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Cannabis as an Adjunct to or Substitute for Opiates in the Treatment of Chronic Pain

Philippe Lucas, M.A.[a]

Abstract — There is a growing body of evidence to support the use of medical cannabis as an adjunct to or substitute for prescription opiates in the treatment of chronic pain. When used in conjunction with opiates, cannabinoids lead to a greater cumulative relief of pain, resulting in a reduction in the use of opiates (and associated side-effects) by patients in a clinical setting. Additionally, cannabinoids can prevent the development of tolerance to and withdrawal from opiates, and can even rekindle opiate analgesia after a prior dosage has become ineffective. Novel research suggests that cannabis may be useful in the treatment of problematic substance use. These findings suggest that increasing safe access to medical cannabis may reduce the personal and social harms associated with addiction, particularly in relation to the growing problematic use of pharmaceutical opiates. Despite a lack of regulatory oversight by federal governments in North America, community-based medical cannabis dispensaries have proven successful at supplying patients with a safe source of cannabis within an environment conducive to healing, and may be reducing the problematic use of pharmaceutical opiates and other potentially harmful substances in their communities.

Keywords — addiction, cannabis, harm reduction, opiates, substitution effect

The medical use of cannabis can be traced back at least 5,000 years. The oldest reports originate in China and Egypt. It appears in a medical context in the Vedas, India's oldest religious text, and there are reports of its use as a medicine from fragments of Assyrian texts dating back to 700 B.C. The famous Chinese doctor Hua T'uo (approx. 100 A.D.) reportedly made use of a wine and cannabis mixture as an anaesthetic for surgical operations (Russo 2007; Fankhauser 2002).

There are numerous reports of the medicinal properties of cannabis from early in the nineteenth century, the most noted of which is an 1839 report titled "On the Preparations of the Indian Hemp, or Gunjah" by the Irish doctor William B. O'Shaughnessy (1843) where he describes diverse applications for cannabis, including rheumatism, rabies, cholera, tetanus, cramps and delirium tremens. A few years later Ernst Freiherr von Bibra published the renowned *Narcotics and the Human Being*, devoting thirty pages to the therapeutic use of cannabis preparations and hashish (Von Bibra 1855).

By the late nineteenth century, cannabis-based preparations were manufactured and marketed by Burroughs-Wellcome & Co. In England; and Bristol-Meyers Squib, Parke-Davis, and Eli Lilly in North America. The development of vaccines to prevent the spread of common infectious diseases, the increased use of opiates (with the introduction of the hypodermic syringe), and the discovery of aspirin at the end of the nineteenth and early twentieth century resulted in cannabis-based medicines losing their prevalence in the market place and Western pharmacopoeia (Grinspoon & Bakalar 1993). The U.S. Pharmacopoeia

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listed cannabis until 1941, stating that it can be used for treating fatigue, coughing, rheumatism, asthma, delirium tremens, migraine headaches, and the cramps and depressions associated with menstruation (Mikuria 1973).

Although modern research into therapeutic applications for cannabis has been seriously stymied by its prohibition in most of the Western world, extensive anecdotal reports and a growing body of laboratory and clinical research suggest that it may have many medicinal uses, including hunger stimulation for wasting syndrome; anti-emetic and anti-nausea properties in AIDS or cancer chemotherapy; antispasmodic properties for multiple sclerosis, epilepsy and other neurological dysfunctions; reducing intra-ocular eye pressure in glaucoma; and analgesic properties in a large number of chronic pain conditions (Hazekamp & Grotenhermen 2010; Ben Amar 2006; Grotenhermen & Russo 2002).

CANNABIS AND CHRONIC PAIN

The Canadian Psychological Association (CPA) defines chronic pain as being pain that doesn't go away, lasts over six months, or extends beyond the expected recovery time after an accident or medical intervention. Additionally, they suggest that chronic pain is a highly variable condition with many different causes:

> There are different types of chronic pain, many of which are not clearly understood. Chronic pain may be associated with an illness or disability, such as cancer, arthritis or phantom limb pain. Some types of chronic pain start after an accident. Others may start as acute episodes but then the pain becomes constant over time, such as low back pain. With some types of chronic pain, like migraine headaches, the pain is recurrent, rather than constant. There are many other kinds of chronic pain, such as chronic postsurgical pain, fibromyalgia, temporomandibular disorders, etc. While in some cases the cause of pain is known, in many other cases it is not clear why pain persists (CPA 2007).

