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Standardization of Forensic Drug Analyses

The subject of standardization of methodology used in the forensic sciences has been a controversial topic studied at length for the past several years. The American Society for Testing and Materials (ASTM) has formed a committee to study standardization of forensic analyses, and the Association of Official Analytical Chemists (AOAC) has sections devoted to forensic sciences and narcotic and dangerous drugs. Members of the legal profession have strongly advocated the use of only "standard" procedures in the examination of evidence for court purposes.

For the purpose of this paper, standard methods may be defined as official or compendia methods, such as those published by AOAC, The Pharmacopeia of the United States of America (USP), and The National Formulary (NF). These methods have been subjected to extensive collaborative studies and have attained quasi-legal status due to the extensive data that support their use. Standard methods have been applied with success to many scientific disciplines in court cases, both for the prosecution and defense. The benefits of such methods are obvious. It is our opinion, however, that the use of standard methods of analysis is not applicable to the field of forensic drug chemistry, and this paper will attempt to explain our position.

Let us first look at the types of samples of drug evidence for which standard methods have been successfully used. Such evidence is collected by Inspectors of the U.S. Food and Drug Administration (FDA) in enforcing the Federal Food, Drug, and Cosmetic (FD&C) Act. The evidence is usually in a bottle or container labeled with the manufacturer's name, active drug components, etc. The composition of the material is known because the product must meet FDA standards or compendia requirements before it can be marketed. The FD&C Act is designed to provide the consumer with a relatively uniform product, and FDA has the responsibility for assuring that marketed products meet the requirements of the Act.

To determine whether or not a drug meets the requirements, it is subjected to physical and chemical tests that have been established to specifically demonstrate that the substance is, or is not, the same as that identified on the label of its container. Since the composition of the material is on file, specific tests, which have been set up for the particular product and subjected to scientific scrutiny, can be used for the examination. Should a substance be present that adversely affects the standardized procedure, then technically the sample is in violation of the Act, even though the correct amount of drug may be present.

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Such a situation is ideal for the use of standard methods. The tests that are used are specific, have been subjected to scientific testing to establish their validity, and are used by both the prosecution and defense so that both parties should readily arrive at the same valid conclusion concerning identity or other physical characteristics of the substance. In summary, areas that could be subjected to scientific debate are minimized as much as possible, and the efficiency of enforcing the statute is enhanced.

One of the definitions of a drug, according to the FD&C Act, is that it be a substance recognized in the official pharmacopeias. To better understand applicability of standardized testing for compendia drug substances, let us examine a brief outline of the types of requirements and tests generally included in a United States Pharmacopeia monograph [*1*]:

Definition, wherein purity limits are included. (These limits relate to the *Assay* results.)

Description

Identification (Usually infrared and ultraviolet spectrophotometry, but often color tests and sometimes chromatographic qualitative tests are performed.)

Solubility

Specific Rotation

Loss on drying (where applicable)

Residue on ignition (where applicable)

Melting (or Boiling) range

Assay

Thus, it can be seen that standards for each substance are clearly defined, and specific identification and assay procedures can be set up and scientifically validated.

A substance not appearing in a pharmacopeia is also recognized as a drug according to the FD&C Act if it is used in the diagnosis, cure, mitigation, treatment, or prevention of disease, or if it is intended to affect the structure or any function of the body. For many of these substances regulatory agencies have set up mechanisms for choosing, validating, and publishing approved and standardized methods of analysis through organizations such as the AOAC. The methods published by the AOAC are subjected to collaborative studies, requiring demonstration of the reliability of the particular method in a number of different laboratories [*2*].

Occasionally, however, chemists of the FDA are faced with unusual exhibits of drug evidence that require them to devise their own analytical system capable of examining, both qualitatively and quantitatively, the ingredients of the sample. Such is the case when criminal charges are brought against distributors of contaminated drugs that are dangerous to public health.

