Forschende Komplementärmedizin
Research in Complementary Medicine

Forsch Komplementärmed 1999;6(suppl 3):40–43

The Future of Medical Marijuana

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Key Words
Cannabis: medicine, synthetic analogs, cannabinoids, medical potential, classification, regulation

Summary
The medical value of marijuana is becoming increasingly clear, as it proves to be a remarkably versatile, safe, and inexpensive drug. Arrangements now being proposed for making cannabis constituents medically available include quasi-legal buyers clubs, restrictive classification as a prescription drug, the isolation of individual cannabinoids, and the manufacture of synthetic analogs. Careful analysis potentially of this inexpensive drug shows that all these proposals are unworkable. Furthermore, cannabis has so many beneficial uses that the strictly medical ones should not be singled out for approval, and its medical potential cannot be fully realized as long as its use for any other purpose is prohibited. Therefore cannabis should be made available under laws similar to those now applied to alcohol.

Schlüsselwörter
Cannabis: Medizin, synthetische Analoge, Cannabinoide, medizinisches Potential, Klassifikation, Gesetzgebung

Zusammenfassung
Die Zukunft der medizinischen Verwendung von Marihuana
Der medizinische Wert von Marihuana wird immer deutlicher ersichtlich, da es sich als ein bemerkenswert vielseitiges, sicheres und zudem potentiell preiswertes Medikament erweist. Ausgestaltungen, die heute für die medizinische Verfügbarkeit von Cannabisbestandteilen vorgeschlagen werden, umfassen quasi-legale Einkaufsgemeinschaften, die restriktive Klassifizierung als ein verschreibbares Medikament, die Isolierung individueller Cannabinoide sowie die Herstellung synthetischer Analoga. Eine sorgfältige Analyse zeigt, dass all diese Vorschläge nicht funktionieren. Darüber hinaus bietet Cannabis so viele segensreiche Anwendungsmöglichkeiten, dass die strikt medizinischen bei einer Zulassung nicht besonders hervorgehoben werden sollten. Sein medizinisches Potential kann nicht vollständig verwirklicht werden, so lange seine Nutzung für andere Zwecke verboten ist. Daher sollte Cannabis unter ähnlichen Gesetzen verfügbar gemacht werden wie sie heute für Alkohol gelten.

'A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die and a new generation grows up that is familiar with it.' Max Planck

The medical value of marijuana has become increasingly clear to many physicians and patients. There are three reasons for this. First, it is remarkably versatile, useful in treating a diverse array of symptoms and syndromes. Second, it is also remarkably non-toxic. Compared to medicines for which it will be substituted, it has minimal short-term and long-term side effects. Third, once patients no longer have to pay the prohibition tariff, it will be much less expensive than the medicines it replaces. The question is whether its medical potential can be realized as long as its use for any other purpose is prohibited and harshly punished.

The American public is becoming increasingly impatient for a legal means of obtaining medical cannabis. The most dramatic manifestation of that impatience have been the referenda allowing distribution of medicinal marijuana that have been passed in several states. In 1996, when California became the first state to approve such a law, more than a dozen cannabis clubs or cooperatives opened to help sick people in need of relief, and the membership

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of one quickly grew to 8,000. Many Americans believe that this is the best temporary approach to the problem, but they disagree on how the clubs should be organized.

One model follows the conventional delivery system for medicine, in which the buyers club acts as a pharmacy, with a note of recommendation from a physician as the equivalent of a prescription. The second model, exemplified by the recently closed San Francisco Cultivators Club, resembles a social club. The dispensary contains lounge chairs and sofas, tables, magazines, and newspapers. Most patients, after buying their medicine, stay to smoke and talk or listen to music. It is a blend of Amsterdam-style coffeehouse, American bar, and medical support group.

Because of its on-site cannabis use and informal atmosphere, this model may seem more casual in its commitment to confirming medical need. But the value of sociability and warmth should not be underestimated, especially for people who might otherwise be isolated in misery. It has become increasingly clear that social support is important in battling illness and improving the quality of life. The informal San Francisco buyers' club provided a kind of supportive group therapy for patients, partly because people using cannabis find it easier to share difficult thoughts and feelings. Unfortunately, the initiatives passed more recently in several states will not permit clubs of the San Francisco type, and in any case, buyers clubs have to be regarded as a stopgap measure. The federal government will not allow the development of a separate quasi-legal distribution system for one medicine. It has already succeeded in closing most of the California buyers clubs.