Although statistics regarding chronic pain are difficult to come by, the CPA website states that:

> About one in ten Canadians has chronic pain. Chronic pain affects both sexes and while it is most common in middle age, it can occur at any age—from infancy to the elderly. Chronic pain can make simple movements hurt, disrupt sleep, and reduce energy. It can impair work, social, recreational, and household activities. People who have been injured in accidents may develop anxiety symptoms as well as pain. Chronic pain can have a negative impact on financial security, and can provoke alcohol or drug abuse. It can disrupt marital and family relationships . . . Given the impact pain can have on quality of life, it is no surprise that more than a quarter of all people who develop chronic pain also experience significant depression or anxiety (CPA 2007).

While numerous products are available for the relief of many different types of pain, there remains a significant group of patients for whom traditional pharmacological pain control is incomplete or ineffective. Existing pharmacological treatments with known side effects are widely used for analgesia, but may show a lack of efficacy in certain conditions (Russo 2008a). These agents include:

- Non-opioid analgesics
- Opioid analgesics
- Anticonvulsants
- Antimigraine drugs
- Tricyclic antidepressants
- Anti-inflammatories
- Steroids

Despite modern progress on the understanding and treatment of pain over the last century as well as a recent North American emphasis on treating pain stemming from other medical conditions, many problems still remain in providing safe and effective analgesia for all those with a legitimate need for pain relief (Russo 2008a).

Chronic pain is highly subjective in nature, and sufferers of the same chronic pain condition may experience very different symptomology. Fibromyalgia, a chronic pain syndrome of unknown origins associated with depression and chronic fatigue is a good example of this effect. It is interesting to note that Russo (2008a, b) has theorized that intractable and difficult to treat pain conditions like fibromyalgia may be related to a condition he terms *clinical endocannabinoid deficiency* (CECD), which is an imbalance in the body's own internal cannabinoid system. Furthermore there are numerous different origins for chronic pain—visceral, somatic, neurogenic, etc.—which may explain why so many sufferers report poor control with standard pharmaceuticals. Therefore chronic pain sufferers are in no way homogeneous, indicating the need for variable and individual treatment regimens and dosages (Mersky & Bogduk 1994).

In Europe, chronic musculoskeletal pain of a disabling nature affects over 25% of elderly people (Frondini et al. 2007). Responses to a 2005 poll indicate that 19% of adults (38 million) in the U.S. have chronic pain, and 6% (or 12 million) have utilized cannabis in attempts to treat it (ABC News 2005). Ware and colleagues (2005) report that 25% of chronic pain sufferers in the U.K. use cannabis, and that medical cannabis was largely associated with "younger age, male gender and previous recreational use." A further assessment of cannabis use and chronic pain by Ware and Beaulieu and Ware (2007) found that "there is increasing evidence that cannabinoids are safe and effective for refractory chronic pain conditions including neuropathic pain associated with multiple sclerosis, rheumatoid arthritis, and peripheral neuropathy associated with HIV/AIDS", concluding that more research is needed.

CANNABINOID RECEPTORS AND ANALGESIA

Over the last 15 years, CB1 and CB2 receptors have been identified (Pertwee 2002). CB1 receptors are of particularly high concentration in the central nervous

system, including several areas of the central nervous system that mediate the perception of pain (Walker et al. 1999). CB2 receptors are found mostly in immune tissue, such as leukocytes, the spleen and tonsils. These receptors are absent from the brain stem, thus explaining the lack of classic opioid side effects such as respiratory depression. This may prove to be an advantage of cannabinoid-based drugs over opiates. Another similarity with the opioid system is the existence of endogenous cannabinoid receptor agonists, the most studied of which is anandamide (Pertwee 2002). Evidence shows that this endocannabinoid can serve as a neuromodulator or neurotransmitter (DiMarzo et al. 1998), and it has been found that cannabinoid receptors outside of the brain and spine are affected when skin or flesh is cut or injured; anandamide is released and helps modulates the pain associated with injury. Rats treated with a chemical blocker for anandamide showed an extended and more severe response to pain (Calignano et al. 1998). There is recent evidence that anandamide and methandamide can activate vanilloid receptors on sensory neurons. The extent to which exogenous or endogenous cannabinoids can modulate pain through vanilloid receptors that are known to be present on nociceptive sensory neurons has yet to be fully established (Pertwee 2002).

