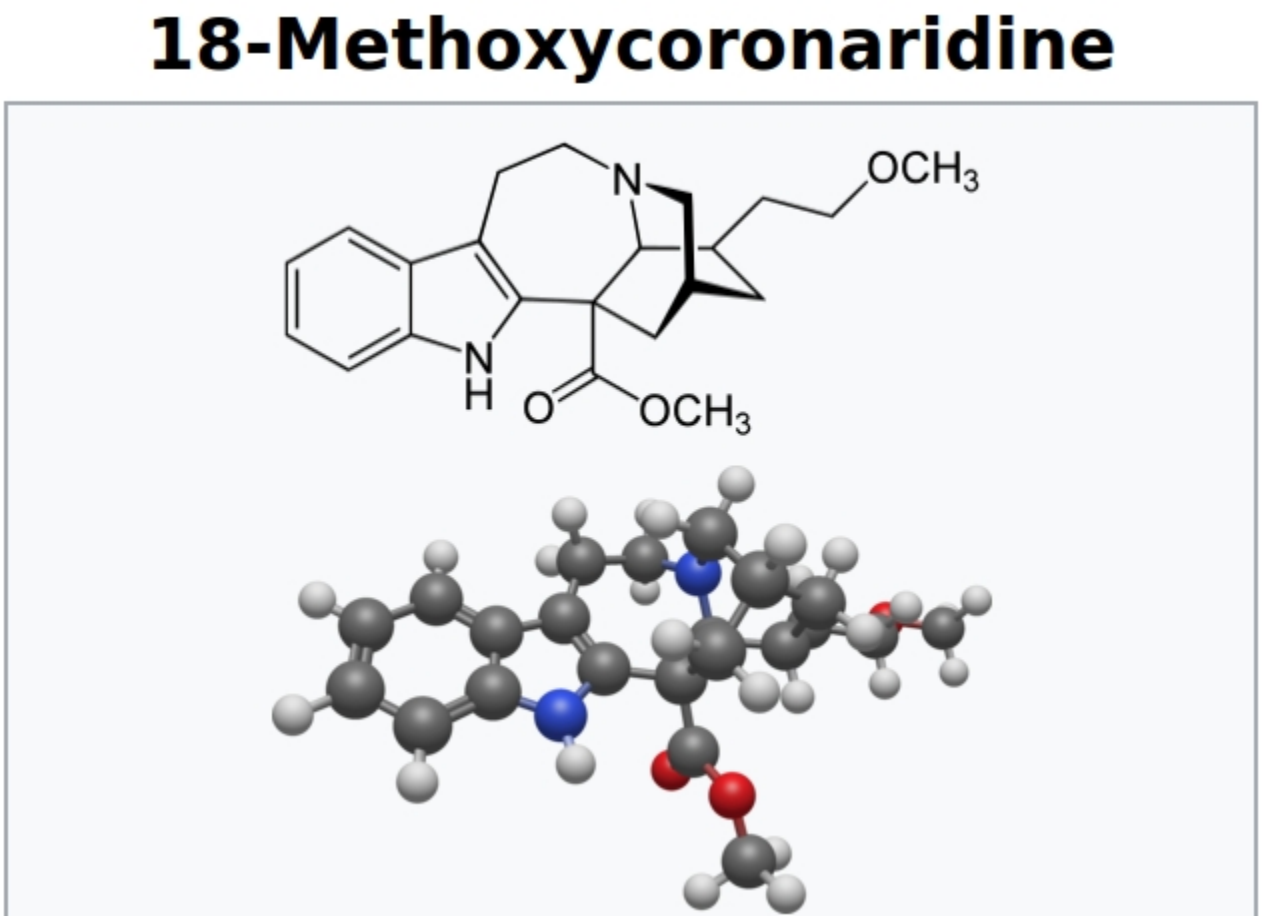
18-MC and Other Coronaridine Analogs as Medicines to Detoxify Drug Addicts

by R. Stuart, AlfredHubbard@protonmail.com, November 2024



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I. Introduction to 18-MC

People who are dependent on addictive drugs are afraid that if they stop using the drug then they will experience two adverse effects: withdrawal symptoms and drug craving. Ibogaine and the rootbark of its botanical source *Tabernanthe iboga* are used to reduce these adverse effects during the detoxification process of addiction treatment. Detoxification is when the addict undergoes the highly uncomfortable process of ceasing to use the addictive drug. To ward off relapse, detoxification must be followed up by a recovery program such as a 12-step group.

