

## Research needed on psychedelic compound for opioid withdrawal

Classified as a Schedule I controlled substance in the United States, ibogaine is used at unlicensed treatment centers in Canada and Mexico to lessen the withdrawal symptoms from opioid addiction and to reduce subsequent craving symptoms. New York, Maryland, Vermont, and New Hampshire have introduced legislation supporting pilot studies of ibogaine for these symptoms, but none have passed to date.

### What is ibogaine?

Ibogaine is a psychedelic compound from the root bark of the West African rainforest shrub *Tabernanthe iboga*. It has been known to induce a dream-like state.

Different dosing regimens of ibogaine have been used in opioid withdrawal sessions. After dosing, an initial phase consists of vivid waking dreams, followed by a stage in which individuals describe gaining personal insight, and finally by a period of mental clarity and calmness.<sup>2</sup>

Ibogaine and its active metabolite interact with multiple neurotransmitters, including the N-methyl-D-aspartate receptor known as NMDA, kappa and mu-opioid receptors, acetylcholine, dopamine, and serotonin.<sup>3</sup> Ibogaine is metabolized through CYP2D6 and, to a lesser extent, CYP2C9 and CYP3A4. Noribogaine is a primary active metabolite and has a prolonged half-life of 28 to 49 hours, compared with only 4 to 7 hours for the parent compound.<sup>3,4</sup>

### Adverse effects

Adverse effects of ibogaine have primarily involved cardiotoxicity. Ibogaine blocks the human ether-a-go-go-related gene (hERG) potassium channels, thereby delaying cardiac repolarization and prolonging the QT interval.<sup>4</sup> This may lead to the development of arrhythmias, including Torsades de pointes. Sudden death has been reported in people with and without underlying cardiovascular disease.<sup>4</sup>

Many individuals and families search online for dietary supplements to assist in managing opioid withdrawal symptoms, despite no evidence of their efficacy.<sup>1</sup> Given its cardiotoxicity, ibogaine

should not be purchased online. One patient who bought ibogaine online developed multiple arrhythmias and a QT interval of 647 msec; normal is less than 420 msec. The prolongation continued for 12 hours after the dose, an effect probably related to noribogaine.<sup>5</sup>

Neurotoxicity has also been associated with ibogaine.



### Evidence

One online survey of 88 adults who had undergone ibogaine detoxification at a Mexican center between 2012 and 2015 assessed their experiences with this compound for opioid addiction.<sup>2</sup> At this center, individuals who had concomitant severe psychiatric and medical disorders, such as a prolonged QT interval, were excluded.

Participants had used opioids for more than 4 years, and 80% reported reduced withdrawal symptoms. More than 60% of respondents indicated that ibogaine was “very effective.” Well-being and mood were increased and persisted for more than 1 month. One-third of this small sample reported not returning to opioids, with one-half maintaining abstinence for at least 1 year.

A 2018 study evaluated 50 participants undergoing a 7-day ibogaine

detoxification regimen for opioid use disorder.<sup>6</sup> Standardized assessment tools were used, including the Addiction Severity Index, Clinical Opioid Withdrawal Scale (COWS), Subjective Opioid Withdrawal Scale (SOWS), and the Brief Substance Craving Scale (BSCS).

The COWS, SOWS, and BSCS instruments were administered 48 and 24 hours before and after the ibogaine treatment. Symptoms of withdrawal and opioid craving were significantly reduced.

### What to tell patients

Like that on marijuana, research on ibogaine in the United States has been limited because of its classification as a Schedule I controlled substance. While this compound may possess benefits in opioid detoxification, rigor-

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ous studies are needed to fully evaluate its potential. Inform patients that ibogaine exhibits cardiotoxicity and should never be purchased online for self-administration, as ibogaine facilities have onsite physicians who are able to manage medical emergencies relating to adverse effects.

### References

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