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Black market products suspected to contain doping relevant ingredients - annual report for 2018

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Abstract

The black market for performance enhancing drugs continues to represent a popular source for recreational/mass sport athletes. Also in 2018, the health risks can be estimated as immense due to poor quality of the majority of analyzed products. Almost half of the ingredients identified as relevant in accordance to anti-doping regulations were not indicated on the container labels. In addition, the lack of medical indication, false administration, or missing clinical studies represent risks for the consumers. There appear to be growing rather than decreasing risks due to the constantly expanding spectrum of drugs traded on the black market. In the last years new substances like hormones and growth factors emerged on the black market, which were confiscated by German customs authorities e.g. statins, Thymosin-β₄, ACTH-analog, modified GHRPs, and modified hGH. In case of modified GHRPs, also Polish and Norwegian customs authorities confiscated these emerging substances.

The analysis of confiscated products is an essential pillar of monitoring the black market. The products analyzed at the Cologne Anti-Doping Laboratory in 2018 included original pharmaceuticals as well as products from underground laboratories, which were confiscated by customs authorities. In total, the European Monitoring Center for Emerging Doping Agents (EuMoCEDA) analyzed 73 products by means of liquid chromatography - mass spectrometry (LC-MS) and gas chromatography - mass spectrometry (GC-MS). 94% of the compounds considered relevant for doping controls accounted for anabolic agents; 4% accounted for hormone and metabolic modulators, and 1% for glucocorticoids.

Another cornerstone of the EuMoCEDA's work includes the collection of information via internet research to probe for the emergence of new products or discussions concerning the application, efficiency or side effects of putative performance enhancing products. For 2018/2019 the focus was set on substances, which were suggested to have potential to appear on the black market, due to the fact that (pre)clinical data were published e.g. for REV-ERB-agonists, HIF stabilizer, sirtuins, and SARMs.

Introduction

In 2018, the European Monitoring Center for Emerging Doping Agents (EuMoCEDA) analyzed a total of 73 products qualitatively and quantitatively. The analysis of confiscated products is an essential pillar of monitoring the black market regarding developments to novel performance enhancing drugs, due to the fact, that the black market for performance enhancing drugs, comprising original pharmaceuticals as well as faked products, continues to represent a popular source for recreational/mass sport athletes [1-3]. Another cornerstone of the EuMoCEDA's work is the collection of information via internet research to probe for the emergence of new products or discussions concerning the application, efficiency or side

effects of putative performance enhancing products.

Drug	Finding	Labelled	Not labelled	
S1 Anabolic agents				Doping relevant
Boldenone	2		2	
-Undecylenate	2	2		
DHCMT	1		1	
Drostanolone				
-Propionate	1	1		
Metandienone	7	2	5	
Methyltestosterone	1		1	
Nandrolone				
-Decanoate	6	5	1	
-Phenylpropionate	3	2	1	
SARMs				
RAD-140	1	1		
Stanozolol	4	1	3	
Testosterone	6		6	
-Cypionate	4	4		
-Caproate	1	1		
-Decanoate	1	1		
-Enantate	12	7	5	
-Phenylpropionate	3	3		
-Propionate	13	6	7	
Trenbolone				
-Acetate	3	1	2	
-Enantate	2	2		
S4 Hormone and metabolic modulators				
Anastrozole	1		1	
Letrozole	1	1		
Tamoxifen	2	2		
S9 Glucocorticoids				
Cortisol	1	1		
23 Doping relevant drugs	78	43	35	
Unspecific / other drugs				Currently not doping relevant
Amino acids	2	2		
Caffeine	1		1	
Caffeine	2	2		
Dapoxetine	1	1		
Tadalafil	4	4		
Sildenafil				
In total 73 products with 28 analytes	88	52	36	

Table 1: Identified drugs in black market products

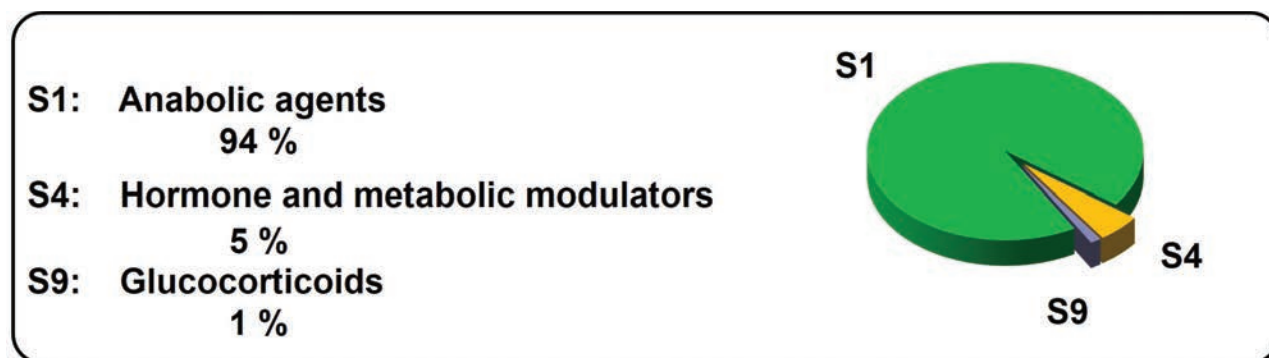


Figure 1: Apportionment of identified doping relevant drugs in analyzed black market products 2018

