Why computer simulations should replace animal testing for heart drugs

March 27 2018, by Elisa Passini, Blanca Rodriguez And Patricia Benito

Credit: AI-generated image (disclaimer)

Safety is imperative before new medicines are given to patients – which is why drugs are tested on millions of animals worldwide each year to detect possible risks and side effects. But research shows computer simulations of the heart have the potential to improve drug development for patients and reduce the need for animal testing.

Animal testing has, to date, been the most accurate and reliable strategy for checking new drugs, but it is expensive, time consuming and – for some – highly controversial.

There is also the potential for some side effects to be missed due to the differences between animals and humans. Drug trials are particularly problematic for this reason and it's clear that new testing methods are needed to enable the development of better and safer medicines.

Humans and other animals

A variety of species of animals – including rats, mice, rabbits, guinea pigs, dogs and pigs – are used each year in drug development to predict the possible side effects for the heart in humans.

But while the underlying biology is similar, small differences between animal and human cells are amplified when a patient takes a drug. It means predicting the risk to patients is limited to an accuracy rate of around (75% to 85%), research shows, and it also leads to drug withdrawals from the market because of cardiovascular safety issues.

However, it's now possible to test a new heart drug in a "virtual human". Our recent research at the University of Oxford's Department of Computer Science demonstrates that computational models representing human heart cells show higher accuracy (89-96%) than animal models in predicting an adverse drug effect, such as dangerous arrhythmias – where the heart beat becomes irregular and can stop.

It shows that human computational models would bring additional advantages by reducing the use of animal experiments in early stages of drug testing; improving drug safety, thereby lowering the risk for patients during clinical trials; and speeding up the development of medicines for patients in urgent need of healthcare.

Computer models of the heart

British biologist Denis Noble first began experimenting with computer models of the heart in Oxford in 1960. Since then, the technology has evolved and it is ready to be integrated into industrial and clinical settings.

Thanks to human experimental data, human computer models are now available at different scales, from single cells to whole hearts, and they can be used to explore the behaviour of the human heart in healthy or diseased conditions, and under drug action.

Instead of a one-model-fits-all method, there are also new population-based approaches. Everyone is different, and some drugs can have harmful side effects only for certain parts of the population, such as people with a specific genetic mutation or disease.

The study by the Computational Cardiovascular Science team demonstrated that human computer models of heart cells are more accurate than animal experiments at predicting the drug-induced side effects for the heart in humans. This research won an international prize because of its potential to replace animal testing in labs.

We incorporated the technology into software, dubbed Virtual Assay, which is easy for non-experts to use in modelling and simulations.

The software offers a simple user interface for Microsoft Windows in which a control population of healthy cardiac cells with specific properties, based on human data, can be built. It can then be used to run computer-simulated – known as in silico – drug trials, before analysing the results. The whole process is very quick: it takes under five minutes using a modern laptop to test one drug in a population of 100 human cardiac cell models.

Several pharmaceutical companies are already using and evaluating Virtual Assay, which is available with a free academic licence and can be used by clinicians and pharmaceutical companies.

This research is part of a wider move towards the integration of computer models for drug safety testing which includes the Comprehensive in vitro Proarrhythmia Assay initiative, promoted by the US Food and Drug Administration and other organisations.

Pushing computer science boundaries

While simulations of heart cells can run in a few minutes, 3-D computer models of the whole heart still require a huge amount of computational power. One heartbeat, for example, can take about three hours in a supercomputer with almost 1,000 processors.

We're now working on 3-D simulations of the heart to explore drug cardiac safety and efficacy on a larger scale. It includes an exploration of diseased conditions, such as acute ischemia – where the blood flow in one of the arteries around the heart is obstructed. This research is also part of the European CompBioMed project to build computer models for the whole human body: a virtual human.

By bringing together academia, the pharmaceutical industry and regulatory agencies we hope to accelerate the uptake of human-based in silico methodologies for the evaluation of cardiac drug safety and efficacy.

Computer simulations are a faster, cheaper and effective alternative to animal experiments – and they will soon play an important role in the early stages of drug development.

This article was originally published on The Conversation. Read the

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