HUMAN STUDIES ON CANNABINOIDS AS ANALGESICS

Although human studies on the therapeutic effects of cannabis have been significantly limited by a restrictive legal regime and the unavailability of cannabis products to conduct such studies, available research suggests that cannabis has strong potential as an analgesic. An early study of synthetic delta-9-tetrahydrocannabinol (hereafter referred to as "THC" for the rest of this paper) administered orally in 10 to 25 mg doses was shown to relieve pain in cancer patients without significant effects on mood (Davies et al. 1974). A study by Blake and colleagues (2006) examining the effects of Sativex, an oromucosal whole plant cannabis extract with a THC/CBD ratio of 50:50, on rheumatoid arthritis reported significant analgesic effect compared to placebo. Although some mild or moderate adverse effects like dizziness were reported by the active treatment group, Sativex was generally well-tolerated.

In a study to determine the effect of smoked cannabis on pain related to HIV-associated sensory neuropathy and an experimental pain model, researchers found that smoked cannabis was well tolerated and effectively relieved chronic neuropathic pain (Abrams et al. 2007). A study by Wilsey and colleagues (2008) on smoked cannabis and neuropathic pain compared the effect of high THC (7%) cannabis with low THC (3.5%) cannabis and placebo. The results showed that both active preparations were effective at reducing pain, with no apparent correlation between dose levels and pain relief. Although some moderate adverse effects were identified, the treatment was well-tolerated.

Ware and colleagues (2010) recently published results from a randomized clinical trial on smoked cannabis and chronic pain, finding that 9.4% THC cannabis used three times daily for five days reduced the intensity of pain and improved sleep in patients compared to placebo, and was well tolerated by the 21 patients who concluded the study. Although study participants reported mild or moderate adverse effects, these were comparable to the adverse effects of non-smoked pharmaceutical cannabinoid medicines.

CANNABINOIDS AND OPIOIDS IN THE TREATMENT OF CHRONIC PAIN

Opiates are among the most widely prescribed treatments for chronic pain in the world (Dhalla, Mamdani & Sivilotti 2009; Compton & Volkow 2006). Evidence of the medical use of opiates dates back at least to the Ebers Papyrus from 1500 B.C. (Brownstein 1993), and there is little doubt that despite the potential for serious side effects, including death, and the ongoing development of alternative approaches to pain relief, pharmaceutical opiates will continue to be one of the most effective tools available for the treatment of chronic pain. However, a major personal and public health concern associated with the use of pharmaceutical opiates is dependence. In fact, according to the US Substance Abuse and Mental Health Services Administration, the dependence on and abuse of pharmaceutical medications is currently the fastest growing form of problematic substance use in North America (SAMHSA 2007). As a result of this increase in the use and abuse of prescription pharmaceuticals, Moore and colleagues (2007) report that serious adverse events and deaths resulting from prescription drug use in the U.S. nearly tripled between 1998 and 2005. Addiction to and abuse of pharmaceutical opiates has been identified as one of the main personal and public health concerns associated with this trend (Dhalla, Mamdani & Sivilotti 2009; Fischer et al. 2008; Compton & Volkow 2006).

The following research suggests that when used in conjunction with opiates, cannabinoids can lead to a greater cumulative relief of pain, which may in turn result in a reduction in the use of opiates (and associated side effects) by patients in a clinical setting (Cichewicz et al. 1999). This may not only have positive impact on patient pain levels and overall quality of life, but also on the overall morbidity and mortality associated with pharmaceutical opiates, and on the high levels of opiate addiction in both patients and the general population.

A randomized double-blind crossover placebo-controlled study of oral medication for pain in ten terminal cancer patients comparing 5, 10, 15, and 20 mg of THC in

single doses with placebo found a significant dose-related analgesic effect at the two higher doses (Noyes et al. 1975a). A larger follow-up study of 36 terminally ill patients with cancer pain was designed to compare 10 and 20 mg THC with 60 and 120 mg codeine and placebo. The results suggest that 10 mg THC was slightly less effective than 60 mg codeine, and that 20 mg THC was slightly more effective than 120 mg of codeine (Noyes et al. 1975b).