Banes [*3*] cites an example in which isoniazid tablets were contaminated by a substance which caused an estrogenic response in several young females in a California institution for tubercular patients. It was desirable to try to isolate and identify the substance responsible for the estrogenic response. Recognizing that most potent estrogenic substances are phenolic compounds, while isoniazid is nonacidic, a suitable extraction in immiscible solvent systems was accomplished, and the infrared absorption spectrum of the purified substance in a potassium bromide dispersion disk was identical with that of diethylstilbesterol. The ultraviolet absorption spectrum and chromatographic properties of the contaminant also matched those of diethylstilbestrol.

Obviously, no standard method of analysis can be drawn up and subjected to collaborative study for situations such as that described above. The chemist must utilize his

education and experience in adapting many of the various techniques available in the field of analytical chemistry. Moreover, it is to the advantage of the chemist to use several different techniques in order to substantiate his conclusion. This is of great importance because the chemist must be able to prove his conclusion beyond a reasonable doubt in a court of law, should criminal charges be brought against the party responsible for the violation of the statute.

Now let's look at the type of drug evidence submitted by Special Agents of the Bureau of Narcotics and Dangerous Drugs (BNDD) or police department narcotics squad officers. Such evidence is frequently obtained in undercover buys in unmarked containers; it may be a pure drug or may be cut with diluents or excipients. The illicit manufacturer is not a member of the Pharmaceutical Manufacturers Association (PMA), and the illicit distributor, frequently referred to as the pusher, is not concerned with labeling his product. The old statement "Let the Buyer Beware!" is one that every narcotics agent has had ingrained in his brain. "Don't get burned!" "Don't buy Turkey!" These phrases are familiar to those who enforce narcotics laws. As reported by Johnson and Gunn [*4*], Marshman and Gibbons [*5*], and others, the drug user never really knows what he is taking, and potency of the active drug ingredient is one of the primary unknowns. As an example, Johnson and Gunn [*4*] described the cutting of heroin by using playing cards or other haphazard methods to cut in diluents or excipients. As a result of these cutting procedures the heroin potency, as determined by the BNDD laboratories, has been found to vary from close to zero, up to nearly 100 percent. Also described were LSD tablets varying greatly in potency, one source producing tablets varying anywhere from 5 to 248 μg per tablet.

Johnson and Gunn [*4*] also indicated that potency variation is not the only unknown factor in the abuse drug preparations. Identity of the ingredients, both primary and secondary, has been seen to vary widely. By primary we are referring to the main ingredient; the drug is frequently something other than what it is claimed to be. Illustrating this point, in one year 23 percent of all suspected heroin exhibits examined in BNDD laboratories were not heroin. Approximately 2 percent contained no drug substance and 21 percent contained some drug substance other than heroin. These substances included cocaine, methamphetamine, propoxyphene, aspirin, methapyrilene, morphine, methadone, LSD (lysergic acid diethylamide), MDA (3, 4-methylenedioxyamphetamine), PCP (phencyclidine hydrochloride), and beta-(4-hydroxy-4-phenylpiperidino) propiophenone. Often the substitute materials will give similar results when analyzed, that is, false positive screening tests for the drug they are purported to be.

The secondary ingredients to which reference was made are the excipients or other substances with which the primary ingredient is mixed. Heroin is cut with many different materials. Among those materials that have been found to be used for this purpose are starch, lactose, dextrose, brown sugar, talc, quinine, quinidine, procaine, methapyrilene, salicylic acid, phenylpropanolamine, caffeine, ephedrine, mannitol, benzoic acid, boric acid, methamphetamine, and magnesium carbonate.

What may also be classified as a secondary ingredient is the compound that is often added to the drug by the illicit manufacturers to disguise the drug. This is often in the form of a dye and is sometimes added to make an analysis more difficult to perform.

Thus, it can readily be seen that although the forensic drug chemist may be presented with a substance purported to be heroin or any other drug, there is no assurance that heroin will be present. Further, if heroin is present, the potency level and other materials present vary to a great extent.

But what does this all mean to the chemist examining the suspected drug? In short,

because there is a great variance in the type of material being submitted for his examination, it is necessary to use a wide range of methodology in analyzing the material. Where one method of analysis may be suitable in several instances, the same method may give inconclusive results in other situations.

