

Cannabis

Fact Sheet



Information

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Cannabis

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1. Introduction

Cannabis remains controversial, both in its status as an illegal drug and as a possible treatment for MS. This document discusses some of the historical and legal background to cannabis and cannabis-based medicines. It also provides an overview of current research into cannabis-based medicines as a treatment for MS.

Research into cannabis-based medicines for MS remains important because the way it works and its long-term effects are still not wholly understood. To date, no medicine derived from cannabis plant is licensed for use for any condition in the UK. However, Sativex, a cannabis-based medicine, is now available on a named patient basis in the UK - see our Sativex factsheet for further information.

2. Background

Cannabis is one of the oldest plants in cultivation, and has been used to make textiles, fuel, paper, and rope as well as medicines. In addition it has been used recreationally as an intoxicant. Botanically, there are three recognised plants: cannabis sativa, cannabis indica, and cannabis ruderalis, only some of which have strong psychoactive properties. There are a number of common names for cannabis, including hemp, hashish, marijuana, skunk, weed, pot, grass and ganja.

Cannabis was legal in the UK until 1928, when the Dangerous Drugs Act outlawed private use but allowed medicinal use. The United Nations Single Convention on Narcotic Drugs 1961 did not recognise cannabis as having any medical or scientific benefit. UK law fully implemented this convention with the Misuse of Drugs Act 1971, which imposed penalties for possession and supply.

3. Current legal position of cannabis

Cannabis is an illegal drug. Under the Misuse of Drugs Act 1971, illegal drugs are classed on a scale from Class A to Class C - most to least dangerous drugs. There is no clear protocol to state what effects a drug must have to warrant a specific classification. Drugs may be added to the Misuse of Drugs Act 1971, and reclassified within it, at any time. The law provides for some illegal drugs, such as morphine, which is derived from heroin, to be prescribed in certain circumstances. Currently, cannabis is not recognised in law as having any medicinal value. The legal arrangements for providing Sativex are therefore exceptional.

Unless Sativex is prescribed, the penalties for possessing or using cannabis are still significant. In January 2004, the government reclassified cannabis as a Class C drug. Class C drugs are illegal and carry the following penalties: two years' imprisonment and/or a fine for personal possession of cannabis, and five years' imprisonment and/or a fine for possession with intent to supply. Supplying and dealing in Class C drugs carries a maximum penalty of 14 years' imprisonment. Recent legal cases have indicated that the law makes no exception for people using or supplying cannabis to help relieve medical symptoms. Similarly, the Government has indicated that the classification of cannabis will revert to a Class B drug in the near future, with higher penalties for possession and supply.

Research studies have suggested that excessive use of recreational cannabis in young people may lead to long-term mental health problems. One recent, very small study in people with multiple sclerosis who smoke cannabis has demonstrated a significant adverse effect on mental processes, particularly cognition.¹ There is no evidence that cannabis-based medicine causes any similar cognitive effects, although a recent review cautions that more research is needed in this area.²

The indications are that cannabis-based medicines will be licensed and available in the UK only when research trials prove unequivocally that the medicines are effective.

4. Current research into cannabis-based medicines

Cannabis is known to work on parts of the brain known as cannabinoid receptors. However, how it works is not fully understood and is the subject of considerable research. Cannabis plants contain more than 60 different cannabinoids, which can affect these receptors. Only some cannabinoids are believed to help in MS.

Cannabis-based medicines may be based on the whole plant, or contain specific cannabinoids. Additionally, some medicines are available that are manufactured to be the synthetic chemical equivalent of some cannabinoids.

At the moment, two specific cannabinoids are believed to be of benefit in MS:

- delta-9 tetrahydrocannabinol (THC) - known to be the part of cannabis that is psychoactive - that gives a 'high'; also thought to be responsible for some of the physical effects of cannabis, such as relaxation
- cannabidiol (CBD) - a cannabinoid with few or no psychoactive properties, and some painkilling effect. It is thought to mitigate some of the unwanted effects of THC alone, such as feelings of drowsiness, weakness and cognitive impairment.

Drugs used in the research trials outlined below contain one or both of these substances, or are based on the whole cannabis plant. It is worth remembering that the cannabis-based drugs used in these research trials have been quality-controlled and therefore may differ from street cannabis.

