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The Use of Oral Fluid and Sweat Wipes for the Detection of Drugs of Abuse in Drivers*

ABSTRACT: Blood, urine, oral fluid (by spitting or with a Salivette®), and sweat samples (by wiping the forehead with a fleece moistened with isopropanol) were obtained from 180 drivers who failed the field sobriety tests at police roadblocks. With quantitative GC-MS, the positive predictive value of oral fluid was 98, 92, and 90% for amphetamines, cocaine, and cannabis respectively. The prevalence of opiate positives was low. The SAMHSA cut-off values for oral fluid testing at the workplace, proved their usefulness in this study. The positive predictive value of sweat wipe analysis with GC-MS was over 90% for cocaine and amphetamines and 80% for cannabis. The accuracy of Drugwipe® was assessed by comparing the electronic read-out values obtained on-site after wiping the tongue and the forehead, with the corresponding GC-MS results in plasma, oral fluid, and sweat. The accuracy was always less than 90% except for the amphetamine-group in sweat.

KEYWORDS: forensic science, forensic toxicology, oral fluid, sweat, driving, substance abuse, cannabinoids, amphetamines, cocaine, opiates

In March 1999, the Belgian parliament adopted a law on driving under the influence of certain illicit drugs. A driver is sanctioned if Δ^9-tetrahydrocannabinol (THC), cocaine, benzoylecgonine, morphine, amphetamine, 3,4-methylenedioxy-*N*-methylamphetamine (MDMA), 3,4-methylenedioxy-*N*-ethylamphetamine (MDEA) or *N*-methyl-1-(3,4-methylene-dioxyphenyl)-2-butanamine (MBDB) are detected in plasma in concentrations higher than the analytical cut-off values mentioned in the law (1). Similar "per se" laws were introduced in Germany in 1998 and in Sweden in 1999 (2,3). In Belgium, an initial suspicion of impairment is established using a drug recognition test battery, based on external signs of substance abuse and on some well-defined psychomotor tests, followed by a urine screening test. One of the key elements in the enforcement process is the possibility to perform screening tests rapidly at the roadside, to take immediate administrative measures (disqualification from driving for minimum 6 h) and to select drivers for blood sampling.

As for drug screening at the workplace, oral fluid and sweat testing offer a non-invasive way of screening at the roadside and hence the possibility of direct supervision of sampling. This is a major advantage in comparison to urine testing (4–6). In Belgium, police officers are eager to participate in the evaluation of on-site tests for screening of oral fluid and sweat. Since oral fluid sampling can be time consuming because of a decrease in salivary flow after amphetamine use or cannabis smoking, and the high viscosity of the collected specimen, an on-site test should only require a small volume of sample. The sampling procedure with the Drugwipe® is very simple as it consists of wiping the tongue or some part of the skin e.g., the forehead (7). Orasure Technologies (Bethlehem, PA, USA) have obtained FDA approval for the screening of a panel of drugs of abuse in oral fluid using the Intercept Micro-Plate EIA, but this is a laboratory-based technique. However, very recently, the same company received FDA clearance for their oral fluid point-of-care test for opiates (UPlink®).

Oral fluid analysis is considered as the main alternative to blood to document recent use of medicines or drugs of abuse. Some drugs might have a larger detection window in oral fluid than in blood e.g., weakly basic drugs, smoked drugs (4,8). However, the collection protocol and the route of administration significantly influence the concentrations detected in an oral fluid sample (4,8,9).

The time window when the drug is expected to arrive on the surface of the skin is very broad (5,10), but in most cases, drugs will appear later in sweat than in oral fluid. Because of the longer delay of appearance of drugs in sweat, it seems more difficult to use a sweat test to indicate recent drug consumption. However, as an indication of relatively recent drug abuse and in addition to the drug recognition test battery, sweat testing might be useful in a driving under the influence of drugs (DUID) situation (11).

During this study, newly trained police officers evaluated drivers at special enforcement roadblocks. For 180 and 135 subjects, respectively, oral fluid and sweat samples were quantitatively analyzed and compared to the corresponding plasma and, if available, urine laboratory results. The reliability of Drugwipe® is assessed by comparing its on-site results with confirmatory GC-MS results in plasma, oral fluid, and sweat.

