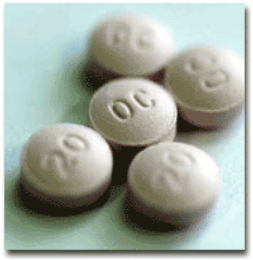
# A Brief Discussion of Pharmacokinetics in Forensic Toxicology



I was retained as an expert in a recent case where, as is common, pharmacokinetic modeling was necessary to answer the questions at hand. Prior to my deposition, I had spent many hours constructing and considering my pharmacokinetic models. I agonized over every assumption that had to be made. Was it fair and unbiased? Was there some reason to select a constant value other than the median of the published range? I dutifully searched the literature for obscure references to bioavailability, absorption rate, half-life, volume of distribution, etc. I calculated the high and low values based on the published ranges of pharmacokinetic constants. In keeping with Daubert, I calculated the potential error of my estimates. In short, I was prepared to answer any questions the opposing attorney or any of their experts could devise. However, when I began my deposition, much to my astonishment, the opposing counsel didn't challenge my credentials or my assumptions or conclusions, he challenged the whole concept of pharmacokinetics and demanded that I supply proof in the literature that such a science even existed! As one of the attorneys that retained me remarked in response, "That is like asking an accident reconstructionist to supply a physics book."

So what is pharmacokinetics? As quoted from the *Journal of the American Medical Association*, "Pharmacokinetics is a science falling under the broader umbrella of the well-established discipline of pharmacology. Pharmacokinetics is concerned with the study and characterization of the time course of drug absorption, distribution, metabolism, and excretion, and with the relationship of these processes to the intensity and time course of therapeutic and adverse effects of drugs. It involves the application of mathematical and biochemical techniques in a physiologic and pharmacologic context."[1]

So what does that all mean? Well, in short, pharmacokinetics is the study of what the body does to drugs. It mathematically describes the absorption, distribution, metabolism and excretion of drugs that are taken into the body. A competent forensic toxicologist can use these mathematical parameters to model the time course of drug concentration in the body and thus make predictions of a drug's concentration at any time, based on a known dosing regimen, or even calculate backwards or forwards from an analytically known concentration.

Pharmacokinetics is not the creation of forensic toxicologists; pharmacokinetic calculations are routinely used in pharmacology to determine proper dosing regimens for individual patients. These calculations rely primarily on two simple equations, a few pharmacological constants, and a few variables, such as the weight of the patient, dosing regimen, or the desired drug concentration. The validity of these two equations has been proven over and over, as evidenced by the literally hundreds of pharmacology texts and peer-reviewed scientific literature that make use of them. In fact, these equations are so well-established that they are typically discussed in the first chapter or chapters of pharmacology textbooks as basic information prior to proceeding to other matters.

While these equations are used by clinicians in determining dosing regimens or explaining various pharmacological events, the utility of these equations is not limited to that application. Since these are algebraic equations, one can also solve for any unknown variables as long as enough of the other variables or pharmacological constants are known. These pharmacological constants are derived from controlled clinical studies that are conducted before a drug is placed on the market, and often these constants are further proven or more accurately determined by studies after the drug reaches the marketplace. While referred to as "constants", these values are only truly constant in a given individual. Therefore, when one consults the literature for these values they are often given as a range of values gleaned from various studies of the population. Therefore, the trained toxicologist must make some assumptions as to what value or values to use. The potential error in pharmacokinetic calculations caused by these assumptions can be estimated by the application of basic statistics.

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As opposed to clinicians, whom often have a full set of clinical parameters such as dosing regimen, etc. in which to employ their pharmacokinetic models, forensic toxicologists, as a rule, are operating in much the reverse fashion; forensic toxicologists are often working from an analytically derived drug concentration and are trying to determine a potential dosing history or a drug concentration at a previous time. This is, in major part, due to the circumstances in which forensic toxicologists find themselves, that is, either trying to determine these values in the absence of dosing information brought about by fifth amendment protections of a defendant, an individual's fabrication of his or her dosing, or the fact that the individual in question is deceased and thus can provide no dosing information.

Probably the most familiar use of pharmacokinetic modeling in forensic toxicology is the back-extrapolation of blood alcohol values. This concept has been admitted in the courts on countless occasions. The primary difference in the use of pharmacokinetics in blood alcohol calculations and its use in calculations for other drugs is that blood alcohol adheres to a slightly different elimination equation.

In summary, pharmacokinetic modeling is a well-established and vital tool to the forensic toxicologist. Properly applied by the knowledgeable expert, pharmacokinetic modeling is invaluable to the interpretation of many otherwise complicated toxicological cases.

I have considerable experience in the proper application of pharmacokinetic modeling. If I can assist you in interpreting your case involving illegal drugs, alcohol or pharmaceutical products, please give me a call or send an Email.

1. Gibaldi M, Levy G: Pharmacokinetics in clinical practice. JAMA 235:1864-1867, 1976

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