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Thesis

On the future of cannabis as medicine

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Abstract

The use of herbal marijuana as a medicine is here to stay. Both its safety and efficacy have been well established through much anecdotal and clinical experience. Pharmaceutical cannabinoid products will be developed, some of which may successfully compete with the de facto gold standard, legally available herbal marijuana.
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The recent publication by Abrams et al of a controlled study using inhaled herbal marijuana for the treatment of AIDS-related neuropathic pain has been greeted as a landmark study because it demonstrated the efficacy of cannabis in the treatment of this difficult-to-treat type of pain [1]. However, this study deserves to be singled out not so much for what it has newly revealed about cannabis as an analgesic, but more for the extraordinary perseverance of the research team in the face of a variety of US government obstacles placed in the path of those who wish to study herbal marijuana, including the mandate to use government-produced marijuana of inferior quality. Both AIDS patients and others suffering from neuropathic pain, and open-minded, astute clinicians have known for more than a decade that this is arguably the most efficacious and least toxic way to approach this difficult symptom; they know this from their own clinical experience. Neuropathic pain is but one of a large number of symptoms and syndromes which emerge from a mountain of anecdotal data that have long established herbal marijuana as a safe and effective medicine. One might ask: given the enormously enhanced interest in cannabis-related research, why have there not been more controlled clinical studies such as this? The answer is largely money.

Today drugs must undergo rigorous, expensive and time-consuming tests to win approval by the appropriate regulatory agency (the Food and Drug Administration in the United States, FDA) for marketing as medicines. The purpose of the testing is to protect the consumer by establishing both safety and efficacy. Because no drug is completely safe or always efficacious, a drug approved by this agency as a medicine has presumably satisfied a risk-benefit analysis. First, the drug's safety (or rather, limited toxicity) is established through animal and then human experiments. Next, double-blind controlled studies are conducted to determine whether the drug has more than a placebo effect and is more useful than an available drug. As the difference between drug and placebo may be small, large numbers of patients are often needed in these studies for a statistically significant effect. Medical and governmental authorities sometimes insist that before herbal marijuana is made legally available to patients, this kind of study should be performed for each of the indications for which it is believed to be useful. But it is doubtful whether these regulatory rules should apply to herbal marijuana. First, there is no question about its safety. It has been used for thousands of years by millions of people with no reported deaths and very little evidence of significant toxicity. Similarly, no double-blind studies are needed to prove marijuana's efficacy. Countless clinicians and patients the world around who have had experience with the medicinal use of cannabis have observed that it often provides better relief with fewer serious side effects than conventionally prescribed medicines. To impose this regulatory protocol on herbal marijuana is tantamount to making the same demand of aspirin, which was accepted as a medicine more than 60 years before the advent of the double-blind controlled study. Many years of experience have shown us that aspirin has many uses and limited toxic-

ity, yet today it could not be marshaled through the FDA approval process. The patent has long since expired, and with it the incentive to underwrite the substantial cost of this modern seal of approval.

Ordinarily, pharmaceutical companies who own the patent on a promising therapeutic are willing to invest the large sums of money necessary to complete the double blind controlled studies required by the FDA for approval of the potential new medicine. Because there is no possibility of acquiring a patent on herbal marijuana, the drug companies have no direct interest in it. The Abrams' study was financed by the State of California; future controlled studies of the variety of already obvious medicinal utilities of cannabis will have to await funding from private or government sources. Given that the official position of the US government is that "marijuana is not a medicine", it is highly unlikely that it will underwrite this large investment to establish a "more scientific" refutation of its position than that already provided by the compelling body of anecdotal data.