A later single-patient study examining the analgesic effects of oral doses of 5mg of THC, 50 mg of codeine, and placebo showed that both active preparations were significantly more effective than placebo at relieving MS-related pain. The only major reported difference between the active drugs was that THC relieved spasticity better than codeine (Maurer et al. 1990).

A study by Pinsger (2006) on the effects of nabilone (a synthetic cannabinoid) as an adjunct to existing chronic pain therapy resulted in reduced pain and improved quality of life. Although some mild to moderate side effects were noted, the majority of patients reported overall benefits when compared to their usual chronic pain treatment.

A clinical study by Nurmikko (2007) examining the effects of Sativex as an adjunct to existing stable analgesia in patients suffering from peripheral neuropathic pain showed that 26% of participants reported more than 30% reductions in pain intensity, compared with 15% in those using placebo. Adverse events were few and largely mild or moderate.

A randomized clinical study by Skrabek and colleagues (2008) on nabilone as an adjunct treatment for 15 patients affected by fibromyalgia reported significant benefits in pain and overall function. Mild side-effects were reported, including weight gain, but participants indicated overall increases in quality of life.

Narang and colleagues (2008) conducted a phase 1 and phase 2 study examining the efficacy of dronabinol as an adjunct to opioid therapy for the treatment of chronic pain. Both studies showed that dronabinol decreased pain intensity and increased quality of life compared to baseline opiate therapy. The findings also reported mild to moderate side effects including drowsiness, but patients also reported an improvement in the quality of sleep and overall satisfaction with the treatment compared to placebo.

Additionally, studies also show that cannabinoids can prevent the development of tolerance to and withdrawal from opiates (Cichewicz & Welch 2003), and can even rekindle opiate analgesia after a prior dosage has become ineffective (Russo 2008a; Cichewicz & McCarthy 2003). Furthermore, research by Blume and colleagues (2011) and Ramesh and colleagues (2011) suggests that cannabinoid receptors might interrupt signaling in the opioid receptor systems, affecting both cravings for opiates and withdrawal severity.

GATEWAY OR SAFER SUBSTITUTE?

Despite its low potential for individual harm or abuse and minimal impact on public health and associated social costs, the medical use of cannabis remains controversial with police, physicians, and policymakers. One of the main concerns cited by opponents is that it could lead to either dependence on cannabis, or potentially be a "gateway" to the use of and addiction to hard drugs. The premise of the *gateway* or *stepping stone* hypothesis is that the use of one substance may subsequently lead to the use of another. In regards to illicit substance use, this theory suggests that the use of cannabis may facilitate the use of potentially more harmful/addictive substances such as opiates, cocaine, or amphetamines. The evidential foundation for this theoretical construct is based on research indicating that most people who use so-called "hard" drugs such as heroin or cocaine report a prior use of cannabis. Lessem and colleagues (2006: 499) state that:

> The "gateway theory" is comprised of two interrelated observations. The first is that marijuana use is associated with later, non-marijuana, illicit drug use, and the second is that there is a temporal ordering of substance experimentation in which lower order substances, which are more commonly used, precede the use of higher order substances. Thus, typically one licit substance such as alcohol or cigarettes is used first in a sequence. Marijuana is usually the first illicit substance used before progressing on to using other illicit substances.

While most studies have focused on the social or economic determinants that could lead cannabis users to experiment with other substances (Wagner & Anthony 2002; Pacula et al. 2002), some research suggests that this progression may be due to biological changes in individuals exposed to cannabis (Lessem et al. 2006).

However, both social and clinical research has convincingly debunked the gateway or stepping stone hypothesis. The Senate Special Committee on Illegal Drugs final report on cannabis (Nolin et al. 2002) reviewed all of the available evidence on the topic and drew the following conclusions:

> We feel that the available data show that it is not cannabis itself that leads to other drug use but the combination of the following factors:
> - Factors related to personal and family history that predispose to early entry on a trajectory of use of psychoactive substances starting with alcohol;
> - Early introduction to cannabis, earlier than the average for experimenters, and more rapid progress towards a trajectory of regular use;
> - Frequenting of a marginal or deviant environment;
> - Availability of various substances from the same dealers.

