MEDICHEM®

DIAGNOSTICA·VERFAHRENSENTWICKLUNG

Hair Reference Materials

- Amphetamines
- Benzodiazepines
- Cannabinoides
- Cocaine
- Ethyl Glucuronide
- Fatty Acid Ethyl Esters
- Hallucinogens
- Opioids
- Substitution Drugs

D Deutsche Version:
www.medichem.de/PDF/HI_D.pdf

F Version française:
www.medichem.de/PDF/HI_F.pdf

About hair analysis

Hair analysis has become a powerful tool for the detection of chronic and past drug consumption and is now a routine technique in forensic toxicology laboratories that offers a wide range of applications.

The advantages of hair over traditional matrices, like urine and blood, are obvious: collection is non-invasive, relatively easy to perform, and in forensic situations it may be achieved under close supervision of law enforcement officers to prevent adulteration or substitution. Most importantly, hair analysis extend the window of drug detection dramatically to weeks, months or even years and provides a historical profile of an individual's exposure to drugs and other substances of interest.

Hair analysis today is an analytical tool not only to investigate retrospectively drug abuse histories in post-mortem toxicology and criminal cases, with outstanding importance for the detection of drug facilitated crimes, but it is also employed in situations in which continuous abstinence is required: Mostly within the bounds of workplace drug testing programs and in the expert assessment of judging driving ability (driving ability assessment), for example by testing for the metabolites ethyl glucuronide (EtG) and fatty acid ethyl esters (FAEEs) to determine previous alcohol intake or to document alcohol abstinence.

Studies comparing hair with other matrices demonstrated the capacity of hair analysis to increase detection rates of drug abuse significantly, in forensic populations as well as in clinic population, for example in transplant patients or pregnant women at both prenatal and postnatal stages. It can generally be assumed, that an objective assessment of exposure to ethanol and other drugs of abuse is essential for early prevention and intervention and that the establishment of hair as a complementary technique in toxicology is a direct result of the success of the matrix in medico-legal cases.

Although the number of analytical methods and tested substances continue to increase, quality control materials with reliable values and homogeneity are not available for the most part and often with concentration levels much higher than the cut-offs proposed by the international Society of Hair Testing (SoHT), the European Workplace Drug Testing Society (EWDTS) and others.

For that reason MEDICHEM started to develop new techniques for the preparation of hair reference materials, with special emphasis on preserving the structural integrity of the hair by avoiding any form of pulverization, which is important for method development and validation, internal quality control and proficiency tests.

Development of Hair Reference Materials for Forensic Toxicology

MEDICHEM's aim is to set a new standard in manufacturing reference materials for hair analysis. Since the homogeneity of solid mixtures is one of the main aspects to be considered for their use as suitable quality assurance standards, particular attention was given to the crucial homogenization process. To reduce the particle sizes without loss of their structural integrity, the donor hairs have been homogenized non-destructively, i.e. without grinding, using a special cutting method developed by MEDICHEM.

This unique method is characterized by the defined length of each hair particle: after cutting the hair fibers, equal segments of 1mm length do remain. This is of vital importance, since hair reference materials, like all solid mixtures, depend on size-based migration patterns, which lead to typical segregation particularly while processing and bottling of larger quantities. This effect (known from popcorn and muesli bags) is the more significant, the more the particles do differ from each other in their sizes: It leads to a concentration of smaller particles in the lower and larger particles in upper areas of the solid mixture. In order to avoid heterogeneity of this kind of reference material effectively, a closely spaced distribution of the particle size inside of a batch is crucial.

Based on this technology, several batches have now been prepared in different ways: by spiking, by incorporation and as authentic samples:

Spiked Hair

Drug-free hair samples from multiple donors have been homogenized thoroughly, divided into equal parts and loaded (fortified) with drugs at a known concentration by precipitation on the hair surface.

- Analytes are extractable easily (most similar to a powdered hair)
- Results are very slightly affected by the effectiveness of the respective extraction procedure
- All preparations were done gravimetrically by stepwise dilution of the same stock solution containing all analytes

Authentic Hair

Authentic hair samples from drug addicts, no further treatment besides cutting and mixing.

