Marijuana Ruling Exempts Federally Funded Research

It's What the Court Didn't Say

By A.J.S. Rayl

"In the case of the Controlled Substances Act, the statute reflects a determination that marijuana has no medical benefits worthy of an exception (outside the confines of a government-approved research project)." --Justice Clarence Thomas

The Supreme Court's recent ruling against manufacturing and distributing medicinal cannabis does not appear to have had any immediate impact on either basic or clinical research studies under way. Some investigators, however, remain leery about the potential for research being compromised in the future.

The ruling comes at a time when research into cannabis, and its active ingredient delta-9-tetrahydrocannabinol (THC), is booming. Just last year, the nation's first Center for Medicinal Cannabis Research (CMCR) opened at the University of California, San Diego, and more projects involving the infamous weed have been approved in the last couple of years than ever before. But it's been a long time coming, and "it hasn't been easy," says University of California, San Francisco physician-researcher and professor Donald Abrams, who spent five years getting his first study on smoked marijuana funded.

Government officials have been reluctant to discuss the issue in any detail. The National Institute on Drug Abuse (NIDA), the agency that retains sole authority to supply marijuana for research, has been referring calls to National Institutes of Health headquarters. There, a spokesperson, who requested to remain nameless, said simply: "The Supreme Court's decision will have no impact on [cannabis] research." Quoting from an NIH Web site, she added "the NIH will review grant applications on the medical utility of marijuana ... that meet accepted standards of scientific design." 2

The case-U.S. v. Oakland Cannabis Buyer's Cooperative-began with a 1998 federal injunction to prevent an outlet in Oakland, Calif., and five other state-regulated centers, from distributing marijuana. The cooperatives opened following the passage of California's Proposition 215 in 1996, which legalized cannabis for patients with doctor's recommendations. Seven other states have since legalized medical marijuana, and other distribution centers opened.

The Controlled Substances Act, a federal law enacted by Congress in 1970, lists cannabis, or marijuana, as a Schedule I drug, meaning that it has no medical value, so it is illegal to possess and/or distribute. The Supreme Court's recent ruling affirms the existing
federal law. Medical cannabis dispensaries, wherever they are located in the United States, the majority held, are illegal under federal law regardless of state laws allowing for medicinal cannabis use.

Since the ruling was handed down, Thomas' frequently quoted summary comment has proved to be the most incendiary, igniting discussions within the cannabis research community. Ruling aside, it's what the justices chose not to consider or say that had many researchers on both the basic and clinical fronts collectively wincing. "That its decision should be based on such an outdated body of knowledge is amazing," states Daniele Piomelli, professor of pharmacology at University of California, Irvine.

"The Court did not acknowledge that an increasing number of studies indicate the medicinal benefits of cannabis for a number of disorders and ailments, while basic science studies are now opening the window on the natural cannabinoid system in the human body, something that will increase knowledge on many fronts," elaborates Montana physician Ethan Russo.

The Court had access to any number of government-generated documents, as well as science journals and other articles detailing new as well as old, recovered research. In recent years, reports issued by the Institute of Medicine and the NIH concluded cannabis does appear to have therapeutic benefit for some people with various conditions and encouraged research.3,4 On other fronts, the community now has its own Journal of Cannabis Therapeutics, and an increasing number of studies are being published in mainstream science journals.

Cannabis also has quite an extensive pharmaceutical history. Between 1842 and 1942, it was a standard medical treatment in Western Europe and the United States, readily available as an extract and used extensively in pain treatment, including migraines.5 According to Russo it was also used to treat addictions to alcohol or narcotics. Cannabis was used regularly until 1937 when the Tax Act made it, essentially, unavailable.

There are very different cultural attributes given to recreational drugs, Piomelli explains. "Cannabis-marijuana-has for decades suffered from a negative social image, and even as a research drug, cannabis is not considered as serious as cocaine or even nicotine."