Thus, while it may be true that many people who use "hard" drugs have also used cannabis, the reasons range

from social factors such as poverty to the illegal status of the substance, which results in black market control over its distribution. As the Canadian Senate discovered, drug use trends in Canada simply do not support the *gateway* or *stepping stone* hypothesis, concluding that "if we come back to trends in drug use in the population, while more than 30% have used cannabis, less than 4% have used cocaine and less than 1% heroin" (Nolin et al. 2002: 126).

The counterpoint to gateway theory is *substitution effect*, an economic theory that suggests that variations in the availability of one product (through changes in cost or social policy), may affect the use of another:

> Within a behavioral economic framework, reinforcer interactions are classified into multiple categories; two commodities may be "substitutes" for one another (e.g., two forms of opioid drugs); they may be "complementary," whereby the value of one is enhanced by consumption of the other; or they may be "independent," such that the reinforcing functions of one are not altered by the presence or absence of the other (Hursh et al. 2005: 24).

Changes in the use of cannabis, opiates, or other drugs—whether for medical or recreational use—can be the result of: (a) economic shifts affecting end-user costs; (b) changes in policy which effect availability; (c) legal risk and associated repercussions; or (d) psychoactive/pharmacological substitution. In regards to psychoactive substitution, Hursh and colleagues (2005: 25) suggest that "pharmacological therapies for the treatment of drug abuse can also be conceptualized as alternative commodities that either substitute for illicit drug use (e.g., agonist therapy) or reduce the potency of illicit drugs directly (e.g., narcotic antagonist therapy)." Perhaps the best example of the viability of psychoactive substitution is the now-common prescription use of methadone as a substitute to injection heroin use. This substitution reduces some of the risks associate with injection drug use, including overdose and disease transmission, since drug levels are constant and predictable, and methadone is taken orally rather than injected. Additionally, since methadone is less expensive than heroin (and is subsidized by provincial health registries in Canada), this substitution has the added potential benefit of reducing drug-related theft and crime. However, many methadone patients have reported health concerns associated with its use as well, and recent research suggests that prescription heroin or opiates may be a safer and more effective alternative for users than either black-market heroin or methadone (NAOMI Study Team 2008).

As suggested earlier, not all psychoactive substitution is the result of a deliberate decision made on an individual basis. At the population level it is often the unintended result of public policy shifts or other social changes, such as cost, criminalization or availability. In an examination of hospital drug episodes in 13 U.S. states that decriminalized the personal recreational use of cannabis in the 1970s, Model (1993) found that users shifted from using harder drugs to marijuana after its legal risks were decreased. Findings from Australia's 2001 *National Drug Strategy Household Survey* (AIHW 2002) specifically identify substitution effect, indicating 56.6% of heroin users substituted cannabis when their substance of choice was unavailable. The survey also found that 31.8% of people who use pharmaceutical analgesics for nonmedical purposes reported using cannabis when painkillers weren't available. This evidence strongly suggests that the increased availability of cannabis (through a reduction of penalties or actual regulated, legal access) might lead to a population level reduction in the licit and illicit use of opiates and pharmaceutical analgesics and the associated personal, social and public health harms and costs.

The illegal status of cannabis across most of the world has made clinical trials on cannabis as a treatment for problematic substance use nearly impossible, but a number of studies on both humans and animals suggest that the cannabinoid system plays a role in dependence and addiction to both licit and illicit substances. Current research shows that behavioral effects and motivational responses induced by nicotine can be modulated by the endocannabinoid system (Balerio, Aso & Maldonado 2006).

Additionally, a study by the New York State Psychiatric Institute on people with cocaine dependence and comorbid attention deficit hyperactivity disorder has shown that cannabis users were more successful than other patients in abstaining from cocaine use (Aharonovich et al. 2006). An earlier study by Labigalini Jr. and colleagues (1999) also noted this effect on people with a dependence on crack cocaine, reporting that 68% of the 25 subjects who self-medicated with cannabis in order to reduce cravings were able to give up crack altogether. Researchers theorized that this phenomenon is biological and psychological. Addiction to stimulants result in a decline in the cerebral activity involving serotonin transmitters, which is believed to result in increased impulsiveness and craving. Cannabinoids act as seratoninenergic agonists, and as serotonin levels increase, impulsiveness and craving decline. Reports from study subjects also suggested that the ritual of preparing cannabis to smoke helped reduce the habituated psychological dependence associated with the preparation of crack cocaine.

