Reefer madness

Marijuana is medically useful, whether politicians like it or not.

IF cannabis were unknown, and bioprospectors were suddenly to find it in some remote mountain crevice, its discovery would no doubt be hailed as a medical breakthrough. Scientists would praise its potential for treating everything from pain to cancer, and marvel at its rich pharmacopoeia – many of whose chemicals mimic vital molecules in the human body. In reality, cannabis has been with humanity for thousands of years and is considered by many governments (notably America's) to be a dangerous drug without utility. Any suggestion that the plant might be medically useful is politically controversial, whatever the science says. It is in this context that, on April 20th, America's Food and Drug Administration (FDA) issued a statement saying that smoked marijuana has no accepted medical use in treatment in the United States.

The statement is curious in a number of ways. For one thing, it overlooks a report made in 1999 by the Institute of Medicine (IOM), part of the National Academy of Sciences, which came to a different conclusion. John Benson, a professor of medicine at the University of Nebraska who co-chaired the committee that drew up the report, found some sound scientific information that supports the medical use of marijuana for certain patients for short periods – even for smoked marijuana. This is important, because one of the objections to marijuana is that, when burned, its smoke contains many of the harmful things found in tobacco smoke, such as carcinogenic tar, cyanide and carbon monoxide. Yet the IOM report supports what some patients suffering from multiple sclerosis, AIDS and cancer – and their doctors – have known for a long time. This is that the drug gives them medicinal benefits over and above the medications they are already receiving, and despite the fact that the smoke has risks. That is probably why several studies show that many doctors recommend smoking cannabis to their patients, even though they are unable to prescribe it. Patients then turn to the black market for their supply.

Another reason the FDA statement is odd is that it seems to lack common sense. Cannabis has been used as a medicinal plant for millennia. In fact, the American government actually supplied cannabis as a medicine for some time, before the scheme was shut down in the early 1990s. Today, cannabis is used all over the world, despite its illegality, to relieve pain and anxiety, to aid sleep, and to prevent seizures and muscle spasms. For example, two of its long-advocated benefits are that it suppresses vomiting and enhances appetite – qualities that AIDS patients and those on anticancer chemotherapy find useful. So useful, in fact, that the FDA has licensed a drug called Marinol, a synthetic version of one of the active ingredients of marijuana – delta-9-tetrahydrocannabinol (THC). Unfortunately, many users of Marinol complain that it gets them high (which isn't what they actually want) and is not nearly as effective, nor cheap, as the real weed itself.

This may be because Marinol is ingested into the stomach, meaning that it is metabolised before being absorbed. Or it may be because the medicinal benefits of cannabis come from the synergistic effect of the multiplicity of chemicals it contains.

Just what have you been smoking?

THC is the best known active ingredient of cannabis, but by no means the only one. At the last count, marijuana was known to contain nearly 70

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The first wonderdrug? Marijuana can help control nausea, appetite loss, pain and anxiety, without serious side-effects. Many cancer patients could benefit from it, but only a tiny minority can get it on prescription

different cannabinoids, as THC and its cousins are collectively known. These chemicals activate receptor molecules in the human body, particularly the cannabinoid receptors on the surfaces of some nerve cells in the brain, and stimulate changes in biochemical activity. But the details often remain vague – in particular, the details of which molecules are having which clinical effects.

More clinical research would help. In particular, the breeding of different varieties of cannabis, with different mixtures of cannabinoids, would enable researchers to find out whether one variety works better for, say, multiple sclerosis-related spasticity while another works for AIDS-related nerve pain. However, in the United States, this kind of work has been inhibited by marijuana's illegality and the unwillingness of the Drug Enforcement Administration (DEA) to license researchers to grow it for research.

Since 2001, for example, Lyle Craker, a researcher at the University of Massachusetts, has been trying to obtain a licence from the DEA to grow cannabis for use in clinical research. After years of prevarication, and pressure on the DEA to make a decision, Craker's application was turned down in 2004. Today, the saga continues and a DEA judge (who

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No one would argue for chewing willow bark when aspirin is available

presides over a quasi-judicial process within the agency) is hearing an appeal, which could come to a close this summer. Dr Craker says that his situation is like that described in Joseph Heller's novel, *Catch 22*. "We can say that this has no medical benefit because no tests have been done, and then we refuse to let you do any tests. The US has gotten into a bind, it has made cannabis out to be such a villain that people blindly say 'no'."

Anjuli Verma, the advocacy director of the American Civil Liberties Union (ACLU), a group helping Craker fight his appeal, says that even if the DEA judge rules in their favour, the agency's chief administrator can still decide whether to allow the application. And, as she points out, the DEA is a political organisation charged with enforcing the drug laws. So, she says, the ACLU is in this for the long haul, and is already prepared for another appeal – one that would be heard in a federal court in the normal judicial system.

Verma's view of the FDA's statement is that other arms of government are putting pressure on the agency to make a public pronouncement that conforms with drug ideology as promulgated by the White House, the DEA and a number of vocal anti-cannabis congressmen. In particular, the federal government has been rattled in recent years by the fact that 11 states have passed laws allowing the medical use of marijuana. In this context it is notable that the FDA's statement emphasises that it is smoked marijuana which has not gone through the process necessary to make it a prescription drug. (Nor would it be likely to, with all of the harmful things in the smoke.) The statement's emphasis on smoked marijuana is important because it leaves the door open for the agency to approve other methods of delivery.

High hopes

Donald Abrams, a professor of clinical medicine at the University of California, San Francisco, has been working on one such option. He is allowed by the National Institute on Drug Abuse (the only legal supplier of cannabis in the United States) to do research on a German nebuliser that heats cannabis to the point of vaporisation, where it releases its cannabinoids without any of the smoke of a spliff, and with fewer carcinogens.

That is encouraging. But it does not address the wider question of which cannabinoids are doing what. For that, researchers need to be able to do their own plant-breeding programmes.

In America, this is impossible. But it is happening in other countries. In 1997, for example, the British government asked Geoffrey Guy, the executive chairman and founder of GW Pharmaceuticals, to come up with a programme to develop cannabis into a pharmaceutical product.

In the intervening years, GW has assembled a 'library' of more than 300 varieties of cannabis, and obtained plant-breeder's rights on between 30 and 40 of these. It has found the genes that control cannabinoid production and can specify within strict limits the seven or eight cannabinoids it is most interested in. And it knows how to crossbreed its strains to get the mixtures it wants.

Nor is this knowledge merely academic. Last year, GW gained approval in Canada for the use of its first drug, Sativex, which is an extract of cannabis sprayed under the tongue that is designed for the relief of neuropathic pain in multiple sclerosis. Sativex is also available to a more limited degree in Spain and Britain, and is in clinical trials for other uses, such as relieving the pain of rheumatoid arthritis.

At the start of this year, the company made the first step towards gaining regulatory approval for Sativex in America when the FDA accepted it as a legitimate candidate for clinical trials. But there is still a long way to go.

And that delay raises an important point. Once available, a well-formulated and scientifically tested drug should knock a herbal medicine into a cocked hat. No one would argue for chewing willow bark when aspirin is available. But, in the meantime, there is unmet medical need that, as the IOM report pointed out, could easily and cheaply be met – if the American government cared more about suffering and less about posturing.