PharmaCannabis

A Canadian cannabis researcher gets a prescription to the first marijuana–based medicine available in North America. Does the spray work as well as smoked cannabis?

By Philippe Lucas

In June of 2005, Bayer Canada began to distribute GW Pharmaceuticals' whole-plant cannabis spray called Sativex. Though Sativex is officially prescribed for MS-related neuropathic pain, as a long-time medical cannabis user, I was able to obtain it as an "off-label" prescription for the treatment of hepatitis C-related nausea, loss of appetite, localized pain and stress.

This experiment was not meant to be either an endorsement or a criticism of Sativex, but rather one person's experience with it. I'd also like to point out that while a five-day trial is admittedly too short to determine the long-term effects of Sativex on my condition, I believe that it's entirely adequate to make a preliminary and personal evaluation of estimated time to onset of effects; dosage, intoxication and short-term side-effects; taste/mode of ingestion; and initial symptom relief.

In 1982, I was infected with the hepatitis C virus as a result of Ontario's tainted blood supply, and since my diagnosis in 1995 I've used cannabis daily to alleviate nausea and localized pain, and to stimulate my appetite. I also believe that the relaxant effects of cannabis help me to deal with the psychological stress of having a chronic condition like hep C.

I've attended many presentations on Sativex given by GW-sponsored researchers. The evidence I've seen and read suggests that Sativex does indeed have at least some of the same therapeutic effects as raw plant cannabis, be it edibles, tinctures or in smoked form.

Prior to Sativex, the only cannabis-related pharmaceutical products available have been Solvay's Marinol (dronabinal) and Lilly's Cesamet (nabilone). Both are synthetic forms of cannabinoids that are primarily prescribed as anti-emetics—to treat nausea, vomiting associated with cancer chemotherapy, and appetite loss associated with weight loss due to AIDS and cancer. Unfortunately, my experience with both of these has been less than satisfactory. Since both are orally ingested in pill form, it can be very difficult to find the right dose on a regular basis. Additionally, oral ingestion means that the initial onset of effects can take from 60 to 90 minutes, limiting their therapeutic potential considerably, particularly in comparison to the rapid therapeutic relief and ease of titration offered through smoked inhalation.

Sativex is different from both of the above-mentions drugs in that it's not a synthetic cannabinoid; it's made by extracting and re-combining cannabinoids from raw-plant

cannabis. While Mariniol and Cesamet come in capsule form, Sativex is administered sublingually by spraying a liquid under the tongue or on the inside of the cheek, resulting in rapid entry into the bloodstream through oromucosal absorption. The combination of THC (tetrahydracannabinol), CBD (cannabidiol) and minor cannabinoids is currently approved for use by MS victims suffering from chronic neuropathic pain, but GW is researching its potential in increasing appetite, relieving post-operative pain, and many other conditions helped by raw-plant smoked or vaporized cannabis.

I should also mention that the Vancouver Island Compassion Society (VICS), a non-profit medical cannabis dispensary and research organization that I founded in 1999, has been distributing an oromucosal spray of our own for over two years, and I was eager to compare the two products. In order to give Sativex a fair shot, I used it exclusively for five days.

PRODUCT ORDER & ARRIVAL

Though I'm certain that this will eventually improve, I was disappointed to find that it took 17 days for Sativex to arrive at the pharmacy following my initial order. The price is extremely prohibitive, and though Bayer Canada suggests that many private companies will eventually cover some of the cost, my 51-spray vial cost C$138 (US$114)—approximately C$.2.70 (US$2.24) per individual spray. GW estimates that the average patient uses five sprays per day. Since the average VICS user goes through about 1.5 grams of dried cannabis a day, this puts Sativex at about the same price as black-market cannabis, and a bit more expensive than the average daily cost of using compassion club cannabis, which ranges from $6-10 a gram. At a cost of $20 for 900 doses (or about $.02 a spray), however, VICS' highly effective but somewhat less sophisticated Cannamist is the most affordable of all of these options.

