

ToxUpdate

Alabama Poison Information Center, Birmingham, AL

www.childrensal.org/apic

1-800-222-1222

Nitrous Oxide – A Medicine or A Party Drug

By Vishva Patel, PharmD Candidate 2023, Samford University

For more than 200 years, nitrous oxide (N₂O), often known as “laughing gas” or “nos”, has been used recreationally and medicinally.¹ Discovered in 1772 by English scientist Joseph Priestley, nitrous oxide is a nonflammable, water soluble, colorless, and slightly sweet-smelling gas. It is used as an anesthetic and analgesic agent for minor dental procedures and as general anesthesia. Because it does not influence food flavor, it can also be used as a propellant in products like whipped cream and cooking oil spray.²

Adolescents and young adults frequently misuse nitrous oxide inhalants. It was initially used as a recreational drug in early 19th century Britain by the upper class at “laughing gas parties” for the fleeting feeling of exhilaration it gave. Nitrous oxide recreational use occurs at raves, university parties, music festivals, clubs, private residences, and parks. In the United States, inhalant abuse is most common among people aged 12 to 17, and its prevalence continues to increase. In 2019, 3.0% of adolescents and 1.7% of adults aged 18 to 25 reported using inhalants.³ The most popular way to consume nitrous oxide is through whipped cream dispensers, also known as “whippits” or “nangs”, often inhaled using a balloon, due to the immediate euphoric effects, low cost, and ease of access. This method is relatively lower risk compared to using full-sized gas cylinders.¹

NMDA receptor antagonism causes the euphoric effects of nitrous oxide. Acute toxicity of nitrous oxide is due to hypoxia. Chronic use can cause functional B12 deficiency. This can lead to inhibition of myelin and DNA synthesis, which may cause demyelination of the spinal cord resulting in paresthesia, ataxia, and weakness of the extremities. In recent studies, it has also been found that chronic use of nitrous oxide may cause acute venous thromboembolism.³

Treatment of acute toxicity of nitrous oxide involves airway management and administration of supplemental oxygen. For chronic toxicity, vitamin B12 supplements should be provided as well as supplemental oxygen to enhance elimination of the gas.⁴

Using or transporting nitrous oxide is currently not explicitly prohibited by law. However, as of 2016, possession of nitrous oxide to sell the substance for the use of its euphoric characteristics is illegal.¹

(References on Page 3)



ALABAMA
POISON
INFORMATION
CENTER

800-222-1222

Special Interest Articles

- Nitrous Oxide
- Cannabinoids in Medicine
- Mounjaro®

Did you know?

While some small objects swallowed by children may be managed by monitoring for passage out of the GI tract, ingestion of a button battery is an emergency that calls for immediate medical attention.

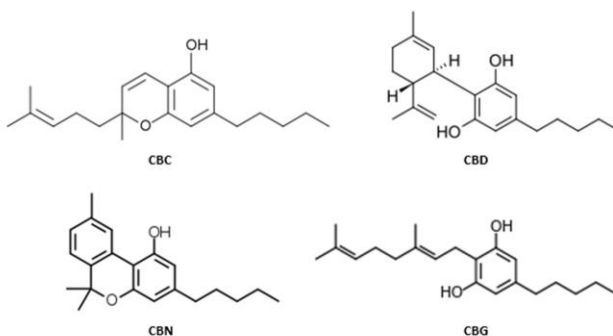
Button batteries are small circular batteries used to power small electronic devices such as calculators, watches, and toys. These batteries can become lodged in the esophagus where they can create an electrical current which produces hydroxide at the anode of the battery. This can lead to serious burns within only a few hours.

Any child who is suspected to have swallowed a button battery requires urgent evaluation to determine the location of the battery and immediate removal if it is lodged in the esophagus.

