Point of Care Diagnostics

DIPSCAN 10 PLUS

with extra opiates

(AMP, BUP, BZD, COC, MET, MTD, OPI, OXY, TRA, THC)

MULTI DRUG SCREEN TEST

INTENDED USE

Dipscan 10 Plus is an immunochromatography based one step in vitro test. It is designed for qualitative determination of drug substances in human urine specimens. This assay may be used in the point of care setting. Below is a list of drug groups and their cut-off concentrations used in this test:-

AMP	Amphetamines	300 ng/ml of d-amphetamine
BZD	Benzodiazepines	200 ng/ml of oxazepam
BUP	Buprenorphine	10 ng/ml of Buprenorphine-3-β-d-glucoronide
COC	Cocaine	300 ng/ml of benzoylecgonine
MTD	Methadone	300 ng/ml of methadone
MET	Methamphetamines	300 ng/ml of (+)methamphetamine
OPI	Opiates	300 ng/ml of morphine
OXY	Oxycodone	100 ng/ml of oxycodone
THC	Cannabinoid (THC)	50 ng/ml of 11-nor-^{9}-THC-9-COOH
TRA	Tramadol	200 ng/ml of Tramadol

NB. ***Dipscan 10 Plus*** is set to the AS/NZS 4308 Australian/New Zealand Standards cut-off levels for AMP, BZD, COC, MET, OPI, THC. Cut-off levels for BUP, MTD, OXY, TRA are not specified in the Standards.

TEST PROCEDURE

1. Collect at least 50ml of urine.
2. Remove the test card from sealed foil pouch.
3. Remove the protective cap and place the revealed strips into the urine sample.
4. Hold there until the urine is seen to visibly migrate up each of the ten test windows. Do not allow the urine to touch the plastic section of the device.
5. Remove from the urine, replace the cap and place the test on a flat dry surface.
6. Read the results at 5-8 minutes after adding the sample. *Do not interpret the result after 10 minutes.*

INTERPRETATION OF RESULTS

Negative:

The appearance of a line next to the Control "C" and Test "T" indicates a negative result. The negative result does not indicate the absence of drug in the specimen; it only indicates the level of tested drug in the specimen is less than the cut-off level. Please note that the colour intensity of Test "T" lines can vary.

Positive:

The appearance of a line next to the Control "C" and the absence of a line next to the Test "T" indicates a positive result. This is an indication the level of tested drug(s) in the specimen is above the cut-off level.

Invalid:

The absence of a line in the Control "C" arean is an invalid result. Retest the sample with a new device. Follow the test procedure closely.

PRINCIPLE

Each component strip of ***Dipscan 10 Plus*** is based on the principle of specific immunochemical reaction between antibodies and antigen to analyze particular compound in human urine specimen. The assay relies on the competition for binding antibody. When drug is present in the urine specimen, it competes with drug conjugate for the limited amount of antibody-dye conjugate. When the amount of drug is equal or more than the cut-off, it will prevent the binding of drug conjugate to the antibody. Therefore, a positive urine specimen will not show a coloured band on the test line zone, indicating a positive result, while the presence of a coloured band indicates a negative result.

A control line is present in the test window to work as procedural control. This coloured band should always appear on the control line zone if the test device is stored in good condition and the test is performed appropriately. The Control line serves to validate the results.

STORAGE AND STABILITY

The test device should be stored at 2 to 30°C and will be effective until the expiration date stated on the package. The product is humidity-sensitive and should be used immediately after being open.

PRECAUTIONS

1. For in vitro diagnostic and forensic use only.
2. Do not use the product beyond the expiration date.
3. Handle all specimens as potentially infectious.
4. Do not open foil pouch until it is ready to be tested.
5. Use a new urine specimen cup for each sample to avoid cross contamination.

SPECIMEN COLLECTION AND PREPARATION

Samples greater than 50ml are required for this test. Fresh urine does not require any special handling or pretreatment. Specimen should be collected in a clean, dry, plastic or glass container. If the assay is not performed

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immediately, urine specimen may be refrigerated at 2-8 °C or frozen up to 7 days. Specimens should be brought to room temperature before testing. Urine specimens exhibiting a large amount of precipitate or turbidity should be centrifuged or allowed to settle before testing.

QUALITY CONTROL

The control band is an internal reagent and procedural control. It will appear in each of the test's ten windows if the test has been performed correctly and the reagents are reactive.

Control standards can be used to validate reagent performance and establish test reliability. Controls, which are not provided with this test, are commercially available.

