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Nutritional Supplements – A Risk Assessment
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Nutritional Supplements – A Risk Assessment

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Introduction

Several studies have demonstrated that there is a considerable risk that dietary supplements may contain not only what is declared on the label, but also substances prohibited by the International Olympic Committee/World Anti-Doping Agency. It remains unknown whether the reason is bad production control or intentional addition. The Norwegian Olympic Committee and Confederation of Sport has, in co-operation with *Det Norske Veritas* (DNV), prepared guidelines for attitude and advice connected to nutrition and use of dietary supplements, as well as a risk assessment for dietary supplements which is meant to be advisory for the athletes. Analytical findings at the Norwegian Doping Control Laboratory, Aker University Hospital, support the risk assessment, in agreement with previous results [1-6].

Guidelines for athletes

Elite athletes affiliated with Olympiatoppen, the organisation for olympic sports on a top level in Norway, are instructed to follow guidelines concerning the use of dietary supplements. The guidelines are summarized below:

Nutrition: An optimised diet promotes health and performance. Elite athletes undertake to optimise their diet and training methods before, and while, using dietary supplements, if any.

Competence: Knowledge of the connection between diet, health, restitution, performance is of vital importance.

Dietary Supplements: Dietary supplements must only be used after an individual assessment and medical examination.

Responsibility: All use of dietary supplements and the possible consumption of banned substances through dietary supplements are the responsibility of the athlete.

Marketing: Elite athletes are role-models for children and young people. All should be aware of the responsibility and not take part in distribution, sale and marketing of dietary supplements, unless approved by the federation.

Risk assessment

The purpose of the risk assessment is to provide athletes with information concerning the risk that different types of dietary supplements may contain prohibited substances and so help to reduce the risk of inadvertently consuming prohibited substances. A summary of the risk assessment is presented in Table 1. The list is not exhaustive or final. It will be reviewed continuously and changed if new information so dictates.

Analytical results

The Norwegian Doping Control Laboratory, Aker University Hospital, has established an analytical method based on GC-MS for the analysis of nine different pro-hormones in nutritional supplements. The procedure was carried out according to Geyer et al [2]. Method parameters and validation parameters are presented in Table 2. A number of nutritional supplements were analysed. These supplements were obtained from the Internet, mainly from "suspicious" producers, companies and products that either previously were connected to a positive doping case for norandrosterone, or from companies that offer prohibited substances on their web site. The results are presented in Table 3. In 20 of 25 nutritional supplements different pro-hormones were found, which were not declared on the label. The amounts ranged from ten nanograms to several hundred micrograms per gram. Four of these "positive" nutritional supplements were subjected to excretion studies, and two gave rise to levels of norandrosterone above the reporting threshold.

Conclusion

The risk that nutritional supplements may contain substances prohibited by the IOC/WADA depends strongly on the quality control during manufacturing. The risk can be considerably reduced when the manufacturers (including the suppliers of raw material) and distributors comply with the demands to document good manufacturing practice (GMP) or other adequate requirements in every link of the producing chain. Analytical results confirm that under poor production control, the risk for contaminated supplements that may lead to a positive doping test is considerable. It seems like the risk is increased, when purchasing dietary supplements from suppliers that also provide products that are prohibited by the IOC/WADA. In relation to athletes it is important to focus on nutrition in preference to dietary supplements as well as to contribute to an awareness of the risk for contamination of supplements. In the end, the responsibility for intake of prohibited substances through contaminated nutritional supplements rests on the athlete himself.

