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Detection of Drugs in Drug Facilitated Sexual Assault (DFSA) Cases Using Onsite Screening Devices: A Forensic Review

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Abstract

Drug Facilitated Sexual Assault (DFSA) has now become the most prevalent crime in the today's scenario. It is an offence in which criminal uses the drug to influence the victim for committing assaults, rape, murder, etc. It is a kind of violent act in which the individual is incapacitated with certain mind altering substances resulting in impairment of victim's ability to respond and prevent her from remembering the assault. A wide variety of Central Nervous System (CNS) depressants namely flunitrazepam or rohypnol, GHB (Gamma Hydroxy Butyric Acid), over the counter and prescription drugs involving benzodiazepines, non benzodiazepines hypnotics and sedatives like zolpidem, zopiclone and other psychotropic substances like ketamine, etc., are introduced secretly into the drinks or food material of the victim without eliciting any noticeable taste or colour change. Since benzodiazepines are most commonly abused in these crimes, much difficulties arise in their detection firstly due to their commercial availability in large numbers and secondly because they get rapidly metabolized into multiple forms.

These cases are therefore remains underestimated and hence not being reported to the police personnel. Detection of these drugs being a serious challenge in the field of toxicology because routine analytical procedures cannot be opted for their analysis hence a highly rapid, sensitive and specific technique for their detection is required. Immunoassay techniques are used widely for detection of these drugs due to their rapidity, flexibility and ability to facilitate a preliminary indication of the presence of a particular drug or an array of drugs in the matrix analyzed. The testing is based on binding of an antibody, specific for a particular drug or a drug group and its label that will be used later as a part of complex formed between antigen and antibody detected by means of some fluorescence. The technique mainly functions on the basis of competitive binding between the antibody and the drug antigen. These can be used onsite for the detection of the drug. This binding between the two depends more on a typical immune response generated when the antibodies in the biological tissues combines with the antigen and neutralize them. In the present paper an attempt has been made to consolidate the information regarding the onsite drug detection devices available for the qualitative detection and identification of drugs.

Keywords: Drug facilitated sexual assault; Detection; Immunoassay techniques; Drugs; Onsite analysis

Introduction

The advancement in the field of forensic toxicology leads to a widespread use of drugs for committing drug facilitated crimes. The most common is Drug Facilitated Sexual Assault (DFSA), an offence in which criminal uses the drug to influence the victim for committing assaults, rape, murder, etc., drug facilitated sexual assault is a kind of violent act in which the individual is incapacitated with certain mind altering substances resulting in impairment of victim's ability to respond and prevent her from remembering the assault [1].

A wide variety of drugs including Central Nervous System (CNS) depressants namely flunitrazepam or rohypnol, GHB (Gamma Hydroxy Butyric Acid), GBL (Gamma Butyrolactone), certain over the counter and prescription drugs involving benzodiazepines, non benzodiazepines hypnotics and sedatives like zolpidem, zopiclone and other psychotropic substances like ketamine, opiates, amphetamines, methamphetamines, cannabisetc are being used for committing such assaults by introducing them either secretly into alcoholic or non-alcoholic beverages, or in food material, without noticeably changing taste or colour or taken voluntarily by the person. The use of these drugs especially of benzodiazepine group is mainly associated with suicidal poisoning [2]. Similarly diclazepam, another potent drug of this class is being used apparently in these crimes and detected in biological samples along with its metabolite lorazepam due to its longer detection window. The half-life of benzodiazepines varies widely depending on the particular drug. For ex alprazolam has an average half-life of 12 h while average half-life of estazolam, flurazepam, quazepam, temazepam and zolpidem is 16, 1, 36, 11, 2.9 and 2.3 h respectively. Since benzodiazepines are most commonly abused, many difficulties arise in their detection firstly due to their commercial availability in large numbers and secondly because they get rapidly metabolized into multiple forms (Table 1) [3].

