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The role of illicit, licit, and designer drugs in the traffic in Hungary

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ABSTRACT

The aim of this study was to investigate the prevalence and pattern of psychoactive substances among suspected DUID (Driving Under the Influence of Drugs) drivers in Hungary in 2014 and 2015. Blood and/or urine samples of 1252 suspected drivers (600 in 2014 and 652 in 2015) were analyzed for classical illicit and licit drugs, stimulant designer drugs (SDDs), and for synthetic cannabinoids, with 78.3% and 79.6% positive cases for at least one substance in 2014, and 2015, respectively. Impairment was proven in 39.2% (2014) and 35.7% (2015) of all drivers tested, based on the legal criteria of Hungary. Classical illicit drugs were found to be present in blood or urine of 89–61%, drivers tested. Drivers also tested positive for legal medications in 20–22%, SDDs in 21–28%, and synthetic cannabinoids in 15–19% of all cases. This indicates a drop in prevalence for classical illicit drugs and a slight but statistically non-significant increase for the other three substance groups. The distribution of drug types in each category were: [1] classical illicit drugs: cannabis (432), amphetamine (321), and cocaine (79); [2] medicines: alprazolam (94) and clonazepam (36); [3] SDDs: pentedrone (137) and α-PVP (33); [4] synthetic cannabinoids: AB-CHMINACA (46) and MDMB-CHMICA (30). The average age of illicit drug and SDD users was 30 years, while legal medications users were 36 years old on average, and the mean age of synthetic cannabinoid users was 26.5 years. The presence of both alcohol and at least one drug in samples was found in about 10% of the cases, both years. The ratio of multi-drug use was 33.0% in 2014 and 41.3% in 2015.

Compared to former years the number of drivers who tested positive for drugs doubled in Hungary, but it is still low compared to alcohol positive cases. The relatively low detected rate of DUID can be explained by (1) combined alcohol consumption masking drug symptoms, (2) the absence of road-side tests for illicit and designer drugs and, (3) police officers not adequately trained to recognize milder symptoms of impairment. Targeted education of police officers, prompt medical examination and the use of a symptom-focused on-site survey, could improve the efficacy of DUID investigations.

Our findings are not comparable with drug consumption habits of the general driving population. The last roadside survey (DRUID EU-6 Project) was performed in Hungary in 2008–2009, prior to the mass

Abbreviations: SDDs, stimulant designer drugs; 4-BMC, 4-bromomethcathinone; 4-CMC, 4-chloromethcathinone; mCPP, m-chlorophenyl-piperazine; EDDP, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine; 4F-α-PEP, 4-fluoro-α-pyrrolidinoheptiophenone; 2-FMC, 2-fluoromethcathinone; 4-MA, 4-methylamphetamine; 4-MeBu, 4-methylbuphedrone; 4-MEC, 4-methylethcathinone; 2-MeOD, 2-methoxy-diphenidine; 3-MMC, 3-methylmethcathinone; MeOPh, methoxyphenidine; MPA, methiopropamine; bk-MPA, 2-(methylamino)-1-(thiophen-2yl)propan-1-one; α-PEP, α-pyrrolidinoheptiophenone; α-PHP, α-pyrrolidino-hexanophenone; α-PVT, α-pyrrolidino-pentiothiophenone; α-PVP, α-pyrrolidinovalerophenone; AB-CHMINACA, *N*-[(2*S*)-1-amino-3-methyl-1-oxobutan-2-yl]-1-(cyclohexylmethyl) indazole-3-carboxamide; AB-FUBINACA, *N*-[(2*S*)-1-amino-3-methyl-1-oxobutan-2-yl]-1-[(4-fluorophenyl)methyl]indazole-3-carboxamide; AKB 48, *N*-(1-adamantyl)-1-pentylindazole-3-carboxamide; AB-PINACA, *N*-[(1*S*)-1-(aminocarbonyl)-2-methylpropyl]-1-pentyl-1*H*-indazole-3-carboxamide; ADB-FUBINACA, *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamide; AKB 48F, *N*-(adamantan-1-yl)-1-(5-fluoropentyl)-1*H*-indazole-3-carboxamide; 5F-AB-PINACA, *N*-[(2*S*)-1-amino-3-methyl-1-oxobutan-2-yl]-1-(5-fluoropentyl)indazole-3-carboxamide; JWH-018 (mb), **JWH-018 *N*-pentanoic acid**: 5-(3-(1-naphthoyl)-1*H*-indol-1-yl)pentanoic acid; MAM-2201, (1-(5-fluoropentyl)-1*H*-indol-3-yl)(4-methyl-1-naphthalenyl)-methanone; MAB-CHMINACA, *N*-[(2*S*)-1-amino-3,3-dimethyl-1-oxobutan-2-yl]-1-(cyclohexylmethyl)indazole-3-carboxamide; MDB-CHMICA, methyl (2*S*)-2-{[1-(cyclohexylmethyl)-1*H*-indol-3-yl]formamido}-3,3-dimethylbutanoate; MDMB-CHMICA, methyl (2*S*)-2-{[1-(cyclohexylmethyl)-1*H*-indol-3-yl]formamido}-3,3-dimethylbutanoate; PB-22, 1-pentyl-1*H*-indole-3-carboxylic acid 8-quinolinyl ester; UR-144 (mb), UR-144 *N*-pentanoic acid: 5-(3-(2,2,3,3-tetramethylcyclopropanecarbonyl)-1*H*-indol-1-yl)pentanoic acid; 6AM, 6-acetylmorphine; BZE, benzoyl-ecgonine; CNS, central nervous system; DUID, Driving Under the Influence of Drugs; HIFS, Hungarian Institute for Forensic Sciences; NPS, new psychoactive substances.