Methods

Sample Selection

Figure 1 explains the legal procedure applied in a DUID case and the study protocol for the evaluation of the alternative matrices. During the course of police controls from November 1999 until

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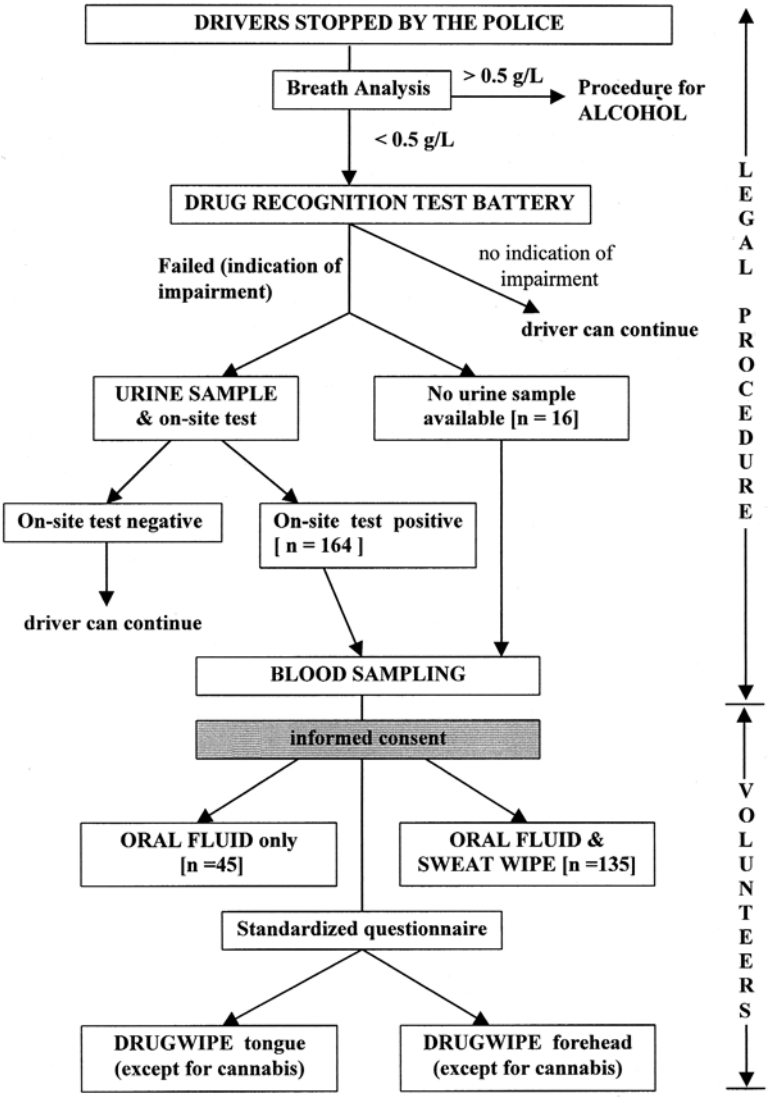

FIG. 1—*Study protocol based on the legislation for driving under the influence of drugs in Belgium, comparing oral fluid and sweat data with the corresponding results for plasma and urine. The Drugwipe test for cannabis was not used because previous experiments had shown that it lacked sensitivity.*

November 2000, 180 subjects agreed to provide oral fluid samples on a voluntary basis (written informed consent) in addition to plasma and urine. In 135 subjects sweat samples were also collected. Only drivers that screened negative for alcohol (legal limit 0.5 g/L) and that scored positive in the drug recognition test battery were included in the study. The police used specially designed sanitary vans to collect a urine specimen at the roadside, taking into account the necessary requirements to ensure the privacy of the subject. The on-site urine test Dipro drug screen 5 panel (VanDePutte group, Boechout, Belgium) was used to screen for amphetamines, methamphetamines, cannabinoids, cocaine, and opiates. The cut-off values stated by the manufacturer were 1000 ng/mL d-amphetamine, 500 ng/mL d-methamphetamine, 50 ng/mL cannabinoid metabolites, 300 ng/mL cocaine metabolite, and 300 ng/mL morphine. The panel test was extensively evaluated in our laboratory (12) and showed an excellent cross-reactivity with MDMA and MDA. When the on-site test was negative for the complete panel of illicit drugs, the driver was not included in the study and the procedure stopped. If the driver was unable to provide a urine sample but the police had a strong suspicion of impairment, the legal procedure for driving under the influence of drugs was followed anyway and blood was collected.

By means of standardized questionnaires, members of the medical staff obtained information on the kind of drugs that were taken and the route and time of administration. Self-reported drug use remained confidential and was not passed on to the police or the prosecutor as additional evidence.

