

**Master of Science (M.Sc.) Department of Clinical Sciences (Thesis) (Program start:
autumn 2024 or winter 2025)**

Project title: Vatinoxan in rabbits - pharmacokinetic and pharmacodynamic study

Project description:

Rabbits (*Oryctolagus cuniculus*) are the gold standard laboratory animals in biomedical experimentation and owing to their resemblance to humans they are utilized to test a wide range of human pathologies, both genetic and acquired. In addition, they are popular pets and therefore frequently presented to veterinarians for diagnostic or surgical procedures. Many of these procedures require sedation or general anaesthesia. Unfortunately, the number of deaths associated with anaesthesia or sedation in rabbits remains disproportionately high compared with other species, and many of these deaths appear to be due to cardiorespiratory causes. Alpha-2 adrenoceptor agonists (α_2 -agonists) are a class of drugs commonly used in veterinary medicine because of their reliable sedative and analgesic effects. However, they also have profound adverse cardiovascular effects. Due to the activation of postsynaptic α_2 -adrenergic receptors on vascular muscle cells, they cause constriction of the vessels (vasoconstriction) resulting in a 'reflex' reduction in heart rate (bradycardia) which can lead to cardiac arrhythmias.

Although the scientific evidence regarding the safety of α_2 -agonists in rabbits is controversial, there have been reports of an increased risk of bradycardia, cardiac arrest and death in rabbits following their use.

Vatinoxan is a new drug that counteracts the effects of α_2 -agonists, therefore called an α_2 -antagonist, which may help to reduce adverse cardiovascular side effects. Compared with the α_2 -agonists, vatinoxan is unable to cross the blood-brain barrier and its effects are therefore limited to the peripheral actions of the α_2 -agonists, namely the neutralisation of the vasoconstrictor effects. Studies in other animal species have shown higher heart rates in animals receiving a combination of an α_2 -agonist and vatinoxan compared with administration of an α_2 -agonist alone.

The aim of this study is therefore to determine the pharmacokinetics and pharmacodynamics of vatinoxan in rabbits and to assess its impact on the cardiovascular changes associated with the administration of an α_2 -agonist in rabbits.

Role of the candidate:

The successful candidate will be involved in the various stages of the study, including handling of the rabbits, monitoring the animals in the pre- and post-experimental phases, monitoring the rabbits during sedation, carrying out sedation assessments using a validated scale, taking blood samples, preparing blood samples for analysis, analysing the data and interpreting the results.

In addition to being able to contribute to the advancement of animal welfare, the successful candidate will acquire in-depth knowledge of animal research. Furthermore, they will have the opportunity to present their work at an international congress. Moreover, in the context of this research project, the successful candidate will be able to commence or continue their scientific career with the publication of one to two first author scientific articles.

To be eligible, you must:

- hold a degree in veterinary medicine; candidates who have completed studies in pharmacology or biology may be considered
- have a strong research interest
- be experienced in handling rabbits
- be experience in handling blood samples
- have good organisational skills
- have good interpersonal skills
- be patient and meticulous in your work

Salary:

\$20,000 (i.e. \$10,000 per year), internal and external grant applications will be required to complement the salary. A wide variety of scholarships are offered by the UdeM.

How to apply:

For more information or to apply, send your CV, your university transcript(s), a cover letter and the email addresses of 2 referees to inga-catalina.cruz.benedetti@umontreal.ca before June 7th, 2024.