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Oral Fluid and Driving Under the Influence of Drugs (Duid): A Brief Review

Brief Review

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Abstract

This review deals with different aspects of driving under the influence of drugs (DUID).Cannabis, cocaine, opiates, amphetamines and methamphetamines are the most prevalent illegal drugs detected in the surveys carried out by the police and involved in traffic accidents. The use of oral fluid matrix to detect drugged drivers as well as pharmacokinetics of illegal drugs in oral fluid, correlation with blood, times of elimination and on-site drugs tests has been considered. A brief description of the marketed on-site test devices is provided. The relationship between drug use and impairment driving, and articles published in the specialized literature have been consulted. Data has been obtained from MEDLINE base date during the last years. Although oral fluid is a suitable fluid for analysis and the a steady progress has been done along the time, in the devices for screening, more effort must be achieved regarding to its performance and reliability regarding to parameters as sensibility specificity and recovery, specially for cannabis, the most prevalent drug detected. Standardized protocols referring to sample collection, established cut-offs, analytical confirmatory methods are issues that may be established to avoid erroneous results and interpretation. At present, legislation around the world using the oral fluid in legal procedure is not well defined but some countries are applying these methods to sanction drivers. In Spain, in Catalonia region, qualitative results are being utilized to fine drivers and courts are admitting the proofs.

Keywords: Oral Fluid; Drugs Abuse; Toxicology; On-Site Drug Tests; Driving Under the Influence; Legal Medicine.

Abbreviations: OF: Oral Fluid

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Introduction

Driving under the influence of drugs (DUID) has focused the attention in many countries and prevention measures, administrative, judicial procedures and policies have been studied to deal with the problem, trying to find effective solutions. Many papers are being published referring to the presence of drugs of abuse in drivers and analytical results of samples of the population are being provided.

Matrices as blood, urine and oral fluid (OF) have been tested with different and acceptable results. Reviews about the use of OF in drug analysis and in therapeutic and toxicological monitoring are numerous as the one reported by Shikha et al., [1] where the sample integrity problems and the advantages and limitations of OF in drug screening programmes are examined, as well as the relation to the pharmacokinetics of drug metabolism and excretion in this matrix. Parent drugs are often found in OF where only their metabolites may be found in urine. OF offers the possibility of comparison of unbound pharmacology active drug concentrations to pharmacodynamic effects, but with a shorter detection window than urine [2].

However, the lack of concordance studies examining both urine and OF drug levels and kinetics in the clinical setting is of some concern [3]. The utility of OF as a sample matrix for the detection of drugs abuse is known time ago, since it can be used in various settings and situations, such as roadside drug testing and clinical and forensic case studies. OF is widely recognised as a tamper-resistant screening method, which can identify drug use as accurately as blood testing, given the high correlation between the two fluids. Hold et al., [4] have reviewed OF as a biological sample to contribute to the interpretation of drugs concentration.

Advances in analytical techniques, particularly chromatography linked to tandem mass spectrometry, are helping to promote OF

analysis. This matrix is used testing by immunoassay biochemical test where the presence or concentration of a substance is detected. Nevertheless, it is a screening test and confirmatory analytical technique may be used after the screening test when positive results are obtained as Gas Chromatography/Mass Spectrometry (GC/MS) or Liquid Chromatography/mass Spectrometry (LC/MS). Confirmatory analysis, GC/MS or LC/MS, must be carried out to meet the desired sensibility because low amounts of sample are usually available for analysis [5].

OF has some disadvantages. For example, the volume of specimen collected may be too low for testing and for subsequent laboratory confirmation testing.

The aims of this review is to report studies published about this issue in the last years carried out using OF as matrix to detect drivers under the influence of drugs of abuse Data base MEDLINE has been consulted from 2000 until now. Results were focused on cocaine (COC), opiates (OPI), cannabis (THC), amphetamines (AM) and methamphetamines (MAM) analytes. Reference to testing devices, pharmacokinetic, correlation OF/blood results and drugs and impaired driving are also provided in this review.

Background

Several surveys have been performed since the 1980s using OF as matrix for detection of drugs of abuse and medicaments. In 1990's when devices suitable for the use of this matrix were developed and marketed, researchers encountered problems related to insufficient sample volume and insufficient sensitivity of the analytical methods. Along the time progress has been shown in sample collection, knowledge of toxicokinetics in OF, performance of on-site and laboratory-based immunoassays and confirmation methods.