Sampling

Oral fluid was collected by asking the subject to spit in a dry polypropylene tube (obtained volume: 1–2 mL). In some cases, especially where cannabis use was suspected, a neutral Salivette® (Sarstedt, Belgium) was used to obtain a sample. The subject was asked to keep the cotton roll between cheek and gum for two minutes without touching it with the hands. Sweat was collected by wiping the forehead with a cotton fleece of 5 cm × 4 cm (supplied by Securetec, Germany) moistened with 0.5 mL of 70% isopropanol.

Special precautions were taken in this study to avoid a significant decrease in analyte concentration in the different matrices

caused by storage and transport. Urine, oral fluid, and sweat samples collected at the roadside were frozen (dry ice) in plastic tubes until analysis in the laboratory. Blood samples were collected in two 7-mL glass Vacutainer® tubes using sodium fluoride and potassium oxalate as anticoagulant. The tubes were either cooled to +4°C (cool box) and centrifuged the next day or centrifugation was performed on-site and the corresponding plasma was frozen (dry ice) until analysis.

Analytical Procedures

Urine and plasma—On-site data for urine were confirmed by laboratory screening with FPIA and subsequent quantitation of 11-*nor*-Δ^9-tetrahydrocannabinol-9-carboxylic acid (THC-COOH), amphetamine, methamphetamine, MDMA, 3,4-methylenedioxy-*N*-amphetamine (MDA), MDEA, MBDB, benzoylecgonine, morphine, 6-acetylmorphine (6-MAM) and codeine by GC/MS, using the appropriate cut-off values (12). The parameters that tested positive in urine, when available, were confirmed in plasma with GC-MS using previously published extraction and derivatization techniques for cocaine and its metabolites, for opiates and for cannabinoids (13–15). Amphetamine, methamphetamine, and the designer amphetamines were extracted from plasma using solid phase extraction (SPE) with mixed-mode C8-cation exchange columns (Bond Elut Certify, Varian Belgium) and ethylacetate/ammonia (98:2, v/v) as eluent; heptafluorobutyric anhydride was used as derivatization agent. Quantitative analyses were performed using the deuterated analogues of all the analytes of interest on an Agilent 6890 gas chromatograph equipped with an autosampler (HP7673A) and interfaced with an Agilent 5973 mass selective detector. Analytical conditions were optimized for the detection of (1) cocaine, benzoylecgonine, anhydroecgonine methylester (AEME), ecgonine methyl ester (EME), morphine, 6-MAM and codeine; (2) amphetamine, methamphetamine, MDA, MDMA, MDEA, MBDB; (3) THC, 11-hydroxy-Δ^9-tetrahydrocannabinol (OH-THC) and THC-COOH. The MS was operated in SIM mode. At least three ions were monitored for the analytes and two ions for the internal standards. The methods are permanently evaluated through participation in external quality control programs (SFTA, France; GTFCh, Germany). In this study, plasma was considered positive for the amphetamine group if the concentration of the relevant amphetamine was higher than a defined cut-off level: the limit of quantitation (LOQ) (Table 1) or the legal limit (Table 2). A plasma sample was considered positive for cannabinoids, cocaine, or opiates if respectively, THC, benzoylecgonine/cocaine or morphine were present in a concentration higher than the LOQ (Table 1) or than the legal limit for confirmation (Table 2).

TABLE 1—*Limit of detection (LOD) and limit of quantitation (LOQ) for each analyte in the different matrices. For urine, plasma, and oral fluid obtained by spitting, values are expressed as ng/mL; for sweat wipes and Salivette® values are expressed as ng/wipe or ng/Salivette.*

	LOD	LOQ
Cannabinoids		
Urine		
THC-COOH	5.0	10.0
Plasma, oral fluid (spitting)		
THC	0.8	1.0
OH-THC	0.8	1.0
THC-COOH	1.0	5.0
Sweat wipe and Salivette		
THC	3.0	5.0
Amphetamines		
Urine		
Amphetamine/MDA	10.0	25.0
Others	5.0	25.0
Plasma, Oral Fluid, Sweat		
Amphetamine/MDA	10.0	20.0
Others	5.0	10.0
Cocaine		
Urine		
Benzoylecgonine	10.0	20.0
EME/Cocaine	20.0	40.0
Plasma, Oral Fluid, Sweat		
Cocaine/EME/AEME	3.0	5.0
Benzoylecgonine	1.0	2.5
Opiates (6-MAM, morphine, codeine)		
Urine	10.0	20.0
Plasma, Oral Fluid, Sweat	1.0	2.5

