



SCIENTIFIC ADVISOR

Morris Faiman Ph.D. (<http://pharmacy.ku.edu/morris-faiman>) is Professor Emeritus of Pharmacology and Toxicology at the University Of Kansas School Of Pharmacy in Lawrence, Kansas. Dr. Faiman received his Master's Degree and Ph.D. from the University of Minnesota. He conducts research at the Life Span Institute where he is a recognized leader in the fields of Pharmaceutical Chemistry and Pharmacology. His research program is focused on studies on the mechanism of action of agents used in the treatment of alcohol abuse and the studies of the mechanism by which alcohol can become addictive. His laboratory has been carrying out studies investigating the mechanism of action of disulfiram for the treatment of alcohol and other substance use disorders for some 35 years. The focus of the research has been to 1. Identify the various metabolites formed during disulfiram's bioactivation, 2. Identify that disulfiram is a prodrug, and that the metabolite of disulfiram which inhibits ALDH2 is S-methyl N, N-diethylthiocarbamate sulfoxide, 3. Understand their role in disulfiram's mechanism of action, and 4. To determine the effect of some key metabolites on CNS neurotransmitters. His laboratory has now identified and synthesized most of the metabolite intermediates formed from the bioactivation of disulfiram and determined the effect of carbamathione on dopamine, GABA, and glutamate in the nucleus accumbens and prefrontal cortex.

Dr. Faiman is a member of The American Society for Pharmacology and Experimental Therapeutics, The Society of Toxicology, American Association for the Advancement of Science Research Society on Alcoholism, American Association of Pharmaceutical Scientists and the International Society for Biomedical Research on Alcoholism. He is the recipient of numerous awards and honors, served as an Editorial Reviewer for the leading journals in his field of research, was a member of many Committees that conducted ad hoc NIH study sections focused on toxicology and pharmacology, as well as for AIDS and other related diseases. Amongst Dr. Faiman's accomplishments, he has received numerous grants from the National Institute of Health.

Dr. Faiman has authored a vast number of scientific articles, some of which are listed below;

1. Yourick, J.J. and Faiman, M.D., "Disulfiram Metabolism as a Requirement for the Inhibition of Rat Liver Mitochondrial Low Km Aldehyde Dehydrogenase." *Biochem. Pharmacol.* 42:1361-1366, 1991.
2. Hart, B.W. and Faiman, M.D., "In Vitro and In Vivo Inhibition of Rat Liver Aldehyde Dehydrogenase by S-Methyl N,N-Diethylthiocarbamate Sulfoxide, A New Metabolite of Disulfiram." *Biochem. Pharmacol* 43: 403-406, 1992.
3. Madan, A, Parkinson, A., and Faiman, M.D., "Identification of the Human and Rat P450 Enzymes Responsible for Sulfoxidation of S-Methyl N,N-Diethylthiocarbamate (DETC-Me), the Terminal Step in the Bioactivation of Disulfiram". *Drug Metabolism and Disposition* (23: 1153-1162, 1995).
4. Faiman MD, Kaul S, Latif SA, Williams TD, Lunte CE. S-(N, N-Diethylcarbamoyl)glutathione (Carbamathione), a Disulfiram Metabolite and its Effect on Nucleus Accumbens and Prefrontal Cortex Dopamine, GABA, and Glutamate: a Microdialysis Study, *Neuropharmacology*. 2013 75: 95-105, 2013.
5. Yourick, J.J. and Faiman, M.D., "Comparative Aspects of Disulfiram and its Metabolites in the Disulfiram-Ethanol Reaction in the Rat." *Biochem. Pharmacol.* 38:413-421, 1989.1,2,3,4
6. Hart, B.W. and Faiman, M.D., "In Vitro and In Vivo Inhibition of Rat Liver Aldehyde Dehydrogenase by S-Methyl N,N-Diethylthiocarbamate Sulfoxide, A New Metabolite of Disulfiram." *Biochem. Pharmacol* 43: 403-406, 1992.