More recently, a study by Reiman (2009) of 350 cannabis patients who purchased their medicine from a community-based dispensary in Berkeley suggests that many patients report using it as a substitute for other potentially more dangerous substances, particularly pharmaceuticals. Results show that 40% report using cannabis as a substitute for alcohol, 26% as a substitute for illicit drugs, and 66% as a substitute for prescription drugs. Patients cited a number of reasons for using cannabis instead of pharmaceutical drugs: 65% reported less adverse

side effects, 57% cited better symptom management, and 34% found that cannabis had less withdrawal potential than their other medications. A similar survey study of 400 patients is currently underway in four medical cannabis dispensaries located in British Columbia, Canada.

Finally, exploratory research suggests that cannabis use does not interfere with formal substance abuse treatment. Data from the California Outcomes Measurement System (CalOMS) were compared for medical (authorized) marijuana users (N = 18) and non-marijuana users who were admitted to a public substance abuse treatment program in California. Behavioral and social treatment outcomes recorded by clinical staff at discharge and reported to the California Department of Alcohol and Drug Programs were assessed for both groups, and although the sample was small, cannabis use did not seem to compromise substance abuse treatment among the medical marijuana using group, who (based on these preliminary data) fared equal to or better than nonmedical marijuana users in several important outcome categories (e.g., treatment completion, criminal justice involvement, medical concerns) (Schwartz 2010).

MAXIMIZING THE POTENTIAL BENEFITS OF MEDICAL CANNABIS USE

While much of the research cited above suggests that cannabinoids can be safe and effective adjuncts or alternatives to pharmaceutical opiates, the illegality of cannabis and the associated stigma in patients who might benefit from its use has significantly hampered research into therapeutic potential of both whole-plant preparations and pharmaceutical cannabinoid treatments (Lucas 2009). As a result, the international prohibition on cannabis has not only led to significant social costs with little impact on overall usage rates in the general population, it may also be inadvertently leading to increased suffering and addiction in patients suffering from chronic pain.

In light of recent evidence that cannabis not only helps relieve the symptoms of a number of serious conditions, but might also increase the success rate of both HIV/AIDS and hepatitis C treatment (Abrams et al. 2007; Sylvestre, Clements & Malibu 2006), it can be argued that the governments throughout the world have a moral, ethical obligation to ensure that this medicine is legally available to patients who might benefit from its use. The same argument could be made if cannabis is shown to be effective in reducing the non-prescription use of other potentially more dangerous licit and illicit substances, including pharmaceutical opiates.

In an essay on the globalization of ayahuasca, which is an entheogenic plant-based medicine from the Amazon basin that, like cannabis, has a long history of traditional use, Tupper (2007:5) suggests that:

> . . . a shift to a generative metaphor of drugs as "tools" offers a much more nuanced way to conceiving of the risks and benefits posed by ayahuasca practices. Rather than essentializing psychoactive substances as inherently dangerous, to regard them as tools—ancient technologies for altering consciousness . . . allows for a realistic assessment of their potential benefits and harms according to who uses them, in what contexts and for what purposes.

Although this may appear reflective of a harm reduction approach to drugs, Tupper insists that conceptualizing drugs as "tools" necessitates a move beyond policies simply based on reducing potential harms, suggesting that benefits also need to be explored and where possible, maximized by government policies and practices. He continues:

> The philosophy of harm reduction is also further illuminated by a shift to the generative metaphor of drugs as tools. To the extent that policy-makers or practitioners emphasize a behaviour's potential risks, the harm reduction policy approach is justified. However, the tool metaphor for psychoactive substances warrants a corollary notion of "benefit maximization," the other side of the harm reduction coin. Instead of approaching drug policy from a deficit perspective . . . the tool metaphor opens discursive avenues for realistic policy considerations of benefits as well as harms.

As with ayahuasca, the concept of harm reduction may not be wholly appropriate to maximize the potential health benefits of medical cannabis. A great deal of research indicates that cannabis is far less dangerous than licit substances like alcohol and tobacco, and safer than many over-the-counter or prescription pharmaceuticals (Grotenhermen & Russo 2002; Grinspoon 1999; Grinspoon & Bakalar 1998), and many have suggested that the greatest potential harms of cannabis use are based on a its illegal status, including arrest or the vagaries of the black-market (Nolin et al. 2002). In this light, harm reduction policies associated with the use of other substances that are designed to prevent the spread of infectious disease, reduce the likelihood of overdose and stem addiction and related crime—such as needle-exchange, safe consumption sites, heroin maintenance or opiate substitution—don't readily apply to the use and distribution of medical cannabis.