Oral Fluid—GC-MS confirmation was performed for those drug classes that already showed a positive result in urine or plasma or a positive on-site Drugwipe® result. Oral fluid samples obtained by spitting were thawed and centrifuged for 10 min at 4000 rpm. The supernatant was extracted and derivatized using identical methods as for plasma. The Salivette® device was centrifuged and internal standards were added directly to the roll. Cannabinoids were extracted from the dried cotton roll with a mixture of hexane and ethyl acetate (9:1 v/v). If the presence of more than one drug had to be confirmed, the wet Salivette® was extracted with methanol, the organic phase evaporated and further cleanup on mixed-mode C8

TABLE 2—*The number of plasma samples that were positive by GC-MS for a particular drug class, taking either the LOQ or the legal cut-off value for confirmation into account, and the median plasma concentration of the most prevalent analytes.*

	Plasma + (> LOQ)	Plasma + (> Legal Cut-off)	Legal Cut-off (ng/mL)	Median Concentration (ng/mL)
Amphetamine group	76	74		
Amphetamine			50	97
MDMA			50	315
MDEA			50	…
MBDB			50	…
Cannabinoids	101	91		
THC			2	6.4
Cocaine	26	21		
Benzoylecgonine			50	148
Cocaine			50	…
Opiates	7	5		
Morphine			20	32

SPE-columns allowed sequential elution of cannabinoids with hexane/ethylacetate (9:1, v/v) and basic drugs with ethylacetate/ammonia (100:2, v/v) and dichloromethane/isopropanol/ammonia (80:20:2, v/v/v). These procedures resulted in extraction recoveries of 80–90% for all basic drugs and THC.

Oral fluid was considered positive for the amphetamine group if the relevant amphetamine exceeded a pre-established cut-off level: the LOQ (Table 1) or a confirmation cut-off for oral fluid based on the most recently proposed SAMHSA cut-offs for amphetamine and methamphetamine (50 ng/mL) (Sam Niedbala, personal communication). An oral fluid sample was considered positive for cannabinoids, cocaine, or opiates if respectively, THC, benzoylecgonine or morphine exceeded the LOQ (Table 1) or met the requirements of SAMHSA: THC $>$ 2 ng/mL, benzoylecgonine $>$ 8 ng/mL, morphine $>$ 40 ng/mL and 6-MAM $>$ 4 ng/mL (6,16).

Sweat—GC-MS confirmation was performed for those drug classes that already showed a positive result in urine or plasma or a positive Drugwipe® result on-site. Internal standards were added to the wipe. Sweat wipes were extracted with acetate buffer 0.1 M pH 4.0 for cocaine, opiates, and amphetamines. For cannabinoids, direct extraction of the wipe with a mixture of hexane and ethyl acetate (9:1 v/v) was performed. If analysis of cannabinoids and other drugs was needed, the cotton fleece was dried, extracted with acetate buffer for cocaine, opiates, and amphetamines, centrifuged and extracted with the nonpolar solvent mixture for cannabis. The extracts were further analyzed with identical clean-up and derivatization procedures as for plasma samples. These procedures resulted in extraction recoveries of 80–90% for all basic drugs and THC.

Sweat was considered positive for the amphetamine group if the relevant amphetamine exceeded the LOQ (Table 1). A sweat sample was considered positive for cannabinoids or opiates if respectively THC or either 6-MAM or morphine were present in a concentration exceeding the LOQ (Table 1). A sweat sample was considered positive for cocaine if either the benzoylecgonine or cocaine concentration exceeded the LOQ (Table 1).

Validation of Analytical Methods—Table 1 represents the estimated limits of detection (LOD) and limits of quantitation (LOQ) in the different matrices. The limit of detection (LOD) was estimated from extracted pools of blank urine, plasma, oral fluid, blank sweat wipes, or Salivette® rolls, spiked with decreasing concentrations of the analytes, where the response of the quantitation ion was equal to 10 times the response in the appropriate blank matrix. The LOQ was defined as the lowest concentration of analyte that could be measured reproducibly and accurately in a certain matrix (coefficient of variation lower than 20%, accuracy between 80 and 120%). Concentrations of internal standards varied according to the matrix. A six-point standard curve was prepared using the internal standard method for quantification. Calibrators were prepared by spiking blank matrix material and the control samples were measured daily in the same sequence as the unknown samples.

