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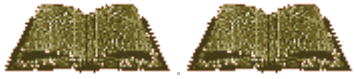
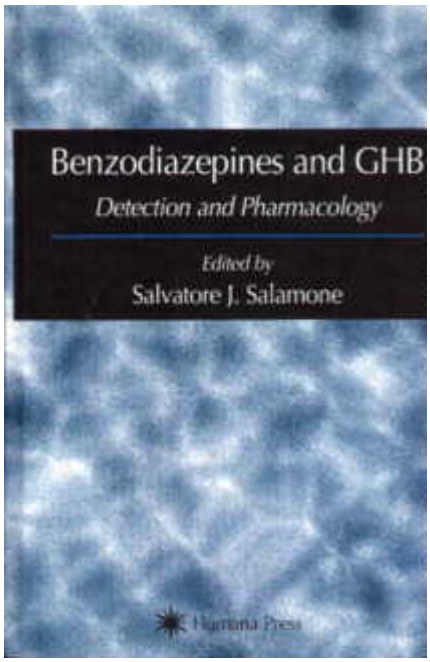
 (N.B. Please increase your screen resolution to 1600 x 1200 dpi or more, for best viewing)

OTHER REVIEWS IN THIS ISSUE
[Technical Books Section] Pages: |1| 2| 3| 4| 5| 6| 7| 8| 9| 10| 11| 12| 13| 14| 15| 16| 17| 18| 19| 20| 21| 22| 23|
[Popular Books Section] Pages: |1| 2| 3| 4| 5| 6| 7| 8| 9|
[Animated Reviews] Pages: |1| [Software/Multimedia] Pages: |1|2|
REVIEWS IN THE PREVIOUS ISSUE | NEXT ISSUE

ALL ABOUT PHARMACOLOGY AND DETECTION OF GHB AND BENZODIAZEPINES

Benzodiazepines and GHB: Detection and Pharmacology, 1st Edition *edited by* Salvatore J. Salamone,

(A Book from *Forensic Science and Medicine* Series by Humana Press)
Humana Press Inc., 999 Riverview Drive, Suite 208, Totowa, New Jersey 07512; xii + 148 pages pages: ISBN 0-89603-981-1 (alk. Paper). Publication Date 2001: Price, $79.50.



Benzodiazepines and GHB (Gamma Hydroxy Butyrate) rank among the top abused drugs today. Both are known to induce a sleep like state, a relaxation of muscles and a few other CNS affects, which taken together are perceived by many to be desirable effects, and hence the frequency of abuse. The first benzodiazepines came to the market in 1960 and since then there have been considerable efforts to produce analogues which can produce similar effects in lower doses. These new species of benzodiazepines have a shorter duration of action and a faster clearance rate too. Although desirable for the patients, these forms have posed a new challenge to the forensic toxicologist, as he is faced with the prospect of detecting these in infinitesimally low quantities.

GHB was synthesized by a French Navy Surgeon Henry Laborit and his associates in 1960. The structures of GABA and GHB are remarkably similar, with just an OH group (in GHB) for an NH_2 group (in GABA). Laborit and his associates were actually looking for a GABA analogue for possible use in the treatment of seizure disorder. They were thinking that since GHB could readily cross the blood brain barrier, it could easily go there and perhaps facilitate the synthesis of GABA. A fairly reasonable guess.. . but it didn't work. However it was found to have some very desirable pharmacological properties, some of them being that it mimicked natural sleep, had cardiotonic effects and permitted slow induction of anaesthesia. GHB is also required in very small quantities to produce its effects.

The forensic detection of both Benzodiazepines as well as GHB is obviously not an easy task for the forensic toxicologist. The book under review comes as a succor to those forensic toxicologists who are faced with the unenviable task of detecting infinitesimally low quantities of these drugs in various body fluids of their subjects.

The book comprises of seven different chapters, each written by a specialist or a group of specialists in that particular field. In all thirteen experts - ranging from countries as diverse as France, Switzerland and the US - have contributed material for this book. Most of the chapters are devoted to benzodiazepines and their analogues, but one - chapter six - is entirely devoted to GHB, and is a veritable treasure trove of information on this drug.

