Available online at www.sciencedirect.com
ScienceDirect
Journal of Steroid Biochemistry & Molecular Biology 101 (2006) 161–178
The Journal of Steroid Biochemistry & Molecular Biology
www.elsevier.com/locate/jsbmb

Review

Metabolism and excretion of anabolic steroids in doping control—New steroids and new insights

Peter Van Eenoo *, Frans T. Delbeke

Doping Control Laboratory (DoCoLab), Ghent University (UGent), Technologiepark 30, B-9052 Zwijnaarde, Belgium

Received 10 April 2006; accepted 29 June 2006

Abstract

The use of anabolic steroids in sports is prohibited by the World Anti-Doping Agency. Until the 1990s, anabolic steroids were solely manufactured by pharmaceutical companies, albeit sometimes on demand from national sports agencies as part of their doping program. Recently the list of prohibited anabolic steroids in sports has grown due to the addition of numerous steroids that have been introduced on the market by non-pharmaceutical companies. Moreover, several designer steroids, specifically developed to circumvent doping control, have also been detected. Because anabolic steroids are most often intensively subjected to phase I metabolism and seldom excreted unchanged, excretion studies need to be performed in order to detect their misuse.

This review attempts to summarise the results of excretion studies of recent additions to the list of prohibited steroids in sports. Additionally an update and insight on new aspects for "older" steroids with respect to doping control is given.

Keywords: Doping; Anabolic steroid; Metabolism; Sport; Prohormone

Contents

* Corresponding author at: Ghent University (UGent), Department of Clinical Biology, Microbiology and Immunology, Doping Control Laboratory (DoCoLab), Technologiepark 30, B-9052 Zwijnaarde, Belgium. Tel.: +32 9 3313290; fax: +32 9 3313299.
E-mail address: Peter.VanEenoo@UGent.be (P. Van Eenoo).

0960-0760/$ – see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jsbmb.2006.06.024

1. Introduction

The first characterized androgen was androsterone, which was isolated from urine [1]. Shortly thereafter, in 1935, the characterisation [2] and synthesis [3,4] of testosterone resulted in the Nobel prize for chemistry for Butenandt and Ruzicka. The possible beneficial effects on physical strength, after the subcutaneous administration of testis-glycerol extracts, were already reported earlier [5]. In 1954, the first reports appeared of athletes using anabolic steroids searching for an increase in weight and power [6]. As a result, the misuse of anabolic steroids in sports led to a ban by the International Olympic Committee of these substances in 1974 and testing was implemented on a large scale at the 1976 Montreal Olympic Games via radio-immunoassays [7]. However, this technique only allowed for a non-specific detection of a limited number of exogenous steroids. Rapid developments in mass spectrometry allowed for the development of comprehensive screening methods for anabolic steroids in the 1980's [8].

The abuse of the endogenous steroid testosterone remained undetectable until the introduction of the testosterone to epitestosterone ratio (T/E) as a biomarker [9,10]. Based upon population studies an upper limit of 6 was calculated for T/E [10,11,12] and in 1983 the International Olympic Committee introduced this value as a criterion for testosterone abuse, although subsequently it was discovered that in some cases naturally elevated levels could occur [13,14]. Besides testosterone a range of anabolic steroids were synthetised by pharmaceutical companies as regular drugs and in some cases steroid preparations, e.g. a mixture of testosterone and epitestosterone, were already custom made for doping purposes [15].

In 1994, the Drugs Supplement Health and Education Act (DSHEA) was approved in the United States [16] and several new steroids were commercialized as nutritional supplements. Initially these new steroids were precursors of testosterone, commonly referred to as 'prohormones'. Late 2004, the US Congress approved the Anabolic Steroid Control Act (ASCA), restricting the sale of anabolic steroids as nutritional supplements [17]. However, by 2004 a range of prohormones derived from other steroids, including 19-nortestosterone, boldenone and even 17α-alkylated steroids were available as over-the-counter preparations. Moreover, several anabolic steroids specifically designed to circumvent doping control have been developed in recent years [18]. The introduction of these steroids on the market resulted in their incorporation on the list of prohibited substances of the World Anti-Doping Agency (WADA) [19]. On this list steroids figure in three classes of forbidden substances, namely anabolic steroids as well as corticosteroids and substances with anti-estrogenic properties [19].

Although several review papers have been published on the metabolism and detection of steroids commercialized by pharmaceutical companies [8,20–25] an overview on the phase I metabolism of steroids that were recently added to the WADA list of prohibited substances is lacking. Moreover, the recent (r)evolution on the steroid market and the discovery of new metabolites call for an updated review. This paper gives a general overview on the metabolites detected in recent excretion studies with anabolic steroids and prohormones, which could contribute to the detection of misuse of such substances. It should be noted that identification of the substances administered and metabolites detected in most studies incorporated in this review is based on chromatographic-mass spectrometric techniques and only in rare cases NMR was used as an additional technique. Especially for studies where the parent drugs were of non-pharmaceutical origin, it can not be excluded that the steroid specified on the label did not correspond to the administered steroid.

2. Testosterone prohormones

The first steroids introduced on the prohormone market were dehydroepiandrosterone (DHEA) and androst-4-ene-3,17-dione in 1996, shortly thereafter followed by androst-4-ene-3β,17β-diol, androst-5-ene-3β,17β-diol and androst-5-ene-3,17-dione. These steroids can be regarded as prohormones of testosterone as they are claimed to metabolise to testosterone after oral administration. A tentative overview