Data Analysis—Different types of results were obtained in this study: true positives (TP, the number of positive oral fluid (or sweat) samples matching a positive plasma sample); true negatives (TN, the number of negative oral fluid (or sweat) samples matching a negative plasma sample); false positives (FP, the number of positive oral fluid (or sweat) samples that were not confirmed in plasma); false negatives (FN, oral fluid (or sweat) samples that were negative but corresponding to a positive plasma result). Based on these results, sensitivity (the ability of oral fluid (or sweat) analyses to identify those plasma samples that truly contain a concentration of target analyte above a certain cut-off level) and positive predictive value (PPV, probability that a positive oral fluid (or sweat) result will show a positive plasma result) can be calculated. Since as a consequence of the study protocol the number of TN was so low, the specificity and negative predictive values were not calculated and Receiver Operating Characteristic curves (ROC) analysis was not performed (17).

On-site Screening of Oral Fluid and Sweat

Oral fluid and sweat were screened by wiping the Drugwipe® (Securetec, Germany) over the tongue or on the forehead, respectively, before oral fluid and sweat samples were collected for confirmation. Separate strips were available for opiates, cocaine, and the amphetamine group. The results of the urine test, the self-reported drug use, or the suspicion of the police determined the parameters to test for. The coloration of the detection field changed from light pink to red depending on the concentration of drugs collected. In contrast to an early small-scale study with Drugwipe® (18), in this study, the color reaction in the test-area of the device was measured with the Drugread® hand photometer (reflectometer prototype provided by Securetec), providing an electronic read-out after two minutes. The proposed digital cut-off values are arbitrary reflectance values that correspond to 25 ng of heroin-HCl, 10 ng of cocaine-HCl and 10 ng of methamphetamine-HCl. Due to the lack of sensitivity for THC, the manufacturer decided not to include the Drugwipe test for cannabinoids in the study.

Results and Discussion

Analysis of Plasma Samples

The number of positive plasma samples per drug class, using either the LOQ or the legal limit as a cut-off value, is presented in Table 2. Median concentrations of the target analytes in plasma clearly exceeded the legal cut-off level. In 34% of the subjects, THC was the only analyte detected in plasma; in 20% of the samples only amphetamine and/or MDMA were identified. Methamphetamine is practically not abused in Belgium. Almost half of the drivers were positive for at least two types of drugs, amphetamines and cannabis representing the most frequent combination in plasma. The prevalence of cocaine positives was 13%, with 70% of them stopped at roadblocks in the surroundings of discotheques.

Analysis of Oral Fluid Samples

Spitting was found to be the easiest way of obtaining an oral fluid specimen without stimulation and at the roadside. Handling of the Salivette® was somewhat more complicated, because subjects' hands can be contaminated through handling of cigarettes (marijuana) or tablets (ecstasy).

THC concentrations detected in oral fluid samples obtained by spitting were often in the low ng/mL range, whereas after extraction of the Salivette® cotton roll, THC levels exceeding 100 ng/salivette were observed, even for similar corresponding plasma THC concentrations (Table 3). THC levels detected in oral fluid recovered after centrifugation of the Salivette® device were negligible and the variability in the volume recovered was substantial (50-1000 μL). The cotton roll in the device should be extracted directly with an organic solvent mixture like hexane/ethyl acetate (9:1 v/v) or with methanol, which was reported by Kauert (19). Although the

TABLE 3—*Selection of oral fluid samples from cannabis users, collected by spitting and/or with a Salivette®, and compared to the corresponding urine and plasma results. THC concentrations in plasma are presented in ascending order.*

	Urine (ng/mL)	Plasma (ng/mL)			Oral Fluid (ng/mL)	Salivette® (ng/salivette)
ID	THC-COOH	THC	OH-THC	THC-COOH	THC	THC
X4	88	<LOD	<LOD	<LOQ		45
X5	166	<LOD	<LOD	9		61
X3	<LOQ	1.2	<LOD	7		>100
T4	200	2.4	1.0	15	4.6	71
U6	>1000	3.1	1.2	40	5.4	72
Z9	41	3.9	<LOD	9		>100
H3	>1000	4.4	1.8	37	11.0	
H4	>1000	5.2	3.7	81	83.0	
O1	106	6.4	3.6	38	9.4	>100
O3	134	7.9	2.6	23	21.3	>100
O5	107	8.0	3.0	11	15.5	>100
H2	840	11.7	4.8	218	2.2	
O2	516	12.4	3.7	32	3.5	
Z1	187	12.4	6.0	60		>100
I2	>1000	13.1	4.2	88	24.2	
Z3	316	14.2	3.2	51		>100
F5	771	17.8	8.8	90	2.7	
X1	>1000	20.6	3.3	65		>100