Cannabinoids in Medicine

“It is important that patients choosing to use these products realize they are not strictly regulated and different products may contain variable concentrations of the various cannabinoids and varying amounts of THC”

By Benjamin Marsella, PharmD Candidate 2023, Samford University



The use of cannabinoids in medicine is a controversial topic. The Agriculture Improvement Act of 2018 (also known as the “Farm Bill”) was signed into law to allow hemp to be legally grown in the US. This bill stipulates that the crops grown must contain 0.3% or less delta-9-tetrahydrocannabinol (THC), the psychoactive molecule in hemp and marijuana.¹ Cannabichromene (CBC), cannabigerol (CBG), and cannabinol (CBN) are three of the less psychoactive molecules found in marijuana responsible for anxiolytic effects and reduction of pain and inflammation.² Importantly, these substances are legal and are used by many patients.

CBC is one of the cannabinoids that has shown inhibition of pain and inflammation along with limited studies indicating possible neuroprotection and neurogenesis. Udoh et al. found that CBC selectively binds to cannabinoid receptor 2 (CB2), which is primarily distributed within the immune system. CBC is non-psychoactive as it does not interact with the CB1 receptors that are found abundantly in the brain and contribute to the intoxication effect of marijuana.³ Three common formulations of CBC oil are as a sublingual tincture, a food or drink additive, or a topical agent.⁴

CBG is another non-psychoactive cannabinoid with evidence for benefit in gastrointestinal conditions, such as irritable bowel disease. Similar to many of the other cannabinoids, limited data is available on the efficacy or safety in humans and the existing information is primarily anecdotal or in non-human test subjects.⁵

Another product gaining popularity is CBN. CBN is mildly psychoactive, producing slight intoxication, which has the potential to lead to dependence. CBN binds to both CB1 and CB2 with higher affinity to CB2. CBN is thought to act as an appetite stimulant, pain reducer, and treatment for insomnia. At this time, very little is known about the side effects of CBN oil.⁶

With any of these products, several considerations, such as age, weight, and body chemistry, factor into the proper dosing of CBD derivatives. Additionally, these products are metabolized by various CYP enzymes, allowing for interactions that may lead to suprathreshold or subtherapeutic dosing. Further research is needed to better understand drug interactions with these products. It is important that patients choosing to use these products realize they are not strictly regulated and different products may contain variable concentrations of the various cannabinoids and varying amounts of THC, factors which can also lead to users testing positive for THC on certain drug screens.

1. Farm bill. USDA. <https://www.usda.gov/farmbill>. Accessed May 26, 2022.
2. Comparison of cannabinoids. Pharmacist's Letter. <https://pharmacist.therapeuticresearch.com/en/Content/Segments/PRL/2018/Sep/Comparison-of-Cannabinoids-12640>. Published April 2022. Accessed May 26, 2022.
3. Udoh M, Santiago M, Devenish S, McGregor IS, Connor M. Cannabichromene is a cannabinoid CB2 receptor agonist. *British Journal of Pharmacology*. 2019;176(23):4537-4547. doi:10.1111/bph.14815
4. Julia N. What is CBC Oil Good For? benefits, uses, & effects. CFAH. <https://cfah.org/what-is-cbc-oil/>. Published May 24, 2022. Accessed May 26, 2022.
5. Navarro G, Varani K, Reyes-Resina I, et al. Cannabigerol action at Cannabinoid CB1 and CB2 receptors and at CB1–CB2 heteroreceptor complexes. *Frontiers in Pharmacology*. 2018;9. doi:10.3389/fphar.2018.00632
6. Sreenivas S. CBD vs CBN: What's the difference? WebMD. <https://www.webmd.com/pain-management/cbd-cbn-what-is-difference>. Published October 29, 2021. Accessed May 26, 2022.

Mounjaro™ Approved May 2022

By Dustin Latham, PharmD Candidate 2023, Samford University



Mounjaro - Getting Patients Started. <https://www.mounjaro.com/hcp/getting-patients-started#dosing>

Mounjaro (tirzepatide) is a once-weekly subcutaneous injection for the treatment of type 2 diabetes mellitus (T2DM), approved by the U.S Food and Drug Administration in May 2022.¹ Mounjaro should be used as an adjunct to diet and exercise. While Mounjaro is indicated for T2DM, it is commonly used off-label for weight management. Initially, it is dosed as a 2.5 mg injection weekly for four weeks and then increased to 5 mg weekly. The dose may be increased by 2.5 mg per week if needed to reach therapeutic goals.²