At the end of the 90s, in this context, the European Union launched to develop road site drug testing devices for drugs of abuse. The Roadside Testing Assessment (ROSITA) project (ROSITA 1 and ROSITA-2) continued evaluating the usability and analytical reliability of the onsite OF drug testing devices as the integrated project DRUID (Driving Under the Influence of Drugs and Medicaments) trying to find information concerning the use of drugs or medicines affecting ability to drive safely. Analytical techniques for detection of drugs in OF were reviewed with emphasis on applications used in European Union roadside testing projects. Project DRUID was a part of the 6th Framework Programme 1 to fight against substance dangerous for road safety. ESTHER (Evaluation of oral fluid Screening devices by TISPOL to Harmonize European police requirements) were programs and organizations included in DRUID Project as well as DVLA (Driving vehicle licensing agency) in Great Britain. All these projects were evaluating the performance of different devices.

With time, the new technologies have enabled the development of the kits evaluated in these projects with enhanced performance.

Cut-Offs

In OF on-site drug screening, detection limits are set by the laboratory or the device manufacturer and there are significant differences among them. It is important to set the adequate cut-offs for their detection and confirmation. As a rule, the detection limit values used were those set by the National Institute on Drug Abuse (NIDA), In the ROSITA project, the Substance Abuse and Mental Health Services Administration (SAMHSA) guidelines recommended a confirmation cut-off level in OF [6].

Several studies have reported results establishing different cut-offs. Engblom et al., [7] investigated AM concentrations in both OF and whole blood samples of persons suspected of DUID. The cut-off for OF samples was 25μg/L and for whole blood sample 20μg/L. The results nevertheless indicated that the cut-off used for AM in OF (25μg/L) could be higher to correspond to the window of detection given by the level of 20μg/L in whole blood.

When using equivalent cut-off concentrations other studies indicate that the prevalence of drugs in samples of OF is the same as the prevalence in blood. The cut-offs in OF may be higher or lower than that in blood in accordance with the median OF to blood concentration ratio (OF/B), but it is also influenced by the skewness of the distribution of OF/B ratios. Regression formulae for the concentrations corresponding to selected percentiles in OF versus the same concentration percentiles in blood were determined. The accuracy when multiplying the cut-off thresholds in blood with the average and median OF/B ratios to estimate equivalent cut-offs in OF fluid was also investigated. These results were obtained from a population of 4080 subjects. Prevalence regression gave the most accurate results [8].

Pharmacokinetics

Although there are a number of factors that affect drug concentration in OF, there appear to be a reasonable correlation between blood and OF concentrations of drugs but local absorption of drug, in situations where drug may be present in the oral cavity (smoking or sublingual absorption) may influence in the results Drug may be also deposited by intranasal administration which must be considered. Moreover, contamination of the sample by food, beverages, or other adulteration agents may pose additional problems to the analytical method [9]. Drugs generally appear in OF by passive diffusion from blood. Drug metabolites can be also detected in OF. Several studies agree that there may be a close correspondence between drug and metabolite concentrations in OF and in blood, but interpretation of OF results for drugs of abuse should evaluate the test results in the context of program requirements [10].

Several studies deals with the transference mechanisms of drug transfer from blood into OF and the influencing factors, as the methods of sample collection, preparation, analysis of the abused drugs in OF and the relationship between abused drugs content in OF and in blood. It should be interesting to estimate abused drugs concentrations in blood by via their saliva concentrations [11]. Another fact that can influence the OF with plasma drug concentration correlation is that depending upon the lipophility and pKa of the drugs and its metabolites concentration in OF can be much higher or lower than in plasma [12].

Drugs concentrations are generally lower in OF than in urine [13]. In general, drug testing of OF detects drug use during the previous 24–48 hours [14], regardless of the route of administration although the selection of cut-offs plays an important role in the length of the detection window. OF/B ratios vary from drug to drug, from person to person, and even intraindividually making therapeutic drug monitoring in OF challenging [15].

Correlation

Recently this relationship was evaluated by studying the linear correlation of concentrations and calculating the OF/B ratios for different substances The median OF/B ratios were, for AM 19-22, for OPI 1.8-11, for COC and metabolites 1.7-17, for THC 14; results also confirmed that there was a lot of inter-individual variation in the OF/B ratios. For all substances, except THC a correlation between the OF and whole blood concentrations was observed but due to large variation seen here, drug findings in OF should not be used to estimate the corresponding concentrations in whole blood (or vice versa) as it would be desirable [16].

