

ToxTalk

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» » » Happy Holidays to All!

REGULAR FEATURES

- President's Message
- Elmer Gordon Open Forum
 - Career Opportunities
 - Professional Calendar
 - Journal Club
- Toxichem + Krimtech (Xylazine)

NEW DRUGS

- 2 Zaleplon (Sonata®) (D. Anderson)
- Oxcarbazepine (Trileptyl®) (J. Ropero-Miller)

SOFT 2002 DETROIT AREA!!

Hyatt Regency, Dearborn, MI

October 13-17, 2002

ToxTalk is mailed quarterly (bulk mail) to members of the Society of Forensic Toxicologists, Inc. It is each member's responsibility to report changes of address to the SOFT mailing address (Mesa, AZ - above). Non-members may now receive ToxTalk for \$15 per calendar year. Make your check payable to SOFT and mail it directly to the ToxTalk Editor.

DEADLINES: Feb. 1, May 1, Aug. 1, and Nov. 1.

NEXT DEADLINE: FEBRUARY 1, 2002

PRESIDENT'S MESSAGE by Mick Smith, Ph.D.

Not unexpectedly many of the good accomplishments this year were overshadowed by the terrorist attack on our country on September 11, 2001. I'm going to be no different than the media by focusing on this attack first. As I discussed at the business meeting in New Orleans during our annual meeting, many of us wonder what we can do as forensic toxicologists to help our country. I will provide some facts and let each of you make the connection to possible helpful actions.

Fact 1: Over 80% of the world's heroin is produced from opium grown in Afghanistan. For Europe the amount is over 90%. It is estimated that the Taliban made \$15 to \$24 million annually in the past from taxes on the only trade and used much of this money to buy arms. Al Qaeda made an unknown amount of money providing protection for transport and distribution of opium. Beginning September 11 the price of crude opium on the world market began dropping rapidly from \$700/kg to less than 1/10 this amount.

Fact 2: Quoting Michael Elliot, "We Will Not Fail", Time, Oct 1, 2001: Fighting terrorism as outlined by the President "is a fight in which the forensic processes of the criminal justice system promises to be augmented by the thud

and thump of military action." I know many of you are already involved in this forensic process.

Fact 3: When asked if troops were ready for combat, a Defense Department source stated "Our troops are well trained and drug-free. We are ready." An effective drug testing program certainly preceded this observation. I also think this statement could have been made by any number of CEO's regarding an effective workforce that is needed in these tough economic times.

I will only mention in passing our expertise in chemical toxins used as weapons and move on to more pleasant subjects, the outstanding accomplishments for this past year. The annual meeting in New Orleans was a tremendous success. Kudos to Pat Pizzo and her crew for the incredible planning and scientific content. Kudos also for Tim Rohrig, Guest Editor, Christine Moore, Adam Negrusz, & Lance Presley, Associate Editors, for the SOFT Special Issue of the Journal of Analytical Toxicology. Tinsley Preston, Publisher, and Julie Weber-Roark, Managing Editor, have kept this tradition alive and we continue to thank them for one of our premier educational products. Your Board this year attacked a number of issues from ethics to education. I want to personally thank them for making my job easier. My thanks to Joe Monforte for ToxTalk and for stimulating philosophical conversations. We should all pass on our thanks to Bruce Goldberger for his hard work in keeping the website active and one of our best information sources.

The President's last letter is necessarily filled with thanks because so many members helped in so many ways. It is easy to forget those who have helped so much and so often that we take their contribution for granted. I don't want to forget someone very important to me, so I especially thank my wife, Marilyn Huestis. I have had the good fortune to have a past president giving me advice on tough issues. This has also been a tough year in general and Marilyn has given me a lot of needed emotional support. Thanks, Beautiful Lady.

The best to all of you. . .

SOFT / AAFS Forensic Laboratory Guidelines - Proposed 2002 Revision

Submitted by Graham R. Jones. Ph.D., DABFT, Chairman, Joint SOFT/AAFS Forensic Toxicology Guidelines Committee

The original SOFT/AAFS Guidelines were approved by the SOFT and AAFS Toxicology Section membership when they were introduced in 1991. In 1997, the Guidelines were redrafted to include both the main Guidelines document and the material originally published as the Appendix, and again in 2000 to re-format in "point style", in order to make individual sections in the document easier to refer to.

However, the practice of forensic toxicology has progressed a great deal since the original document was first published, and very few substantive changes have been made to the Guidelines since that time. Therefore, over the past year, the Guidelines Committee has drafted several changes to reflect the enhanced practice of forensic toxicology since 1991. This draft document is available for review as an Adobe PDF file on the SOFT web site (http://www.soft-tox.org). There is an index to the changes on the first page of the document, with hypertext links to each affected paragraph. Deletions are indicated by "strikeout" text, and additions by yellow highlighting. Paragraph numbering will be updated once changes to the text have been approved.

