

PROJECT REVIEW

"Pharmacological properties of inhaled beta2-agonists in athletes with special emphasis on Salmeterol and Terbutaline"

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Since 2010 the World Anti-Doping Agency (WADA) has changed their restrictions towards certain beta2-agonists on the prohibited list. As of 2013, the beta2-agonists salbutamol, formoterol and salmeterol are allowed by inhalation in therapeutic doses, and no longer require athletes to acquire a therapeutic use exemption. To distinguish allowed therapeutic use from suprathreshold misuse, urinary thresholds and decision limits have been introduced for salbutamol and formoterol, but due to limited pharmacokinetic studies of salmeterol and terbutaline, no urinary thresholds has yet been established for these beta2-agonists on the prohibited list.

Detection of salmeterol in biological fluids is difficult due to very low concentrations, which only gives a window of approximately 8 to 12 hours of detection in urine samples. However, the metabolite of salmeterol, Alpha-hydroxysalmeterol, is present in much higher concentrations in the urine than unaltered salmeterol and the metabolite may therefore be a suitable biological marker for excessive use of inhaled salmeterol.

Some athletes with asthma or exercise-induced bronchoconstriction (EIB) use combination therapy of both short and long-acting beta2-agonists. Combined inhalation of various beta2-agonists may affect the excretion of each substance. Lastly, asthmatic athletes usually take their beta2-agonists prior to or during competition and training. Therefore pharmacokinetic studies of beta2-agonists with applicability for the prohibited list should simulate sport-specific situations.

The main objective of the present study is to help establish urinary thresholds for salmeterol and terbutaline on the prohibited list as done with salbutamol and formoterol. A secondary objective is to address how combined inhalation of beta2-agonists influences the excretion of each substance in the urine. Lastly, an objective is to investigate the relationship between the specific gravity of urine samples and the concentrations of each beta2-agonist.