Now, he says, "the Supreme Court has opened the door * to an interpretation that is potentially dangerous for science. The risk is if [the ruling] is interpreted to mean there is no actual value in the investigating of the medicinal properties of marijuana because the law is explicitly stating there are no such properties. This could create an intellectual atmosphere of 'let's try to stay away from cannabis because it's a problem.' And that is exactly the atmosphere that has delayed tremendously our understanding of cannabis pharmacology," concludes Piomelli, who is currently working under grants from NIDA and CMCR for basic research on THC.
Those who have been on the cannabis research front lines have experienced extreme difficulty in getting projects funded. "It has been an uphill battle at the very best, and impossible at worst, to get research funded, particularly for projects involving smoked marijuana," says Russo. No one knows that better than Abrams. After four years of grant applications and revisions on a protocol to test the therapeutics of smoked cannabis as an appetite stimulant on AIDS wasting syndrome, he finally conceded to shifting his focus from efficacy to safety to get his first study approved, investigating the impact of smoked marijuana on the immune system in AIDS patients taking protease inhibitor drugs. In his study (recently submitted to a medical journal), Abrams reports that cannabis did not produce immune problems in people taking protease inhibitor drugs and did lead to weight gain.

Russo hasn't been as lucky. He first applied to the Food and Drug Administration in 1997 for an Investigational New Drug application to test cannabis on acute migraines. He says he was put through "a classic bureaucratic runaround" between the FDA and the NIH. In 1999, he finally hooked up with FDA ombudsman Jim Morrison. "He led me to understand that the FDA had not been following its own procedures, and indicated things would be different from then on," Russo recalls. By September of that year, he had finally secured approval from both the FDA and NIDA. "Then, NIDA changed its policy and ultimately rejected my grant application for a variety of reasons, including the requirement that participants be exposed to marijuana only once."

Russo has now aligned with GW Pharmaceuticals of the United Kingdom, the only company in the world that produces cannabis for research. The company, he says, "is currently in negotiation with the FDA and the [Drug Enforcement Administration] and if they get approved for trials, my migraine project may finally see the light of day."

For now, investigators are cautiously optimistic that their research will continue on track and that cannabis is-at least in scientific circles-beginning to rise above its troubled past. "I think the trend at the federal level, at the NIH, is that this is an area worthy of scientific study," says physician-researcher Igor Grant, CMCR director. "I think there's a kind pressure building scientifically and medically that we need to get some answers."

Still, the fact that NIDA is the sole official and legal distributor of marijuana for research may portend more stormy days ahead. Given NIDA's prime objective, says Russo, "I just don't know if the agency could ever look favorably on a study that indicated medicinal benefit from smoked marijuana." And, he says, such studies exist already. "In one recent report, material gathered by several state commissions back in the late 1970s and 1980s on trials involving smoked cannabis versus synthetic THC versus standard medicines found in many of the cases people had 100 percent response rate to smoked cannabis in preventing nausea and vomiting with chemotherapy, with lesser degrees of relief from the synthetic versions and other medications."

"The use of marijuana per se [in its organic form] as an analgesic for the greater population-not in the compassionate sense of a particular cancer patient-I don't think [will] be possible," says Piomelli. "This system that cannabis is disclosing for us offers
enormous opportunities for drug discovery-new drugs-not necessarily THC [derived]-but drugs that have higher selectivity and effects that are more suitable to a medicine."

To that end, more research is needed. "This is one of the most exciting areas in neuropharmacology and the neurosciences at large right now," says Piomelli. "But you have to be extremely persistent and have dogged determination," cautions Russo. "And you have to have a high tolerance for frustration," adds Abrams, who is going through the regulatory hoops for his next two studies that will investigate the effect of smoked cannabis on patients suffering from peripheral neuropathy and pain from bone metastases caused by breast and prostate cancer. "Even now, with the research we're trying to do, we need to go through seven regulatory reviews, each one making their own comments and suggestions on how to change it, so it's very hard to keep track of your revised protocol in this field."

For researchers considering investigating cannabis, Piomelli advises, don't think about the politics, "think about the science."

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References


4. NIH Workshop. August 1997