DRUG GROUPS TESTED:-

Amphetamines (AMP)

Amphetamines are a class of potent sympathominetic agents with therapeutic applications. The most common amphetamines are d-amphetamine and d,l-amphetamine. Amphetamines are central nervous stimulants that cause the neutrotransmitters epinephrine, norepinephrine and dopamine to be released into the brain and body giving users feelings of euphoria, alertness, and increased energy. Chronic abuse of amphetamines leads to tolerance and drug reinforcement effect. Cardiovascular responses to amphetamine include increased blood pressure and cardiac arrhythmias. More acute responses produce anxiety, paranoia, hallucinations and psychotic behavior. Amphetamines are metabolised by a number of pathways. In general, acid urine promotes excretion whereas alkaline urine retards it. In 24 hours, approximately 79% of the amphetamine dose is excreted in acid urine and about 45% in alkaline urine. Typically, about 20% is excreted as unchanged amphetamine. Unchanged amphetamine can be detected up to 10 days after use.

Benzodiazepines (BZD)

Benzodiazepines are a class of widely prescribed central nervous system depressants which have anxiolytic, hypnotic, anticonvulsant and muscle relaxant effects. Chronic abuse can result in addiction and tardive dyskinnesia. Acute higher doses lead to drowsiness, dizziness, muscle relaxation, lethargy, coma and possible death. The effects of benzodiazepines use last 4 – 8 hours. Many of the benzodiazepines share a common metabolic route, and are excreted as oxazepam and its glucuronide in urine. Oxazepam is detectable in the urine for up to 7 days after drug use.

Buprenorphine (BUP)

A derivative of thebaine, buprenorphine is an opioid that resembles morphine structurally but has a longer duration of action than morphine and can be administrated sublingually as an analgesic. In October 2002, FDA approved the use of a buprenorphine monotherapy product, Subutex, and a buprenorphine/naloxone combination product, Suboxone, for the treatment of opioid addiction. It has been shown that buprenorphine has abuse potential and may itself cause dependency. In addition, a number of deaths have been recorded as a result of overdose with intravenously injected buprenorphine in conjunction with other psychotropic drugs such as benzodiazepines. Buprenorphine is metabolized primarily by n-dealkylation to form glucuronide-buprenorphine and glucuronide-norbuprenorphine.

Cocaine (COC)

Derived from the leaves of cocoa plant, cocaine is a potent central nervous system stimulant as well as a local anesthetic. Some of the psychological effects induced by cocaine are: euphoria, confidence and a sense of increased energy, accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating. Continued ingestion of cocaine could induce tolerances and physiological dependency which leads to its abuse. Cocaine is used by smoking, intravenous, intranasal or oral administration and excreted in the urine primarily as benzoylecgonine in a short period. Benzoylecgonine has a biological half-life of 5 – 8 hours, which is much longer than that of cocaine (0.5 – 1.5 hours), and can be generally detected for 12 – 72 hours after cocaine use or exposure.

Methadone (MTD)

Methadone is a synthetic opioid, clinically available. It is used clinically for the treatment of severe pain and in maintenance programs for morphine and heroine addicts. Methadone acts on the central nervous and cardiovascular systems to produce respiratory and circulatory depression. Methadone also produces miosis and increases the tone of smooth muscle in the lower gastrointestinal tract while decreasing the amplitude of contractions. Acute higher doses induce analgesia, sedation, respiratory depression and coma. After methadone administration, the major urinary excretion products are methadone and its metabolites, EDDP and EMDP. Large individual variations in the urine excretion of methadone are output of methadone from 5-22%. Typically, following a 5 mg oral dose, methadone and EDDP account for 5% of the dose in the 24-hour urine. In those individuals on maintenance therapy, methadone may account for 5 to 50% of the dose in the 24-hour urine and EDDP may account for 3 to 25% of the dose.

Methamphetamine (MET)

Methamphetamine is the most popular synthetic derivative of the amphetamines. It is a potent sympathomimetic agent with therapeutic applications. Acute large doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, reduced appetite, and a sense of increased energy and power. More acute response produces anxiety, paranoia, psychotic behavior, and cardiac dysrhythmias. Methamphetamine is excreted in the urine as amphetamine and oxized and deaminated derivatives. However, 10-40% of methamphetamine is excreted unchanged. Methamphetamine is generally detectable in the urine for 3 to 5 days after use.

Opiate (OPI)

Opioid analgesics comprised of a large group of substances that control pain by depressing the central nervous system. Acute high dose used by abusers or addicts can cause depressed coordination, disrupted decision, decreased respiration, hypothermia and coma. Morphine is excreted unmetabolized and is the marker metabolic product of opiates. Morphine and morphine glucuronide is detectable in urine for several days after opiates dose.