Perhaps the biggest surprise of this bioassay (a.ka. drug test) came when I went to pick it up my Sativex from the drugstore. The little box of four vials (about the size of two packs of cigarettes) was delivered to my pharmacy in a huge (20 in. x 20 in. x 16 in.) box containing a cooler and artificial cooling packs; since the box is literally covered in "skull-and-crossbones" poison signs six inches wide and big red flaming "flammable" signs, it terrified both the delivery person and my pharmacist. Considering that cannabis is non-lethal, I was extremely concerned about the psychological impression created by treating this product like it was nitroglycerine, rather than a benign, plant-based medicine.

DAY 1

At 5 P.M. I try Sativex for the first time, using just one spray as instructed in the dosing regimen included with the product. My initial experience is kind of frightening: a slight (but not imperceptible) burning sensation under my tongue followed by a taste of cannabis, mint, and a slightly bitter/chemical flavor which lingers for a few minutes after use. I notice no effect at this dosage regimen (and find that my appetite is weak despite the approach of dinner time), so at about 7 P.M. I up the dosage to two sprays. Much like

with Cannamist, I feel the initial effects within the first five minutes (GW claims that it takes 20 to 40 minutes, but if this were true, they could hardly claim to be getting any oromucosal absorption). I definitely feel more relaxed and actually start to get hungry. I take another two sprays before bed, and report no change in my sleep/dream patterns (like many regular users, when I deprive myself of cannabis, I go through a very active dream cycle for a couple of days).

My total use for Day 1 was five sprays, or $15 worth of Sativex.

DAY 2

Today I awoke with significant nausea, which is unusual for me when I have a regular supply of dry cannabis. Since I normally don't feel nauseous or the need to smoke in the morning, I've always assumed that the residual cannabinoids ingested the night before continue to have an anti-nauseant effect through much of the next day; this does not appear to be the case with Sativex, at least after the first night. I take two sprays of Sativex, noting that the burning is still there, and feel a bit of relief from my nausea, and then have my usual breakfast. It's almost 1 P.M., and I take two more sprays to stimulate my appetite for lunch. Interestingly, I find myself uncomfortably dizzy, disoriented, and intoxicated as I finish typing this entry, suggesting that I haven't quite figured out my proper dosage yet (and that yes, you can get high off of Sativex). By the way, this also suggests that the GW spray is somewhat stronger than the VICS Cannamist, with which my usual dose is three sprays every two hours (which equals 24 puffs a day) for relief without significant intoxication.

As I finished writing yesterday's report, I'd just been overcome by an uncomfortable level of intoxication, and since I'm very cannabis-experienced and rarely encounter significant adverse effects in even high doses of smoked ingestion, I highly doubt that this intoxication was due to THC overdose. This leads me to consider two further options: that this discomfort was CBD-related, since I would've only had exposure to low doses of this cannabinoid in commercial/medical strains; or I experienced enough "first-pass effect" to convert a significant amount of the THC in Sativex into 11-hydroxy THC, which is about four times stronger than THC. Since I've long been a lightweight with edibles, I favor the latter explanation. Additionally, GW's research has suggests that many people whocouldn't handle high doses of THC alone often find that the addition of CBD helped. In other words, CBD should've helped limit my intoxication and reduce the potential side-effects of ingesting too much THC.

Regardless of the cause, the intoxication/dizziness lasts about three to four hours (once again suggesting a conversion to 11-hydroxy THC), and admittedly freaked me out a bit, forcing me to cut back on my dosage regimen. I end up using four more sprays over the next eight hours at the rate of about a single spray every two hours. I suffer no further adverse consequences, sleep well, and experience nothing unusual in my dream patterns.

My total use for Day 2 was nine sprays, or $27 worth of Sativex.

