

TOXALERT

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Gammahydroxybutyrate and Analogues

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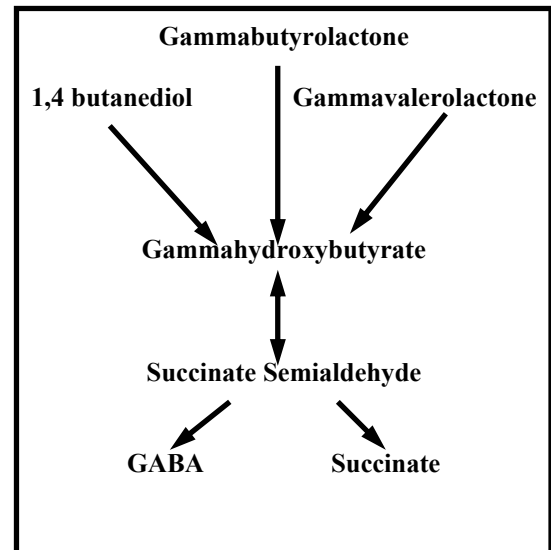
First synthesized in 1960 as an anesthetic agent in Europe, gammahydroxybutyrate (GHB) became popular in the late 1980's and early 1990's as a dietary supplement, sleep aid, dietary aid, bodybuilding agent and recreational drug. It is believed to be used and abused recreationally because of its disinhibitive and aphrodisiac effects. Currently in the USA, GHB is being studied as a treatment for refractory sleep disorders.

GHB became famous in 1990, when, in response to several deaths and considerable morbidity, the Food and Drug Administration issued an advisory limiting its availability. Congressional movement to ban GHB was slow and was hindered by the Dietary Supplement Health and Education Act of 1994, which created some protection for dietary supplements such as GHB. In March 2000, the Drug Enforcement Agency made GHB a Schedule I drug (with some exceptions). To circumvent the legal issues associated with GHB trafficking, people turned to GHB alternatives or analogues.

Analogues such as gammabutyrolactone (GBL) and 1,4 butanediol (1,4 BD) share a similar molecular structure with GHB. GBL undergoes spontaneous hydrolysis by lactonases to form GHB in the blood and liver. 1,4 BD requires enzymatic oxidation by alcohol dehydrogenase in order to form GHB. Analogues have pharmacologic properties similar to those of GHB. There are many different names for these

analogues as people got creative about their products (see table 1). GHB/analogues are available as colorless and almost tasteless liquids or as white powders packaged into capsules.

Lately, a substance called gammavalerolactone (GVL) has gained



popularity as a GHB precursor in Arizona. GVL is prohibitively expensive and may not be a worthy investment for the marketer.

Epidemiology

In 1996, it was estimated that 94% of GHB users were Caucasian and that 91% of the time, it was used recreationally. The first GHB exposure reported to the Maryland Poison Center (MPC) was in 1998. In 1999, 23 exposures were reported. 92% of

Gammahydroxybutyrate (continued)

exposures implicated GHB and 8% analogues. In 2000, the total number of exposures has remained essentially the same, but the proportion of exposures implicating the analogues has increased to 71%. Most of the exposures have occurred in the 17-50 years of age group. Some overdoses have resulted in hospitalizations and prolonged ICU admissions. GHB/analogues exposures have been reported to the MPC from Anne Arundel, Baltimore, Carroll, Harford, Montgomery, Prince George, Wicomico and Worcester counties, as well as Baltimore City.

Pharmacology

GHB receptors have been identified in the mammalian brain and reside in the basal ganglia. There is still debate on whether GHB is a neurotransmitter or a neuromodulator. GHB has been linked to an increase in dopamine and acetylcholine activity in the brain. It has a minor pro-GABA role. GHB promotes REM and non-REM sleep and may have endogenous cerebroprotective effects.

GHB/analogues are rapidly metabolized. The elimination half life is approximately 1 hour. Time to peak serum concentration may be delayed by the co-ingestion of food.

Clinical manifestations

GHB/analogues ingestion has been associated with rapid onset of CNS depression, depressed respirations, apnea and coma. Pupils are not constricted. In one case series, 30% of patients experienced spontaneous emesis. The duration of action of GHB/analogues is very short, an average of 2.6 hours. Complete recovery is expected within a few hours.

Management

The treatment of GHB/analogues ingestion remains largely supportive. Naloxone is not effective at reversing the sedative effects of GHB/analogues. Neither is flumazenil. Careful monitoring and prompt intubation of the patient presenting with severe respiratory

depression is recommended. Careful neurological examination for possible concurrent head trauma is also prudent.

Complications following acute overdoses of GHB/analogues include aspiration pneumonia and caustic oropharyngeal injuries. Aspiration of gastric contents can occur in the field, pre-intubation or in the hospital during extubation or self-extubation. Some clinicians have purposefully sedated the intubated patient further by propofol infusions in order to perform extubation under optimal conditions, usually in the morning. Caustic injuries stem from the process required to make GHB, which involves addition of large quantities of sodium bicarbonate or other alkali to the preparation.

Diagnostic testing

Detection of GHB/analogues in body fluids remains an elusive problem. GHB/analogues can be detected in the urine for a few hours after exposure if mass spectrometry assay of the urine is performed.