Mounjaro works by targeting the glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. This enhances insulin secretion and reduces glucagon levels, both in a glucose-dependent manner. It should be noted that Mounjaro carries a black box warning for an increased risk of thyroid C-cell tumors and is contraindicated in patients with a personal or family history of these cancers.¹

Mounjaro concentrations peak in 8 to 72 hours with an elimination half-life of 5 days. It is 99% bound to albumin and is converted to active metabolites which are excreted in the urine and feces. It is anticipated that overdose effects will be similar to adverse effects reported at therapeutic doses.² Adverse effects usually consist of injection site reaction, cardiovascular effects, nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain. However the incidence of these effects is low. Potentially more serious issues have included hypoglycemia when taken with an insulin secretagogue (e.g. sulfonylureas) or insulin, hypersensitivity reaction, severe GI disease (gastroparesis), pancreatitis, gallbladder disease, diabetic retinopathy, and acute kidney injury secondary to severe dehydration.³ Mounjaro delays gastric emptying which may affect oral drug treatments. Caution should be taken in patients that are receiving concurrent medications that decrease gastric emptying due to the potential for Mounjaro to compound this effect.

Toxic doses of Mounjaro have yet to be established. It is recommended that a maximum dose of 15 mg injected subcutaneously once weekly should not be exceeded. The safety and effectiveness in children 18 years and younger have not yet been studied. Patients should be educated on signs and symptoms of hypoglycemia prior to initiating this medication. If toxicity is suspected, supportive measures should be taken.⁴

1. Lexicomp. Tirzepatide. Accessed September 9, 2022. https://online-lexi-com.ezproxy.samford.edu/lco/action/doc/retrieve/docid/patch_f/7224042?cesid=3al7Adasuld&searchUrl=%2Ffco%2Faction%2Fsearch%3Fq%3Dmounjaro%26t%3Dname%26acs%3Dtrue%26acq%3Dmounjaro#mop
2. Tirzepatide Mechanism of Action - Clinical Pharmacology. Accessed September 9, 2022. <https://www-clinicalkey-com.ezproxy.samford.edu/pharmacology/monograph/5403?sec=monmech&n=MOUNJARO>
3. Mounjaro (tirzepatide) | GIP and GLP-1 Receptor Agonist for T2D. Accessed September 9, 2022. <https://www.mounjaro.com/hcp>
4. Drug Result Page - Quick Answers - Toxicology - Range of Toxicity. Accessed September 9, 2022. <https://www-micromedexsolutions-com.ezproxy.samford.edu/micromedex2/librarian/PFDDefaultActionId/evidenceexpert.DolntegratedSearch?navitem=topHome&isToolPage=true#>

References for Nitrous Oxide – A Medicine or A Party Drug (page 1)

1. Nitrous Oxide (Laughing Gas) - Everything You Need to Know - Drug Science. [drugscience.org.uk](https://www.drugscience.org.uk/drug-information/nitrous-oxide/#1614731714218-19bf1003-2a6c). Accessed September 9, 2022. <https://www.drugscience.org.uk/drug-information/nitrous-oxide/#1614731714218-19bf1003-2a6c>
2. Nitrous Oxide | AACC.org. [www.aacc.org](https://www.aacc.org/science-and-research/toxin-library/nitrous-oxide). <https://www.aacc.org/science-and-research/toxin-library/nitrous-oxide>
3. Schaffer D, Goldfine C. Nitrous Oxide Misuse and Abuse. www.acep.org. Published June 25, 2021. Accessed September 9, 2022. <https://www.acep.org/toxicology/newsroom/jun2021/nitrous-oxide-misuse-and-abuse/#:~:text=Nitrous%20oxide%20and%20toxicity&text=in%20the%20United%20States%2C%20inhalant>
4. Schneir A. NITROUS OXIDE. In: Olson KR, Smollin CG, Anderson IB, Benowitz NL, Blanc PD, Kim-Katz SY, Lewis JC, Wu AB, eds. Poisoning & Drug Overdose, 8e. McGraw Hill; 2022.