Other present approaches to making marijuana medically available have even more serious drawbacks. Under federal law, cannabis is now classified as a Schedule I drug, which makes clinical research extraordinarily difficult. But even if it were moved to Schedule II, so that studies leading to FDA approval became possible, the money to finance those studies would be difficult to find. Drug companies spend vast sums on development for the sake of the profits they make on a patentable drug, but marijuana cannot be patented. That leaves the U.S. government, which unfortunately has a record of obstructionist opposition to research on the medical uses of cannabis. The government will ultimately have to provide some support for this research because of public pressure, but it will arrive there slowly and grudgingly. A study of marijuana in the treatment of the AIDS wasting syndrome has recently been approved and funded after 4 years of obstruction, probably because the political climate has changed since the California initiative. Even so, the main focus of the study had to be changed from medical efficacy to safety.

But suppose that the necessary studies are somehow completed, and physicians are allowed to prescribe marijuana for some specific medical purpose – let us say, the weight reduction syndrome of AIDS. This will present unique problems. When a drug is approved by the FDA for one medical purpose, physicians are also generally free to prescribe it 'off-label' for other conditions. The only present exception is dronabinol (Marinol®), a synthetic form of tetrahydrocannabinol, which was approved in 1986 for the treatment of nausea and vomiting in cancer chemotherapy, and later for the weight reduction syndrome of AIDS. Only a few physicians have been willing to defy the administrative ruling against off-label prescription. If marijuana is approved as a medicine, how will this issue be dealt with? It is an especially important issue because cannabis has so many potential medical uses. For example, a physician might sensibly and safely prescribe it for muscle spasms and chronic pain resulting from a variety of conditions, from paraplegia to premenstrual syndrome. If the government challenges physicians every time they prescribe it for any new patient or any new purpose, there will be constant conflict, and patients will turn to the illicit market for relief.

As a Schedule II drug, marijuana would be classified – inaccurately on both accounts – as having a high potential for abuse and limited medical use. Restrictions on these drugs are tight and becoming tighter, and the drug enforcement authorities police physicians who prescribe them closely. Pharmacies would be reluctant to stock marijuana, and physicians would hesitate to prescribe it for fear that they would lose their reputations, licenses, and careers. The potential for harassment would be extremely discouraging. Because cannabis has so many potential medical uses, many patients might try to persuade their doctors that they had a legitimate claim to a prescription. Physicians would not want the responsibility of making such decisions if they were constantly under threat of discipline by the federal government. Since the passage of the medical marijuana initiative in California, I have heard from many patients who say their doctors are afraid to recommend marijuana because of threats from the government.

Even the current and proposed state arrangements for medical cannabis (except the California initiative) almost always specify that it must be used only for the treatment of illnesses described as 'serious', 'life-threatening', 'terminal', or 'debilitating'. These restrictions are presumably necessary because cannabis is so dangerous. But how dangerous is it? Consider some typical over-the-counter (OTC) drugs, regarded as so safe that patients are allowed to use them without a doctor's permission or advice. Aspirin takes 'only' 1,000–2,000 lives a year in the U.S., and acetaminophen accounts for 'only' 10% of cases of end-stage renal disease. The public is also allowed to consume many untested herbal remedies which may be dangerous and probably have only placebo effects. By contrast, marijuana has been extensively studied, and its extraordinarily low toxicity has been well established. It has minimal effects on important physiological functions and has never caused an overdose death.

Another question is who will provide medical cannabis. The federal government would certainly not produce marijuana for many thousands of patients receiving prescriptions, any more than it does for other prescription drugs. But if production is contracted out, will the farmers have to enclose their fields with security fences? How would the marijuana be distributed? If through pharmacies, how would they provide secure facilities capable of holding fresh supplies? When urine tests are demanded for workers, how would patients who use marijuana as a medicine be distinguished from those who use it for disapproved purposes? In the setting of the present prohibition laws, all these problems and more would have

to be addressed. A system designed to navigate this minefield would be so inefficient and bureaucratically cumbersome that patients would continue to grow their own or buy it on the illicit market instead. In other words, they would find themselves in the same situation they are in today.

The authors of a recent report by the Institute of Medicine, among others, believe that a solution will be found in the isolation of individual cannabinoids, the manufacture of synthetic cannabinoids, and the development of analogs. Supposedly these drugs, sometimes in combination, will make the natural product superfluous. I believe this view is wrong. In certain limited circumstances, individual cannabinoids and analogs may be preferable to whole smoked or ingested marijuana. For example, cannabidiol may be more effective as an anti-anxiety drug when it is not taken along with THC, which sometimes causes anxiety. Other cannabinoids and analogs may occasionally prove useful because they can be administered intravenously. For example, the cannabinoid analog dexanabinol has recently been shown to protect brain cells from damage after a stroke or head injury, and, unlike whole cannabis, it can be given intravenously to an unconscious person. Nasal sprays, vaporizers, skin patches, pills, and suppositories can also be used to avoid exposure of the lungs to the particulate matter in marijuana smoke. But these developments are unlikely to make marijuana itself medically obsolete. Prescription dronabinol was expected to do that, but patients have generally found it to be less useful than whole smoked marijuana and often more expensive.