S. No	Drug	Metabolites detected
1	Alprazolam	4-Hydroxy-alprazolam, α-hydroxy-alprazolam
2	Diazepam	Oxazepam, nor-diazepam
3	Lorazepam	Conjugated with glucuronic acid

4	Clonazepam	7-Aminoclonazepam
5	Triazolam	4-Hydroxy-triazolam α-hydroxy-triazolam
6	Oxazepam	Oxazepam glucuronide
7	Temazepam	Oxazepam
8	Clorazepate	Nor-diazepam which is then further metabolized to oxazepam.
9	Flunitrazepam	7-aminoflunitrazepam
10	Chlordiazepoxide	nor-chlordiazepoxide, which is further metabolized to demoxepam-nor diazepam-oxazepam

Table 1: Major metabolites of commonly abused benzodiazepines.

This problem of DFSA is always misinterpreted and remains hidden and restraining the victim to put forth the complaint of this serious crime to the law enforcement agencies. These cases are therefore underestimated and hence not being reported to the police personnel which causes a delay in the appropriate sample collection and thereby detection of the drug. The routine analytical procedures cannot be opted for the analysis of these drugs so detection of these drugs remains a challenge for the law enforcement agency, hence requires a highly rapid, sensitive and specific technique for their detection [4].

One of the detection devices employed for testing of these drugs works on the principle of immunoassay. Immunoassay techniques are used widely for detection of drugs due to their rapidity, flexibility and ability to facilitate a preliminary indication of the presence of a particular drug or an array of drugs in the matrix analyzed. The testing is based on binding of an antibody which is specific for a particular drug or a drug group and its label that will be used later as a part of complex formed between antigen and antibody detected by means of some fluorescence. The technique mainly functions on the basis of competitive binding between the antibody and the drug antigen. This binding between the two depends more on a typical immune response generated when the antibodies in the biological tissues combines with the antigen and neutralize them. These devices are used only as an initial method for drug screening utilizing either blood or urine or oral fluid as a sample of analysis. The conventional biological matrix employed for testing is blood but due to the short window of detection of the drugs mainly benzodiazepines (48 hours) other matrices including urine and oral fluid, hair are also being used nowadays. Urine is one of the preferred matrices for analysis of benzodiazepine group drugs because of the higher concentration their metabolites. The windows of detection of these substances vary from 1 day to several weeks in urine matrix after consumption of the drug. Unlike, urine, oral fluid matrix is also considered as an optimal matrix of choice for drug monitoring and detection with a detection window between 24 hours-48 hours after drug administration (Figure 1) [5].

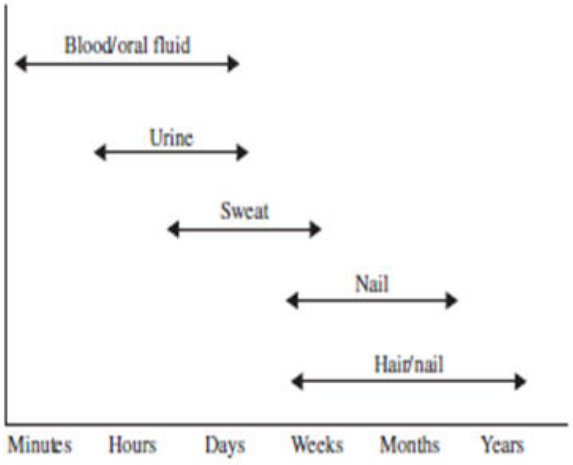

Figure 1: Detection window of drugs in different biological matrices.

Literature Review

These methods of preliminary analysis of drugs in the biological fluids employs automated immunoassay techniques as point of care devices which aids in only qualitative testing of drug or its metabolite. These immunoassay tests are rapid which can be performed with ease and are used by laboratories as a first line screening method for the detection of drugs or metabolites above a certain threshold concentration in the biological matrix (Figure 2) [6].