theoretical saliva-to-plasma (S/P) ratio of THC is low, the cannabinoids in the marijuana smoke are sequestered in the mouth (4,6,8). Presumably, they stick to the gingival mucosa and get adsorbed to the cotton roll rather than dissolve in the aqueous fluid of the oral cavity. The probability to obtain a positive oral fluid result for cannabis seemed higher with the Salivette® than after collection by spitting. However, this technique might be too sensitive, as in some cases the corresponding plasma sample was negative, while the urine was positive (Table 3). In a recently published controlled study (20) THC could be measured reproducibly in oral fluid collected with a different sampling device, the Intercept DOA Oral Specimen collection device (Orasure Technologies, Bethlehem, PA).

Table 4 presents PPV and sensitivity for oral fluid analyses, calculated using different cut-off values: (A) applying the limits of quantitation of the GC-MS procedures (B) applying the legal limits for plasma and the proposed SAMHSA cut-off values for oral fluid (6, 16, Sam Niedbala—personal communication). Using both sets of criteria, results exceeding 89% were obtained for cannabis, amphetamines (including MDMA-only samples) and cocaine. The results for opiates need to be interpreted with caution because of the low prevalence of positives in this study.

Figure 2 shows the percentage of matching plasma and oral fluid samples for all four drug classes, when the limits of quantitation of the GC-MS analyses were applied.

Agreement is almost 100% for amphetamines. Median S/P ± SD ratios for amphetamine and MDMA were 13 ± 12 and 10 ± 8 respectively. Oral fluid concentrations of MDA were generally much lower than MDMA concentrations.

In this study, cocaine was predominantly abused intranasally or by smoking, resulting in high concentrations of the parent drug in the collected oral fluid samples. In one case, cocaine, and benzoylecgonine were clearly present in oral fluid and in urine but not in plasma (Fig. 2). Contamination of the oral cavity has been shown in cocaine users after smoking or sniffing (21) but only during the first hours. AEME was typically present after smoking. In cases where benzoylecgonine was present in plasma and in oral fluid, the median S/P ratio was 0.53 ± 0.64.

TABLE 4—*Prediction of the presence of cannabis, amphetamines, cocaine and opiates in plasma by GC-MS analysis of the corresponding oral fluid samples. Positive predictive values (PPV) and sensitivity (SENS) were calculated based on the number of true positives, false positives and false negatives using either the limits of quantitation for GC-MS or the legal limits for plasma and the proposed SAMHSA cut-off values for oral fluid.*

	Plasma: LOQ Oral Fluid: LOQ		Plasma: Legal Cut-off Oral Fluid: SAMHSA	
Cut-off Values	PPV	SENS	PPV	SENS
Cannabis	90%	91%	89%	91%
Amphetamines	98%	98%	100%	100%
Cocaine	92%	100%	90%	100%
Opiates	87%	100%	83%	100%

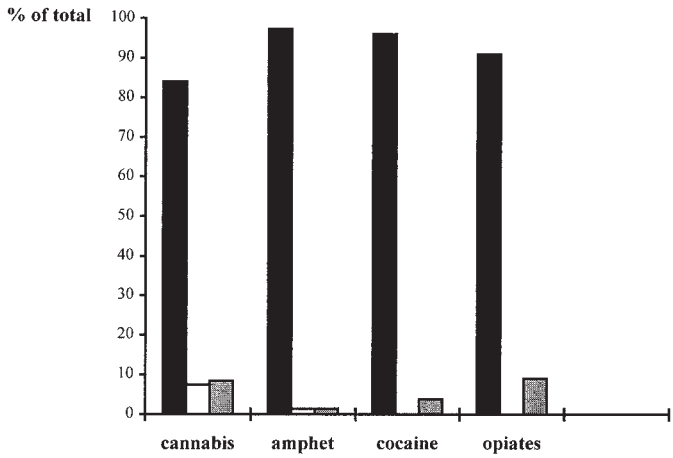

FIG. 2—*Comparison of plasma and oral fluid analysis by GC-MS, using the analytical limits of quantitation as cut-off values: ■ plasma and oral fluid in agreement, □ plasma positive, oral fluid negative, ■ plasma negative, oral fluid positive.*

TABLE 5—*Comparison of selected opiate positive samples after different administration routes documented by standardized questionnaires on-site: intravenous injection (IV), inhalation (SM) or sniffing (SN) of heroin. Concentrations are expressed as ng/mL.*