Research suggests that community-based medical cannabis dispensaries appear to both reduce the potential harms and maximize the benefits of medical cannabis use by removing some of the social stigma associated with the therapeutic use of cannabis and by separating medical cannabis access from the potential dangers of the black market (i.e. lack of safety and quality assurances, pressure to try other illicit substances, prohibition–associated harms such as arrest and prosecution) (Lucas 2010, 2009, 2008; Reiman 2009, 2006; Belle-Isle & Hathaway 2007; Belle-Isle 2006). Additionally, they increase access to a safe consistent supply of medical cannabis within an environment conducive to health and healing, which may be directly

and indirectly leading to a reduction in the use of pharmaceuticals, alcohol and illicit substances in their community. Moreover, nonprofit dispensaries like the Vancouver Island Compassion Society (VICS) contribute to the overall social capital of their client-members through membership, joint knowledge creation, and inclusion and participation in a social movement informed by public health, harm reduction and human rights (Lucas 2009; Belle-Isle & Hathaway 2007; Belle-Isle 2006; Reiman 2006). As such this community-based, patient-centered model is growing in both legitimacy and popularity, and is now the predominant means for patients access in Canada and in many U.S. state-run medical cannabis programs (Lucas 2010, 2009; Reiman 2006).

DISCUSSION

Evidence is growing that cannabis can be an effective treatment for chronic pain, presenting a safe and viable alternative or adjunct to pharmaceutical opiates. Addiction to pharmaceutical opiates has been noted by the medical community as one of the common side-effects of extended use by patients (such as those suffering from chronic pain), and a growing body of research suggests that some of the biological actions of cannabis and cannabinoids may be useful in reducing this dependence. Therefore cannabis has the potential to both relieve suffering for those suffering from chronic pain, and to reduce morbidity and mortality often associated the use and abuse of pharmaceutical opiates.

Since both the potential harms of pharmaceutical opiates and the relative safety of cannabis are well established, research on substitution effect suggests that cannabis may be effective in reducing the use and dependence of other substances of abuse such as illicit opiates, stimulants and alcohol. As such, there is reason to believe that a strategy aiming to maximize the therapeutic potential benefits of both cannabis and pharmaceutical cannabinoids by expanding their availability and use could potentially lead to a reduction in the prescription use of opiates, as well as other potentially dangerous pharmaceutical analgesics, licit and illicit substances, and thus a reduction in associated harms. The resulting public health benefits would include lower rates of alcohol-related automobile accidents, less domestic violence, reductions in drug-related crimes such as break-ins and petty theft, and reduced drug and alcohol-related morbidity and mortality.

International experience appears to support this premise. A recent report by the European Monitoring Center for Drugs and Drug Addiction shows that the Netherlands long-time policy of de facto cannabis decriminalization has resulted in some of the lowest drug-induced death rates in Europe, while countries with more severe cannabis laws and drug policies, such as Norway and Sweden, rank among the highest (EMCDDA 2009). Despite such compelling evidence, much of the world's current and long-standing prohibitionist approach to cannabis continues to act as a barrier to these potential personal and public health benefits, and to criminalize otherwise law-abiding citizens as well as many critically and chronically ill patients.

Community-based dispensaries have emerged as a disjointed but effective social movement focused on the principles of harm reduction and human rights. Although they remain largely unregulated or even illegal in much of Canada and U.S., these dispensaries have been successful in establishing a safe and consistent supply of medical cannabis, advocating for patient rights, and adding to society's knowledge and understanding of the therapeutic potential of cannabis through scientific research. Additionally, evidence suggests that they are reducing the problematic use of opiates, alcohol and other substances in their communities. If we are to ever benefit from drug policies based on science, reason and compassion, national governments will need to abandon the misinformation that underscores drug prohibition, and to start promoting and supporting research into cannabis and cannabinoids as both a relatively safe and effective medicine in the treatment of chronic pain and other serious medical conditions, and as a potential "exit drug" for problematic substance use.

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