

PROJECT REVIEW

“Factors affecting pharmacokinetics of inhaled salbutamol in athletes: Application of 4O sulfate metabolite analysis to improve predictive value of AAFs”

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Salbutamol is a short-acting beta2-agonist used for asthma and exercise induced bronchoconstriction and is permitted in inhaled doses up to 1600 µg in 24 h, not exceeding 800 µg in 12 h. A corresponding urine threshold of 1000 ng/mL and decision limit of 1200 ng/mL has been established to discriminate permitted inhalation from prohibited misuse. If an athlete exceeds the decision limit in doping control, this is recorded as an Adverse Analytical Finding (AAF) that may result in the athlete being charged with an anti-doping violation.

While salbutamol has been available for half a century, knowledge about its pharmacokinetics in relation to athletes and anti-doping control is incomplete. A handful of clinical trials underpin that high urine concentrations of salbutamol, relative to the dose inhaled, can occur, indicating that the risk of AAFs reported for salbutamol is possibly greater than previously assumed. These observations are further substantiated by the fact that several supplements and medications may interfere with the metabolism and subsequent excretion of salbutamol, which to our knowledge, are unexplored with respect to the salbutamol decision limit. Thus, athletes are exposed to several factors that may affect the pharmacokinetics of inhaled salbutamol, including, but not limited to strenuous exercise, dehydration, diet and supplements, and other medication.

This project will provide a comprehensive investigation into the factors that affect the intra- and inter-individual pharmacokinetics of salbutamol in female and male athletes. The primary objective is to model the peak urine excretion rate and peak urine concentrations of unchanged salbutamol and its major 4'O sulfate metabolite after permitted inhalation and prohibited oral ingestion to possibly improve the predictive value and accuracy of the decision limit for salbutamol.