References

1. Ayotte C., Nutritional supplements and doping controls, New Studies in Athletics, 14 (1999) 37

2. Geyer H., Mareck-Engelke U., Reinhart U., Thevis M., Schänzer W., Positive dopingfälle mit norandrosterone durch verureinigte nährungsgänzungsmittel, Dtsch. Z. Sportmed. 51 (2000) 378

3. Catlin D., Leder B.Z., Ahrens B., Starcevic B., Hatton C.K., Green G.A., Finkelstein J.S., Trace contamination of over-the-counter androstendione and positive urine test results for a nandrolone metabolite, JAMA, 284 (2000) 2618

4. Ayotte C., Lévesque J.F., Cléroux, Lajeunesse M., Goudrealt D., Fakirian A., Sport nutritional supplements: Quality and doping controls, Can. J. Appl. Physiol. 26 (2001) 120

5. De Cock K.J.S., Delbeke F., Van Eeno P., Desmet N., Roels K., De Backer P., Detection and determination of anabolic steroids in nutritional supplements, J. Pharm. Biomed. Anal. 25 (2001) 843

6. Geyer H., Mareck-Engelke U., Wagner A., Schänzer W., The Analysis of „Non-Hormonal" Nutritional Supplements for Prohormones, In: Schänzer W., Geyer H., Gotzmann A., Mareck-Engelke U. (eds) Recent Advances in Doping Analysis (9). Sport und Buch Strauss, Köln (2001) pp. 63-72

Table 1. Risk assessment. Classification of dietary supplements in risk groups.

	LOW RISK	UNKNOWN RISK	HIGH RISK	BANNED SUBSTANCES
Purity	Low risk of consuming banned substances	Unknown risk of consuming banned substances	High risk of consuming banned substances	Banned substances or precursors of banned substances
Product	i.e. Vitamins Minerals Trace Elements Antioxydants Fatty acids Cod Liver Oil Energy bars, energy drinks Proteins Carbohydrates Colostrum supplements	i.e. Creatine Free Amino Acids Herbal preparations, as Ginseng, Echinacea Drinks with caffeine and guarana in concentrations < 150 mg/l	i.e. Supplements companies manufacturing stimulating substances, hormones, or precursors of the above banned substances Drinks with caffeine and guarana in concentrations > 150 mg/l (i.e. Red Bull)	i.e. Herbal supplements with ephedrine (i.e Ma Huang) Herbal products with claimed anabolic effect (i.e. Tribulus Terrestris) Supplements with prohormones (i.e DHEA, androstenedione, norandrostenedione, norandrostenediol)
Purchase	Supplements purchased in Norway involve less risk than products obtained abroad. Purchase at pharmacies involves less risk than i.e. health food shop. Most risk is involved when the products are purchased over the Internet.			
Manufacturer and documentation	Dietary supplements from drug and food manufacturers with the GMP[1] standard may have a lower risk than dietary supplements from unknown manufacturers without the GMP standard. Natural products that are approved natural medicines[2] may have a lower risk than natural products that are not approved natural medicines. Dietary supplements have a high risk if manufactured by comapanies manufacturing prohibited substances.			

1. GMP is a standard for "Good Manufacturing Practice". Products with the GMP standard satisfy set requirements with regard to production and labelling.
2. Approved natural medicines are preparations approved by the Norwegian Medicines Agency

Table 2. Method parameters and validation parameters for prohormones in nutritional supplements

	Method parameters					Validation parameters			
Compound	Derivative	MW[a]	*m/z* (SIM)[b]	RT[c] (min)	RRT[d]	LOD[e] (ng/g)	Intra assay precision (CV%)	Inter assay precision (CV %)	Recovery (%)
19-nor-5-androstenediol	Bis-O-TMS	420	315, 330, 420	8.31	1.079	1.0	1.6	8.7	59
19-nor-4-androstenediol	Bis-O-TMS	420	330, 405, 420	8.43	1.095	1.6	1.6	17	74
DHEA	Bis-O-TMS	432	327, 417, 432	8.84	1.148	1.5	1.7	5.4	104
19-nor-4-androstenedione	Bis-O-TMS	416	194, 401, 416	8.89	1.155	3.1	8.7	8.9	87
4-androstenediol	Bis-O-TMS	434	405, 419, 434	8.93	1.160	2.1	8.5	20	94
5-androstenediol	Bis-O-TMS	434	239, 434	9.07	1.178	2.9	1.1	22	56
Nandrolone	Bis-O-TMS	418	194, 403, 418	9.15	1.188	-[f]	-[f]	-[f]	-[f]
1,4-Androstadienedione	Bis-O-TMS	428	323, 413, 428	9.27	1.204	1.5	17	11	97
19-nor-5-androstenedione	Bis-O-TMS	416	169, 401, 416	9.30	1.208	-[f]	-[f]	-[f]	-[f]
4-androstenedione	Bis-O-TMS	430	169, 415, 430	9.48	1.231	1.0	6.9	14	130
Boldenone	Bis-O-TMS	430	206, 325, 430	9.52	1.236	4.7	14	33	56
Testosterone	Bis-O-TMS	432	209, 417, 432	9.72	1.262	1.2	6.1	4.4	75
5-Androstene-3,7,17-triol	Tris-O-TMS	522[a]	417, 432	11.1	1.442	-[f]	-[f]	-[f]	-[f]
19-Noretiocholanolone d_3 ISTD 1	Bis-O-TMS	423	408, 423	7.7	1.00	-[f]	-[f]	-[f]	-[f]
Methyltestosterone ISTD2	Bis-O-TMS	446	301, 446	10.9	1.415	-[f]	-[f]	-[f]	-[f]

