



Selected References Dealing with Absorption, Distribution, Metabolism and Excretion of Ethanol in Humans

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Introduction

The acronym ADME is easily recognized by pharmacists, pharmacologists and toxicologists and hopefully also by members of IACT, because it stands for Absorption, Distribution, Metabolism and Excretion of drugs in the body.

In short, ADME is what the body does to an administered drug and is therefore synonymous with the term pharmacokinetics. The latter word, however, is derived from two Greek words *pharmakon* meaning a drug or poison and *kinesis*, which refers to movement or motion, hence the path taken by a drug or poison in the body.

IACT members need to know a lot about the disposition and fate of ethanol in the body, because they are often required to testify in court as expert witnesses or write affidavits and opinions, and/or give a deposition in criminal cases involving DUI or DWI. A common request is to perform so-called Widmark calculations (named after Erik MP Widmark, 1889-1945, a Swedish pioneer in forensic alcohol research). These calculations might entail back-extrapolating a person's blood- or breath-alcohol concentration (BAC or BrAC) from the time of sampling to the time of driving, which sometimes is several hours earlier. Another common request is to calculate the amount of alcohol (grams) absorbed and distributed in all body fluids and tissues based on the measured BAC or BrAC.

Sometimes the aim of a Widmark calculation is to estimate a person's BAC or BrAC from information gleaned about the amounts of alcohol consumed (number of drinks, drinking pattern and dose of ethanol). The outcome of this particular calculation is more uncertain because accurate information about the types of drinks consumed, their ethanol content, the volume of each drink etc., is often lacking. Another problem with making a prospective estimate of BAC or BrAC is that the bioavailability of orally ingested ethanol is rarely 100 percent. Indeed, under some circumstances, such as when alcohol is consumed together with or immediately after a large meal, the bioavailability might be as low as 50 percent. There are various reasons for this, such as an appreciable first-pass metabolism as the portal venous blood passes through the liver, or oxidation of ethanol already in the stomach by enzymes (alcohol dehydrogenase) located in the gastric mucosa. A third explanation is that some of the ethanol molecules bind to constituents of the diet, such as the amino acids and fails to reach the systemic blood circulation. All these issues are tightly linked to the physiological processes that govern ADME of ethanol.

The best advice I can give IACT members whenever they are required to write expert statements about the ADME of ethanol or testify in court as expert witnesses is to read and know the relevant published research articles on this topic. Many law firms in all 50 US states specialize in defending drinking drivers and some of the attorneys, in my opinion, are very knowledgeable and well-informed about the disposition and fate of ethanol in the body. Moreover, many DUI defense lawyers belong to professional organizations that arrange seminars

and training classes about the science and law of drunken driving. Invited speakers to these meetings discuss various pitfalls with forensic alcohol testing in an attempt to raise a reasonable doubt and to challenge the prosecution evidence. People attending these DUI or DUID seminars obtain copies of research articles and are given examples of model questions to ask prosecution experts about ethanol ADME during cross-examination.

The present contribution to the IACT newsletter contains over 350 literature citations to journal articles dealing with various aspects of ethanol ADME in humans. These represent a small fraction of the thousands of papers I have collected during my career spanning over 40 years. Many of the older articles have been scanned into pdf files and newer ones were obtained directly in electronic (pdf) format by downloading them from websites and/or homepages of the publisher of the respective journals.

In selecting the articles in my list, I have mainly focused on experimental studies published in English language journals with a peer-review of the manuscript prior to publication. Accordingly, I did not include book chapters or encyclopedia entries, because in my experience these are not subjected to the same rigorous peer review as journal articles. Another source of highly relevant information about ethanol ADME is the German language journal *Blutalkohol* (Blood Alcohol), which recently celebrated 50 years of scientific publishing. However, I have purposely omitted these from this compilation because they are less useful to IACT members, owing to the language barrier.

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How to obtain articles

The above compilation of literature references can be used in various ways. I suggest first and foremost that the accuracy of the citation is verified by use of PUBMED (www.ncbi.nlm.nih.gov/pubmed). The best way to do this is to enter the name of one of the authors of the article along with the year of publication e.g. for the last reference in the above list, one would enter Zelner I and 2013. This would retrieve all articles in the database by a person with a family name of Zelner and first initial I published in the year 2013. Sometimes PUBMED contains an abstract of the article and also a list of related references, which are also useful to review. Note however that not all scientific journals are included in the PUBMED database. The pdfs of many scientific articles can be found by an appropriate search of Google or Google Scholar by entering the title of the article and ending with ext:pdf. This will hopefully locate a pdf file if one is available on the internet.

Another information resource to consider using is ResearchGate (www.researchgate.net), which is a fairly recent database of scientific publications and the authors are encouraged to upload electronic versions of their articles. Access

to ResearchGate is gratis and pdf files of articles, if they exist, can then be downloaded for individual usage. So I strongly recommend that IACT members consider joining ResearchGate as a source of research articles.

Most of the articles listed have appeared in relatively few scientific journals, mainly those specializing in analytical toxicology, forensic science, legal medicine, and alcohol and addiction research. Electronic copies of the more recent articles (since about 1995) are available as pdf files if electronic versions of the journals are held by university or medical school libraries. For articles published prior to 1995 there is often no alternative but to visit the library and make a photocopy. However, some of the larger publishing houses (e.g. Elsevier, Springer, and Wiley) have scanned in all back issues of their most prominent journals (e.g. *BMJ*, *JAMA*, *Lancet*, *Nature*, or *NEJM*). This means that an article published in the 1800s is available to purchase and download as a pdf file.

Alternative ways to categorize references

The citations included in this bibliography are listed alphabetically after the name of the first author. They could have been listed according to the journal where the research work was published (e.g. *JAT*, *JFS*, *FSI* etc.) or chronologically by the year the article appeared in print. An even more useful compilation might have been to categorize the references into certain sub-groups according to the subject matter or the scientific question addressed. Examples of various sub-categories include drug-alcohol interactions (e.g., histamine-2-antagonists), the effects of gender on ADME, beverage type (beer, spirits, wine),

obesity (body mass index), having food in the stomach before drinking etc., etc. Such a classification by research topic will be published in an upcoming issue of the IACT newsletter in which I focus attention on my own contributions to knowledge about the ADME of ethanol in humans.

One of our colleagues, Jim Wigmore (Toronto, Canada), a veritable collector of scientific articles has accumulated thousands of papers spanning the entire subject of forensic alcohol toxicology. Jim keeps these articles in folders (ring binders) and he arranges them in alphabetical order by the name of the first author, as done with the present compilation. However, Jim has gone one step further and includes a summary of the main findings/conclusions from the research and the individual articles are searchable via a bibliographic database program called ENDNOTE (Thomson Reuters, endnote.com). More recently, Jim has produced a book entitled *Wigmore on Alcohol – Courtroom Alcohol Toxicology for the Medico-legal Professional* (Irwin Law, Inc. Toronto, 2011). The articles in Jim's book are arranged under various sub-headings and/or subject categories covering the typical sort of questions that arise in court testimony about ADME of ethanol and the impairment effects on performance and behavior. Moreover, the publisher also issues occasional electronic updates to the list of articles included in Jim's book.

I hope that IACT members find the information in this article of interest and that it will prove to be useful in their future casework and expert testimony.