reproducibility of capsaicin 8% patch in producing skin nerve denervation in healthy subjects.
-To investigate the temporal relationship between skin nerve denervation and regeneration (intra-epidermal nerve fibre density [IENFD]) and functional changes (quantitative sensory testing [QST], videothermography) after topical cutaneous application of 8% capsaicin.
-To investigate the reproducibility of somatic pain tests over a 3 month period.
-To investigate the relationship between immonogenicity, acute capsaicin reactions and nerve regeneration capacity in healthy subjects.
-Investigation of confounding factors on responses.
-Explore logistics, practicalities and potential refinement of techniques.

### Study design

This will be a randomized, single-blind, placebo-controlled, study to

investigate the pharmacodynamics, safety and tolerability of cutaneous capsaicin in healthy adult subjects. Subjects will be randomised to receive a capsaicin crème and placebo crème. All subjects will receive a capsaicin patch on their non-dominant leg. This will be done in combination with already established somatic pain tests. Subjects will first come to the clinic for a screening visit. Eligible subjects will subsequently come for 1 study visit of 8 hours as outlined in the study schedule and 4 follow-up visits of 4 hours each.

### Intervention

- 8% Capsaicin patch (Qutenza)
- 0.075% Capsaïcine crème FNA [Formularium der Nederlandse Apothekers]

### Study burden and risks

Potential for pain an discomfort associated with blood sample, skin biopsies, pain tests and capsaicin applications. No benefit to the individual is expected.

## Contacts

**Public**
Centre for Human Drug Research

Zernikedreef 10
Leiden 2333CL
NL
**Scientific**
Centre for Human Drug Research

Zernikedreef 10
Leiden 2333CL
NL

## Trial sites

### Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

- Agree to and be capable of signing an informed consent form.
- Healthy male and female subjects;
- Age: 18 to 65 years at screening (inclusive);
- Body mass index between 18-30 kg*m-2 (inclusive);
- Able to refrain from strenuous physical exercise from 48 hours prior to admission and during each stay at the CHDR clinic;
- Able to refrain from use of all (methyl)xanthenes (e.g. coffee, tea, cola, chocolate) from 12 hours prior to admission and during each stay at the CHDR clinic;
- Able to refrain from alcohol use from 24 hours prior to admission and during each stay at the CHDR clinic;
- Ability to communicate well with the investigator in the Dutch language; and
- Ability for female subjects to attend study day 0 while in the follicular phase (3-13 days after onset of menstruation).

## Exclusion criteria

- Legal incapacity or inability to understand or comply with the requirements of the study;
- Clinically significant findings as determined by medical history taking, physical examination, ECG and vital signs;
- Hemodynamic status at screening: systolic <100 and >160 mmHg, diastolic <50 and >95 mmHg, heart rate <45 and >100 bpm measured on the non-dominant (non-leading/non-writing hand) arm;
- Any current, clinically significant, known medical condition in particular any existing conditions that would affect sensitivity to cold (such as atherosclerosis, Raynaud*s disease, urticaria, hypothyroidism), pain (disease that causes pain, hypesthesia, hyperalgesia, allodynia, paraesthesia, neuropathy, etc.) or capsaicin (eczema, etc);
- Pregnancy;
- Dark skin (Fitzpatrick skin type V or VI), wide-spread acne, tattoos or scarring on back or upper leg;
- Subjects indicating nociceptive tests (including capsaicin formulation) intolerable or insensitive at screening;
- Have a urine drug screen detecting illicit drug of abuse (morphine, benzodiazepines, cocaine, amphetamine, THC, methamphetamines, MDMA) or a positive alcohol breath test at screening;
- Consume, on average, >8 units/day of (methyl)xanthines (e.g. coffee, tea, cola, chocolate)

and not able to refrain from use during each stay at the CHDR clinic;
- History or clinical evidence of alcoholism or drug abuse;
- Smoking of >5 cigarettes/day or equivalent and not able to abstain from smoking cigarettes during each stay at the CHDR clinic;
- Use of prescription, illicit or herbal drugs within 7 days of nociceptive assessments;
- Use of over-the-counter medications within 3 days of nociceptive assessments; and/or
- Participation in a clinical trial within 90 days of screening or more than 4 times in the previous year.

# Study design

## Design

**Study type:** Interventional

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| Masking: | Single blinded (masking used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 09-01-2013 |
| Enrollment: | 12 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | FNA [Formularium der Nederlandse Apothekers] |
| Generic name: | 0.075% Capsaicin creme |
| Registration: | Yes - NL outside intended use |
| Product type: | Medicine |
| Brand name: | Qutenza |
| Generic name: | Capsaicin |
| Registration: | Yes - NL outside intended use |

# Ethics review

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| Approved WMO Date: | 18-09-2012 |
| Application type: | First submission |
| Review commission: | METC Leids Universitair Medisch Centrum (Leiden) |
| Approved WMO Date: | 21-12-2012 |
| Application type: | First submission |
| Review commission: | METC Leids Universitair Medisch Centrum (Leiden) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2012-003898-26-NL |
| CCMO | NL41898.058.12 |