For those who do not have Internet access, or for whatever other reason are unable to view the draft Guidelines, a copy may be obtained from the committee Chairman, Dr. Graham Jones, Office of the Chief Medical Examiner, 7007 -116 Street, Edmonton, Alberta, Canada T6H 5R8; phone 780-427-4987; fax 780-422-1265; e-mail: graham, jones@gov.ab.ca. Comments and suggestions are welcome. It is hoped that the new Guidelines can be adopted by AAFS Toxicology Section members at the business meeting in Atlanta, February 2002, and by SOFT members at the

business meeting in Detroit, October 2002.

SOCIETY OF FORENSIC TOXICOLOGISTS 2002 ANNUAL MEETING

DEARBORN, MICHIGAN OCTOBER 13-17, 2002

PRELIMINARY INFORMATION

Plan now to attend the 2002 Annual Meeting of the Society of Forensic Toxicologists at the beautiful Hyatt Regency in Dearborn, Michigan conveniently located between the Metropolitan Wayne County Airport and Downtown Detroit. The meeting will feature workshops on Sunday and Monday and scientific sessions Tuesday through Thursday. Many special events will be featured including a gala President's reception Wednesday evening at the Henry Ford Museum. Additional information on the meeting will be available from the SOFT website and in future issues of ToxTalk. Abstract forms and registration materials will be available in the March issue of ToxTalk and from the SOFT website. We look forward to seeing you in Southeast Michigan for the 2002 Fall Foliage Season!

Bradford Hepler, PhD Meeting Co-Host Bhepler@co.wayne.mi.us

Daniel Isenschmid, PhD Meeting Co-Host Disensch@co.wayne.mi.us Amanda Jenkins, PhD Program Chair cccotox@inetmail.att.net

Visit the SOFT Web-site at www.soft-tox.org

Visit the new SOFT web-site at www.soft-tox.org and get the latest information on items of interest to SOFT members. Web Master Bruce Goldberger welcomes comments.

To gain access to SOFT's on-line membership directory and drugs and driving pages, you must type the username: drugs and password: #cocaine!

CALL FOR CASE NOTES

We need your contribution! This need not take much time.

Your case note should be about 1/2 page in length, no more than a full page.

Material and/or a disk (arial font, size 10, Microsoft Word 6.0 preferred) may be submitted to:

Joseph R. Monforte, Ph.D., DABFT, **ToxTalk** Editor **e-mail: DrMonforte@aol.com**42408 N. Sombrero Rd., Cave Creek, AZ 85331-2821
Or fax: 480-595-MONF (6663). PLEASE remember that Arizona is hours behind the East Coast.

Other items of interest to SOFT members are also welcome.

Pay your SOFT annual dues before January 1st and avoid the late fee

NEW DRUGS

Oxcarbazepine (Trileptyl®)

Submitted by: Jeri D. Ropero-Miller, Ruth Winecker and Matthew Lambing Office of the Chief Med Exam, Chapel Hill, No.

Structure:

10,11-D lhydro-10,11-trans-dihydroxycarbam azepine

Manufacturer: Novartis Pharma AG; Basel, Switzerland

FDA Status: January 14, 2000 for treatment adjunctive and monotherapy in adults and adjunctive

therapy for children ages 4-16 with partial epileptic seizures.

Available in 150, 300, and 600 mg tablets and as an oral suspension of 300 mg/5 mL (60 mg/mL).

CAS registry number: 28721-07-5

Chemical Name: 10,11-Dihydro-10-oxo-5H-dibenz[b,f]azepine-5-carboxamide

Molecular Formula: C₁₅H₁₃N₂O₂

Molecular Weight: 252.29

Therapeutic Category: Anticonvulsant or antiepileptic drug (AED). The exact mechanism by which oxcarbazepine exerts its antiseizure activity is unknown. However, it is believed that it produces a blockage of voltage-sensitive sodium channels, resulting in stabilization of hyperexcited neural membranes, inhibition of repetitive neural firing, and diminution of propagation of synaptic impulses.

Metabolism: Cytosolic enzymes rapidly reduce oxcarbazepine to its active metabolite, 10-monohydroxycarbazepine (MHD) in the liver. MHD is further metabolized by conjugation with glucuronic acid. Oxcarbazepine is also oxidized to a minor (<4% of dose) inactive metabolite, 10,11-dihydro-10,11-trans-dihydroxycarbamazepine (DHD).

Bio-availability: Based on MHD concentrations following administration of Trileptyl[®] tablets or suspension, both the parent and active metabolite have similar bio-availability.

Protein Binding: MHD-40% (predominantly albumin).