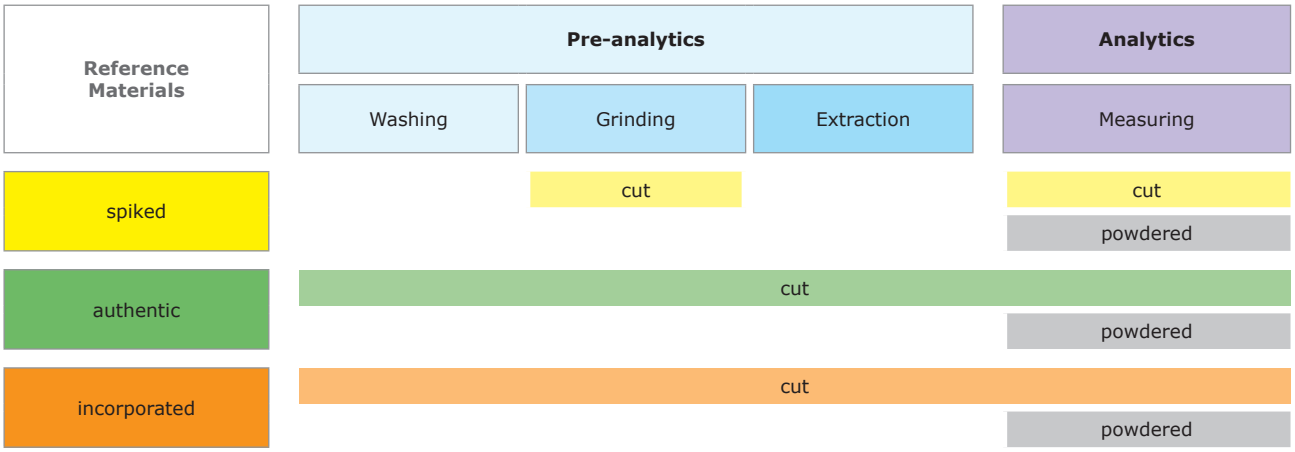
- The extractability of analytes is supposed to be "normal".
- Depending on various and generally unknown factors (e.g. the influence of aging processes, hair care habits and cosmetic treatments on the structural integrity and porosity) authentic hair samples can show large differences regarding the extractability of analytes.

Incorporated Hair

Drug-free hair samples have been altered by incorporating analytes into the hair matrix ("soaked") and washed repeatedly after incorporation to eliminate remaining analytes on the hair surface as well as to reduce the amounts of easily extractable analytes.

- Small amounts of easily extractable analytes due to the specific preparation.
- Efficient extraction procedures are required for analysis.

Application of hair reference materials for quality control



Which Kind of Hair Reference Material provides the best Control of the Analytic Process?

The comparability of a matrix reference material to a patient sample is ideally maximum in order to exclude analytical matrix effects. Admittedly the simulation of the broad variety of matrix characteristics found in potential patient samples must remain incomplete if only a single reference material is used. Also the hair employed for the manufacturing of so called "authentic" reference materials represents more or less a random choice of matrix characteristics which remain mostly unknown.

Beside obvious and easily recognizable cosmetic treatments of hair – such as bleaching or coloration for example – it remains predominantly unexplained how similar or dissimilar an "authentic" sample is to a "typical" patient sample respective to its analytical behavior. Many potential disturbances and affecting values of the hair matrix towards the analytical process - i.e. other substances contained in the hair sample - are not examined sufficiently yet. Before a precise definition of the term "authentic" can be made, it has to be concretized which criteria a sample matrix must verifiably comply with in order to be comparable to a "standard patient sample".

There is a general consensus about the evaluation of hair samples whose analyte concentrations were increased artificially by spiking or incorporation: For these samples as well, a limited comparability with "authentic" samples must be supposed – equally as for urine, serum or whole blood reference materials with artificially raised levels of their analytical compounds. It is therefore generally necessary to consider whether potential limitations are tolerable or not – depending on the analytical problem and its particular requirements (see table on next page).

Characteristics of different hair reference materials and their application for quality control

Application		spiked sample	authentic sample	incorporated sample
Control for washing procedures	cut	not possible due to mainly superficial adsorbtion of analytes	**possible,** if available in sufficient quantity and homogeneity	**possible**, if superficially adsorbed analytes are removed after incorporation - as it is done by MEDICHEM reference materials
	powdered	not possible	not possible	not possible
Control for grinding procedures	cut	**possible**	**possible,** if available in sufficient quantity and homogeneity	**possible**
	powdered	not possible	not possible	not possible
Control for extraction yield	cut	not possible due to mainly superficial adsorbtion of analytes	**possible,** if available in sufficient quantity and homogeneity **but less sensitive than incorporated and washed samples!** [1)]	**possible**, since the analyte is incorporated in the structure of the hair by the special method developed by MEDICHEM [1)]
	powdered	not possible	not possible	not possible
gravimetric value assignment for additional verification of values assigned by analysis		**possible** using the specific method developed by MEDICHEM for gravimetrical doping of cut hair without loss	not possible	not possible

1) Hair samples washed after incorporation contain a minor quantity of easily extractable analytes when compared to unwashed authentic hair samples (depending on the used washing method). The lower the quantity of easy to extract analytes in the sample, the more the extraction yield differs depending on the actual effectiveness of the extraction method and the better variations in the quality of extraction can be discriminated.

