PROJECT REVIEW

“Conversion of 4-Norandrostenedione 4-Norandrostenediol and 5-Norandrostenediol to Nandrolone in Human Subjects”
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According to the Dietary Supplement Health and Education Act, prohormones like DHEA, androstenedione and norandrostenedione are sold as nutritional supplements in the USA. Manufacturers are claiming that these hormone precursors are converted to the active hormone after oral ingestion. Because these prohormones are currently marketed legally in the USA, athletes are using these compounds as an alternative to the illicit anabolic steroids to enhance muscle size and strength and to improve performance.
Within a clinical study the conversion of 4-norandrostenedione (estr-4-ene-3,17-dione), 4-norandrostenediol (estr-4-ene-3B,1 7B-diol), and 5-norandrostenediol (estr-5-ene-31!,1 7B-diol) to nandrolone shall be found out. Until now there has not been any research dealing with this problem. The purpose of this investigation is to determine the exact plasma levels of physiological active nandrolone after administration of nandrolone prohormones.
Six to eight male volunteers are planned to attend the study. Single oral doses of the following products, available on the US nutritional supplement market, will be administered to the subjects:
4-norandrostenedione 100 mg capsule, 4-norandrostenedione 25 mg lozenge, 4-norandrostenediol 100 mg capsule, 4-norandrostenediol 10 mg lozenge, 5-norandrostenediol 100 mg capsule. Pharmacokinetic data will be evaluated for plasma nandrolone and the respective prohormones. Plasma concentrations will be established by venous sampling at baseline and prescribed intervals: 10’, 20’, 30’, 45’, 60’, 90’, 2h, 3h, 4h, 6h, 8h, 10h and 24h from the t=0 point. Analyses will be done by means of gas chromatography/mass spectrometry (GC/MS).
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Results and Conclusions

A new analytical method was developed and validated in order to determine plasma levels of 19-norsteroids, which are linked to the administration of the nandrolone precursors 4-norandrostenedione and 4-norandrostenediol. Compared to urine analysis, blood analysis enables the detection of the applied prohormones themselves and the intermediately formed nandrolone in addition to the main metabolites norandrosterone and noretiocholanolone.

Within this project, excretion studies with commercially available nutritional supplements containing 4-norandrostenedione and 4-norandrostenediol, which are advertised as potent nandrolone precursors, were conducted. Both active components were administered to eight volunteers as capsule (100 mg) as well as in form of sublingual formulation (25 mg). Compared to application of capsules sublingual administration provided faster absorption and higher bioavailability of these prohormones due to circumvention of the gastrointestinal passage and first pass effects of the liver.

Our main attention was focused on the generation of unconjugated nandrolone after administration of 4-norandrostenedione and 4-norandrostenediol. These concentrations are an indication for a hormonal activity caused by ingestion of aforementioned nutritional supplements. In fact, relevant plasma levels of unconjugated nandrolone were determined. Within a period of two hours after administration of the different nandrolone precursors, unconjugated nandrolone was detected in plasma samples of most volunteers. After application of only a single dose of both tested formulations containing 4-norandrostenedione, concentrations of generated nandrolone were determined which allow physiological intervention. Administration of sublingual tablets containing 4-norandrostenediol seemed to be particularly suitable for the generation of effective plasma levels of unconjugated nandrolone. While detecting only a marginal concentration after application of 4-norandrostenediol capsules, administration of 4-norandrostenediole sublingual tablets resulted in amounts of unconjugated nandrolone comparable to acute therapeutic treatment with nandrolone pharmaceuticals in all volunteers. Even though these concentration levels were present for only 2-3 hours after administration of a single dose, hormonal action can not be ruled out, especially by considering multiple intake of the respective supplement.

In conclusion, administration of 4-norandrostenedione and 4-norandrostendiol gives rise to pharmacologically relevant plasma concentrations of unconjugated nandrolone. Considering the results of this study, distribution of these particular prohormones as nutritional supplements as done in the past has been irresponsible. In fact, these effective nandrolone
precursors should be classified as drugs. Since the commencement of the Anabolic Steroid Control Act of 2004 at the beginning of this year, steroid precursors are banned and classed as Schedule III drugs. Based on this, sales of these products have been officially prohibited, and thus, the development of the black market concerning steroid precursors should be watched carefully in the future.

References


Anabolic Steroid Control Act of 2004


Guidance for Industry, Bioanalytical Method Validation