Oxycodone (OXY)

Oxycodone is known as Oxycontin, Roxicodone and is an ingredient of Percodan, Percocet, Roxicet and Tylox. Oxycodone is a semi-synthetic opiate derived from opium. Like other opiates, oxycodone is characterized by its analegestic properties, and the tendency for users to form a physical dependency and develop tolerance with extended use. Oxycodone is usually administered in combination with non-opiate analegesics such as acetaminophen and salicylates for the relief of moderate to severe pain. Oxycodone is a central nervous system depressant that may cause drowsiness, dizziness, lethargy, weakness and confusion. Toxicity in an overdose of oxycodone can lead to stupor, coma, muscle flaccidity, severe respiratory depression, hypotension, and stripiac arrest. Oxycodone is metabolized by N- and O-demethylation. One of the metabolites, oxymorphone, is a potent narcotic analgesic, while the other, noroxycodone, is relatively inactive. Between 33 to 61% of a single dose of oxycodone is excreted in a 24 hour urine collection and consists of 13-19% free oxycodone, 7-29% glucuronide conjugated oxycodone, 13-14% glucuronide conjugated oxymorphone and an unknown amount of noroxycodone. The detection time window of oxycodone is 1-3 days following use.

Marijuana (THC)

The agents of Marijuana that cause various biological effects in humans are called cannabinoid. Cannabinoid is a central nervous stimulant that alters mood and sensory perceptions, produces loss of coordination, impairs short term memory, and produces symptoms of anxiety, paranoia, depression, confusion, hallucination, and increased heart rate. Large doses of cannabinoid could cause the development of tolerances and physiological dependency and lead to abuse. A tolerance to the cardiac and psychotropic effects can occur and withdrawal syndrome produces restlessness, insomnia, anorexia and nausea. Δ^9-THC is the primary active ingredient in cannabinoids. The main metabolite excreted in the urine is 11-nor- Δ^9-THC-9-COOH, which are found within hours of exposure and remain detectable in the urine for 10-30 days after smoking, longer for chronic users.

Tramadol (TRA)

Tramadol is a quasi-narcotic analgesic used in the treatment of moderate to severe pain. It is a synthetic analog of codeine, but has a low binding affinity to the mu-opioid receptors. Large doses of tramadol can develop

tolerance and physiological dependency and lead to its abuse. Tramadol is extensively metabolized after oral administration. Approximately 30% of the dose is excreted in the urine as unchanged drug, whereas 60% is excreted as metabolites. The major pathways appear to be N- and O- demethylation, glucoronidation or sulfation in the liver.

LIMITATION OF PROCEDURE

The assay is designed for use with human urine only. A positive result with any of the tests indicates only the presence of a drug/metabolite and does not indicate or measure intoxication. There is a possibility that technical or procedural error as well other substances in certain foods and medicines may interfere with the test and cause false results. Please refer "SPECIFICITY" section for lists of substances that will produce either positive results, or that do not interfere with test performance. If a drug/metabolite is found present in the urine specimen, the assay does not indicate frequency of drug use or distinguish between drug of abuse and certain foods and medicines.

EXPECTED RESULTS

Dipscan 10 Plus is a qualitative assay. It identifies the drug(s) in human urine at its cut-off concentration or higher. The concentration of the drug(s) can not be determined by this assay. The test is intended to distinguish negative result from presumptive positive result. All positive results must be confirmed using an alternate method, preferably GC/MS as outlined in the AS/NZS 4308 Standards.

PERFORMANCE CHARACTERISTICS

A. Accuracy

The accuracy of the ***Dipscan 10 Plus*** were evaluated in each component strip and in comparison to GC/MS method at the following concentration: d-amphetamine 300ng/ml (AMP), oxazepam, 200 ng/ml (BZD), buprenorphine-3-β-d-glucoronide 10ng/ml (BUP), benzoylecgonine 300ng/ml (COC), methadone 300 ng/ml (MTD), (+)methamphetamine 300ng/ml (MET), morphine 300 ng/ml (OPI), oxycodone 100ng/ml (OXY), 11-nor-Δ^9-THC-9-COOH 50ng/ml (THC), Tramadol 200 ng/ml (TRA). The results of each component strip are listed below:

1. **Amphetamine** The accuracy of the amphetamine test was evaluated in comparison to GC/MS method at a cut-off of 300 ng/ml. Eighty one (81) urine specimens with GC/MS confirmed d-amphetamine concentration were evaluated in this study. The results are summarized and presented below:

Positive % agreement: 92, Negative % agreement: 98

Four specimens were found discrepant between the RapidAMP and the GC/MS method. When compared those data, 50% (2 out of 4) of the discrepancy specimens were found between +25% to –25% of cutoff concentration (225-375).

