

## **Promotoren**

---

### **Prof. Ann Van Eeckhaut**

#### **Prof. Ralph Clinckers**

Department of Pharmaceutical Chemistry,  
Drug Analysis and Drug Information  
Vrije Universiteit Brussel

## **Copromotor**

---

### **Prof. Yvette Michotte**

Department of Pharmaceutical Chemistry,  
Drug Analysis and Drug Information  
Vrije Universiteit Brussel

## **Leden van de examencommissie**

---

### **Prof. Ann Van Schepdael**

Laboratory for Pharmaceutical Analysis  
Katholieke Universiteit Leuven

### **Prof. Jean-Michel Kauffmann**

Department of Instrumental Analysis and  
Bioelectrochemistry  
Université Libre de Bruxelles

### **Prof. Kristien De Paepe**

Department of Toxicology, Dermato-Cosmetology  
and Pharmacognosy  
Vrije Universiteit Brussel

### **Prof. Yvan Vander Heyden**

Department of Analytical Chemistry and  
Pharmaceutical Technology  
Vrije Universiteit Brussel



Vrije Universiteit Brussel

FACULTEIT GENEESKUNDE EN FARMACIE

## **Doctoraat in de Farmaceutische Wetenschappen**

Academiejaar 2011-2012

## **UITNODIGING**

Voor de openbare verdediging van het  
doctoraatsproefschrift van

**Naser Yousef SHRAIM**

Woensdag 23 mei 2012

U wordt vriendelijk uitgenodigd op de openbare verdediging van het proefschrift van

**Naser Yousef SHRAIM**

**'Intracerebral Microdialysis as a Tool to Investigate the Blood-Brain Barrier Passage and Brain Pharmacokinetics of Drug Substances'**

Op **woensdag 23 mei 2012** om **17 uur** in auditorium **P. Brouwer** van de Faculteit Geneeskunde & Farmacie Laarbeeklaan 103, 1090 Brussel

### **Situering van het proefschrift**

---

Intracerebral microdialysis is a well-established technique for *in vivo* monitoring of the free extracellular brain concentrations of exogenous or endogenous compounds. It has been extensively used primarily for the characterization and assessment of the neuropharmacodynamic profile of drugs in *in vivo* rodent as well as non-human primate studies. This technique also allows to study the brain accessibility and blood-brain barrier passage of systemically applied drugs. Intracerebral microdialysis can therefore be considered as the preferential monitoring technique for pharmacodynamic and pharmacokinetic studies of a multitude of drugs acting on the central nervous system. In this thesis we developed and validated two analytical methods which are tailored to the analysis of brain microdialysates. We first developed and validated a microbore LC–UV method for the determination of the selective non-peptidergic AT<sub>2</sub> receptor agonist compound 21 in striatal dialysate samples of the rat. This method was used to investigate the *in vivo* passage of this compound to the striatum of rats. Consecutively, a LC method with fluorescence detection was developed and validated for the quantification of the antidepressant reboxetine in rat brain microdialysates and plasma. The method was found to be suitable for pharmacokinetic profiling in both biological fluids. In a final study we investigated the impact of implantation of three commercially available high cut-off microdialysis probes on blood-brain barrier permeability using fluorescence microscopy. Concomitantly, the impact on nanobody brain disposition was quantified using intracerebral microdialysis in combination with  $\mu$ SPECT/CT.

### **Curriculum Vitae**

---

Naser SHRAIM was born on February 10th, 1977 in Qaliliya, Palestine. In 2000, he graduated with the degree of honor as a pharmacist from An-Najah National University, Nablus, Palestine. Then he worked for two years in a community pharmacy before following a master program of pharmaceutical sciences at the University of Jordan, Amman (2002). Naser successfully defended his master thesis entitled "The Effect of Crude Extract of Licorice on the Pharmacokinetics of Ciprofloxacin in an Animal Model" and got his M.Sc. in pharmaceutical sciences with excellent rating in 2004. Immediately, he was appointed at the college of pharmacy at An-Najah National University as a full time lecturer. He was teaching several courses i.e. biopharmaceutics and pharmacokinetics, physical pharmacy -both theoretical and practical parts- and drug delivery systems. In 2009, Naser got a scholarship from the Erasmus Mundus organization to do a Ph.D. in the Department of Pharmaceutical Chemistry, Drug Analysis and Drug Information (FASC) at the Faculty of Medicine and Pharmacy - Vrije Universiteit Brussel. In May 2009 he started his Ph.D. project under the supervision of Prof. Dr. Ann Van Eeckhaut and Prof. Dr. Ralph Clinckers. His project was focused on the use of intracerebral microdialysis to study the blood-brain barrier passage and the brain pharmacokinetics of drug substances. The project generated 3 first-author articles.