Curriculum vitae

2021-2024: PhD candidate in Health Sciences, Ghent University

2014-2015: MSc Analytical Toxicology, King's College London

2011-2014: BSc Forensic Science, University of Lincoln

Key publications

C. Cutler *et al.* Investigation of the metabolism of the selective androgen receptor modulator LGD-4033 in equine urine, plasma and hair following oral administration. *Drug Test Anal* (2020).

C. Cutler *et al.* Equine metabolism of the selective androgen receptor modulator AC-262536 *in vitro* and in urine, plasma and hair following oral administration. *Drug Test Anal* (2021).

C. Cutler *et al.* Identification of equine *in vitro* metabolites of seven non-steroidal selective androgen receptor modulators for doping control purposes. *Drug Test Anal* (2022).

C. Cutler *et al.* Equine metabolism of the growth hormone secretagogue MK-0677 *in vitro* and in urine and plasma following oral administration. *Drug Test Anal* (2022)

C. Cutler *et al.* Detection of the selective androgen receptor modulator S-23 and its metabolites in equine urine and plasma following oral administration. *Drug Test Anal* (2024)

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FACULTY OF MEDICINE AND HEALTH SCIENCES

In vitro and *in vivo* models to compare metabolism of online 'supplement' products, to improve detection in human and equine doping control analyses

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Summary

Selective androgen receptor modulators (SARMs) are a large class of structurally diverse compounds that have been developed primarily for androgen replacement therapy. They have better oral bioavailability, improved tissue selectivity and fewer androgenic side effects than traditional steroids, while having the positive anabolic effects on muscle and bone. No SARMs are available therapeutically but are widely available to purchase online as 'supplement' products, alongside other related compounds often sold under the umbrella of SARMs. This wide availability and potential for performance enhancing effects makes them a significant threat to the integrity of sport. To increase chances of detecting doping with these substances it is essential to determine their metabolism, to identify the best possible analytical targets for doping control testing.

Aims

The aims of this thesis were:

- to investigate the equine and human metabolism of a range of SARMs and related compounds
- to identify the best analytical targets for these compounds for doping control testing of both species
- to compare the metabolite profiles obtained with *in vitro* and *in vivo* models
- to compare the equine and human metabolite profiles
- to assess the feasibility of using the equine as a model for human metabolism

Approach

The metabolism of nine different SARM compounds and one growth hormone secretagogue was investigated *via* controlled administration studies to Thoroughbred racehorses as well as with a simple phase I *in vitro* system using equine and human liver microsomes. A selection of leftover human urine samples found to contain SARMs and/or related compounds were analysed using the same methods as the equine post-administration samples to allow direct comparison of the metabolites detected. Metabolite identification was carried out using liquid chromatography high resolution mass spectrometry.

Conclusions

This research advances anti-doping efforts by identifying analytical targets for detecting a range of SARMs in both human and equine doping control laboratories. The results suggest that equine studies are of great use for identifying potential targets for human doping control where human data is not yet available.

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