		6-MAM		Morphine		Codeine	
ID	Route	Plasma	Oral Fluid	Plasma	Oral Fluid	Plasma	Oral Fluid
E6	IV	<LOD	19	13	25	<LOQ	7
J2	IV	<LOD	61	34	163	10	98
B4	SM	<LOQ	6,600	40	6421	9	434
E1	SM	<LOQ	300	158	5000	23	460
J6	SM	LOQ	594	36	332	7	43
E2	SN	<LOD	20	15	95	3	91
I1	SN	4	572	32	323	6	50
L7	SN	<LOD	5	<LOD	19	<LOD	3

The presence of substantial concentrations of 6-MAM in oral fluid is shown in Table 5. Detection of morphine, codeine and 6-MAM in the collected oral fluid samples also depended upon the route of administration. The one false positive result in oral fluid (Fig. 2), also corresponding to a positive urine result, was probably caused by a residual contamination of the buccal cavity after sniffing of heroin (22) as the subject admitted abuse 6–12 h before sampling.

Plasma and oral fluid results for cannabis showed an agreement of 84%, based on sampling by spitting, resulting in a median S/P ratio of 1.6 with substantial inter-subject variability. The percentage of FN and FP results was 7.5% and 8.5% respectively, using only the LOQ as cut-off value. For THC, the use of Salivette® to collect an oral fluid sample would decrease the number of FN results but would increase the number of FP results if no suitable cut-off values were applied.

Analysis of Sweat Wipes

In all cases, the parent drug was the predominant analyte in sweat. The amount of analyte detected in the sweat wipes was very variable, which might be explained to a certain extent by the lack of reproducibility of sampling, the longer detection window of sweat and by accumulation of the drug after repeated dosage.

Median sweat concentrations of amphetamine and MDMA were 248 ng/wipe and 1771 ng/wipe, respectively.

In the opiates group, all sweat samples contained both 6-MAM (median 90 ng/wipe) and morphine (median 12 ng/wipe). The sweat samples with the lowest concentrations of the parent drug corresponded to a negative plasma sample or a plasma sample with a low concentration of analytes, but the number of data for opiates is low.

Sweat levels of benzoylecgonine (median 14 ng/wipe) were much lower than cocaine concentrations (median 354 ng/wipe). Two samples showed cocaine levels of 19 ng and 83 ng/wipe, respectively, but no benzoylecgonine. In the latter case, the corresponding oral fluid concentrations of cocaine were high and the plasma cocaine exceeded the level of benzoylecgonine, which indicated recent abuse. Huestis et al. also showed the absence of benzoylecgonine in several of the fast sweat patches that were applied to the skin for 30 min at different times after a controlled administration of cocaine (10).

For cannabis, the determination of a suitable cut-off level for THC in sweat seemed difficult because there was no quantitative correlation between the THC levels in the sweat wipes (median > 100 ng/wipe) and the corresponding plasma concentrations. SAMHSA cut-off values for sweat are proposed for eluates of sweat patches, which are applied to the skin for days or weeks, rather than for sweat wipes.

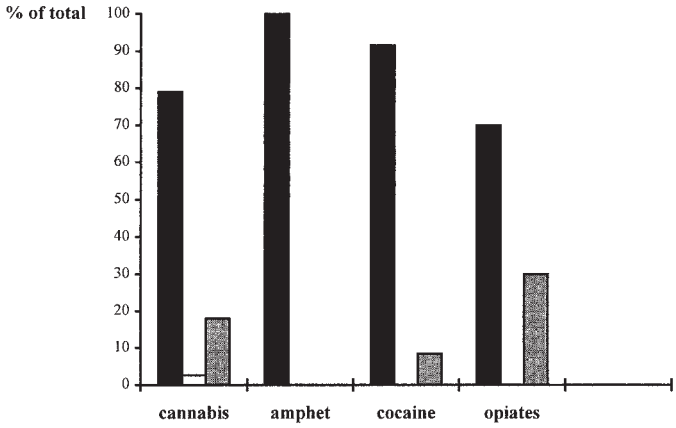

FIG. 3—*Comparison of plasma and sweat analysis by GC-MS, using the analytical limits of quantitation as cut-off values:* ■ *plasma and sweat in agreement,* □ *plasma positive, sweat negative,* ▒ *plasma negative, sweat positive.*

The probability that a positive sweat wipe result matched a positive plasma result (PPV) was lower than for oral fluid in the cannabis (80%) and opiates (70%) class, but remained high (> 90%) for cocaine and amphetamines. Figure 3 illustrates the correlation between sweat and plasma confirmatory results. The high percentage of FP results in the cannabis and opiates class probably reflects the longer detection window of sweat in comparison to plasma and the "depot" effect which is more significant than for oral fluid. The numerous factors that influence the excretion of sweat and the uneven distribution of the sweat glands (5,10) will necessitate further research to compare further the different sampling locations and the reproducibility of the sampling process.