Molecule	Therapeutic concentrations in the blood (µg/l)	Toxic concentrations in the blood (µg/l)	$T_{1/2}$ (hours)
Alprazolam	5-50	75	12-15
Alimemazine	50-400	>500	6-18
Bromazepam	80-200	300-500	8-19
Cetirizine	250-450	NA	6.5-10
Chlordiazepoxide	400-2 000	5 000	20-40
Clobazam	100-600	NA	10-20 (metab: 50)
Clonazepam	10-80	100-120	19-40
Clotiazepam	10-700	1 000-5 000	4
Diazepam	250-1 500	5 000	20-30
Cyamemazine	50-400	NA	10
Estazolam	55-100	1 000	10-24
Doxylamine	50-400	NA	10
Flunitrazepam	1-15	50	20
Haloperidol	5-40	>500	10-40
Hydroxyzine	50-90	>100	13-27
Loprazolam	5-10	NA	6-23
Lorazepam	20-250	300	12
Lormetazepam	1-25	NA	10
Meprobamate	5 000-20 000	>50 000	6-17
Midazolam	40-100	1 000-1 500	2-3
Nitrazepam	10-180	200-500	20-25
Nordazepam	200-2 000	2 000	65
Oxazepam	200-2 000	3 000	8
Prazepam	10-200	1 000-5 000	metab: 65
Temazepam	20-900	1 000	5-8
Tetrazepam	50-600	6 000	10-26
Triazolam	2-20	200	1.5-3 (metab: 4)
Zolpidem	30-300	500	1.5-4.5
Zopiclone	10-50	150	3.5-6.5

Figure 2: Detection window or half-lives ($T_{1/2}$), therapeutic and toxic concentrations of few benzodiazepines.

These devices although are used widely all over the globe for detection of various drugs abused in DFSA but not adequately screened benzodiazepine group drugs. It poses a limitation in interpretation of the results due to variable immune reactivity of the antibodies which leads to diverse structural differences of the benzodiazepine class of drugs and thereby increases the chances of obtaining false positives and false negatives while screening. Since the drugs are present in low concentration in the sample there must be a specific, sensitive and validated method available for their screening. The method opted can be used on the spot not only for the detection of benzodiazepines and its metabolites but also for determination of their detection limit.

Detection in urine

Urine being an aqueous media is considered as a suitable sample matrix for analysis because collection of such specimens is non-invasive and the detection window for the drug or its metabolite is substantially longer in urine compared to blood. These drugs are available for detection in urine depending onto their metabolic pathway and the route of administration. These drugs after administration either by enteral or parenteral route undergo some degree of metabolism by phase I or phase II reactions involving hydrolysis, oxidation or reduction of the drug which might show certain degree of activity or toxicity. The process of metabolism takes place by one of the major form of enzyme group *i.e.,* the hepatic microsomal cytochrome P450 enzyme system (CYP enzymes) by oxidation. During the metabolism, drug having reactive species of hydroxyl group undergo phase I reaction (a process used mainly for lipophilic drugs). This is followed by phase II reactions in which drugs/metabolites become more polar or water soluble by the addition of glucuronide, acetate or sulphate group. The process of metabolism then leads to excretion of the final products. This enables the excretion of final products of drug metabolism *via* kidneys and their accumulation in urine matrix which in turn may be available for detection for up to several days from the initial drug administration.

Discussion

The drugs and metabolites can be detected in urine up to 2-3 days after lastuse. The most prevalent drug of this class abused nowadays is flunitrazepam, presence of which can be ascertained in the urine sample by immunoassay screening showing a high concentration of its metabolite 7-aminoflunitrazepam as compared with the parent drug itself. Similarly other drug of this class is clonazepam which is more potent in nature than flunitrazepamand has a longer half-life with effects experienced for around 30 to 60 minutes after ingestion and last up to 12 hours that can be screened using immunoassay devices (Table 2) [7].

Drug	Detection window in urine
Amphetamine	2 days
Methamphetamine	2 days
Barbiturates	
Short acting (for example, pentobarbital)	1 day
Long acting (for example, phenobarbital)	21 days
Benzodiazepines	
Short acting (for example, Alprazolam, Lorazepam)	3 days
Long acting (for example, diazepam, etc.)	30 days
Marijuana	2-3 days after single use
(As 11-nor-A-tetrahydrocannabinol- 9-carboxylic acid)	30 days in chronic abuser

	2 days after single use
Cocaine (as benzoylecgonine)	4 days after repeated use
Opiates	
Morphine	2-3 days
Codeine	2 days
Heroin (as morphine)	2 days
Methadone	3 days
Oxycodone	2-4 days
Phencyclidine	14 days
Methaqualone	3 days
Propoxyphene	6 h-2 days

Table 2: Window of detection of various drug of abuse in the urine specimen.