Wille et al., [17] also studied the relationship between the OF/B ratios and scatter plots and trend lines of the blood and OF concentrations were calculated for AM, COC, OPI and THC. A wide range was also found, >1 for AM (0.5-182), COC 22 (4-119), OPI 2 (0.8-6) for THC an OF/B ratio of 15 (0.01-569) was found although the time of last administration and the dose and the route of administration was unknown. It is important to stand out that these results agree with previous results reported and also confirm that the wide range of the ratios did not allow calculations of the blood concentration of drugs from OF data.

Regarding to the presence of one or more drug in OF and correlation with blood was studied by Toennes et al., and variability of OF analysis results in relation to blood/serum. In a sample of 177 cases in 45% of the cases single-drug use was found, and in 50% poly-drug use was found. Cannabis was most prevalent (78%) and 70% of these individuals were also positive for THC in serum. Overall, 97% of OF samples positive for any substance were also positive in serum [18]. Garcia- Repeto et Soria [19] has also reported the correlation of psychoactive substances between OF and blood.

Bogstrand et al., [20] investigated the association between drug type and arrest for driving under the influence of drugs by calculating odds ratios (ORs) using a case-control design in drivers; 794 subjects involved in road traffic crashes and 1944 arrested for other reasons, The controls were random drivers in normal traffic. Blood samples from cases and OF samples from controls were analyzed for 15 drugs. The most prevalent illicit drug in the control group was THC (0.58%), which was also commonly found in samples from drivers arrested due to road crash or other reasons (15.6%, 21.8% respectively) AM/MA was most prevalent among arrested drivers involved in crashes (30.6%) and drivers arrested for other reasons (56.9%), whereas only 0.18% of the control group was positive for AM/MAM. The single-use substances which gave highest OR for police arrest were AM/MA. Combinations of two or more drugs yielded higher ORs than the use of single substances.

Times of Elimination

In the area of pharmacokinetic another variable of interest is the course and time of elimination of drugs and. Controlled studies that have measured drug concentrations in OF following dosing regimens have been identified over the last years. These studies show that the AM including designer AM, COC, THC usually have similar time-courses to that in plasma. Following common doses peak OF concentrations exceed 0.1µg/mL and often even 1µg/mL. The drug concentration will depend on whether a dilution occurs with when a buffer solution is used as part of the sampling procedure. Results can be affected and it must be considered [21].

Additional evidence for interpreting COC and metabolite concentrations in OF was provided in another controlled study [22] carried out on a closed research unit for up to 10 weeks under constant medical supervision, to determine time of elimination and half life of COC; 19 participants were administered 75 mg/70 kg subcutaneous COC and 14 received 150 mg/70 kg. The disposition of COC, and its metabolite benzoylecgonine (BE) and ecgonine methyl ester (EME) into OF was determined after administration. In OF, COC first appeared, 0.08 to 0.32 hours after dosing and was rapidly eliminated with half-lives of 1.1 to 3.8 hours. BE and EME were first detected 0.08 to 1.0 hours after dosing with longer half-lives of 3.4 to 13.8 (BE) and 2.4 to 15.5 hours (EME). OF and plasma concentrations were significantly correlated for COC, BE, and EME There were no significant differences in first and last detection times with the 8-µg/L cut-off proposed by the SAMHSA or the 10-µg/L cut-off from DRUID.

Due to its high prevalence cannabis is one of the illegal drugs most studied and THC pharmacokinetics has been reported in occasional and chronic users. Toennes et al., [23] have studied the elimination half-life (1.6+/- 0.4 h); the OF/serum ratios were 0.3 to 425 without differences between the two groups. The large variability observed precludes a reliable estimation of THC serum concentrations from OF.

Van der Linden et al., [24] carried out other controlled study to determine time of elimination of THC in OF during roadside surveys. 2957 subjects were asked to report their use of drugs during the previous two weeks and to indicate the time of their last intake. THC was analyzed and frequencies in the time categories were calculated and compared with toxicological results. Diagnostic values were calculated for the time categories in which positive findings were to be expected (<4h and <24h, respectively for THC and its metabolite THCCOOH in blood, <12h for THC in OF. Most of subjects self-reported cannabis use was more than 12h before driving. The sensitivity of the questionnaire was low, while the specificity and accuracy were high. As conclusion self-report largely underestimates driving under the influence of cannabis, particularly recent cannabis use; therefore analysis of biological samples is necessary.