Screening at the Roadside with Drugwipe®

Oral Fluid—The percent agreement of the Drugwipe® results obtained after oral fluid and sweat testing is calculated based on the results of the GC-MS analysis of plasma, oral fluid and sweat and is shown in Table 6.

When the LOQ is applied as a cut-off level for confirmation, the accuracy of Drugwipe® to test oral fluid was only 79% for amphetamines and even lower for opiates (67%) and cocaine (63%). There is only a weak indication that the FN results for the amphetamines and cocaine correspond to the oral fluid samples with

TABLE 6—*Accuracy of Drugwipe® results (DW) after wiping the tongue or the forehead, using the cut-off values for the electronic reader, and GC-MS results, using the LOQs for oral fluid and sweat and the legal limit for plasma.*

	Oral Fluid (>LOQ) DW (Tongue)	Sweat (>LOQ) DW (Forehead)	Plasma (>Legal Limit)	
			DW (Tongue)	DW (Forehead)
Cannabis	…	…	…	…
AMPH/MDMA	79%	95%	77%	95%
Cocaine	63%	68%	71%	76%
Opiates	67%	75%	82%	75%

the lowest concentrations of the relevant analytes. The application of higher confirmation cut-off values will therefore not alter the results significantly. However, for opiates, the oral fluid samples with the lowest concentrations corresponded to the negative Drugwipe® results on the tongue.

Sweat—The accuracy of Drugwipe® after wiping the forehead is 75%, 68% and 95% for opiates, cocaine, and amphetamines respectively. Similarly to oral fluid, there is only a vague indication of a correlation between the test results and the concentration of analytes in the screening matrix. Application of higher confirmation cut-off values will not change the conclusions significantly.

The agreement between the Drugwipe® results (applying the manufacturers' cut-off values for screening) and plasma results (using legal cut-off values for confirmation), only exceeded 90% for amphetamine and/or MDMA when using sweat as the screening matrix.

Conclusions

The overall results of the study indicated that:

- A positive oral fluid result was closely related to the presence of drugs in plasma.
- The choice of collection protocol was extremely important for the detection of recent cannabis use with oral fluid testing and the in-vitro recovery of THC when using a special collection device needs to be evaluated carefully.
- A controlled and reproducible sampling technique will be a key issue in the design of a reliable screening test.
- The cut-off levels of the screening test should be chosen in order to optimize the detection of positive plasma (blood) samples since plasma or blood analysis will remain the most widely accepted confirmation method for DUID cases.
- The proposed SAMHSA cut-off values for oral fluid drug testing at the workplace can also be used for the interpretation of traffic safety related oral fluid data. Application of the most recently proposed cut-off values for confirmation resulted in positive predictive values and sensitivities of oral fluid analyses exceeding 90%, when the corresponding plasma results were interpreted according to the Belgian legal limits for confirmation.
- A positive sweat test seemed a good indication of recent use of cocaine and amphetamines although in most cases the possibility of external contamination of the skin could not be ruled out.
- A positive sweat result for THC was merely an indication of relatively recent use and was not necessarily related to a positive plasma result.
- The positive predictive values for sweat in this study are better or similar to what has already been reported for urine in a comparable pre-selected driver population (23). Since the police definitely prefer sweat to urine as a screening matrix, sweat testing might be part of future roadside programs as a second step after drug recognition tests.
- The use of oral fluid and sweat would facilitate the procedure to screen for recent drug use at the roadside. Even when sanitary vans are available, the collection of a urine sample is not very practical and a few attempts of adulteration and substitution have been observed during the study.
- An important advantage of urine testing is the accuracy of the on-site tests to detect drugs of abuse in fresh urine samples (23). Unfortunately, the current situation for on-site oral fluid testing is by no means comparable to urine on-site testing.
- Although very user-friendly, the use of the version of Drugwipe® that was available during the study for oral fluid analysis is not recommended, even with an electronic reader to facilitate the interpretation of the immunoassay result. An accuracy of more than 90% was only obtained for amphetamine and MDMA when wiping the test on the forehead.

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