Experimental

The sample preparation depends on the formulation (oily solution, lyophilized, etc.), they were solved or extracted with water, acetic acid (2% aq.), and/or acetonitrile (50:50 v/v) and subsequently diluted to yield an adequate concentration of labeled drug content. To screen the most common target analytes in black market products, high performance liquid chromatography/mass spectrometry (HPLC-MS) experiments were conducted in single-reaction-monitoring (SRM) mode. Anabolic agents, stimulants, growth factors, natural and synthetic insulins, IGF-1 and synthetic analogs as well as growth hormone releasing factors could be determined by high performance liquid chromatography/high resolution mass spectrometry (HPLC-HRMS)-experiments in full-scan mode. Qualification and quantification of analytes were obtained by conducting product-ion scans with substance specific fragmentation pathways. For gas chromatography/mass spectrometry (GC-MS) experiments, analytes were derivatized and measured in full-scan mode. Qualitative and quantitative analysis were accomplished by using reference substances and/or reference databases. Included substances were anabolic agents, stimulants, beta-2-agonists and narcotics [1]. The samples were screened by HPLC-ESI-MS using an Agilent 1100 series HPLC interfaced via electrospray to a Thermo Scientific TSQ Vantage system. For HRMS experiments a Thermo Q-Exactive plus, and an Agilent 6550 iFunnel Q-TOF mass spectrometer were used. GC-MS experiments were performed on a HP 6890 series GC-system and a 5973 Mass Selective Detector, furthermore GC-experiments were conducted on a Trace 1310 Gas Chromatograph in combination with a TSQ 8000 Evo Triple Quadrupole Mass Spectrometer from Thermo.

Results and Discussion

A total of 73 suspicious (illicit) black market products were analyzed at the Center for Preventive Doping Research in 2018. Doping-relevant findings accounted in 78 cases for 23 different drugs (multi-findings included), from which 45% of the ingredients were not or falsely declared (Tab.1). As shown in Fig. 2, 94% of the identified doping relevant compounds accounted for anabolic agents (predominantly testosterone esters); 5% accounted for hormone and metabolic modulators, and 1% related to glucocorticoids. The analytes, which were currently not doping relevant, were stimulating, dermatologic, and virilizing agents as well as amino acids. Findings of modified GHRP-2 and GHRP-6 emerged in 2016 in Germany and Norway. The confiscation of Glycine-GHRP-2 was reported recently also by polish

researchers [5,6]. This represents an indication for the global impact of black market trafficking. The research via internet showed that the community of recreational sport misusing performance enhancing drugs discusses new developments of putative performance enhancing pharmaceutical substances. Aspects are: fields of application, efficiency, side effects, and forms of application. Drug candidates are investigated scientifically and pass through preclinical studies. Therefore, the substances are produced and sold by chemical vendors. Most investigated substances fail the clinical trials, but are still available via internet. Table 2 summarizes the status of diverse pharmaceutical candidates from substance classes REV-ERB-agonists, HIF stabilizers, sirtuins, and SARMs.

Drug	Begin of monitoring by ZePräDo / EuMoCEDA	No. of chemical vendors ⁽⁴⁾	Clinical trial	Advertised in performance enhancing product	Identified in black market product
REV-ERB-agonist	2016				
SR9009		26	x	✓	✓
SR9011		15	x	x	x
SR10067		6	x	x	x
GSK4112		25	x	x	x
HIF-stabilizer	2008				
Roxadustat		70	✓ <small>(approved in China)</small>	x	x
Sirtuin	2013				
SRT1720		42	x	x	x
SRT2104		28	✓	x	x
PPARδ-agonist	2009 / 2016				
GW1516		69	✓	✓	✓
GW0742		36	x	x	x
L165041		47	x	x	x
SARM	2013				
RAD-140		23	✓	✓	✓

Table 2: Status of potentially emerging drugs of black market products in 2018/2019

Conclusions

The athletes of recreational sports still risk their health by misusing black market products. Especially faked and falsely labeled preparations represent a particular problem. Anabolic agents and peptidic hormones are still the most popular products to improve body shape. Remarkable is the recent finding of glycine-GHRP-2 in Poland. This indicates the international distribution of black market products of substandard production quality or intentional modification by manufacturers. In both cases, the risks for athletes are unpredictable. The Cologne Anti-Doping Laboratory's commitment under the umbrella of EuMoCEDA, yielded the detection of emerging drugs, as well as the compilation of informations concerning availability, handling and forms of misuse of black market products. This confirms once again the requirement of continuous monitoring of the black market and the investigation of distributed products.

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