Devices

Reliable rapid on-site oral fluid tests are needed to be used in police controls to detect impaired and drugged drivers Description of numerous devices is not the objective of the review although we report some of them. Along the time testing technology is improving for accurate and sensitive detection of drug use. However, manufacturers do no publish OF or analyte's recoveries thus placing the burden to document these factors on individual investigators. Rosita-1 y Rosita-2 projects focused to evaluate the effectiveness of point of collection OF drug detection. The devices were evaluated for their ability to meet manufacturers' claims and proposed cut-offs concentration for illegal drugs. Drugwipe, Securetec, Ottobrunn, results were compared after confirmatory mass spectrometry analysis [25].

Peherson et al., [26] evaluated the performance of two on-site oral fluid drug-testing devices. The evaluation was performed for:

AM, THC, COC, and OPI. Both tests seemed to perform quite well for AM and THC although an evaluation of COC and OPI tests was not applicable because of the very low number of positive cases.

The performance of eight devices was assessed using cut-offs at a low levels In Belgium, Finland and the Netherlands as a part of the EU-project DRUID The sensitivity of OPI results ranged between 69 and 90% and acceptable results were found for AM. The THC and COC tests of the devices showed a still lack of sensitivity [27].

Within the same project and based in the toxicological cut-off as set in DRUID project the performance of the Rapid STAT DrugWipe 5/5+ and Dräger Drug Test 5000 on-site oral fluid devices was evaluated with random OF specimens from car drivers in North Rhine-Westphalia and results of OF and urine on-site tests were compared to serum. The sensitivities obtained showed wide range (50%-95%) THC specificity was especially low, 29% and 47% due to low cut-off concentrations. These data were similar to those obtained from the literature. In DRUID project was evident that OF devices still show a lack of sensitivity for MA and specificity for THC. The sensitivity for THC came out higher than compared to the literature, but specificity was not yet satisfactory (<90%) [28].

DrugWipe5/5+, was evaluated by Finish police. The device performed quite well in detecting AM, but the performance of the THC, OPI and COC tests was not at the same level [29].

Goessaert et al., [30] evaluated the Varian Oralab 6 and collected OF samples from 250 subjects, one with the Varian Oralab6 and one with the StatSure Saliva Sampler. Two cut-off values were used in the evaluation (Varian and DRUID cut-off values).The conclusion was that specificity of the Oralab 6 is generally good. For both cut-offs, sensitivity was low for COC and THC. As conclusion, the Varian Oralab 6 test was not sensitive enough to be applied during roadside police controls.

Advanced studies have evaluated the efficacy of using IgG concentration, or any other endogenous marker, as a measure of OF specimen validity. Preliminary rinsing experiments with different volumes of water did not reduce the OF IgG concentration below proposed specimen validity criteria [31].

Recently Roche DAT has marketed another homogeneous screening assay for illegal drugs. Sensibility and specificity were > 94% and agreement was >96% which means a good performance [32].

Research to evaluate applicability of four commercial on-site OF devices was carried out by Stran-Rossi et al to determine sensitivities of COC, THC and AM with different results [33].

Wille et al., [34] evaluated three devices that demonstrated respectively a good sensitivity. For COC screening, sensitivities were lower. One of the devices, the DrugTest 5000 test cassette, a newer version, demonstrated a sensitivity of 93%, indicating an increased detection of THC using new generation OF screening tests with lowered cut-offs.

Cozart DSS 801 device was tested to establish statistical parameters of the tests for THC and COC [35]. The sensitivity, specificity, predictive positive value, predictive negative value, likelihood positive ratio and likelihood negative ratio for COC and THC were calculated. Accuracy was 91% for COC and 86% for THC. OF samples were compared with collected OF and urine samples and performance of two devices established to detect drug use in an investigation of drug impaired driving in a sample of 92 subjects. Overall, 41% of these drivers were confirmed positive for the presence of one or more drugs. The most frequently detected drugs were THC (30%), and COC (10%). The most notable difference in performance was the DDT5000's better sensitivity in detecting marijuana use compared to Affiniton Drugwipe device [36].

In DUID context, a pilot study was developed in the Gauteng and Western Cape provinces (South Africa) to test four substance use screening devices developed in Germany in a sample of motorists, to assess the utility for detecting driving under the influence of drugs as part of the standard road block operations of local law enforcement agencies; 14% of the 269 drivers drug-screened tested positive for drugs. AM, MA and COC were the most common drugs of impairment detected. The results suggest that under normal enforcement procedures only 76% of drivers impaired by alcohol and other drugs would have been detected. One advantage was that in more than 70% of cases the tests were administered within 5min and this is likely to improve with more regular use [37].