[a] Molecular weight of bis-O-TMS-derivative, except Androstentriol, tris-O-TMS-derivative
[b] m/z monitored in SIM aquisition mode; ions for quantitation are underlined
[c] Retention time
[d] Relative retention time to 19-Noretiocholanolone
[e] Limit of detection
[f] Not validated

Table 3. Analysis of nutritional supplements from selected producers

No	Prod-ucer	Product	Prohibited substances declared on label?	Producer offering prohibited substances?	Cont-aminated?	Norsteroids ng per serving unit	Total pro-hormones ng per serving unit	Excretion studies		
								Serving size	Total amount norsteroids	Maximum norandro-sterone conc. in urine
1	A	Ribose capsules	No	Yes	**Yes**	40	100			
2	A	Ribose capsules	No	Yes	**Yes**	200	390	3 capsules	0,6 µg	-
								10 capsules	2 µg	0.8 ng/ml (after 2 h)
3	A	Ribose capsules	No	Yes	**Yes**	20	+			
4	A	Creatine capsules	No	Yes	**Yes**	+	90			
5	A	Chrysine capsules	No	Yes	**Yes**	33600	38950	1 capsule	33.6 µg	8.6 ng/ml (after 5 h)
								1/3 capsule	11 µg	16 ng/ml (after 2 h)
6	B	Pyruvate tablets	No	Yes	**Yes**	60	430			
7	B	Pyruvate tablets	No	Yes	**Yes**	230	1070	10 capsules	2.3 µg	0.2 ng/ after 2 h)
8	B	Pyruvate tablets	No	Yes	**Yes**		40			
9	B	Pyruvate tablets	No	Yes	**Yes**		+			
10	B	Pyruvate tablets	No	Yes	**Yes**	70	1850			
11	B	Alpha Dopa Growth Poppers	No	Yes	**Yes**	130	730			
12	B	Chrysine Tablets	No	Yes	**Yes**		58150			
13	B	EcDyBOL Explo capsules	No	Yes	**Yes**	60	120			
14	C	Stenandiol tablets	No	Yes	**Yes**		+			
15	C	Stenandiol tablets	No	Yes	**Yes**	8502	19530			
16	D	Phosphagen powder	No	Yes	**No**					
17	D	HMB capsules	No	Yes	**Yes**		+			
18	E	Trioxalon capsules	No	Yes	**Yes**	70	8440			
19	E	Creatine	No	Yes	**No**					
20	F	Tribulus terrestris	No	Yes	**Yes**		20			
21	F	Natural phen-fen capsules	No	Yes	**Yes**		12180			
22	G	Chrysine capsules	No	Yes	**Yes**	63990	204020	1 capsule	64 µg	37 ng/ml (after 4 h)
23	H	Fuel Plex	No	Yes	**No**					
24	I	HMB powder	No	Yes	**No**					
25	I	HMB powder	No	Yes	**No**					

+ Concentrations not estimated