Anecdotal evidence commands much less attention than it once did, yet it is the source of much of our knowledge of synthetic medicines as well as plant derivatives. As Louis Lasagna has pointed out, controlled experiments were not needed to recognize the therapeutic potential of chloral hydrate, barbiturates, aspirin, curare, insulin, or penicillin [2]. He asks why regulators are now willing to accept the experience of physicians and patients as evidence of adverse effects but not as evidence of therapeutic effects. Anecdotes present a problem that has always haunted medicine: the anecdotal fallacy or the fallacy of the enumeration of favorable circumstances (counting the hits and ignoring the misses). If many people suffering from, say, muscle spasms caused by multiple sclerosis take herbal marijuana and only a few get much better relief than they get from conventional drugs, those few patients would stand out and come to our attention. They and their physicians would understandably be enthusiastic about cannabis and may proselyte for it. These people are not dishonest, but they are not dispassionate observers. Therefore, some may regard it as irresponsible to suggest on the basis of anecdotes that herbal marijuana may help people with a variety of disorders. That might be a problem if marijuana were an especially dangerous drug, but it is in fact remarkably safe. Even in the unlikely event that only a few patients get the kind of relief that many observant physicians have now seen, it could be argued that it should be available to them because the risks are so small and it costs so little to produce.

While it is early in the history of the effort to "pharmaceuticalize" cannabis, the few products that have so far been developed do not measure up to the de facto gold standard, herbal marijuana. Dronabinol (Marinol), encapsulated THC in sesame oil, was introduced two decades ago with expectations (particularly on the part of the US government, which supported Unimed's development of this pharmaceutical) that it would be every bit as medically useful as marijuana and thereby obviate the necessity to find a way to allow patients to use herbal marijuana legally. However, Marinol has not succeeded in displacing marijuana because it is not as effective or useful as marijuana, whether ingested as a food such as brownies or smoked. I have yet to know of a patient who has had the opportunity to use both marijuana and Marinol who prefers the latter. One reason is that like the 19th century oral preparations of cannabis indica, with their slow time of onset, the appropriate dose of dronabinol is much more difficult to titrate than smoked cannabis, whose therapeutic effects are experienced within a few minutes. The most common reason people who have an opportunity to choose between these two forms of cannabis elect dronabinol is because it is legal. Sativex, a more recent addition of cannabinoid medicines which are meant to fly under the legal radar, has been referred to as liquid marijuana. It is a liquid formulation of two cannabinoids, tetrahydrocannabinol and cannabidiol, extracted from marijuana. It was developed as a means to make use of the medicinal capacities of marijuana without exposing the patient to the twin "dangers" of getting “high” and smoking. There are many who now question both the harmfulness of the "high" and whether the psychoactive effects are always separable from those that are therapeutic. While smoking anything may cause chronic bronchitis, smoked marijuana has never been demonstrated to have serious pulmonary consequences [3], but in any case the technology to inhale these cannabinoids without smoking cannabis already exists as vaporizers that allow for smoke-free inhalation. Sativex is administered as drops to be held under the tongue to facilitate buccal mucosal absorption. However, in part because it has such a disagreeable taste, some if not most of it is swallowed. While the time of the onset of that part of the dose absorbed by the buccal mucosa is about 20 minutes, that part which is absorbed by the gastrointestinal tract requires at least an hour and a half and thus its capacity for titration is closer to that of Marinol than to inhaled marijuana. It also shares with Marinol a cost to the patient which is greater than that of herbal marijuana, even with its heavy prohibition tariff.

I have no doubt that the use of herbal marijuana as a medicine is here to stay. Nor do I doubt that the present effort directed at the "pharmaceuticalization" of cannabis will eventually lead to some good cannabinoid pharmaceuticals. However, I question how many of them would be able to compete with herbal marijuana on a level playing field, i.e. effectiveness, limited toxicity, versatility, ease of titration of dose, expense and, of course, legal access. Presently we are beginning to see two powerful forces collide: the growing acceptance of medical cannabis and the proscription against any use of herbal marijuana, medical or non-medical. There are few signs that we are moving away from absolute prohibition to a regulatory system that would

allow responsible use of marijuana. As a result, we appear to be heading toward two simultaneous distribution systems for medical cannabis: the conventional model of legal pharmacy-filled prescriptions for officially approved medicines, and a model closer to the distribution of alternative and herbal medicines, legal or illegal.

References

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