A recent evaluation of a second-generation handheld OF testing device, the Alere DDS2 Mobile Test System (DDS2), was probed. Drivers randomly stopped at various locations across California, in 2012, were asked to submit voluntarily to a questionnaire regarding their drug use. OF samples were collected and 50 drivers were asked to submit an additional OF sample using the DDS2 collection device; samples were analyzed by using the DDS2 mobile test system. In 24%, the device failed to provide a valid result. Thirty-two of the 38 collected samples were negative for all drugs; five were positive for THC and one was positive for MA using the mobile device. These results corresponded exactly with the laboratory-based results from the Quantisal OF collection [38].

More specific results of these devices and their performance are not supplied in this review and may be consulted in corresponding published articles.

OF Reports Published In Specialized Literature

In a number of Australian States police services conducted a research to provide the prevalence of drugs driving in a sample of motorists in Queensland. 3.5% of the sample was confirmed positive for al least one illegal substance. THC was the most common drug detected in OF followed by AM [39].

In the same country at least one illicit drug was detected in 96% of drivers in 853 OF samples submitted by Victoria Police. In this sample the most common drug was the MA (77%) followed by THC (42%). COC was detected in 8% of the cases [40].

In Norway, drug use, was examined analysing OF samples. Alcohol or drugs were found in 1.9% and 6.6% of the samples of the truck drivers and car drivers [41]. Prevalence of driving with blood drug concentration above legal limits in blood based on drug concentration in OF was estimated. 3.8% were positive for drugs in OF [42].

In south eastern Norway comparison of drug use in drivers by analyzing OF, by urban and rural areas, was carried out in a roadside survey in 2005-2006. Samples of OF were analyzed for alcohol or drugs, for a total 28 psychoactive substances. Illegal drugs were significantly more frequently detected in samples from drivers in urban areas than in rural areas, The time of the sampling was a variable of importance since the illegal drugs were most commonly found in samples collected during late night on weekdays or weekends (2.8%-3.2%). The most prevalent substance was cannabis THC (1.1%), The prevalence of driving with drug concentrations above the Norwegian legislative limits for blood was estimated to be 0.6 % for illegal drugs [43].

In Denmark, OF samples were collected randomly from 3002 drivers using a sampling scheme stratified by time, season, and road type while 0.3% of the drivers tested positive for one or more illicit drug at concentrations exceeding the Danish legal limit. THC, COC, and AM were the most frequent illicit drugs detected [44].

Another random sample of night drivers in British Columbia indicates that cannabis and COC were also the drugs most frequently detected; 10.4% of 78 samples tested positive for illegal drugs [45]. More data are provided for British Columbia in road survey issues. Beirness et Beasley [46] reported a 31.8% of COC, 11.9% OPI, 4.8% AM and 4.4% MAM in Columbia roadside study of drivers and accounted in 8.3% of all positive drug cases. In Belgium 18% of results COC positives were found in a sample of drivers [47].

In South-East Hungary in the framework of the DRUID EU-6 project, to determine the and the most frequent illicit drug consumption (AM, THC, OPI, COC) a roadside survey was conducted in the population, 3110 drivers; illicit drugs were detected in 27 cases (0.99%). Illicit drug consumption was the highest among young men, during the spring, and on the week-end nights. Authors conclude that In comparison to international European averages, the alcohol and illicit drug consumption was low [48].

According to data reported for Finland among drivers suspected of driving under the influence of drugs, there is a high percentage of licit and/or illicit drug use. The drugs of most concern are AM and AM-type substances, COC, THC, OPI, among other psychoactive drugs [49].

In The Netherlands and Belgium randomly selected car drivers and drivers of small vans were included between 2007 and 2009. Blood and OF samples were analyzed for 23 substances, whereas the single illicit drugs were more common in Dutch traffic (2.2%) than in Belgian traffic (0.6%) [50].

Spain has achieved random, roadside controls of 3302 representative sample of Spanish drivers, including OF analysis for 24 psychoactive substances; 11% were found positive to any illicit drug. The most common illicit drugs among Spanish drivers were THC (7.7%) or COC (3.5%) either alone or combined with other substances. Alcohol and COC positive cases were more frequently found among drivers of urban roads. Alcohol and drugs cases were also more likely found those driving on urban road (OR=2.17) and driving at night time [51].

