

# FOR YOUR INFORMATION



## PHARMACY NEWSLETTER



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### **GHB – A Drug of Abuse**

#### **INTRODUCTION**

Gama-hydroxybutyrate (GHB) is a naturally occurring fatty acid derivative of the inhibitory neurotransmitter, gama-aminobutyric acid (GABA) found in every human cell. It was first synthesized in 1960 and initially investigated as an alternative anesthetic to aid in surgery. However, most studies had to be stopped due to its minimal analgesic effect and the association with seizure activity including tonic-clonic jerking movements of the limbs or face.

GHB has been used as a dietary supplement for muscle building, and insomnia. It has also been tested for treatment of opiate and alcohol withdrawal. In the late 1970's, GHB was first investigated for narcolepsy and meanwhile there are ongoing clinical trials still underway. During the thirty years since the discovery of this chemical, the scientific reports on GHB unanimously claimed that it was low in toxicity, and lacking in long-term negative effects.

In 1990, the over-the-counter sale of GHB in the United States was banned based on numerous reports of GHB-linked poisoning. However, in the summer of 2002, it was then approved as a prescription drug in the U.S. for the treatment of cataplexy attacks in patients with narcolepsy. In recent years, GHB has gained the public attention and concerns due to its increasing popular use as a recreational drug and "date-rape" drug. Common street names for GHB include Liquid E, Liquid Ecstasy, Liquid X, Salty Water, Soap, Nature's quaalude, Scoop and many others.

#### **PHARMACOKINETICS**

GHB is rapidly absorbed following oral administration due to its lipophilic properties, which also render to its ability to cross the blood-brain-barrier readily. Peak serum levels occur 20 to 45 minutes post-ingestion. Absorption may be dose-dependent, with the time to peak progressively lengthening as the dose increases. The half-life is only 20 minutes, which makes GHB

unlikely to accumulate in the body. When GHB is taken with food, the bioavailability may be reduced.

GHB is not easily detected by routine serum or urine toxicology screens because of its rapid excretion as carbon dioxide through exhalation, with little unchanged drug eliminated in the urine. GHB is virtually undetectable in the urine 12 hours after ingestion. The difficulty in tracing this drug in the body could be one reason why it is chosen as a date-rape drug.

#### **PHARMACOLOGY**

GHB is a central nervous system depressant. It is both a metabolite and precursor of GABA and is normally found in concentrations 1/1000 that of GABA. In the brain, the highest amount is found in the hypothalamus and basal ganglia.

GHB affects the activity and levels of many neurotransmitters in the brain including dopamine, acetylcholine and serotonin. It is believed to increase the dopamine concentration through interactions with GABA receptors. Research indicates that GHB induces hypothermia and mediates memory.

The use of GHB as a muscle builder is based on the findings of some studies that GHB stimulate pituitary growth hormone release. However, these findings are derived from reports of small-scale studies.

What accounts for GHB's use for narcolepsy is its ability to promote a natural pattern of REM and slow wave sleep. GHB is believed to cause the induction of "remarkable hypotonia" (muscle relaxation) which lends to its use as an aid to childbirth in the European countries such as France and Italy.

#### **AVAILABILITY**

GHB is scheduled as a controlled substance in Canada and is not currently marketed as a therapeutic product.

An oral liquid GHB preparation is available from a European pharmaceutical supplier and a patient-specific supply may be obtained following approval by Health Canada's Special Access Programme (SAP). If a Canadian practitioner wants to treat a patient with narcolepsy, it can be obtained by submitting the standard SAP Request Form and must also contact the Bureau of Controlled Substances.

In the U.S., GHB is scheduled as a controlled substance. Xyrem, a GHB brand approved in the U.S. for treating patients with narcolepsy, cannot be imported into Canada for regulatory reasons. It is tightly restricted for distribution through the Xyrem Success Program to ensure safe use of the drug. Under the program, it will be available through a centralized pharmacy. The recommended dose is 4.5 grams as a starting dose up to maximum of 9 grams per day, divided into two equal doses at bedtime at 2.5 to 4 hours apart.

Although GHB is classified as a controlled substance, GHB continues to be widely available through illicit sales, home manufacture and recipes using its chemical precursors, such as gamma butyrolactone and 1,4 butanediol since the body metabolizes these compounds to form GHB. GHB's common form is an odorless, colorless and almost tasteless liquid. It may also be found as a crystalline powder. Poorly made liquid GHB may taste like old seawater or have a strong soapy taste.

## **EFFECTS/TOXICITY**

CNS depression is the hallmark of GHB use. Following an oral dose of GHB, CNS depressant effects usually appear in 15-30 minutes. The degree of CNS depression is dependent on the dosage as well as individuals since each person responds to each dose level differently. Ingestion of an oral dose of 10mg/kg usually produces short-term amnesia and hypotonia.

At 20-30 mg per kg, GHB can cause drowsiness and sleep. Doses exceeding 70mg/kg may produce loss of consciousness lasting one to two hours. Acute overdose of GHB may result in coma, respiratory depression, bradycardia, hypothermia, vomiting, myoclonus and seizures; behaviors like agitation, combativeness, hallucinations may be present despite profound CNS and respiratory depression.

Effects are intensified if taken concomitantly with another CNS depressant such as alcohol, benzodiazepines and neuroleptics. Deaths have been reported due to combining GHB with another CNS

depressant. In a survey study, adverse effects of GHB were found to occur more frequently in daily users and polydrug users than in occasional GHB users.

The diagnosis of GHB intoxication/ingestion will be based mainly on patient history and clinical findings. There is no specific antidote and management involves symptomatic and supportive care. Patients usually recover spontaneously and dramatically from the respiratory depression two to six hours after ingestion.

## **Tolerance / dependence / withdrawal**

Regular use of GHB has been shown to produce both tolerance as well as physical and psychological dependence. Due to its short half-life, people who are dependent on GHB must self-administer every 2-4 hours around the clock to avoid symptoms of withdrawal upon abrupt cessation.

The typical withdrawal symptoms include anxiety/restlessness, insomnia, tremor, confusion, delirium, hallucinations (auditory, tactile, and visual), tachycardia, hypertension, nausea, vomiting and diaphoresis. The onset of GHB withdrawal occurs within 1-3 hours and may last 6-12 days.

## **CONCLUSION**

GHB is a drug of abuse with anesthetic and sedative-hypnotic properties. Since it causes anterograde amnesia and being colorless, tasteless and odorless, it can be easily mixed into beverages. Date-rape victims may not be able to recall incidence of sexual assault. The abuse of GHB can be associated with dangerous consequences such as seizures, coma and deaths. Although GHB is listed as a controlled substance, it is easily and cheaply manufactured in the home and new cases with troublesome and difficult to manage withdrawal symptoms continue to be reported. Health professionals as well as the public should be alerted to the potent addictive and intoxicant properties of GHB. With testimonial evidence presented by those who have addicted to GHB reveal the agony to be ongoing even after abstinence of GHB, one should think twice before anticipating of using it for purposes like muscle-building, sleep-aid or recreational purposes.

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