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Production of metandienone longterm-metabolite, 17β-hydroxymethyl-17α-methyl-18-nor-androsta-1,4,13-trien-3-one, using S. pombe based biotransformation assay

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Abstract

17β-Hydroxymethyl-17α-methyl-18-norandrosta-1,4,13-trien-3-one was introduced into doping screening as long-term metabolite of metandienone in 2006. It was found to be detectable in the urine of test persons via GC-MS up to 19 days after the administration of 5 mg of metandienone. This leads to a significantly increased detection period compared to methods previously applied for the determination of metandienone abuse. However, so far it has not been possible to obtain sufficient reference material of this metabolite, e.g. by chemical synthesis, and to confirm its structure via NMR.

Recently its production could be performed successfully in a whole cell biotransformation assay using the fission yeast *Schizosaccharomyces pombe* as host. The strategy involved the use of recombinant fission yeast strains that express different hepatic and steroidogenic cytochrome P450 enzymes e.g. CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP4Z1, CYP11A1, CYP11B1, CYP11B2, CYP17 and CYP21. The CYP profiling study revealed that 17,17-dimethyl-18-norandrosta-1,4,13-trien-3-one, chemically derived from metandienone, is converted to the desired urinary metabolite by CYP21. Human CYP21 is a microsomal steroidogenic cytochrome P450 enzyme that converts progesterone to 11-deoxycorticosterone as well as 17α-hydroxyprogesterone to 11-deoxycortisol in the body.

The production of this metabolite using the whole cell biotransformation system exhibits a valuable contribution to the fight against doping in sport.

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