In our laboratory, in Spain, we carried out a study focused on the study of prevalence of drugs of abuse in a sample population of drivers of motor vehicles. 3468 OF samples came from local police activities, during the years 2007 until June 2010 in Barcelona. After confirmation results showed a cannabis prevalence in 2064 samples (59.5%), COC in 1952 samples (56.2%) opiates in 258 (7.4%) and AMP in 69 samples. Results show that THC was the most prevalent in the study, followed by COC. Data are valuable in order to initiate sanction proceedings in Spanish legislation and also as signs of recreational drugs consumption, which provide information [52]. The prevalence of COC in our study is higher than in other reports ranging between 0.1-8,4%) but in other studies a higher prevalence was found between 10, 2% and 32, 7% [53-58].

Penning et al, in Netherland, report data studies indicating that 1-15% of drivers are under the influence of drugs when driving. Road side studies show the most test positive for the use of alcohol and or THC [59].

In Belgium in paired samples of blood and OF, 2.949 randomly selected drivers participated in a roadside survey Samples were analyzed for 11 illicit substances or metabolites; 28 (1.0%) had drug concentrations above the legal cut-off in blood and 71 (2.6%) were above the legal cut-off in OF [60].

Vindenes et al reported the study of the Norwegian police in a population suspected of driving under the influence of drugs. If drugs detected in blood were found in OF and if interpretation of OPI findings in OF was as conclusive as in urine was investigated. The three matrixes were collected from 100 drivers suspected of drugged driving. The analysis showed a good correlation between the findings in urine and OF for AM, COC/BE, OPI, COC, opiate metabolite, and 6-monoacetylmorphine (6-MAM) were more frequently detected in OF than in urine. Drug concentrations above the cut-off values were found in samples of OF and urine in the cases positive for OPI. The use of cannabis was confirmed by detecting THC in OF and its metabolite THC-COOH in urine. In 34 of 46 cases the use of THC was confirmed both in OF and urine. All the drug groups detected in blood were also found in OF [61].

Brazil and Norway, two different countries regarding legislation history, enforcement and penalties for DRUID, were compared. The proofs were conducted on week-ends between noon and midnight. Samples of OF were collected for analysis of drugs. High participation rates of 94-97% were obtained in both countries. AM or COC were found in samples from 1.0% of drivers in Brazil and 0.3% in Norway. The prevalence of AM was highest among Brazilian truck drivers (3.6%); THC was found in samples from 0.5% of drivers in Brazil and 1.0% in Norway. Differences for drugs may be related to different patterns in the use of stimulants, cannabis and medicines [62].

Among Brazilian drivers, the prevalence of psychoactive drug was investigated as a part of a larger designed project. About 10% of the 2235 OF samples collected from drivers on Brazilian Federal highways were positive) for at least one analyte investigated. Alone or in combination with other drugs, COC/metabolites were the analytes most detected in the samples (5.8%), followed by amphetamines/metabolite (3.1%), THC (1.1%) and OPI (0.4%). Detection of at least two psychoactive drugs from different classes accounted for 9.3% of the 236 positive samples. COC was found at higher levels in the samples (up to 1165ng/m) [63].

In the same country, Brazil, the use of stimulant drugs to avoid fatigue and to maintain the work schedule was also reported. Among 1250 professional drivers OF samples were collected from truck drivers on the roads during morning hours to investigate the incidence of alcohol and illicit drug use among truck drivers on São Paulo state roads between the years 2002 and 2008. The samples were tested for the presence of, COC, THC and AM/MA. Of the total analyzed samples, 3.1 % were positive 0.64 % for AM, 0.56 % for COC, and 0.40 % for THC. In one case, both COC and THC were detected [64].

In San Francisco 175 drivers and 272 passengers were surveyed among young adults. The survey was achieved in music dance events in young adults aged 18-34 who are at high-risk for crashes to locations where alcohol sales are the principal source of revenue. OF samples were analyzed and up to 30% of these attendees may also use drugs. However, there were no differences in the prevalence of drug use among drivers and passengers. These findings suggest that the effort by young adult drivers to avoid alcohol-impaired driving appears to be reducing the number of drivers with high blood alcohol levels returning from drinking locations, by about one third. However, there is no similar pattern for drugged driving [65].

In the United States association between alcohol and drug use is not uncommon among drivers. Until the 2007 the prevalence of drugs among drinking drivers on U.S. roads was unknown by the national Roadside Survey and surveys were conducted on weekend nights from July-November 2007. Of the 8384 eligible motorists contacted, 85.4% provided a breath sample, 70.0%, an OF sample, and 39.1%, a blood sample. The regression analyses were conducted on 5912 participants with a breath test and an OF or blood test. Illegal drugs (COC, THC, street AM, and OPI) were investigated. 10.5% of nondrinking drivers were using illegal drugs and 26% to 33% of drivers with illegal blood alcohol concentration were using drugs [66].