The only laboratory in Maryland that arranges for assays for GHB in the urine is Friends Lab, located at 5820 Southwestern Blvd, Arbutus, 410-247-4417. The cost of the analysis is \$130. The turn around time is 7 days and a refrigerated urine specimen is preferred.

Is GHB addictive?

There are numerous unpublished and published case reports of chronic GHB abusers who have developed both tolerance and withdrawal with this drug. Chronic ingestions of as little as 20g/day for periods of 1.5-2 years have lead to dependence and

Table 1

GHB

Gammahydroxybutyrate
Sodium Oxybate

Liquid X, liquid ecstasy, cherry meth

GBL

Gammabutyrolactone
Dihydrofuranone
Furanone di-hydro

Renewtrient, Revivarant, Gamma G, Remforce, Blue Nitro, G

1,4 BD

1,4 Butanediol
Butanediol

Butylene glycol
Tetramethylene glycol
Pine Needle Extract, Revitalize Plus, Serenity, SomataPro, Enliven, Zen

Maryland legislators are attempting to pass a bill that will make GHB analogues Schedule 1 drugs.

Visit the Maryland Poison Center website at:
<http://www.pharmacy.umaryland.edu/~mpc/>

withdrawal. The most noteworthy case report was that of a patient who required over 500 mg of intravenous lorazepam over a 4 day ICU stay because of her severe agitation following withdrawal of GHB. GHB/ analogues withdrawal is characterized by disorientation, hallucinations and tremors. Tachycardia, hypertension and nystagmus are found on physical examination. Contrary to the withdrawal associated with other sedative-hypnotics, GHB/analogue

withdrawal is not associated with seizures or fever. In many instances, the withdrawal has been prolonged for 7-10 days.

Maryland House Bill 1347 (a bill that would have made the GHB analogues Schedule I drugs in Maryland) was introduced last year by Delegate Pauline Menes, but did not pass the Judiciary Committee. The issue will be tackled again this year.

Toxicology-Related Websites

The following websites may be useful to health care providers. They should not, however, be used in place of consultation with the Maryland Poison Center.

Organizations

The American Academy of Clinical Toxicology: <http://www.clintox.org/>
American Association of Poison Control Centers: <http://www.aapcc.org/>
 note: individual poison center websites can be found at this site
American College of Medical Toxicology: <http://www.acmt.net/>
Society of Toxicology: <http://www.toxicology.org/>
Maryland Poison Center: <http://www.pharmacy.umaryland.edu/~mpc/>

Drugs of Abuse

Erowid: <http://www.erowid.org/psychoactives/psychoactives.shtml>
Ecstasy: <http://www.ecstasy.org/>
Rhodium: <http://rhodium.lycaeum.org/>
Lycaeum: <http://www.lycaeum.org/>
Inhalation: <http://www.inhalation.net/>

Occupational/Environmental

Duke Occupational & Environmental Medicine: <http://occ-env-med.mc.duke.edu/oem/>
Extoxnet (pesticides): <http://www.ace.orst.edu/info/extoxnet/>
Vermont SIRI Website (MSDS): <http://siri.org/>

Meta sites: Links of Toxicology Links

The Hardin Meta Directory: <http://www.lib.uiowa.edu/hardin/md/tox.html>
Yahoo Health - Toxicology: <http://dir.yahoo.com/Health/Medicine/Toxicology/>
Martindale's Health Science Guide- Pharmacy- Toxicology: <http://www-sci.lib.uci.edu/HSG/Pharmacy.html#PP3-TOX>
MedWeb Plus: <http://medwebplus.com/subject/Toxicology.html>
MedPharm- Toxicology information: <http://www.medfarm.unito.it/toxicol/toxicol1.html>
Web Resources: Toxicology (University of Kentucky): <http://www.uky.edu/Subject/toxicology.html>

Forensics

Alan Barbour's Forensic Toxicology Page: <http://userzweb.lightspeed.net/~abarbour/>

Reference Material

The Merck Index: <http://library.dialog.com/bluesheets/html/b10304.html>
Specialized Information Services - Toxicology: <http://sis.nlm.nih.gov/index.cfm>

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Baltimore, MD



410-706-7701 or 1-800-492-2414

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Toxicology-Related Websites (continued)

Snakes and Spiders

Venomous Reptiles; Snakes: <http://www.herper.com/Venom.html>

Spiders: <http://spiders.ucr.edu/>

<http://www.ufsia.ac.be/Arachnology/Pages/Araneae.html>

Government sites

Center for Disease Control and Prevention: <http://www.cdc.gov/>

CDC Wonder (epidemiology info): <http://wonder.cdc.gov/Welcome.html>

Agency for Toxic Substances and Disease Registry: <http://www.atsdr.cdc.gov/atsdrhome.html>

Food and Drug Administration: <http://www.fda.gov/>

Medline Plus: Poisoning, Toxicology, Environmental Health: <http://www.nlm.nih.gov/medlineplus/poisoningtoxicologyenvironmentalhealth.html>

Drug/Medical Information websites

Clinical Pharmacology Online (requires registration): <http://cp.gsm.com/fromcpo.asp>

Hyper Tox: <http://www.ozemail.com.au/~ouad/toxi0002.htm>