The majority of research trials have focused on relieving symptoms of MS. However, one new trial, the CUPID trial, is looking to see whether cannabis might have a more important role in protecting the brain from damage by MS.

4.1 Completed non-commercial research trials

CAMS (Cannabis in MS) trial

The largest study of cannabis-based medicine as a treatment for MS was funded by a government agency, the Medical Research Council. Results from the trial were published in November 2003.

This was a randomised, controlled, double-blind trial which involved 660 participants at a number of sites around the UK. Participants were allocated to one of:

- cannabis extract (Cannador) - capsules containing extract of cannabis plant, standardised to contain 2.5mg delta-tetrahydrocannabinol (THC)
- dronabinol (Marinol) - synthetic delta-tetrahydrocannabinol (THC)
- placebo - dummy treatment with no active ingredient

The trial investigated the effect of cannabis on various symptoms of MS, primarily on spasticity. A dose level was gradually built up over five weeks, treatment continued for a further eight weeks and was then tapered off over two weeks, with regular assessments for spasticity and mobility.

Results of this study were mixed. Researchers found that cannabis had no significant effect on the primary outcome measure of muscle spasticity using the Ashworth scale. However, some improvement was shown on the time taken to complete a 10 metre walk, which was compared before and after treatment with cannabis.

Participants on the trial were asked to complete their own reports on symptoms. They reported improvements in spasticity, pain and sleep quality. This contrasts with the outcome measures the researchers used.

Importantly, participants on the trial experienced no significant adverse side-effects, and these drugs appeared to be very safe for use in the treatment of MS. There was little difference in the effect on symptoms between Cannador and dronabinol, suggesting that the whole plant or synthetic versions of cannabis may be equally effective.³

Extension trial

After the main 15 week trial had completed, all participants were given the option of continuing with their medication for a further twelve months. Around 80% of participants opted to continue.

Results from this trial suggested that cannabis-based medicine had some effect over the longer period of time on muscle spasticity, most notably in the group taking dronabinol, when compared with Cannador and placebo. However, only a small effect was seen.

In addition, there was some suggestion that dronabinol and Cannador might delay some people's increase in disability over a period of time. The investigators stressed that these results should be treated with caution, but the CUPID trial will investigate this possible effect more fully.⁴

Effect of cannabinoids on psychological factors in MS

This trial with a subgroup of people from the CAMS trial was fully funded by the MS Trust. 150 participants with MS and spasticity were recruited from two centres. The trial's purpose was to evaluate whether cannabis-based medicines have any psychological impact and/or any impact on cognitive performance, mood, pain and fatigue in participants undergoing treatment. The study started in February 2001.

Preliminary results were presented in 2003. They showed that the cognitive scores of all the participants at the start and end of treatment within the study remained within the expected range for people with MS. Researchers have concluded that no significant effect on cognition was shown in people using medicinal cannabis.⁵ Full results from the study are still awaited.

Lower urinary tract symptoms in MS

Anecdotal evidence suggests that cannabis might be beneficial for some bladder problems in MS. This randomised, controlled, double-blind study was designed as a subset of the main CAMS trial, to test the theory that cannabis-

based medicine might improve urgency (the need to empty the bladder at very short notice) and increase day-to-day bladder capacity.

All 657 participants in the CAMS trial were asked to complete diaries about whether they experienced urinary incontinence, and also quality of life questionnaires. 47 of these people also agreed to undergo tests for urodynamics - how the bladder works - and incontinence pad tests.

People taking either Cannador or dronabinol demonstrated an improvement of around 35% compared with placebo on the number of episodes of urge incontinence they experienced. However, there was no evidence of any treatment effect on any of the urodynamic measures, nor on quality of life. Still, these results do suggest that cannabis-based medicine may improve some bladder symptoms in MS.⁶

Tremor in MS

One very small randomised, double-blind, placebo-controlled crossover study looked at oral cannabis extract (Cannador) as a treatment for 14 people with MS who experienced tremor in their arms. No statistically significant difference was seen between cannabis-based medicine and placebo in terms of tremor, although people receiving cannabis-based medicine reported more relief than those who receiving placebo.⁷

Spasticity

57 people with MS undergoing inpatient rehabilitation participated in a randomised, double-blind crossover trial of oral cannabis-based medicine, over a three week period. Active drug was a whole-plant cannabis extract containing 2.5mg THC and 0.9mg CBD in a gelatine capsule. Participants received either active or placebo ingredients for two weeks in the main part of the study. The aim was to investigate whether this helped people who had poorly controlled spasticity.