Volume of Distribution: 49 L

Half-Life (Ty): Oxcarbazepine- 2 hours

MHD- 9 hours

Therapeutic Serum Concentration: 4-9 mg/L

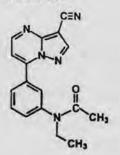
Specimen Preparation: Oxcarbazepine (weak acid/neutral) and its active metabolite, MHD, can be extracted from specimens using solid-support, liquid-liquid extraction utilizing Varian Chem Elut extraction columns followed by derivatization with MTBSTFA with 1% TBDMCS.

Analysis: Oxcarbazepine and MHD can be analyzed using gas chromatography coupled with flame ionization detection (GC/FID) and/or gas chromatography/mass spectrometry (GC/MS). With GC/FID, MHD (RRT 1.03) elutes directly after the chosen internal standard, p-methylphenobarbital and oxcarbazepine follows (RRT 1.16). GC/MS quantification ions include 323, 266, and 423 m/z for oxcarbazepine and 211, 193, and 311 m/z for MHD. Underivatized oxcarbazepine ions include 180, 209, 252, 151 m/z. The inactive metabolite, DHD, can not be analyzed by this methodology because of gas chromatographic degradation.

Zalepion (Sonata®)

Submitted by Daniel Anderson, Los Angeles County Department of the Coroner

Structure:



Manufacturer: Wyeth-Ayerst Laboratories

FDA Status: August 13, 1999 - Approved as schedule IV

CAS registry No.: Unknown

Chemical Name: N-[3-(3-cyanopyrazol [1,5-alpyrimidin-7-yl]-N-ethylacetamide

Molecular formula: C₁₇H₁₄N₅O Molecular weight: 304

TherapeuticCategory: Short acting, rapid onset hypnotic for insomnia

Bio-availability: 30%

Volume of

Distribution (V_d): 1.3 L/kg Dose: 10 mg Half-Life (T_{1/2}): 1.1 hours

Extraction Information:

Liquid/Liquid chlorobutane extraction:

A single step liquid/liquid extraction from a basic solution will work, however, it CANNOT be back extracted into an acidic layer.

Behaves somewhat like a basic drug, however extracts more like a low dose benzodiazepine

Preliminary method: Liquid/Liquid extraction along with solid phase

2-ml sample size (Prazepam as internal standard)

2-ml of 20% sodium carbonate, 5-ml toluene-Rotate 20 minutes, Centrifuge, Decant

Solid phase extraction utilizing a pure silica column

Prep columns with methanol and toluene

Pour on sample

· Wash with toluene, chloroform and hexane

Elute with acetonitrile:methanol (60:40)

Evaporate, reconstitute with methanol

Instrumentation:

GC/NPD:

Oven program: 140-300°C 0.50 min initial hold, 10°C/min ramp,

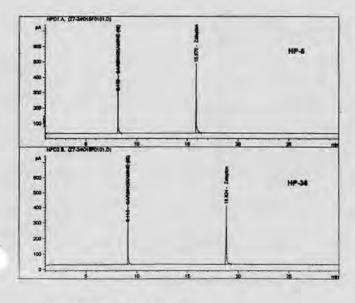
10.5 min final hold, total analysis time 27 min. HP-5 & HP-35 (15m x 0.25 um x 0.25 i.d)

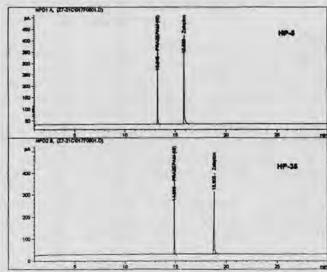
Columns: HP-5 & H
Limit of Detection: 5 ng/ml

Limit of Quantitation: 10 ng/ml

Linearity: At least up to 1000 ng/ml

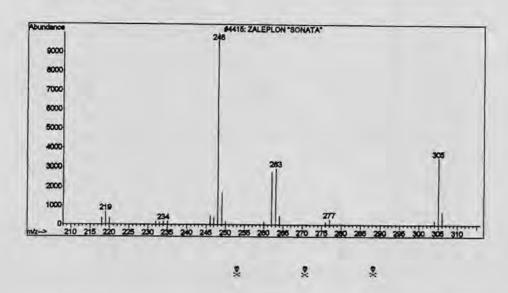
Chromatograms: Carbinoxamine vs. Prazepam as Internal standards





GC/MS:

lons 248, 305 263, 262



"NEW DRUGS" FEATURE

Submit information on new drugs relative to forensic toxicology to:

Daniel Anderson, M.S.

L.A. County Coroner's Dept., 1104 N. Mission Road, Los Angeles, CA 90033

E-mail: danderso@co.la.ca.us Ph: 323-343-0530

Toxichem + Krimtech (2000) 68(1):27

Submitted by Donald Kippenberger, Ph.D.