Ibogaine is hallucinogenic, which has the advantage that its psychedelic effects can be used for psychotherapy and the disadvantage that this has caused legal prohibition and institutional resistance. Although ibogaine is a Schedule I drug in the United States, it is used by underground therapists in the U.S. and in legal clinics in Mexico, Canada, the Caribbean. Additionally, ibogaine is cardiotoxic (some would say “cardio-affecting”), which increases the necessity of careful screening of patients and requires prolonged medical supervision during and after detoxification. At least 33 Westerners have died taking ibogaine mainly in non-clinical settings, in addition to innumerable deaths of natives taking iboga root in African religious ceremonies.

In the 1990s, Stanley Glick’s team at Albany Medical College investigated a series of “ibogaine congeners” (coronaridine analogs). These seem very promising for the detoxification phase of addiction treatment for opioids, cocaine, methamphetamine, alcohol, and — amazingly — nicotine. Rodent studies show that these analogs reduce drug craving and withdrawal symptoms in the same way as does ibogaine. These analogs have advantages over ibogaine with regard to toxicity and psychoactive affects. They are non-psychoactive and appear to be non-toxic in ordinary doses for anti-addiction purposes.

The analog that happened to get the most attention was 18-MC, originally synthesized by Glick’s associates Martin Kuehne and Upul Bandarage at the University of Vermont. However, several related analogs are at least as interesting. ME-18-MC is as effective for detoxification at half the dose used for 18-MC, and would thus be more economical. Another analog, 18-MAC, is more effective at the same dose as 18-MC. The entire series of analogs was covered by the same use patents. For the rest of this document, the reader should understand that everything said about 18-MC also applies to its

analogs, which are not as well known but which might be even more worthy of investigation.

II. 18-MC is an Orphan Drug

Glick and his colleagues sold the use patent for using 18-MC and its analogs for addiction treatment, as well as the use patent for using them as a weight-loss medications. MindMed bought the patents, but did not develop it as a prescription drug. The patent expired without 18-MC being developed into marketable products. Apparently, MindMed's attempt to renew the patent was unsuccessful. Nobody in the United States seems to want to put up the millions of dollars to usher 18-MC through clinical trials. So now 18-MC is a so-called "orphan drug" for addiction and weight-loss applications. Circa 2020, Brazilian researchers at Infan Industria Quimica Farmaceutica Nacional were supposedly planning to test 18-MC in a Phase II clinical trial for treating leishmaniasis parasites.[1] It is unknowns what doses they were planning to use. An article on the MAPS.org website stated:

> 18-MC has proved difficult to manufacture. Obiter Research, a company based in Champaign, Illinois, that specializes in synthesizing experimental chemicals, spent nearly two years refining the process before successfully creating about 200 grams of the substance — just enough to send to Brazil to be administered to human subjects.[2]

III. The Toxicity of Ibogaine

As of 2019, about 10,000 people had ingested ibogaine outside of African religious settings and 32 of them died. (Of course, people also occasionally die from ibogaine during African religious rituals.) This means that ibogaine killed about 1 in 300 people who consumed it. Although many of the deaths were due to the addict concurrently using incompatible drugs such as opioids, some of these fatalities were from heart attacks, even in non-addicts who appeared to have been in great physical shape. There were a couple deaths by patients who took ibogaine under medical supervision at clinics that presumably had properly screened them, and nobody knows why ibogaine killed them. Ibogaine requires repeated monitoring of vital signs for a couple days after administration because some people have heart attacks two or three days after ingestion. This puts an extra layer of expense and labor on the clinical staff. Given human nature, some clinics

are likely to cut corners, with the result that some patients may suffer adverse events that should have been prevented. Ibogaine is metabolized by the liver enzyme CYP2D6, so each patient should be given a genotype test to determine if he is a “poor metabolizer” who should receive a lower dose. This also imposes an extra expense and time delay on treatment.

An ibogaine therapist told me that he believes that ibogaine should be regarded as “cardio-affecting” (rather than cardio-toxic) because its potential toxicity can be managed by skillful intake screening and supervision, as well as adjusting the dosing schedule so that sensitive patients receive much lower doses stretched out over a longer period of time. Nevertheless, circumventing ibogaine’s potential cardio-toxicity requires medical tests and extra staffing requirements during and following administration. This adds an extra layer of expense, time delay, and complexity to the detoxification process.