These drugs abused for commission of sexual assaults are commonly detected in urine sample by use of immunoassay techniques. The technique functions on the basis of competitive binding between the antibody and the drug antigen. Sometimes the performance of these devices gets limited due to highly sensitive and specific nature of the technique along with the inability of the antibody and drug antigen.

Drugs of abuse plus TCA

The screening of benzodiazepine group drugs using immunoassay technique in routine practice is done using oxazepamas the antigen. Clonazepam, a drug of this group gets metabolized by the liver to 7-aminoclonazepam and is able to detect in the urine sample for about 14 to 21 days using the oxazepam as antigen. Although a few benzodiazepines do not metabolize to oxazepam (e.g., clonazepam, lorazepam, alprazolam, and triazolam) and hence will not be detected [8].

Although immunoassay techniques are being used nowadays for the qualitative screening of benzodiazepines but the technique does not detect all the known benzodiazepines after 2-3 days due to the typical high detection limits of immunoassay. Also, there are numerous problems associated with the collection of urine sample including adulteration, dilution or falsification of the sample by addition of various adulterants in order to alter the pH or to reduce the drug level by chemical destruction which intervene the screening process. Dilution of urine lowers the concentration of the drug in the sample and hence makes the detection difficult. Many a times false negative results have also been obtained during the onsite screening process due to addition of various substances in the sample as adulterant a few of them are common household products including bleach, concentrated lemon juice, vinegar, table salt, eye drops etc. Hence, the device used for onsite screening of drugs of abuse in cases of drug assisted assaults must have the appropriate sensitivity for its application [9].

Detection in oral fluid

Drugs abused for committing sexual crime can be tested in oral fluid of the victim because of their excretion into saliva in unchanged forms. Oral fluid can be considered as a convenient and promising matrix for testing due to its ease of collection and minimal privacy invasion. Also, the chances of detecting parent drug or its metabolite are more in such a matrix for approximately up to 48 hours after last use. The testing of drug using this sample is a preferred over urine because the concentration of the drug in this is not affected by the use of breath sprays, mouthwash, or other oral rinses containing alcohol if they are not used up to 30 minutes of sample collection.

The detection of drugs in oral fluid is carried out using techniques which involves either spitting directly into the vials or polypropylene tubes or by the use of an absorbent material (cotton roll, plastic pad) by absorption. For collection of an ample amount of saliva and effective stimulation of the sample in the mouth numerous ways can be applied like chewing of paraffin or use of certain chemical stimulants namely citric acid or other. Collection done with utilization of spitting method involves the addition of a preservative or buffer and an indicator to the plastic tube whereas an absorbent pad is placed inside the mouth for few minutes in cases of collection carried out using an absorbent pad.

The latter method of saliva collection, a non-invasive technique sometimes involves the use of a point of care collection device. A device named saliva sampler (stat sure diagnostic systems, Framingham, MA) is one such device consists of an absorptive cellulose pad with a volume adequacy indicator and a plastic tube containing buffer solution. The collection of oral fluid sample involves placing of the collection pad under the tongue after gathering of ample amount of oral fluid inside the mouth and removed when the indicator window has turned completely blue. The window of the stem turns blue when 1 ml of sample is collected. The pad is then placed into the collection tube. In the laboratory, the collection pad is disconnected from the stem and dropped to the bottom of the tube, and a filter is inserted into the tube to recover the of buffer solution. After collection of ample amount of oral fluid it is then proceed for analysis using these immunoassay techniques. A large number of devices are being used with oral fluid as a sample matrix for detection of drugs abused in DFSA cases. Some of them are listed below:

Rapid STAT device: The rapid STAT device comprises a collection stick, an aroma field to increase salivation, a buffer solution and a test strip. It is collected by rotary movements of the microfiber collector stick inside the cheeks and gums. The collection stick is then put into the buffer bottle and agitated before removal. Seven drops of the buffer fluid mixture are pipetted to each well of the test device. The lid is closed to the first position and left for 4 min. The test is started by pressing down the lid completely to let the buffer flow to the test strips. Red control lines indicate a successful test. A positive screening result is indicated by the absence of a red line in the designated positions. The results should be read within 8 min of the buffer flowing; the total time needed for testing is 7-12 min [10].

