

# Experimental pain models for the evaluation of next-generation analgesics in clinical pharmacology studies

Hijma, H.J.

# Citation

Hijma, H. J. (2022, November 2). Experimental pain models for the evaluation of next-generation analgesics in clinical pharmacology studies. Retrieved from https://hdl.handle.net/1887/3485147

Version: Publisher's Version

License: Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden

Downloaded

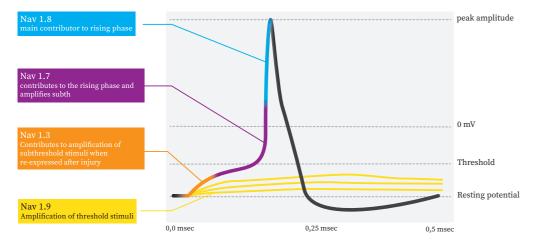
https://hdl.handle.net/1887/3485147

from:

**Note:** To cite this publication please use the final published version (if applicable).

# PAGE 43 / CHAPTER 1 / FIGURE 3

# Illustration of unique role of various $Na_V$ channels in action potential generation. (Adapted from [40])



EXPERIMENTAL PAIN MODELS FOR THE EVALUATION OF NEXT-GENERATION ANALGESICS IN CLINICAL PHARMACOLOGY STUDIES

# FOR THE EVALUATION OF NEXT-GENERATION ANALGESICS IN CLINICAL PHARMACOLOGY STUDIES

## Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Leiden, op gezag van rector magnificus prof.dr.ir. H. Bijl, volgens besluit van het college voor promoties te verdedigen op woensdag 2 november 2022 klokke 10:00 uur

> door Hemme Jacob Hijma geboren te Leiden in 1992

# Design

Caroline de Lint, Den Haag (caro@delint.nl)

# **Cover image**

Stroming, Jaap Hijma

The publication of this thesis was financially supported by the foundation Centre for Human Drug Research (CHDR) in Leiden, The Netherlands

#### **Promotores**

Prof. dr. G.J. Groeneveld Prof. dr. J. Burggraaf

## **Promotiecommissie**

Prof. dr. J.M.A. van Gerven

Prof. dr. J.H.M. van Zundert Maastricht Universitair Medisch Centrum +, Maastricht

Dr. ir. J.R. Buitenweg *Universiteit Twente*, *Enschede* 

Dr. M. Rad HagaZiekenhuis, Den Haag

8 CHAPTER 1 – Introduction: Analgesic drug development: proof-of-mechanism and proof-of-concept in early phase clinical studies

#### SECTION I

- 50 CHAPTER 2 A phase 1, randomized, double-blind, placebo-controlled, crossover study to evaluate the pharmacodynamic effects of VX-150, a highly selective Na<sub>V</sub>1.8 inhibitor, in healthy male adults
- 80 CHAPTER 3 A phase 1, randomized, double-blind, placebocontrolled, single- and multiple dose escalation study evaluating the safety, pharmacokinetics, and pharmacodynamics of VX-128, a highly selective Na<sub>V</sub>1.8 inhibitor, in healthy adults
- 104 CHAPTER 4 Comparative analgesic activity of two distinct sodium channel inhibitors, mexiletine and lacosamide, in healthy subjects

#### **SECTION II**

- 130 CHAPTER 5 Challenging the challenge: a randomized controlled trial evaluating the inflammatory response and pain perception of healthy volunteers after single-dose LPS administration, as a potential model for inflammatory pain in early-phase drug development
- **160** CHAPTER 6 A crossover study evaluating the sex-dependent and sensitizing effects of sleep deprivation using a nociceptive test battery in healthy subjects
- 182 CHAPTER 7 Simultaneous measurement of intra-epidermal electric detection thresholds and evoked potentials for observation of nociceptive processing following sleep deprivation
- 210 CHAPTER 8 Investigation of the sensitizing properties of a topical ethanolic 1% capsaicin formulation, and its applicability in a nociceptive test battery
- 236 CHAPTER 9 General discussion and conclusion

#### **APPENDICES**

- 244 Nederlandse samenvatting
- 253 Curriculum vitae
- 254 List of publications