2. **Benzodiazepine** The accuracy of the benzodiazepine test was evaluated in comparison to GC/MS at a cut-off of 200 ng/ml of oxazepam. Seventy nine (79) urine specimens with GC/MS confirmed oxazepam concentration were evaluated in this study. The results are summarized and presented below:

Positive % agreement: 97, Negative % agreement: 100

One specimen was found discrepant between the RapidBZD and GC/MS method. When compared those data, it was found to be between –25% and +25% cut-off concentration (150-250).

3. **Buprenorphine** The accuracy of the Buprenorphine test was evaluated in comparison to GC/MS at a cut-off of 10 ng/ml of buprenorphine-3-β-d-glucoronide. One hundred and one (101) urine specimens with confirmed buprenorphine-3-β-d-glucoronide concentrations were evaluated in this study. Borderline readings were recorded as negative. The results are summarized and presented below:

Positive % agreement: 96, Negative % agreement: 100.

Two specimens were found discrepant between the RapidBUP and GC/MS method. When compared those data, 50% (1out of 2) of the discrepancy specimens were found between -25% cut-off and cut-off concentration (7.5 – 10 ng/ml).

4. **Cocaine** The accuracy of the cocaine test was evaluated in comparison to GC/MS at a cut-off of 300 ng/ml of benzoylecgonine. Eighty one (81) urine specimens with GC/MS confirmed benzoylecgonine concentration were evaluated in this study. The results are summarized and presented below:

Positive % agreement: 94, Negative % agreement: 100

Two specimens were found discrepant between the RapidCOC and GC/MS method. When compared those data, 100% (2 out of 2) of the discrepancy specimens were found between –25% and +25% cut-off concentration (225 – 375 ng/ml).

5. **Methadone** The accuracy of the methadone test was evaluated in comparison to GC/MS at a cut-off of 300 ng/ml of methadone. One hundred and nineteen urine specimens with confirmed methadone concentrations were evaluated in this study. The results are summarized and presented below:

Positive % agreement: 98.3, Negative % agreement: 98.3.

Two specimens were found discrepant between the RapidMTD and GC/MS method. When compared those data, 100% (2 out of 2) of the discrepancy specimens were found between –25% and +25% cut-off concentration (225 – 375 ng/ml).

6. **Methamphetamine** The accuracy of the methamphetamine test was evaluated in comparison to GC/MS at a cut-off of 300 ng/ml of (+) methamphetamine. Eighty (80) urine specimens with GC/MS confirmed (+) methamphetamine concentration were evaluated in this study. The results are summarized and presented below:

Positive % agreement: 95, Negative % agreement: 100

Two specimens were found discrepant between the RapidMET and GC/MS method. When compared those data, 100% (2 out of 2) of the discrepancy specimens were found between –25% and cut-off concentration (225-375).

7. **Opiate** The accuracy of the opiates test was evaluated in comparison to GC/MS at a cut-off of 300 ng/ml of morphine. One hundred and twenty three urine specimens with GC/MS confirmed morphine and codeine concentrations were evaluated in this study. The results are summarized and presented below:

Positive % agreement: 97.4, Negative % agreement: 91.3

Six specimens were found discrepant between the RapidOPI and GC/MS method. When compared those data, 50% (3 out of 6) of the discrepancy specimens were found between –25% and +25% cut-off concentration (225 – 375 ng/ml).

8. **Oxycodone** The accuracy of the oxycodone test was evaluated in comparison to GC/MS method at a cut-off of 100 ng/ml. One hundred and forty urine specimens with GC/MS confirmed oxycodone concentration were evaluated in this study. The results are summarized and presented below:

Positive % agreement: 100, Negative % agreement: 95

Four specimens were found discrepant between RapidOXY and the GC/MS method. When compared those data, 75% (3 out of 4) of the discrepancy specimens were found between cut-off and +25% of cutoff concentration (100-125 ng/ml).

9. **THC** The accuracy of the THC test was evaluated in comparison to GC/MS at a cut-off of 50 ng/ml of 11-nor-Δ^9-THC-9-COOH. Eighty eight (88) urine specimens with GC/MS confirmed 11-nor-Δ^9-THC-9-COOH concentration were evaluated in this study. The results are summarized and presented below:

Positive % agreement: 95, Negative % agreement: 100

Two specimens were found discrepant between the RapidTHC and GC/MS method. When compared those data, 50% (1 out of 2) of the discrepancy specimens were found between –25% and cut-off concentration (37.5 – 50 ng/ml).

