PROJECT REVIEW

"Enantioselective pharmacokinetics of formoterol and application to doping control"

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Formoterol is a long acting beta2-agonist allowed for use in athletes via inhalation at doses up to a predetermined limit, and is not allowed to be administered orally. The drug is usually administered and measured as a racemic mixture consisting of an active R/R- and inactive S/S- enantiomer, each with a different time course in the body which also differs by route of administration. The inactive S/S-formoterol is preferentially eliminated in urine relative to the active R/R-formoterol. Recent work has demonstrated that the Adverse Analytical Finding (AAF) limit, currently 40 ng/ml in urine, is difficult to reach and some authors have even questioned whether it is worth having an AAF limit for formoterol at all. To date, anti-doping strategies have not capitalised on this difference between formoterol enantiomer elimination from the body. We will use our advanced analytical technique (enantioselective LC-MS/MS) to characterise the urinary levels and ratio of both R/R- and S/S-formoterol enantiomers, as well as the glucuronide metabolite in athletes dosed with formoterol in prohibited regimens; an "acute" treatment regimen that exceeds the current allowable dose via inhalation and an oral regimen consisting of 160 µg/day for 7 days. The secondary objective is to characterise the urinary levels and ratio of formoterol enantiomers and glucuronide metabolite in athletes using repeated "chronic" inhaled rac-formoterol under permitted regimens. Study design will be double-blinded placebo controlled with two "chronic" 7 day treatment regimens; formoterol delivered by inhalation at just below the maximum allowable dose, and approximately half of the maximum allowable dose. This project will allow doping agencies to better discriminate between permitted and prohibited formoterol dosing.