7. Hart, B.W. and Faiman, M.D., "Bioactivation of S-Methyl N,N-Diethylthiolcarbamate to S-Methyl N,N-Diethylthiolcarbamate Sulfoxide: Implications for the Role of Cytochrome P450." *Biochem. Pharmacol.* 46:2285-2290, 1993.
8. Madan, A., Parkinson, A., and Faiman, M.D., "Role of Flavin-Dependent Monooxygenases and Cytochrome P450 Enzymes in the Sulfoxidation of S-Methyl N,N-Diethylthiolcarbamate." *Biochem. Pharmacol.* 46:2291-2297, 1993.5,6,7,8
9. Hart, B.W. and Faiman, M.D., "In Vivo Pharmacodynamic Studies of the Disulfiram Metabolite S-Methyl N, N-Diethylthiolcarbamate Sulfoxide. Inhibition of Liver Aldehyde Dehydrogenase." *Alcohol. Clin. Exp. Res.* 18:340-345, 1994.
10. Madan, A. and Faiman, M.D., "Diethyldithiocarbamate Methyl Ester Sulfoxide, n An Inhibitor of Rat Liver Mitochondrial Low Km Aldehyde Dehydrogenase and Putative Metabolite of Disulfiram." *Alcohol Clin. Exp. Res.* 18:1013-1017, 1994.
11. Madan, A., Williams, T.D., and Faiman, M.D., "Glutathione and Glutathione S-Transferase-Dependent-Oxidative Desulfuration of the Thione Xenobiotic, Diethyldithiocarbamate Methyl Ester (DDTC-Me)". *Mol. Pharmacol* 46: 1217-1225, 1994.
12. Madan, A. and Faiman M.D., "Characterization of Diethyldithiocarbamate Methyl Ester Sulfine as an Intermediate in the Bioactivation of Disulfiram". *J. Pharmacol Exp Ther* 272: 775-780, 1995. 9,10,11,12
13. Madan, A, Parkinson, A., and Faiman, M.D., "Identification of the Human and Rat P450 Enzymes Responsible for Sulfoxidation of S-Methyl N,N-Diethylthiolcarbamate (DETC-Me), the Terminal Step in the Bioactivation of Disulfiram". *Drug Metabolism and Disposition* (23: 1153-1162, 1995).
14. Nagendra, S.N., Faiman, M.D., Davis, K., Wu, J-Y, Newby, X., and Schloss, J.V., "Carbamoylation of Brain Glutamate Receptors by a Disulfiram Metabolite", *J. Biol. Chem.* 272: 24247-24251, 1997
15. Kaul S, Williams TD, Lunte CE, Faiman MD, LC-MS/MS Determination of Carbamathione in Microdialysis Samples from Rat Brain and Plasma, *J Pharm Biomed Anal.* 2010, 51:186-91. 2009.
16. Heemskerk AA, van Haandel L, Woods JM, McCance-Katz EF, Williams TD, Stobaugh JF, Faiman MD, LC-MS/MS method for the determination of carbamathione in human plasma, *J Pharm Biomed Anal.* 2011 54:799-806. 2010.
17. Faiman MD, Kaul S, Latif SA, Williams TD, Lunte CE. S-(N, N-Diethylcarbamoyl)glutathione (Carbamathione), a Disulfiram Metabolite and its Effect on Nucleus Accumbens and Prefrontal Cortex Dopamine, GABA, and Glutamate: a Microdialysis Study, *Neuropharmacology.* 2013 75: 95-105, 2013.
18. McCance-Katz EF, Gruber VA, Beatty G, Lum P, Ma Q, DiFrancesco R, Hochreiter J, Wallace PK, Faiman MD, Morse GD, Interaction of Disulfiram with Antiretroviral Medications: Efavirenz Increases while Atazanavir Decreases Disulfiram Effect on Enzymes of Alcohol Metabolism., *Am J Addict.* 2014 23:137-144, 2013.
19. Winefield RD, Heemskerk AA, Kaul S, Williams TD, Caspers MJ, Prinszano TE, McCance-Katz EF, Lunte CE, Faiman MD. N-acetyl-S-(N,N-diethylcarbamoyl) Cysteine in Rat Nucleus Accumbens, Medial Prefrontal Cortex, and in Rat and Human Plasma after Disulfiram Administration., *J Pharm Biomed Anal.* 2015 25: 518-525, 2015.