Drugs in Hair. Part I. Metabolisms of Major Drug Classes

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ABSTRACT: Currently, hair can be reliably tested for the presence of drugs. However, one major drawback to the use of parent drugs is the question of potential external or environmental contamination. The analysis of metabolites to confirm the use of the parent drugs was proposed in this short review. The development of hair as a test matrix and the incorporation of xenobiotics, in general, into the hair matrix were discussed. What constitutes an appropriate metabolite for drug testing to mirror the use of a parent drug was proposed and discussed. The use of metabolites rather than parent drugs to indicate unequivocal use rather than external exposure was also discussed for amphetamines, cannabinoids, cocaine, opiates (codeine, morphine, 6-acetylmorphine, hydrocodone, hydromorphone, oxycodone, oxymorphone), phencyclidine, fentanyl, benzodiazepines, and ethanol. This, however, was discussed in terms of class and/or individual drug. In addition, selection or potential selection of appropriate metabolites was reviewed. The actual incorporation of drug metabolites into hair versus the metabolism of drugs which was incorporated into hair were also considered.

KEYWORDS: 6-Acetylmorphine, amphetamine, benzodiazepines, benzoylecgonine, bleach, cocaine, codeine, contamination, CYP, ethyl alcohol, ethyl glucuronide, FAEE, fatty acid ethyl ester, fentanyl, glucuronide conjugates, hair, hydrocodone, hydrogen peroxide, hydromorphone, hydroxyamphetamines, hydroxycocaines, 11-hydroxytetrahydrocannabinol, keratin, melanin, metabolism, methamphetamine, methylenedioxyamphetamine, methylenedioxymethamphetamine, morphine, norcodeine, 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid, normorphine, oxycodone, oxymorphone, PCPdiol, pharmacokinetics, phencyclidine, sulfate conjugates, tetrahydrocannabinol, UGT, xenobiotic.

INTRODUCTION

One of the fundamental requirements in clinical and forensic toxicology is to demonstrate the presence or absence of a xenobiotic such as a drug. The mere presence of a controlled substance like benzoylecgonine (BZE) in urine may be sufficient to precipitate discharge from a clinical treatment program or an adverse civil action such as violation of probation. Conversely, the absence of a drug in a patient's random urine may be sufficient grounds to discharge a patient from a clinical rehabilitation program. In addition to their presence in blood/blood products, urine and oral fluid, many drugs and their metabolites are also incorporated in hair; thus they can be detected reliably [171,178]. Thus, hair is a useful matrix for the demonstration of the presence or absence of drugs and/or their metabolites.

Even though the receipt of a final report may be read as absolute, the presence or absence of a substance in toxicology should be linked to a cutoff or limit of detection (LOD) for the report to be forensically or clinically meaningful. An example of hair testing cutoffs taken from the 2004 Proposed Mandatory Guidelines [214] is given below in **Table 1**.

Table 1. 2004 proposed hair testing cutoffs (pg/mg) [214]

Initial Test		Confirmatory Test	
Analyte	**Cutoff**	**Analyte**	**Cutoff**
Marijuana metabolites	1	THCA[a]	0.05
Cocaine metabolites	500	Cocaine	500
		Cocaine metabolites	50
Opiate metabolites	200	Codeine	200
		Morphine	200
		6-Acetylmorphine[b]	200
Phencyclidine	300	Phencyclidine	300
Amphetamines	500	Amphetamine	300
		Methamphetamine[c]	300
MDMA	500	MDMA	300
		MDA	300
		MDEA	300

[a] 11-Nor-Δ^9-tetrahydrocannabinol-9-carboxylic acid.
[b] Specimen must also contain morphine at a concentration greater than or equal to 200 pg/mg.
[c] Specimen must also contain amphetamine at a concentration greater than or equal to 50 pg/mg.

Presence or absence are also toxicologic terms that need to be considered within established timeframes. The whole blood taken from a motor vehicle driver by EMS, 10 minutes post-accident, has an extremely high probability of indicating that the driver was intoxicated by ethyl alcohol if the laboratory result on the whole blood was 0.18 mg/dL [126]. In an entirely different set of circumstances, the finding of cocaine metabolite in an employee's urine using a cutoff of 150 ng/mL [213] cannot be rationalized with a statement such as "I tried some coke in college 5 years ago." For blood and blood products, oral fluid, and urine, other numerous short-term xenobiotic level-timeframe permutations exist. For a timeframe within which an individual may have used a drug, the hair provides a unique "long look-back" or extended window of detection as described below.

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ABOUT THE AUTHOR

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Robert M. White, Sr. received his B.A. in chemistry from Vanderbilt University (Nashville, TN) in 1967 and Ph.D. degree in physical organic chemistry from the University of Florida (Gainesville, FL) in 1972. Dr. White is currently working for the Center for Forensic Sciences, RTI International (Research Triangle Park, NC).

Upon completing his education, Dr. White served two and a half years of active duty in the US Army. After then, he undertook a post-doctoral in clinical chemistry with Dr. John Savory at the University of North Carolina (Chapel Hill, NC). Dr. White has served as the biochemist at Presbyterian Hospital (Charlotte, NC); Director of Life Insurance Testing at SmithKline-BioScience (Nashville, TN); Co-director for Chemistry and Toxicology at Naples Community Hospital and Diagnostic Services (Fort Myers, FL); Blood Bank Director at North American Biologicals, Inc. (Fort Myers, FL); and Health Care Risk Manager for Montgomery Eye Center (Naples, FL). Dr. White was also the scientific director for the Diagnostic Services State of Florida Toxicology Laboratory and Responsible Person for the NLCP-certified laboratory (Fort Myers, FL). Dr. White also served as an Adjunct Professor at Florida Gulf Coast University and Hodges University in Naples/Fort Myers, FL. Dr. White was a full member of the Naples Community Hospital Department of Medicine (Naples, FL). Dr. White has qualified as an expert in toxicology in the criminal, administrative, and civil courts of the State of Florida and Federal Administrative proceedings. Dr. White's major research interests include oral fluid drug testing, biological matrix stabilization for drug testing, urine substitution and adulteration, hair drug testing, and method development.

Dr. White is licensed as a Clinical Laboratory Director in Florida with specialties in Chemistry, Serology/Immunology, and Molecular Pathology. Dr. White is also licensed in the State of Tennessee as a Clinical Laboratory Director and licensed by the State of Florida as a Health Care Risk Manager. Dr. White is a member of the American Chemical Society, the American Association for Clinical Chemistry, the American Academy of Forensic Sciences, and the Society of Forensic Toxicologists. Dr. White is a fellow in the American Board of Forensic Toxicologists and a diplomate to the American Board of Clinical Chemistry in Clinical Chemistry, Toxicological Chemistry, and Molecular Diagnostics.