Driving Impairment

There is a coincidence that OF analytes can indicate the state of a subject if presence of drugs is detected, the impairment of their driving ability and a better correlation between presence of drugs in OF and impairment.

Some papers have reported data referent to driving, drug use and impairment. Driving behaviour and perceptions related to the frequency of driving under the influence of THC and COC have been studied by means of a questionnaire administered to people in treatment for abuse of COC or THC. The results indicate that COC and THC have different effects on driving and reduced driving ability was reported for COC as well as recklessness. The negative physical effects of cannabis may reduce the likelihood of driving under the influence of cannabis [67].

Regarding to THC and COC, the most representative drugs found in population in many countries, some considerations are derived referring to impairment in driving. A study dealing with marijuana and driving investigated the drugs and accident risk in fatally injured drivers where THC was the most frequent detected (10%in this study). THC tended to show negative effect on relative risk when other drug groups showed an increase [68]. This phenomenon has also been seen elsewhere [69, 70]. The reason probably relates to the over compensation of marijuana-using drivers on their driving skills, but risk analysis studies to investigate the contribution of drugs to accident causation are limited. Nevertheless recently various national surveys suggest that THC use is rising nationally. This present a problem for traffic security as research suggest that THC impairs driving ability. In California, cannabis involved driving has increased since 2007 [71].

A survey was performed and impairment observed. Urine, serum and in OF samples were collected and analyzed for THC, AM and its derivatives, OPI and COC. Police and medical officer observations of impairment symptoms were rated and evaluated using a threshold value for the classification of driving inability. Impairment symptoms above threshold were observed (81.5%). Of the cases with drugs detected in serum, 19.1% appeared not impaired which were the same with drug-positive OF. More persons with drug-positive urine samples appeared uninfluenced (32.7%). The data demonstrate that OF is superior to urine in correlating with serum analytical data and impairment symptoms of drivers under the influence of drugs of abuse [72].

No impairment on basic driving skills are showed on drivers under COC and AM although risk taking during driving is increased but few studies looked at the effects on driving of illegal drugs and drugs users are not aware of impairment in driving [59]. Our group has studied the concentration of COC and its relationship with clinical symptoms in drivers suspected of drug use. A total of 154 samples of OF, which tested positive for COC in previous immunoassay screening, Cozart Drug Detector System, were confirmed using GC/MS method. In Catalonia, during 2007-2010, there were 1791 samples positive for COC among a total of 3468 samples taken from drivers who tested positive for any drug of abuse. The evaluation of clinical symptoms was through a questionnaire that was filled in by the police officers that collected the samples. The mean concentration of cocaine was 4.11mg/l and median concentration was 0.38 mg/l (range 0.01-345.64 mg/l). Association between concentration and clinical impairment symptoms such as motor coordination, walking, speech, mood and state of pupils were not significant [73].

However, detection of drugs in OF is a sign of recent drug use and impairment. New pharmacokinetic studies have been conducted, optimal cut-offs have been proposed, and new studies have examined the correlation between impairment and OF drug concentrations.

Discussion

Data provided over DUID let know the magnitude of the problem around the world. It has been estimated that the prevalence of illicit drug use among the general driving population in Europe is in the range of 1-5 %. Studies are more frequent in Europe and United States than in other less developed countries. The prevalence of the illegal drugs depends on the countries but in general THC and COC are the most prevalent drugs. In DUID context has been observed that majority of incidence fell into the evening hours and early morning hours of Saturday and Sunday.

Reported articles highlight the utility of OF. The testing of this matrix presents fewer ethical problems than blood or urine and that presence of a drug correlate better with impairment than the presence of drug metabolites in urine. Its utility to be used to detect drivers under the influence is undoubted. As it has been reviewed epidemiological research is often carried out on offend-

ers and drivers involved in collisions.

During the last years, scientific and technological advances in OF collection, point-of-collection testing devices, and screening and confirmation methods were achieved. By optimizing the sampling and the analytical cut-offs, the potential of OF as a confirmation matrix could be enhanced. In general it is considered that the detection of a psychoactive substance in OF taken at the roadside is highly predictive for the detection of the corresponding drug or its metabolite in serum.