DAY 3

I woke up this morning with no nausea, so yesterday may have been an exception. My appetite is pretty good, though slightly less than usual (I have skipped my usual lunch hour). I've just taken my third sprayof the day (opting to use one spray every two hours, rather than stacking my dosage), and have not experienced any intoxication, and perhaps most significantly, the mild withdrawal symptoms (hyperactivity, irritability, loss of appetite, nausea, overactive dream cycles) I typically experience for the first three days without cannabis. But I have to be honest: I do miss the high-quality organic dried cannabis that has been my medicine for so long.

Taking a single dose every two hours maintains a steady relief against nausea without uncomfortable intoxication, but I have also started to notice a bit of a burnout factor. Despite having a good but short sleep the night before, by the end of Day 3I'm wiped out. I eat dinner without much gusto, and I'm tired but hyperactive all evening, drifting off to a fairly restless night's sleep at about midnight.

My experience so far with Sativex has made me consider it not so much of a breakthrough in regards to being different and novel mode of ingestion, but more like a new and unique high-CBD strain, only instead of using selective breeding to obtain a combination THC/CBD plant, GW has used the advantages of modern science to create something that might have taken breeders years to accomplish naturally. So, if we accept that the mode of delivery is sound (and I can assure you that it works), then all that we're really trying to determine is for whom and for which condition this particular high-CBD strain of medicine is best suited. Clearly, Sativex is an additional option for medi-pot users and not a replacement for all raw cannabis. Though it may work for some, undoubtedly others will quite simply need a different "strain" than Sativex (and whatever other cannabinoid combinations GW may release over the next few years).

My total use for Day 3 was nine sprays, or $27 worth of Sativex.

DAY 4

I once again begin the day with a single spray every two hours or so, but by lunchtime I'm tired and my appetite is down by about 30 percent (though I suffer no nausea), so I up my dose a bit. The strong narcotic effect that I've periodically experienced on Sativex is either the result of the high-CBD ratio in the product (which I have never heard described as being particularly narcotic) or of at least some of the THC being converted into 11-hydroxy THC; it's kind of like eating cannabis cookies or using a strong *indica* all day. I'm slightly intoxicated by the end of the day, but it's not uncomfortable and I rather enjoy the physical relaxation it brought that I miss from smoked ingestion. I have a small supper and sleep deeply but not for very long last night.

My total use on Day 4 was 11 sprays, or $33 worth of Sativex.

DAY 5

The last day of my Sativex trial begins well. I've more or less determined the proper dose for my condition and personal tolerance—one spray every 90 to 120 minutes. This appears to help with both nausea and increases my appetite, despite the slight drawback of minor intoxication (occasional dizziness/disorientation, limited euphoria, difficulty concentrating, low energy). I appreciate the discretion that Sativex offers, using it in our local City Hall prior to a meeting with city officials. I'd never have smoked under the same circumstances. For those without a viable alternative to smoking, Sativex may offer more discreet access to cannabinoids under circumstances in which smoking would be inappropriate or impossible (such as plane travel).

I used Sativex until midnight and then smoked a joint to celebrate the end of this informal experiment. I'm surprised to find that the level of intoxication I experience with the smoked product is only marginally stronger than with Sativex, and am additionally taken aback by how hungry I suddenly feel. Throughout my five days on Sativex, I had experienced modest relief of nausea and appetite stimulation, but I ate with much less gusto and enthusiasm than normal; yet after smoking a single joint I found myself conducting a late-night raid on the fridge.

Over the next few days of smoked ingestion, my appetite returns to normal (it decreased about 30 to 40 percent while on Sativex), my mood is elevated, and I experience known of the dizziness and disorientation like I did while on Sativex. I'm extremely pleased to return to using dried cannabis, which I find very predictable and easy to titrate, and the euphoria associated with this form of ingestion is a welcome side-effect.

My total use on Day 5 was 11 sprays, or $33 worth of Sativex.