IV. The Apparent Non-Toxicity of 18-MC

Because 18-MC operates on fewer neurotransmitter systems, its effects are more specialized. The predominant metabolic pathway for 18-MC is 18-hydroxycoronaridine (18-HC) formation, and this is primarily catalyzed by the liver enzyme CYP2C19.[3] This is a different liver enzyme than that used by ibogaine.

During studies to examine 18-MC’s potential as a weight-loss medicine, rats were given daily doses comparable to the amount required for a single administration for the purpose of minimizing drug craving and withdrawal symptoms. Not a single rat has died yet, nor have rats suffered any adverse medical complications. Although rats are different from people, the approximately three dozen animal studies indicate that 18-MC and related analogs seem to be remarkably non-toxic and do not affect the heart in the same problematic way as ibogaine.

This lack of toxicity is a major advantage for 18-MC.

V. Psychoactive Effects: Ibogaine vs. 18-MC

Ibogaine advocates regard its mind-expanding properties as an advantage. After treatment, many patients appreciate the psychological insight that came from the psychedelic experience. But before treatment (which is when the decision is made about which medicine the patient will be administered)

the last thing that most addicts care about is self-insight. Many people spend their entire lives hiding from the demons in their unconscious minds, and they do not want to have a psychedelic experience. So while ibogaine is popular among some addicts who are already enthusiastic about psychedelics, its hallucinogenic properties might be unappealing to many mainstream addicts who are afraid of mind-expanding substances. The animal models indicate that 18-MC is not psychoactive. Psychotherapy need not be performed at the same time as detoxification. Patients can undergo psychotherapy after they undergo detoxification. 18-MC's lack of psychoactive effects is actually an advantage for several reasons:

1) 18-MC would require fewer staff to conduct the detoxification, reducing expense and complexity of the process.

2) The lack of psychoactivity would bypass institutional resistance by those government regulators and addiction-treatment personnel who still look askance at psychedelics.

3) If 18-MC turns out to be non-toxic to the entire human population, then it could be used for "mass detoxification" of the millions of addicts who currently need substance-abuse treatment. There would be no need for the individualized attention to the psychological needs of each patient.

VI. Production of 18-MC

18-MC is expensive to manufacture because the complex synthesis must be performed by trained chemists operating in a professional lab. The original synthesis had 13 steps.[4] Because there is some wastage at each step, 18-MC has a relatively low yield, meaning that a comparatively small amount of the finished product is produced in comparison to the precursors and other raw materials consumed in production.

Obiter Research is the American chemical company that uses its patented proprietary process to manufacture 18-MC for scientific research. Because this research involves small animals, Obiter only makes small batches. At the present time, Obiter sells 18-MC to researchers for $3800 per gram. They can make it with cGMP quality, guaranteeing a high level of purity. The anti-addiction and weight-loss doses used in the "murine studies" (using rodents) ranged between 10 and 40 mgs/K (milligrams of drug per kilogram of body weight). A 30 mg/K dose of 18-MC for a person weighting 140 pounds (63.5 K) would be 1.9 grams. So this dose for a human being would cost $7,220, which is prohibitively expensive. However, there is an

economy-of-scale consideration here. In 2020, the president of Obiter told me that they could make a large batch at a more-affordable per-unit cost if a legitimate organization wanted to “organize a large-scale campaign.”

If 18-MC becomes accepted as an anti-addiction drug, then I would research simpler production methods that would be less expensive than the Obiter process. Precursors could be extracted from botanical sources such as *Voacanga* or various *Tabernaemontana* species. One Brazilian clinical study used 18-MC manufactured from coronaridine extracted from the stems of *Tabernaemontana catharinensis*, (a.k.a. *Peschiera australis*), a plant easily cultivated in tropical environments.[5] *Tabernamontana coronaria*, which is claimed to be the same species as *T. divicarata*, would also be worthy of investigation. Coronaridine is also present in the aerial (above ground) parts of *Catharanthus roseus*, also called *Vinca rosea* and commonly known as Madagascar periwinkle. This widely cultivated ornamental shrub grows in temperate climates.