Nevertheless literature on proficiency testing to ensure reliability and comparability of results is limited. Although OF testing is now commonplace in many monitoring programs, the greatest current limitation is the scarcity of controlled drug administration studies available to guide interpretation [74]. For that reason is difficult to outline clear conclusions since other variables should be considered. The studies use different devices to collect and test the samples. The tests show different cut-offs, and different sensibility, specificity accuracy and recovery are obtained. Regarding to analytical methods, confirmatory analysis also may differ among different laboratories; methods are developed for laboratories by LC/MS and GC/MS to determine several drugs and are validated according to their specifics conditions, so comparison may be done cautiously. Standardized protocols of sample pretreatment are needed to link the detected concentrations to final conclusions and development of suitable proficiency testing schemes is required. Moreover, time of last administration of drugs, the dose and the route of administration were unknown in many populations. At the same time search is needed on another variable, the detection time and half life time of elimination of drugs in OF with different onsite analysis techniques and sampling. Additional research is needed to identify new biomarkers, determine drug detection windows, characterize OF adulteration techniques, and evaluate analyte's stability. Further more, interpretation of screening of the proofs done by trained personal is not guarantied most of times and errors inter or intraobservators may be was not taken in consideration.

For that reason and despite the steady progress obtained along the time, some more work needs to be done, principally in the areas of the sensitivity and the reliability of on-site screening devices, particularly for cannabis, knowledge about passive contamination and more generalised proficiency testing. A broad scientific knowledge of the many factors involved in determining test outcome must be considered. More recent studies as the discovery of the presence of THC-COOH, metabolite of cannabis in OF, can contribute to solve the issue of false-positive results caused by passive exposure to cannabis. Variables as oral contamination especially for orally consumed drugs must be considered to explain results like MDMA and THC use [75]. Another limitation is that due to large variation seen here, drug findings in OF should not be used to estimate the corresponding concentrations in whole blood (or vice versa).

However, it is important to stand out that the detection of drugs in OF is a sign of recent drug use and OF can be used for qualitative detection of several drugs, in epidemiological prevalence studies.

Related to legal aspects most countries have legislation that covers driving under the influence of alcohol and/or drugs. Some countries have introduced zero-tolerance laws (per se laws), which prohibit the operation of a motor vehicle while an illicit drug or its metabolite is present in the body, whether or not impairment is manifested but only in a few countries legislation allows the use of OF as a matrix for screening or confirmation. In the state of Victoria, Australia, the use of OF for evidentiary testing in the case of THC and MA is allowed [76]. The first legal random drug testing program in OF since 2004 was organized in that state [77]. Derived from ROSITA 2 Project other countries as Finland, Norway and Spain began to consider OF as a matrix to detect drugged drivers.

In Spain, in Catalonia region, police officers are carrying out programs to detect drugged drivers. More than 35000 proofs have been done and results let proofs going on, since OF is considered a proof good enough to detect drugs consumption although no quantitative analysis is being carried out until now. Traffic Legislation fines drivers where qualitative presence of drugs is detected and Spanish court yard and forensic settings are admitting the qualitative results of these proofs.

Guidelines were proposed for workplace OF testing by SHAMSA and DRUID program, and standardization of DRUID research. SHAMSA of OF testing was delayed because questions about drug OF disposition were not yet resolved, and collection device performance and testing assays require improvement.

We have documented the many advances achieved in the use of OF as an alternative matrix that has an important role in DUID, treatment, workplace, and criminal justice programs According to these promising results police officers and judicial experts are keen to use OF for screening of illegal drugs. Their ease of use and diminished amount of false positive results in comparison with urine screening will lead to more roadside tests and more appropriate juridical measures.

A September 2006 meeting of international experts discussed the harmonization of protocols for future research on drugged driving. The principal objective of the meeting was to develop a consensus report setting guidelines, standards, core data variables and other controls that would form the basis for future international research. A modified Delphi method was utilized to develop draft guidelines. The Guidelines Document was divided into three major sections, each focusing upon different aspects of drugged driving research. One of them was roadside surveys, within the critical issue areas of 'behaviour', 'epidemiology' and 'toxicology' providing recommendations in these specific areas. These guidelines improve significantly the overall quality of drugged driving research and facilitate future cross-study comparisons nationally and globally [78].

On the practical aspects of implying a DUID legislation investigation is specially focused on THC screening and quantification since cannabis is one of the most prevalent illegal drugs [79].

In conclusion more publications focus on the usability of OF for this purpose. Laboratory confirmation techniques, OF collection, choice of cut-offs, stability and proficiency testing are important issues influencing interpretation of results of the presence of illegal drugs in OF to detect subjects in DUID context.

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