Drug Wipe 5+/6S device: The drug wipe 5+ device comprises of collector, a detection element, and an integrated liquid ampoule. First, the of collector is detached from the test body. The tongue or the cheek of the tested person is wiped, and the collector is then reattached to the test body. The ampoule is pressed to let the buffer solution flow to the test strips. The results can be read when red control lines indicating a successful test appear on both strips. Positive screening results are indicated by red lines in the designated positions. The total time required for testing is 3 min-10 min.

The drug wipe1 6S device consisted of a sample collector containing 3 small sampling pads, the test cassette and an integrated liquid ampoule. Oral fluid was collected by wiping the sampling pads on the tongue several times until the pads changed colour. The collector was then placed back onto the test cassette, with the pads in contact with the test strips. The device was held vertically; the liquid ampoule was broken by compression and the buffer flowed along the test strips. After 10 the device was placed on a horizontal surface and the results read after 8 min. Result interpretation involves appearance of a visible band which indicates a positive result. (Faint bands were regarded as positive). The device detected the major 4 to 5 group of drugs namely, amphetamines, cannabis, cocaine, opiates and ketamine while the detection of benzodiazepines using this device requires further development and evaluation to increase its sensitivity and accuracy.

Ora check: The ora check device comprised a sampling sponge, a collection chamber and the test cassette. The sponge was placed in the subject's mouth for 3 min (with occasional sweeping motion), during which supposedly 0.5 ml oral fluid would have been collected. The sponge was then firmly pushed into the collection chamber to release the oral fluid. The chamber was inverted and the oral fluid was transferred through the dropper onto the sampling area of the test cassette. After 10 min, results were interpreted; formation of a visible band indicates a negative result. (Faint bands were regarded as negative).

Saliva screen: The saliva screen device consisted of a sampling sponge with volume indicator (1 ml) and a test cassette that extracted the oral fluid and housed the test strips. The subject was first instructed to sweep the sampling sponge inside the oral cavity several times and leave the sponge inside for 7 min (or when the volume indicator turned red, whichever was earlier). The sponge was then pushed into the test cassette to release the oral fluid. The device was left on a flat surface for 10 min, after which results were read. A visible band indicates a negative result. (Faint bands were regarded as negative).

Alere DDS 2 mobile system: The DDS2 device has a collection time of less than 1 min and collect approximately 600 uloforal fluid; with a blue dye indication when adequate amount of oral fluid has been collected. The device system is then checked with positive and negative cartridges and the test cassette is inserted by pushing the pad into the test cartridge that is already in the device. The oral fluid from the pad mixes with the buffer and flows along the test strips in the unit. The mobile test unit analyses five drug classes (THC, cocaine opiates, amphetamine and methamphetamine) within 5 min.

Cozhert drug detection system: This is another device used for the onsite detection of drugs in oral fluid. In the process the oral fluid samples were taken and diluted with CRS buffer (0.05% (w/v) sodium azide, 0.01% (w/v) thiomersal, detergent, and protein] for a 1:3 dilution. The dilution prepared is equivalent to the dilution that would have been obtained along with the kit been used, as is recommended by Cozart. One hundred twenty microliters of the diluted sample was analyzed with CRS following the manufacturer's procedure. The results were obtained by the machine as positive or negative as recorded by the device at a preset cut off 30 pg/l for cocaine or for benzoylecgonine. The CRS instrument software enabled also enables the printing of the instrument response (%) of test band intensity, within 10 minutes [11]. The performance of these devices needs to be evaluated to make it best suitable for particular class drug detection. A table showing the comparative results of the immunoassay devices for detection of drugs in oral fluid matrix based on their performances (Table 3).