In judging the future of cannabis analogs, we must consider what is required for the commercial success of a pharmaceutical product:

(1) It must be more useful than competing medicines for a particular purpose, or it must have a wide variety of approved medical uses.

(2) It must not have more undesirable side effects than competing medicines.

(3) It must have a mode of delivery at least as good as the available alternatives.

(4) It must be priced competitively.

(5) It must have a risk-benefit ratio at least as good as that of competing medicines.

Now compare the anticipated analogs with whole marijuana:

(1) Except for a few situations like intravenous injection in an unconscious person, analogs or combinations of analogs are unlikely to be more useful than natural cannabis for specific symptoms. Nor are they likely to have a wider spectrum of therapeutic uses than the natural product, which contains the cannabinoids (and synergistic combinations of cannabinoids) from which they are derived. Shortly after dexanabinol was found to protect brain cells against damage from the release of glutamate after a stroke or traumatic injury, it was shown that THC and cannabidiol provide the same protection. This suggests that the most important contribution made by the development of new analogs will be the identification of new uses for marijuana in its natural form.

(2) Marijuana has so few medically significant side effects that it is difficult to see how analogs could have fewer.

(3) Inhalation is a highly effective, safe, and rapid means of delivery that allows precise titration of the dose. It will be even safer with the development of devices (vaporizors) that separate the cannabinoids in whole marijuana from the burnt plant products, protecting the lungs from smoke. Except in a few situations such as unconsciousness and pulmonary impairment, a better means of delivery is unlikely to be found for analogs.

(4) Given the costs of development, it can safely be predicted that the new analogs will be much more expensive than whole smoked marijuana even at the inflated prices imposed by the prohibition tariff. Suppose, for example that a new analog is an antinauseant comparable to the prescription drug ondansetron in effectiveness and price. Today a patient suffering from the nausea of cancer chemotherapy might require 1–4 ondansetron pills (8 mg) at $30–40 apiece. The patient could probably get equally effective relief from a few puffs of a marijuana cigarette – cost $5 at today's street price, 30 cents if marijuana is produced as a medicine. This will be particularly important for people who lack health insurance.

(5) The therapeutic ratio of marijuana is not known because it has never caused an overdose death. It has been estimated on the basis of extrapolation from animal data to be 20,000–40,000. The therapeutic ratio of the new analogs may also be high, but it is unlikely to be higher than that of whole marijuana. Because it will probably be physically possible to ingest more of the analogs, they may, in effect, be less safe.

For all these reasons, I believe that the present proposed arrangements for medical access to cannabis and its constituents are unworkable. I have concluded that ultimately, the range of beneficial uses of this substance is so broad that the strictly medical uses should not be singled out for approval. Many people smoke marijuana to ease everyday discomforts, heighten creativity, or help them in their work. It can enhance the appreciation of food, sex, natural beauty, music, and art. It can promote intellectual stimulation and emotional intimacy. Cannabis use simply cannot be made to conform to the boundaries established by present medical institutions. In this case the demand for legal enforcement of a distinction between medical and nonmedical use may be incompatible with the realities of human need.

I know that to say this is to invite the charge that medical marijuana advocates are only using medicine as a stalking horse for the legalization of nonmedical use. This false accusation is actually a mirror image of the view taken by enemies of marijuana. They are unwilling to admit that it can be a safe and effective medicine largely because they are committed to exaggerating its dangers when used for other purposes. Nevertheless, it would be hypocritical to deny that there is a connection. For 26 years I have been urging the legalization of marijuana for general use. At one time I thought medical use could be treated as a distinct issue, because even people who might never see the urgency of legalizing nonmedical use would be willing to respond to medical need. Now I have changed my mind. I believe that making marijuana fully available as a medicine is one of the reasons for general legalization.

Ideally, cannabis should be available under more or less the same rules now applied to alcohol. At present, I fear, the political and le-

gal system is too ossified to accommodate that change. But I believe the enforcement of the laws against marijuana will be increasingly neglected because of the same public pressure that has resulted in the enactment of state marijuana initiatives. Although the prohibition of cannabis will not soon be repealed, the number of people arrested for possession will begin to decline dramatically. Cannabis will be used more freely as a medicine, both in its natural form and in the form of extracts, cannabinoids, and new analogs. As a result, the public will be in a better position to learn about its value, and this new understanding will make oppressive laws still more difficult to enforce. Eventually the era of prohibition will be brought to a de facto end. Only then will it be possible to realize the medical potential of this remarkable drug as part of its full human potential.