

PROJECT REVIEW

"Endogenous erythropoietin stimulation by CO-breathing and by stabilizing HIF-1 by oral Cobalt application"

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Among the misuse of erythropoietic stimulating agents, the application of substances that induce EPO gene expression by stabilizing HIF 1 as cobalt (II) ions or carbon monoxide inhalation seems to be widely distributed. For athletes, the advantages of the misuse of both substances are low costs, high erythropoietic effectiveness, and no risk of detection, because they are not yet included into the prohibited list of WADA.

The aim of this project is to demonstrate significant effects of cobalt and CO-inhalation on the erythropoietic system which can be detected by the Athlete Biological Bloodpass and direct methods. Special aims are: 1. to monitor the physiological effects of different doses of cobalt and carbon monoxide on plasma-EPO, Hb-mass, and aerobic performance, 2. to prove if the effects of cobalt and CO can be detected by the recently developed Bayesian probabilistic inference techniques, which are the basis for the athletes biological passport, 3. to develop and evaluate direct detection methods for cobalt-misuse, and 4. to evaluate whether the endogenously produced EPO after stimulation by cobalt and CO differs from normal native EPO.

In a first study the optimal dosage of cobalt and carbon monoxide on endogenous EPO production will be determined. In a second step, application of either cobalt or CO for 3 weeks will provide data on (1.) performance effects of both drugs, (2.) stimulation of endogenous EPO, (3.) changes of hemoglobin mass, and (4) changes of hematological parameters which will be analyzed by the statistics of the athlete biological passport. Cobalt concentration and EPO isoforms will be analyzed in urine and/or blood samples. We expect to develop methods which can be used for the detection of endogenous stimulation of erythropoietin by cobalt and carbon monoxide.