Parameters	Onsite drug detection devices				
	Rapid STAT device	**Drug wipe 5+ device/6S device**	**Ora check**	**Saliva screen**	**Alere DDS2 mobile system**
Principle	Lateral flow immunoassay	Lateral flow immunoassay	Lateral flow immunoassay	Lateral flow immunoassay	Lateral flow immunoassay
Sample matrix	Oral fluid	Oral fluid	Oral fluid	Oral fluid	Oral fluid
Sample volume	-	-	0.5 ml	1 ml	600 ul
Detection methodology	A positive screening result is indicated by the absence of a red line in the designated positions	Positive screening results are indicated by red	Positive screening is indicated by absence of visible bands.	Positive screening is indicated by absence of visible band	Cut off concentration are shown onto the device screen

Group of drugs detected	Amphetamines, cocaine, Opiates, cannabis, benzodiazepines	Amphetamines, cocaine, opiates and cannabis by drug wipe 5+ ketamine, cannabis, cocaine, opiates and amphetamines by drug wipe 6S	Amphetamines, cocaine, opiates and cannabis	Ketamine, methamphetamine, cannabis, cocaine, MDMA and opiates	Five drug classes: THC, cocaine, opiates, amphetamine and methamphetamine
Detection time	7-12 mins	3-10 mins	10 mins	More than 15 mins	5 mins
Sensitivity	Moderate	Varied more than 80% with opiates and MDMA and highly sensitive for THC	Relatively low	Showed highest sensitivity for detection of ketamine, >80 %, for detection of cocaine and for opiates and methamphetamines and 0% for THC and cannabis	Very low sensitivity
Performance	Requires more evaluation	High, specificity rate above 90% with drug wipe 5+ and with an increased improvement in sensitivity for cannabis detection by drug wipe 6S device shows a specificity of 99%.	Not satisfactory test completion rate is only 52%	Satisfactory test completion rate is 78%	Satisfactory test completion rate 76%, requires further research)

Table 3: Showing a comparative study of onsite screening devices.

The performance of onsite drug screening devices in oral fluid was variable. Out of these devices some showed satisfactory results and detected major drug classes *i.e.,* amphetamine, methamphetamine, opiates, marijuana and cocaine but does not distinguish the drugs within a particular class (*i.e.,* it cannot distinguish between various amphetamines, barbiturates, benzodiazepines, or opiates). These immunoassay techniques are not considered suitable for the analysis of benzodiazepine drugs as none of them detected all the drugs of benzodiazepine group with equal sensitivity and thereby resulted in false positive results [12].

Evidence multi stat analyzer for detection of benzodiazepines

All the interpretation of the evidence related with drug facilitated crimes are crucial therefore the expert or the forensic scientist with his basic knowledge, skill and expertise in the field, should be competent to analyze and interpret the evidence associated with such type of crimes and use such a technology for analysis which is user friendly, rapid, sensitive and specific for drugs abused [13]. As the detection technique chosen for the analysis must include a highly sensitive and rapid method one device namely evidence multi stat analyzer works on the principle of Biochip Array Technology (BAT), an immunoassay based methodology elicit a highly specific response of a large number of drugs abused for committing such crimes. The technology comprises of a solid state device containing an array of discrete test regions possessing certain immobilized antibodies which are specific to different drugs of abuse according to their class. The principle of competitive chemiluminescent immunoassay is employed for the drugs of abuse assays, in which the drug present in the sample and the drug labelled with Horseradish Peroxidase (HRP) show a direct competition for the antibody binding sites. If the amount of the drug present in the sample is more, more it will bind to antibodies region and it leads to reduced binding of drug labelled with HRP and thus a reduction in chemiluminescence being emitted. The light signal generated from each of the test regions on the biochip is detectred using digital imaging technology and compared to that from the cut off material. The number of test analyte present in the sample is determined from the cut off material [14-19].

Conclusion

This device can be considered favorable for the testing of drugs of abuse in drug facilitated sexual crimes as the machine is able to detect some of the metabolites also along with the parent drug in some of the cases. Determination of the limit of detection of such unique metabolites in the sample run will enhance the value of the result. As it's the known fact that the evidence (biological sample from the victim mainly) encountered in these cases being crucial in nature and hence cannot be detected using routine analytical toxicology procedures and therefore requires a highly selective, appropriate, validated method for the detection of drugs and their metabolites in such samples on the spot using devices of high sensitivity. These immunoassay techniques available for onsite detection of drugs in DFSA cases are therefore must be thoroughly evaluated and properly validated for successful identification of benzodiazepine drugs.

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