PROJECT REVIEW

"Synthesis and analysis of metabolites of several beta-blockers for doping control"

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The aim of our project is to prepare metabolites of beta-blockers timolol, bisoprolol, labetalol and carteolol as reference substances to be used in various doping analytical applications. The results of this project will be directly and immediately applicable to the fight against doping in sports. All the above mentioned drugs are included in the World Anti-Doping Agency's list of prohibited substances.

According to the data available (WADA), there have been many positive doping findings where athletes have been caught using these drugs during recent years. In doping analysis, the analytical data obtained from the sample are compared to the data obtained from a negative and positive reference. According to the WADA's International Standard for Laboratories and ISO 17025 standard, well-characterized reference materials are recommended to be used as references in the analysis. Availability of well-characterized reference material increases reliability and legal defensibility of confirmation analyses. Furthermore, reference materials could also be used in quality assurance and in the development of new analytical methods.

The work will be carried out in close collaboration with two research organizations: Faculty of Pharmacy of the University of Helsinki and United Medix Laboratories, Helsinki, Finland. The Doping Control Laboratory of the United Medix Laboratories has been IOC accredited laboratory since 1983 and is now accredited by WADA.

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Result and Conclusion

Beta blockers are a class of antihypertensive drugs that were originally developed for treatment of *angina pectoris*. They have multitude of other indications such as coronary artery disease, congestive heart failure, ischemic heart disease and management of cardiac arrhythmias. By using beta blockers athletes can control effects of performance anxiety such as nervousness, hand tremor and high heart rate.

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The aim of this study was to synthesize phase I metabolites of bisoprolol and timolol, however the synthesis of a timolol metabolite could not be completed. The synthesized bisoprolol metabolite was characterized by NMR and mass spectrometry and compared to the metabolites extracted from urine samples to confirm the structure. Stability studies of the metabolite were also performed. Samples of *O*-desisopropylbisoprolol were provided to the accredited doping laboratories at the Cologne Workshop for Dope Analytics 2013.