Other Matrices: Serum, Whole-blood, Urine and Water

MEDICHEM provides reference material for internal accuracy and precision testing for chemical-toxicological analysis. The product range is completed by calibrators and pure substances.

Precision testing focuses mainly on the longitudinal expansion of the single control test within the quality control batch, i.e. a specific concentration range next to legal or generally applicable boundary values.

Accuracy testing materials are additionally used to review the compliance level of the individual measurement result with the real value of the indicator. The compliance level has to be evaluated trustworthy by a minimum of representative testings with validated, mostly internal standardised and evident methods. Target values determined by gravimetric analysis are verified by independent, accredited forensic laboratories. These analyses are performed by GC/MS and LC/MS(-MS) according to the guideline of the GTFCh (Society of Toxicological and Forensic Chemistry).

We offer reference materials for the following groups of analytes:

- Alcohol consumption
- Barbiturates
- Benzodiazepines
- Drugs of Abuse
- Blank Matrices
- Opioid Substitution Drugs
- Therapeutical Drug Monitoring
- Tranquilizer
- Work Place Drug Testing

For more information please check our website:
→ **www.medichem.de/rm**

MEDICHEM DIAGNOSTICA VERFAHRENSENTWICKLUNG
MEDICHEM Diagnostica GmbH & Co. KG · Kringstr. 3-5 · 71144 Steinenbronn · Germany
Phone +49 7157 53 04-0 · Fax +49 7157 53 04-11 · www.medichem.de · info@medichem.de

Medidrug® Hair Reference Materials

Spiked | Authentic | Incorporated

After an initial quality control the most promising batches were selected as candidate reference materials. The suitability of first batches was confirmed within the bounds of the proficiency tests ethyl glucuronide (EtG) & fatty acid ethyl ester (FAEE) in 2011 and 2012 by the international Society of Hair Testing (SoHT) in cooperation with the BAM Federal Institute for Materials Research and Testing.

These products are going to be available in the second half of the year. For details on availability please refer to the online version of this flyer, available at our website www.medichem.de/hair.

Alcohol biomarkers I *		1/11-C	1/11-B	12-A	12-B	E/12-C	F/12-C	12-D	12-E	12-F
Ethyl glucuronide	pg/mg	12.4	21.6	38.7	68.6	58.0	---	---	---	---
Ethyl myristate	pg/mg	69	252	394	59	---	16	36	63	115
Ethyl oleate	pg/mg	867	1448	1718	398	---	34	160	262	460
Ethyl palmitate	pg/mg	274	517	875	210	---	17	142	243	465
Ethyl stearate	pg/mg	132	99	231	88	---	22	55	77	129
FAEE total	pg/mg	1342	2315	3218	755	---	89	393	645	1169

* determined within the bounds of SoHT proficiency tests in co-operation with BAM Federal Institute for Material Research and Testing

Alcohol biomarkers II **	**EtG**	000	002	004	007	010	020	025	030	040	050	100	200
Ethyl glucuronide	pg/mg	<LOD	2	4	7	10	20	25	30	40	50	100	200

** in co-operation with BAM Federal Institute for Material Research and Testing

Amphetamines		L1	L2	L3	L4
Amphetamine	ng/mg	0.1	0.2	0.5	0.9
MDA	ng/mg	0.1	0.2	0.5	0.9
MDE(A)	ng/mg	0.1	0.2	0.5	1.0
MDMA	ng/mg	0.1	0.2	0.5	1.1
Methamphetamine	ng/mg	0.1	0.2	0.5	1.0

Benzodiazepines		L1
Diazepam	ng/mg	0.05
Norflunitrazepam	ng/mg	0.05
Prazepam	ng/mg	0.05
Alprazolam	ng/mg	0.05
Lorazepam	ng/mg	0.05
Oxazepam	ng/mg	0.08

Cannabinoids I		L1
CBD (Cannabidiol)	ng/mg	0.5
CBN (Cannabinol)	ng/mg	0.5
THC	ng/mg	0.3

Cannabinoids II		L1	L2	L3
THC-COOH	pg/mg	0.2	0.5	10

Cocaine		L1	L2	L3	L4
Anhydroecgonine methylester	ng/mg	---	---	0.12	0.25
Benzoylecgonine	ng/mg	0.2	0.4	0.7	1.4
Cocaethylene	ng/mg	0.2	0.5	0.02	0.04
Cocaine	ng/mg	0.8	1.3	2.5	4.9
EME*	ng/mg	0.06	-	0.2	0.4
Norcocaine	ng/mg	0.4	0.8	0.02	0.05

Opioids		L1	L2	L3
6-MAM	ng/mg	0.1	0.5	1.0
Codeine	ng/mg	0.1	0.5	1.0
Dihydrocodeine	ng/mg	0.1	0.2	0.75
Fentanyl	ng/mg	0.1	0.25	0.5
Morphine	ng/mg	0.15	0.2	1.9
Tramadol	ng/mg	0.5	0.35	0.7