To illustrate some of the problems in conducting a forensic drug analysis, LSD can be used as a typical example. Color tests are routinely used to screen for suspected drugs. These tests, although they are generally not specific for a particular drug, provide the chemist with information that helps to narrow down the investigation to a particular class or group of drugs. For LSD, the color test most frequently used is the test with an acidic solution of p-dimethylaminobenzaldehyde which will produce a blue-purple color in the presence of LSD or other indole compounds. Our laboratories have examined suspected LSD samples that contained blue dye added to the preparation, which, in effect, eliminated the use of the described test. The majority of these dyes can be easily separated from the LSD by utilizing any one of a number of chromatographic procedures; however, the problem in even beginning a *standard* analysis is well illustrated.

To continue with an analysis of LSD the separation or isolation is the most important step as with any of the drugs. Two simple and rapid ways of separating LSD from excipient or diluent materials are by a dry methanolic extraction and by a simple acid-base shakeout with chloroform. Many LSD samples, however, contain materials which interfere with the separation by these methods. In the case of the acid-base shakeout with chloroform, emulsions may form which render the method useless. Our laboratories have received suspected LSD evidence that contained the LSD on ion exchange resins in tablets, capsules, and powder. Simple solvent extractions do not release the LSD; therefore, no positive identification is possible by this method. Suspected LSD exhibits have also been submitted to our laboratories that contain a large amount of dried milk. Not only does the dried milk give a positive color test as described above, but it causes emulsions to form if a liquid-liquid extraction is attempted. In this situation, the chemist will turn to column chromatography as a solution to the problem. A celite column is prepared with citric acid which will remove the impurities and enable a positive identification to be made. In many cases, however, even this technique does not enable the necessary separation to be made, and more complicated separations involving series of columns must be utilized before the LSD becomes separated from the excipient materials.

At this point one might ask, why not utilize the more complicated separation procedure as a standard analysis, thus assuring that all possible interfering substances are removed. The answer is twofold. First, why set a requirement for the more time-consuming procedure if interfering substances are not there; and second, how can there be assurance that an impurity won't be present that will not be removed by the *standard* procedure.

After the suspected LSD finally becomes separated from the impurities, the problem of a positive identification of the LSD must be solved. Many chemists prefer to obtain the infrared spectrum of the material as a positive identifying feature. Few experts would have much problem identifying LSD if the spectrum matches that of an LSD standard. Before establishing infrared spectrophotometry as a standard requirement for the identification of LSD, however, it must be recognized that this method generally requires more than the equivalent of one dose of LSD to prepare a satisfactory dispersion disk. Thus, the suitability of infrared spectrophotometry for the identification of LSD may be questionable if only 1 or 2 dosage units are available for analysis, and frequently only fragments of tablets are submitted for examination. In such situations, more sensitive identification techniques must be used.

The sensitivity problem illustrates the point that the presence of a narcotic or dangerous drug material may not be detectable by a set procedure under certain circumstances, but may be detectable by a different procedure. Lack of detection may also occur due to excipient materials which may mask the presence of the controlled substance in one procedure, but not in another.

The above examples of some of the problems facing the forensic chemist are by no means atypical. Similar problems exist in the analysis of all abused drugs, and each must be handled on an individual basis. The specific examples that have been cited were chosen to point out that standardization of chemical procedures is of value only under controlled circumstances, that is, when dealing with products of known composition or when examining a product to determine whether it meets certain established criteria. When these conditions do not exist, as is the case with drug evidence submitted by BNDD Special Agents and narcotics squad officers of other enforcement agencies, the forensic chemist must be able to use any and all of the techniques available to him. As Sperling [*6*] so aptly stated, "Because of the many problems involved . . . [in forensic drug examinations] . . . the solutions are correspondingly many and varied. There is no one set scheme of analysis that will invariably result in the identification of an unknown drug and there probably will never be. Each sample must be considered separately on an individual basis and a solution devised depending on the particular problems presented by the sample."

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