VII. Conclusion

A city like San Francisco should develop an 18-MC program. San Francisco spends millions of dollars each year managing its huge addict population, much of it homeless, many of whom came after being kicked out of other states. San Francisco could simply ignore FDA requirements, in the same manner as it previously implemented harm-reduction policies such as needle exchange. The city could procure a kilogram of 10-MC, a kilogram of 18-MAC, and a kilogram of ME-18-MC. It could conduct a double-blind study comparing the safety and efficacy of the three analogs in an addict population. Starting with a small sample of drug-addicted volunteers, who would be detoxed under medical supervision, if everything proceeded smoothly, then the program would expand into a major industry of detoxification. Given that the city government has done little to help San Francisco’s tourism industry recover after the pandemic, eliminating the throngs of unsightly and sometimes belligerent junkies around Civic Center and on Market Street, and offering detox to out-of-town addicts after the city cleans up its own mess, would bolster tourism. If the Board of Supervisors passed a resolution declaring that the opioid epidemic is a local emergency necessitating an 18-MC detox program, then the city lawyers could fend off any objections by anybody who complained that the program does not have FDA approval. If 18-MC and its analogs prove to be

particularly useful in addiction treatment, then the San Francisco program could pave the way for streamlined approval on a federal level.

Additionally, an off-shore 18-MC clinic could be profitable. There are many ibogaine clinics in Mexico, Canada, and the Caribbean. An 18-MC clinic could rent a location to set up an off-shore clinic. Additionally, Ukraine is now receptive to novel treatments such as MDMA psychotherapy for PTSD, so maybe the Ukrainians would be supportive of clinics that treat domestic alcoholics and foreign addicts.

I have a master's degree in clinical psychology with a specialization in addiction studies. I would like to establish an addiction-treatment clinic that uses 18-MC to facilitate the detoxification of addicts. This clinic could be located in a Caribbean country such as Jamaica, which has cheap plane flights, a well-developed tourist infrastructure, English as the national language, and no significant regulatory or legal restrictions. The clinic could operate out of a hotel or retreat center to minimize costs at the beginning. Or my program could operate our of an existing addiction-treatment or ibogaine clinic. A local doctor could be hired to monitor the patients till it became clear that 18-MC did not produce adverse events. The primary expense would be obtaining a large quantity of 18-MC or its analogs. A kilogram of 18-MC would probably cost well over a hundred thousand dollars.

If I were successful, competitors would set up similar clinics. But the world has an unlimited supply of addicts, and it would be a good idea to get in on the ground floor and establish the pioneering clinic that promote this new treatment.

Footnotes

1. Infan Industria Quimica Farmaceutica Nacional. 3-19-2020. “Phase 2 Trial to Evaluate 18-Methoxycoronaridine Efficacy, Safety and Tolerability in Cutaneous Leishmaniasis Patients”. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT03084952 accessed 26-June-2024

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3. Koenig, X.; Hilber, K. 29-January-2015. “The anti-addiction drug ibogaine and the heart: a delicate relation”. *Molecules* 20(2): 2208-28. doi: 10.3390/molecules20022208. PMID: 25642835; PMCID: PMC4382526.

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5. Soares, D.C.; Pereira. C.G.; Meireles, M.Â.A.; Saraiva, E.M. 2007. “Leishmanicidal activity of a supercritical fluid fraction obtained from Tabernaemontana catharinensis”. *Parasitology International* 56: 135–139.

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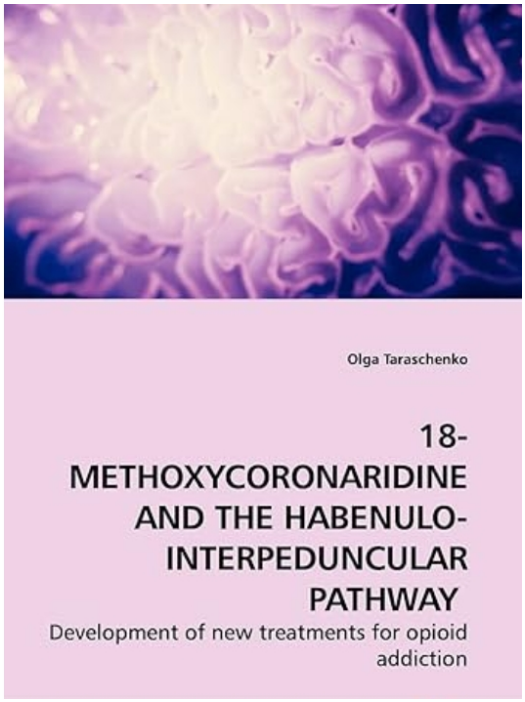

This expensive book contains much of the same information that can be found on PubMed.