TOXIC EFFECTS OF THE VETERINARY TRANQUILIZER XYLAZINE IN MAN U. Hoffman', C.M. Meister², M. Zschiesche¹, K. Golle²

Xylazine (Rompun®, Proxylaz®), a veterinary tranquilizer, is extensively used for sedation, analgesia, or general anesthesia either alone or in combination with other drugs in animals. It has a similar chemical structure and pharmacological properties as the α_2 -andrenergic agonist clonidin. Because of the relatively small therapeutic index, xylazine is a hazardous drug in humans. Intoxications are rare but can lead to collapse or death due to circulatory and respiratory depression.

A 27-year-old farmer attempted to commit suicide by intramuscular injection of about 1.5 g of Xylazine. He was found somnolent with narrow pupils and no response to light and pain stimuli. The patient received gastric lavage and activated charcoal. On admission to the hospital he was comatose, became apnoeic and was placed on a respirator.

Drug screening by gas and thin layer chromatography revealed xylazine in gastric fluid, plasma and urine. Plasma samples were collected for a period of 12 h after ingestion and analyzed by HPLC. The data were fitted by a one compartment model and the plasma half life calculated was $t_{1/2}$ = 4.9 h. The concentrations of xylazine measured two hours after intoxication were 4.6 mg/L in plasma, 446 mg/L in gastric fluid and 194 mg/L in urine. The plasma concentrations were consistent with a fatal overdose. The elimination half life was markedly increased in comparison with the half life found in animals varying (30 – 60 min.). We recommend the need for an awareness of xylazine in humans, especially because of its widespread use in veterinary medicine.

- 1 Institute of Pharmacology, Ernst Moritz Arndt University, F-Loeffler-Str. 23 d, 17487 Greifswald
- 2 Department of Anesthesiology, Central Hospital, Demmin

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2 2 2

Chip Walls and Editor Monforte are working on a new "The Journal Club" format for the next issue of ToxTalk.

ELMER GORDON OPEN FORUM AN OPPORTUNITY FOR INFORMAL DIALOGUE

Send items for this section to Editor Joseph Monforte: E-mail DrMonforte@aol.com or fax to 480-595-6663.

27-year-old Tim Lewis is experiencing extremely difficult physical challenges. Send your words of encouragement and best wishes to Mark and Carol Lewis at Markblewis@aol.com.

The new edition of Clarke's Isolation and Identification of Drugs in Pharmaceuticals, Body Fluids and Post-mortem Material is due for publication in 2002 and will include some 400+ new drug monographs plus several new chapters. While compiling the new drug monographs the editors have identified a number of substances where they have been unable to find mass spectra, IR and UV data and are seeking some assistance from SOFT members with respect to obtaining data relating to MS, UV or IR for a number of the new compounds. If any of our members are interested in assisting with gathering data or would be willing to run samples to obtain UV, MS or IR data, please contact Dr David Osselton at e-mail address "osselmd@aol.com"

This **ToxTalk** will either be late or early. I am having shoulder surgery on 12/03 and hope to get this issue out before that date, but . . . Grateful thanks to those special SO-SOFT ladies who helped make enjoying the New Orleans meeting possible for me. Pat Monforte

Attending the AAFS meeting? Capitol Vial is offering a tour, including transportation and lunch, to their site in Auburn, AL, on Feb. 13th. Contact Ed Bennett at 1-800-832-0737. Limited to 20-25.

Attention camera buffs! Have you got some great shots from SOFT meetings? Start looking through those old boxes. More information in the next issue of **ToxTalk**.

CAREER OPPORTUNITIES

Positions available are listed for the consideration of SOFT members. There is no fee for this service. The information will be repeated in the next issue only if the person who submitted it confirms the information. If you have a job position available, FAX (480-595-6663) or E-MAIL (DrMonforte@aol.com) to ToxTalk or mail to the address below.

Employment opportunities are also listed on the SOFT website. For more information, go to www.soft-tox.org

PROFESSIONAL CALENDAR

SOFT MEETINGS: 2002 - Detroit, MI - Dan Isenschmid /Brad Hepler October 13-17, 2002

2003 - Portland, OR - Kent Johnson

2004 - Washington, D.C. - Marc LeBeau

R F Borkenstein Course on Drugs - "The Effects of Drugs on Human Performance and Behavior" course: March 24-27, 2002, Indiana University, Bloomington, IN. Contact dlindsay@indiana.edu

R F Borkenstein Course on Alcohol, Drugs and Highway Safety: Testing, Research and Litigation: May 2002. Contact dlindsay@indiana.edu

International Association Of Forensic Sciences: September 2-7, 2002, Montpellier, France. Information by e-mail: algosi@mnet.fr

All members and others are encouraged to contribute to ToxTalk.

Please mail your contribution to:

Joseph R. Monforte, Ph.D., DABFT, ToxTalk Editor

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11/19/01 Pat