Forensic Science and Medicine Series of Humana Press

This book is just one of six books published by Humana Press in their excellent *Forensic Science and Medicine* series. Steven B. Karch, MD, is the series editor of this series. This journal has already reviewed one book of this series in one of its earlier issues. This was John H. Trestrail, III's *Criminal Poisoning*. Here is the full listing of the books in this series:

1. Buprenorphine therapy of Opiate Addiction, edited by **Pascal Kintz** and **Pierre Marquet**, 2002
2. On-site drug testing, edited by **Amanda J. Jenkins** and **Bruce A. Goldberger**, 2001
3. Benzodiazepines and GHB: Detection and Pharmacology, edited by **Salvatore J. Salamone**, 2001
4. Toxicology and Clinical Pharmacology of Herbal Products, edited by **Melanie Johns Cupp**, 2000
5. Criminal Poisoning: Investigational Guide for law enforcement, toxicologists, forensic scientists, and attorneys, by **John H. Trestrail, III**, 2000
6. A Physician's guide to clinical Forensic Medicine, edited by **Margaret M. Stark**, 2000

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For instance, the chapter gives us the results of several studies trying to correlate blood concentrations of GHB with the states of consciousness of people taking it. Four states of consciousness were defined: **awake**, when the subject was fully conscious and alert, **light sleep**, when the subject spontaneously came in and out of consciousness, **medium sleep**, when the subject was clearly asleep, but could by roused by various stimuli, and **deep sleep**, when the subject was asleep and could not be roused. The results of one such study have been given in the form of a table on page 96. Some interesting conclusions are immediately apparent from this table. One of the things that is very apparent is that the blood concentrations of GHB display a large overlap across the four states of consciousness just described. If we look at blood concentration of 250 micrograms/mL, we find that the subject could either be in a light, medium or deep sleep state. This is an interesting result, for it shows that it is extremely difficult to predict the state of consciousness of a subject by looking at his blood GHB concentration!

The book gives interesting data on compounds analogous to GHB such as GBL (Gamma Butyrolactone) and 1,4BD (1,4-Butanediol). A very interesting history of the illicit use of GHB, GBL and 1,4BD is also included. The chapter then goes on to discuss the metabolism, distribution, pharmacokinetics and analysis of these three compounds. We are told at one place that GHB can actually increase after death under certain conditions, and this is a possibility forensic toxicologists must well keep in mind.

Another chapter that is very interesting is chapter seven, which deals with the analysis of urine samples in cases of alleged sexual assault. Lately there has been a lot of talk regarding date rape drugs - drugs that are used to facilitate sexual intercourse among acquaintances during dating. A number of drugs have been implicated - GHB, ketamine and flunitrazepam being some of them.

Flunitrazepam is a member of benzodiazepine group of drugs and is among the most frequently prescribed hypnotics in many countries. However - as the book informs us - it has never been available in the United States, for purely commercial reasons. There are however reports that this drug has been illegally smuggled in the US, largely in Florida and Texas. The major manufacturer of

Flunitrazepam is Roche, which manufactures it under the name *Rohypnol*. They have been much worried about the hype surrounding the drug, and this hype has actually caused them to bring about some modifications in its formulation. One of this is the introduction of a color-releasing tablet. With the introduction of this new variety, it would almost be impossible for someone to mix this tablet in, say, a drink of his girl friend to facilitate sexual intercourse!

QUICK NOTES

Some major highlights of *Benzodiazepines and GHB: Detection and Pharmacology* at a glance:

& Comprehensive pharmacological review of benzodiazepines and GHB
& Cutting-edge methods for the detection of benzodiazepines and gamma-hydroxybutyric acid
& Immunological and GC/MS methods of detection for low-dose benzodiazepines
& Guidance on drugs used in cases of sexual assault
& Useful for clinical, analytical and forensic toxicologists, clinicians, pharmacologists, researchers and forensic pathologists

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The book tells us about a very interesting and informative study that the company undertook to find out if *Rohypnol* really was involved in date rape. All rape crisis centers, law enforcement agencies and emergency rooms throughout the US were informed that a testing program was going on, and if any alleged case of date rape came their way, they must collect the urine samples of the victims, and send it for testing. The urine samples were tested by ElSohly Laboratories, Incorporated (ELI) of Oxford, Mississippi. The samples were tested for several drugs, among them alcohol, flunitrazepam, amphetamines, barbiturates, cocaine, GHB, marijuana and opiates. A total of 3303 samples were submitted over a period of four years, and only 11 samples came positive for flunitrazepam and its metabolites. Alcohol was found in the maximum number of samples - an astounding 1358 cases! Marijuana was next with 613 positive samples. Clearly *Rohypnol* did not deserve the bad publicity it had received!

The first five chapters are devoted almost entirely to benzodiazepines, their pharmacology, toxicology and their analysis in various body fluids and hair. Chapter five is devoted entirely to their detection in hair. There is an entire chapter - chapter 4 - on low dose benzodiazepines such as alprazolam, lorazepam, midazolam and triazolam. This is a very informative chapter and tells us how these low dose drugs can be detected by Mass Spectrometry. After giving a full background of the drugs, the authors go on to describe the methods of detection in detail.

This book should be very useful for toxicologists working in all areas, be it forensic toxicology, analytical toxicology or clinical toxicology. Clinicians, pharmacologists, researchers, and forensic pathologists would also find this book very useful. Undoubtedly this book is a very valuable addition to the extant literature on the pharmacology, toxicology and detection of Benzodiazepines and GHB.

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