CONCLUSION

Sativex is a very good preliminary attempt at recreating the benefits of smoked cannabis (rapid onset of effects, ease of self-titration) without irritating the lungs. GW should be commended for obviously considering much of the anecdotal evidence of those who obtain benefit from smoked-ingestion, but in my opinion the latter should still be the benchmark to aim for, and which they have yet to reach (which is surely why GW is now working on an "inhaled" version of Sativex). In my particular situation, the longer onset of effects compared to smoked ingestion makes Sativex less desirable than raw cannabis. Additionally, the high cost (my total for this 5-day trial was 45 sprays, or $135 worth of Sativex) is sure to be prohibitive to many who might otherwise benefit from its use. However, if I didn't have access to a safe and consistent source of whole-plant, organic cannabis, or if I found myself in a situation where smoking might be inappropriate or otherwise impossible, I'd certainly consider Sativex a far superior alternative to either Marinol or Cesamet.

Ultimately, I'll continue to use cannabis in its raw form for a number of reasons, including a personal philosophy that sees me chose to eat an orange rather than taking vitamin C, and a general disinclination to using pharmaceuticals if they can be

avoided. Additionally, the organic cannabis grown by the VICS appears to be more effective in controlling my nausea and increasing my appetite than Sativex; it's simply more predictable than GW's product. I consider Sativex not as a replacement for raw cannabis, but rather as another "strain", and a viable option for those sick and suffering citizens who might not want to smoke their medicine and/or to purchase therapeutic products from anyone but a pharmacist.

Finally, if Sativex is a safe and effective medicine, it's because cannabis is a safe and effective medicine, period. But is Sativex cost-effective compared to the available alternatives? That's a question that both Bayer and GW will have to seriously consider over the next few years.

Philippe Lucas is an experienced medicinal cannabis researcher, producer, distributor, and advocate; he is also one of about 1200 Canadians currently allowed to use cannabis for medical purposes.

For a more direct comparison of the costs, effect and availability of various cannabis-based medicines, please see the chart below.

COMPARING CANNABIS MEDICINES:

Current Options for Some Medicinal Cannabis Users	Year of introduction	mode of ingestion	legal status	manufactured by:	cost per dose[1]	average daily dose	benefits/side effects	comments
Sativex	Approved by Health Canada in 2005	oromucosal	legal in Canada - unavailable in U.S. and Europe	GW Pharmaceuticals (www.**gw**pharm.com)	>$2 per spray	5 sprays	rapid absorption and onset of effects, but overly expensive	effective but expensive alternative to raw cannabis
Marinol	Approved by FDA in 1985	oral	legal and available by prescription	Unimed/Solvay Pharmaceuticals (www.**unimed**.com)	>$2 per pill for 2.5mg; $4 for 5mg, and $9 for 10mg	n/a	expensive and often unpredictable, but legal	poor synthetic substitute for raw-plant cannabis
Cesamet	Approved by FDA in 1985, but never marketed in the U.S.	oral	available by prescription in Canada and U.K - availability in U.S. expected by the end of 2005	Valeant Pharmaceuticals (www.**valeant**.com)	>$3 per pill for 0.5mg; $6 for 1mg	n/a	expensive and often unpredictable, but legal	ditto (see above)
Cannamist	2003	oromucosal	only available through the VICS	The Vancouver Island Compassion Society (www.thevics.com)	$.02 per spray	10-15 sprays	rapid relief at very affordable price	affordable alternative to raw cannabis, but not widely available
Raw Cannabis	Records of therapeutic use date back at least 5000 years (Pen Tsao Ching)	optional (smoked, vaporized, or oral)	illegal and widely used and available	the guy down the street with the blacked-out basement windows, or your friendly neighbourhood compassion society	$5-15 per gram	1-2 grams	effective but illegal; continued concerns over smoked-ingestion	5000 years of recorded use as a medicine, but modern research stymied by drug war

[1] Cost approximate, and may vary slightly from different states and pharmacies.