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spreading of designer drugs. As their appearance has drastically changed the pattern of drug consumption of the population, a new roadside survey, targeting general drivers, would be necessary.
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1. Introduction

Driving under the influence of illicit and licit drugs (DUID) has been punishable in Hungary since July 1999. According to data from Country Police Headquarters approximately 10–15,000 alcohol impairment cases per year were taken to court between 2000 and 2010 (personal communication) but drug impairment was proven in less than 120 cases per year [1]. The real number of DUID cases, however, is probably much higher. A roadside survey demonstrating a higher incidence of DUID was conducted (DRUID EU-6 project) in Csongrád County (South-East Hungary, ~420,000 inhabitants), during which oral fluid samples of 2738 randomly stopped car drivers were analyzed for illicit and licit drugs in 2008–2009. The prevalence of medications that act on the central nervous system (CNS) was 3.14% and that of illicit drugs was 0.99%. Breath alcohol was also tested and was positive in 0.13% of the cases [2]. Among drivers who died in accidents in South-East Hungary (involving four counties with about 1,390,000 inhabitants) 10.7% were positive for licit drugs, 4.92% for illicit drugs, and 33.6% for alcohol during the same investigation period [3]. According to the results of these studies the ratio of DUID drivers must be much higher than it was proved between 2000 and 2010.

The widespread appearance of designer drugs has changed the pattern of drug consumption among drug users in the last five years. As there are no data available describing the frequency of designer drug consumption in general and by suspected DUID drivers in Hungary, the aim of this study was to investigate the frequency of abuse among suspected and proven DUID drivers in 2014–15 of legal psychoactive medications, classical illicit drugs, as well as new psychoactive substances.

2. Materials and methods

Blood and urine samples of 600 suspected DUID drivers were analyzed in 2014 and samples of 652 drivers in 2015. Results of subjects positive for alcohol alone were not included in the current study. Around 80–90% of the nationwide collected samples were analyzed by the National Institute of Forensic Toxicology in Budapest. The samples collected from Csongrád and Pest Counties, as well as from Districts III, VIII, and IX in Budapest were analyzed in other institutes. These regions involve about 18% of the inhabitants in Hungary. Due to the lower number of analytes identified in these institutes their results are not involved in this study.

Initial dilution, protein precipitation and centrifugation of our samples were followed by a liquid chromatography–tandem mass spectrometry assay in which classical drugs and designer drugs were identified by one MRM-transition, except for synthetic cannabinoids and their metabolites, 3,4,5-trimethoxy-amphetamine, 5-MeO-AMT, 4-MeO-α-PVP, 3,4-CTMP, 3-MeO-PCP, 4-MeO-PCP, 2C-P, fentanyl, GHB, morphine and morphine-D6-glucuronide, which were identified by two MRM-transitions. Benzodiazepines and barbiturates were identified by three MRM-transitions. After this primary screening, confirmatory analysis of the positive samples was performed according to Table 1. Details of the confirmatory UHPLC–MS/MS method for synthetic cannabinoids: all targets were identified by three MRM-transitions, default ion allowance was 30% in absolute reference ion mode, S/N values needed to be over 10, in the calibration curve the accuracy of the calibration points had to be within the range of 70%–130%. The mean of the precision for the quantified analytes was 10.2 RSD% at concentration of 0.1 ng/ml and 8.5 RSD% at concentration of

Table 1
Scheme of **v**erification of blood and urine samples tested positive during screening and direct analysis of blood samples.

Groups of substances	Sample	Extraction and derivatization	Instrumental analysis	No. of analytes
Amphetamines, cathinones, other basic drugs	Blood and urine	LLE, toluene, *on-line* deriv. by MBTFA	GC–MS, SIM	150
Ketamine derivatives, methadone, tramadol etc.	Blood and urine	LLE, toluene	GC–MS, SCAN	10
Cannabinoids	Blood Urine	SPE, deriv. by methyl iodide alkaline hydrolysis, SPE	GC–MS, SIM HPLC-DAD	4
Synthetic cannabinoids[a]	Blood Urine	SLE Enzymatic hydrolysis and SLE	UHPLC–MS/MS	100
Cocaine and metabolites	Blood Urine	SPE	HPLC–MS HPLC-DAD, HPLC–MS	3
Opiates	Blood Urine	SPE Enzymatic hydrolysis, SPE, deriv. by MSTFA	HPLC-MS GC–MS	12
GHB	Blood and urine	LLE, deriv. by MSTFA	GC–MS	1
Benzodiazepines and Z-drugs	Blood Urine	SPE	HPLC-DAD, HPLC–MS HPLC-DAD	44

No. of analytes: the total number of different analytes that can be detected by the methods.
LLE: liquid–liquid extraction, SPE: solid phase extraction, SLE: supported liquid extration, MBTFA: *N*-methyl-bis-trifluoroacetamide, MSTFA: *N*-methyl-*N*-(trimethylsilyl) trifluoroacetamide, deriv.: derivatization, GC–MS: gas chromatography–mass spectrometry, HPLC-DAD: high performance liquid chromatography with diode array detection, HPLC–MS: high performance liquid chromatography–mass spectrometry, UHPLC–MS/MS: ultra high performance liquid chromatography–tandem mass spectrometry, SIM: selective ion monitoring mode, SCAN: scanning mode.
[a] Analysis was directed to 64 mother compounds and 36 metabolites.

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