10. **Tramadol** 30 urine samples collected from non-users were tested. All 30 samles were negative at 200 ng/ml cut-off of tramadol. 40 urine tramadol positive samples at a cut-off of 200 ng/ml were tested and all showed positive. Positive % agreement: 100, Negative % agreement: 100.

B. Sensitivity

The cut-off concentrations (sensitivity level) of DOA panel test are determined to be: AMP 300 ng/ml, BZD 200 ng/ml, BUP 10 ng/ml, COC 300 ng/ml, MTD 300 ng/ml, MET 300 ng/ml, OPI 300 ng/ml, OXY 100 ng/ml, THC 50 ng/ml, 200ng/ml of TRA.

C. Precision

The precision of DOA panel tests were determined by conducting the test with spiked controls and interpreted the results by three individuals to verify the random error of visual interpretation. The results of 40 samples each of 50% above and 50% below cut-off specimens are 100% agreed by three observers:

The precision study of was performed by three individuals observing the test result to determine the random error of visual interpretation. The test results were found to have no significant differences between the three observers.

D. Specificity

The specificity for ***Dipscan 10 Plus*** were tested by adding various drugs, drug metabolites, and other compounds that are likely to be present in urine. All compounds were prepared in drug-free normal human urine.

1. Interference testing

Dipscan 10 Plus performance at cut-off level is not affected when pH and Specific Gravity ranges of urine specimen are at 4.5 to 9.0 and 1.005 to 1.035 respectively.

The following substances were tested and confirmed did not interfere with DOA panel tests at the listed concentrations.

Glucose	2000 mg/dl
Human albumin	2000 mg/dl
Human hemoglobin	10 mg/dl
Urea	4000 mg/dl
Uric acid	10 mg/dl

2. Specificity

The following table lists compounds that are detected by ***Dipscan 10 Plus*** which produced positive results when tested at levels equal or greater than the cut-off levels.

Tests	Compounds	Tests	Compounds
Amphetamine	D-Amphetamine D/L-Amphetamine (±)3,4Methylenedioxyamphetamine l-Amphetamine (+)methamphetamine (±)3,4Methylenedioxymethamphetamine	THC	11-nor-Δ^9-THC-9-COOH 11-nor- Δ^8-THC-9-COOH 11-hydroxy- Δ^9-THC Δ^8-Tetrahydrocannabino Δ^9-Tetrahydrocannabinol
Benzodiazepines	Nitrazepam Chloradiazepoxide HCI Clobazam Desmethyldiazepam Oxazepam Temazepam Alprazolam Bromazepam Diazepam Flunitrazepam Lorazepam Clonazepam Flurazepam	Opiate	Morphine Morphine-3--glucuronide Codeine Ethylmorphine Hydromrphone Nalorphine Heroin Hydrocodone Normorphine Norcodeine Naloxone Natrexone Oxycodone
Methamphetamine	(+)Methamphetamine (±)3,4Methylenedioxymethamphetamine d-Amphetamine l-Amphetamine (±)3,4Methylenedioxyamphetamine Chloroquine (-)Ephedrine β-Phenylethylamine Procaine d-Pseudoephedrine Ranitidine	Oxycodone	Oxycodone Dihydrocodeine Codeine Hydromorphone Morphine Acetylmorphine Buprenorphine Ethylmorphine
Cocaine	Benzoylecgonine Cocaine	Buprenorphine	Buprenorphine-3-β-d-glucoronide Buprenorphine
Methadone	Methadone Methadol	Tramadol	N-desmethyl-tramadol O-desmethyl-tramado

The following compounds show no cross-reactivity at concentration up to 100 g/ml unless specified.

Acetaminophen	4-Acetamidophenol	Acetylsalicylic acid	Amikacin	Amitriptyline	Arterenol	Aspartame
Ascorbic acid	Atrophine	Caffeine	Camphor	Chloroquine	Chlopheniramine	Cortisone
Deoxyephedrine	Dextromethorphan	Digitoxin	Digoxin	Diphenhydramine	Ecgonine	
Ecgonine methyl ester	Ephedrine	Epinephrine	Gentisic acid	Guaiacol glycer ester	Histamine	Hydrochlorothiazide
Homatrophine	Ibuprofen	Isoproterenol	Lidocaine	Meperidine	Methaqualon	Methylphenidate
Neomycin	Niacinamide	Perphenazine	Penicillin G	Phenylethylamine-	Phenylpropanolamine	Promethazine
Pseudoephedrine	Quinine antidine	Salicyclic acid	Tetracycline	Tetrahydrozoline	Theophyline	Thioridazine
Trifluoperazine	Tryptophan	Tyramine				

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