titel

my_name

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1 Introduction

Introduction of the research and introduction research questions

The effect of plasma concentration should be related to the concentration of the test substance (so it implies the delayed ventricular regulation). The concentration of the test substance is highly effected by the extent of the delayed ventricular repolarization. Since the plasma concentration is most commonly used as the effective concentration. This research is interested in the ... (mean or the most frequent concentration) ... from drug where it meet cardiac ion channels within heart tissue.

Drug concentration in heart tissue should be of particular interest regarding all possible sites where the drug might meet cardiac ion channels. It should gain even more prominence in light of reports that note that myocardial drug concentration better correlates with a change in QT length4,5 and that the tissue drug concentration profiles do not necessarily correlate with those in plasma.

1.1 Goal

- Describe Goal (not the educational goal but the research goal)
- Describe how you reach the goal (e.g. make model and figures, use different setting)
- formulate hypothesis

This research aims to give a good understanding of the drug concentration over time in different tissue types of the heart. A PBPK (physiologically-based pharmacokinetic) approach has hardly been used in the modeling of drug concentration in various locations within heart tissue so this might be a great opportunity to accelerate research into the role of drugs on many things heart related. In order to

... This part is work in progress...

1.2 Theory

In order to understand the model, the concept of a PBPK model needs to be clear. Simpy put, PBPK is a computer modeling approach that incorporates blood flow and tissue composition of organs to define the pharmacokinetics (PK) of drugs. Alterations in PK properties, such as, absorption, distribution, metabolism, and excretion, can have a substantial impact on achieving the desired therapeutic concentration of a drug. PBPK is a very powerful tool, so a lot of computing power is necessary. The best use for a PBPK model is drug researc, which is the reason this type of model will be used in this research. It can also be, for instance, used by the Pharmaceutical Industry.

The equations which are part of the heart PBPK model are as follows:

(1) • Vmax[mg/h] = Vmax_pmol x CYP x MPPGL x Wli x MW x 60 / 10^9

(2) • CLu int2C8 = Cl int2C8 x fumic x ISEF2C8

(3) • $\frac{\frac{fu_p}{BP} * CLu_{int} * Q_{he}}{Q_{he} + \frac{fu_p}{BP} * CLu_{int}}$

. . . This part is work in progress. . .

2 Methods

2.1 The software model

The tool used for this experiment is called deSolve. This is a R-package which can help solve ODE, or ordinary differential equations. A few parameters were gotten from another research which used a program called: "Simcyp Simulator" to create a PBPK model. This model can predict certain values for tissues like the Kp which is pretty useful in this case. The research talked about just now has also used a package called FME, which performs a model fit based on algorithms. Equation 4 also plays a crucial role in this step.

. . . This part is work in progress. . .

```
library(deSolve)
# code
```

2.2 Model configuration

Chosen parameter- and initial values can be found in the tables below. Do please note that each table corresponds to their own model respectively.

. . . This part is work in progress. . .

3 Results

Introduction of results, how does it answer your research questions.

```
#plot(out)
#code to generate figures with title, subscripts, legenda etc
```

- Describe what can be seen in such way that it leads to an answer to your research questions
- Give your figures a number and a descriptive title.
- Provide correct axis labels (unit and quantity), legend and caption.
- Always refer to and discuss your figures and tables in the text - they never stand alone.

4 Discussion and Conclusion

4.1 Discussion

- Compare your results with what is expecting from the literature and discuss differences with them.
- Discuss striking and surprising results.
- Discuss weaknesses in your research and how they could be addressed.

4.2 General conclusion and perspective

Discuss what your goal was, what the end result is and how you could continue working from here.

References

[1] Soetaert, K., Petzoldt, T., and Woodrow Setzer, R.: *Solving differential equations in R: package deSolve*, J. Stat. Softw., 33, 1-25, 2010.