

VU Research Portal

Structure-based design of AChBP ligands, new insights and applications

Edink, E.S.

2011

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Edink, E. S. (2011). *Structure-based design of AChBP ligands, new insights and applications*.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

vuresearchportal.ub@vu.nl

Structure-based design of AChBP ligands, new insights and applications

Ewald Edink

Structure-based design of AChBP ligands, new insights and applications

Ewald Edink

PerkinElmer and **Shimadzu Benelux B.V.** are greatly acknowledged for their financial support for the printing of this thesis

Printed by Wöhrmann Print Service, Zutphen, The Netherlands

Cover design: by Ewald Edink

Copyright © 2011 Ewald Edink

VRIJE UNIVERSITEIT

**Structure-based design of AChBP ligands,
new insights and applications**

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. L.M. Bouter,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de faculteit der Exacte Wetenschappen
op vrijdag 23 december om 11.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door

Ewald Siegfried Edink

geboren te Delft

promotor: prof.dr. R. Leurs
copromotor: dr. I.J.P. de Esch

"Als je de beperkingen kent, kun je daarbinnen onbeperkt te werk gaan."

Jules A. Deelder

Leescommissie: prof.dr. C.. Abell
 prof.dr. A.B. Smit
 prof.dr. T.K. Sixma
 prof.dr. M.J. Smit

The investigations described in this thesis were carried out in the Division of Medicinal Chemistry and Pharmaceutical Sciences, Faculty of Sciences, Vrije Universiteit, De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands. The work was performed within the framework of the Dutch Top Institute Pharma, project “New approaches for Ligand-Gated Ion Channel (LGIC) drug discovery (D2-103)”.

Table of Contents

| | | |
|-------------------|--|-----|
| Chapter 1: | An Introduction to nicotinic acetylcholine receptors and acetylcholine-binding protein | 9 |
| Chapter 2: | Aim and scope of the thesis | 35 |
| Chapter 3: | Thermodynamic analysis in fragment-based drug discovery | 39 |
| Chapter 4: | Fragment growing induces conformational changes in acetylcholine-binding protein: A structural and thermodynamic analysis | 63 |
| Chapter 5: | Structure-based design, synthesis and structure-activity relationships of dibenzosuberyl- and benzoate substituted tropines as ligands for acetylcholine-binding protein | 95 |
| Chapter 6: | Structure-based design of novel NSAID ester prodrugs: Dual targeting of cyclooxygenase-2 (COX-2) and $\alpha 7$ nicotinic receptors..... | 129 |
| Chapter 7: | Summary and conclusions | 159 |
| | Nederlandse samenvatting..... | 185 |
| | Dankwoord..... | 191 |
| | List of publications | 195 |
| | Curriculum Vitae | 196 |