Substitution + Drugs of Abuse		L1	L2	L3	L4
Methadon	ng/mg	0.05	0.1	0.2	0.5
EDDP	ng/mg	0.05	0.1	0.2	0.5
Buprenorphine	ng/mg	0.05	0.1	0.2	0.5
Norbuprenorphine	ng/mg	0.05	0.1	0.2	0.5
Zolpidem	ng/mg	0.04	0.080	0.15	0.4
THC	ng/mg	0.025	0.050	0.1	0.25

IVD

The provided mixture of the controls and their respective analyte concentrations are for overview purposes only and may differ from the current available batches. For the internal quality control, only the designated specification of the respective batch of the information leaflet is valid.

All products conform to IVD Directive 98/79/EC

Certified quality management according to DIN EN ISO 9001:2008
DIN EN ISO 13485:2003 + AC:2007

Contact us:

+ 49 (0)7157 / 5304 - 100

+ 49 (0)7157 / 5304 - 11

info@medichem.de

Medidrug® Hair Reference Materials

Spiked | Authentic | Incorporated

This set of spiked samples should be particularly suitable to assess the method performance with respect to sensitivity and quantification of concentrations above and below the proposed cut-offs. All preparations were done gravimetrically by stepwise dilution of the same stock solution containing all 47 analytes.

These products are going to be available in the second half of the year. For details on availability please refer to the online version of this flyer, available at our website www.medichem.de/hair.

		L 0	L 1	L 2	L 3	L 4	L 5	L 6
Amphetamines								
Methamphetamine	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
Amphetamine	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
MBDB	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
MDA	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
MDE(A)	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
MDMA	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
Benzodiazepines + Z-Drugs								
Alprazolam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
OH-Alprazolam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
7-Aminoclonazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
7-Aminoflunitrazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Bromazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Diazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Flunitrazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Norflunitrazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Lorazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Midazolam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Nordiazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Oxazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Prazepam	ng/mg	<LOD	0.002	0.024	0.06	0.22	0.55	1.1
Cannabinoides								
THC	ng/mg	<LOD	0.012	0.024	0.06	0.11	0.55	1.1
CBD (Cannabidiol)	ng/mg	<LOD	0.024	0.06	0.12	0.22	0.55	1.1
CBN (Cannabinol)	ng/mg	<LOD	0.024	0.06	0.12	0.22	0.55	1.1
THC-COOH	ng/mg	<LOD	0.00012	0.00024	0.0006	0.0011	0.0055	0.011
Cocaine								
Cocaine	ng/mg	<LOD	0.06	0.12	0.6	1.1	5.5	11
Benzoylecgonine	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	5.5
Ecgonine methylester	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	5.5
Anhydroecgonine methylester	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	2.75
Norcocaine	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	2.75
Cocaethylene	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	2.75
Hallucinogen								
Ketamine	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	2.75
Nor-Ketamine	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	2.75
LSD	ng/mg	<LOD	0.006	0.012	0.06	0.11	0.55	1.1
Phencyclidine	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	5.5
Opioides								
Codeine	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
Dihydrocodeine	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
Morphine	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
6-MAM	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
Fentanyl	ng/mg	<LOD	0.006	0.012	0.06	0.11	0.55	1.1
Norfentanyl	ng/mg	<LOD	0.0006	0.006	0.015	0.055	0.138	0.275
Tilidine	ng/mg	<LOD	0.024	0.06	0.12	0.22	0.55	1.1
Tramadol	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	2.75
Hydromorphone	ng/mg	<LOD	0.024	0.06	0.12	0.22	0.55	1.1
Oxymorphone	ng/mg	<LOD	0.024	0.06	0.12	0.22	0.55	1.1
Substitution								
Buprenorphine	ng/mg	<LOD	0.006	0.012	0.06	0.11	0.55	1.1
Norbuprenorphine	ng/mg	<LOD	0.006	0.012	0.06	0.11	0.55	1.1
Methadone	ng/mg	<LOD	0.06	0.12	0.24	0.55	1.1	2.2
EDDP	ng/mg	<LOD	0.024	0.06	0.12	0.55	1.1	5.5

IVD

CE

The provided mixture of the controls and their respective analyte concentrations are for overview purposes only and may differ from the current available batches. For the internal quality control, only the designated specification of the respective batch of the information leaflet is valid.

All products conform to IVD Directive 98/79/EC

Certified quality management according to DIN EN ISO 9001:2008
DIN EN ISO 13485:2003 + AC:2007

Contact us:

+ 49 (0)7157 / 5304 - 100

+ 49 (0)7157 / 5304 - 11

info@medichem.de