PROJECT REVIEW

"Selection of the most appropriate markers of SARMs misuse. The role of physiological and environmental factors"

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Since 2008, the entire class of androgen receptor modulators has been included in the section S4 "Hormone and Metabolic Modulators" of the World Anti-Doping Agency (WADA) Prohibited List of substances and methods. The development of analytical procedures to reveal the misuse of these emerging drugs became of utmost importance. The relatively short half life of SARMs, the uniqueness of their structure, their effectiveness and the fact that research into their development is still in its infancy, have presented a novel problem for doping authorities everywhere. Indeed, structural modifications of aryl propionamide analogs bicalutamide and hydroxyflutamide led to the discovery of the first generation of SARMs. After that different structural categories of SARM pharmacophores have been designed and synthetized such as for example bicyclic hydantoin, quinolinones, tetrahydroquinoline analogs, benizimidazole, imidazolopyrazole, indole, and pyrazoline derivaties, azasteroidal derivatives, and aniline, diaryl aniline, and bezoxazepinones derivatives. However, this group is continuously expanding with new substances and other chemical structures. Various studies have been conducted to elucidate the metabolic pathways of SARMs and to develop efficacy analytical procedures to detect them in urine samples collected in occasion of doping control tests.

In this project, we plan to extend the data reported in literature by investigating the phase I and phase II metabolism of SARMs (e.g. RAD140, LGD2226, LGD4033) by in vitro assays. The enzymatic isoforms involved in their metabolism together with the effects of physiological and environmental factors will be also investigated. This information will be useful to select the most appropriate marker(s) of use also in the presence of potential confounding factors (e.g., non prohibited drugs).