Results showed no statistically significant differences between cannabis-based medicine compared with placebo. However, minor improvements were seen for

spasm frequency, mobility, and getting to sleep in people on cannabis-based medicine. More side-effects were seen in people receiving cannabis-based medicine rather than placebo, although these were manageable.

The researchers suggest cannabis-based medicine might be useful for people with MS whose spasticity is not responding to other drugs.⁸

4.2 Commercial cannabis-based medicine (Sativex) trials

GW Pharmaceuticals plc have completed Phase III trials* of their cannabis-based mouth spray, Sativex. These used a spray that contains equal proportions of delta-9 tetrahydrocannabinol:cannabidiol, from their own genetically controlled plants. The majority of the trials were double-blind and used a placebo. Sativex was used as an add-on drug rather than replacing any existing medicines. Most participants in the longer-term trials reported side-effects, notably dizziness and nausea.

Details about these trials are given on our Sativex factsheet. However, in summary, trials have been held in the following symptom areas:

- bladder dysfunction in advanced MS: very small study, showed positive results⁹
- multiple symptom relief : spasticity, spasms, bladder problems, tremor and pain. Mixed results only.¹⁰
- multiple symptom relief - long-term follow up study over 14 months. Researchers concluded that long-term use of Sativex remains effective in patients who perceive initial benefit¹¹
- pain relief: trial in 66 people found Sativex is effective for people with MS experiencing dysaesthetic pain (uncomfortable, abnormal sensations, such as pins and needles, burning or crawling feelings, numbness or tightness). Two participants experienced serious heart and circulation-related side-effects that were resolved by coming off the medication.^{12, 13.}
- spasticity: trial involving 189 people found patients reported statistically significant improvements but these were not replicated by the official outcome measure, the Ashworth Scale.¹⁴

4.3 Ongoing non-commercial research trial

CUPID (Cannabinoid Use in Progressive Inflammatory brain Disease)

CUPID is a follow-on study from the CAMS trial. It has recruited 492 people with primary or secondary progressive MS from around 25 hospitals across the UK. Participants have primary or secondary MS, their MS has worsened over the year before entering the trial, and they are still able to walk 20 metres, with or without a walking aid.

This is a long-term study, with each participant followed for three and a half years. It is looking at whether delta-9 tetrahydrocannabinol (THC) can slow the increase of disability in people with progressive MS. Other outcome measures include whether THC provides symptomatic relief for spasticity. The trial will also try to assess the long-term safety of cannabis-based medicines. It is important to note that the cannabis-based medicine used in this trial is different from that used in the CAMS or Sativex trials. This is a randomised controlled trial so people receive either the cannabis-based medicine or a placebo (dummy). All capsules look identical and neither the person receiving it nor the doctor will know which treatment they are receiving.

The trial finished enrolling in June 2008 so results are not expected for several years.

5. Conclusion

The situation for cannabis-based medicine is in a state of flux. The current position, where Sativex is not licensed but is available to some people with MS, is unacceptable in the long-term. The MS Trust would like to see proper, unequivocal results from the research trials that clarify how far cannabis-based medicines are able to relieve MS symptoms leading to regulatory licence approval. We also welcome any new research into the effects of cannabis on the brain, particularly in people with MS. Any work in this area is always welcome, to increase our understanding and offer hope to people whose MS is progressive.

Note

* Drug trials

Phase I trials test a new product on healthy adults to ensure that there are no intolerable side-effects; Phase II trials test on a small number of people in the target group - in this case, people with MS. Phase III trials test therapy on large numbers of people in the target group and are needed before a new substance can be licensed for medicinal use.

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Publications

We hope that you have found this information helpful. The MS Trust offers a wide range of publications, including our quarterly newsletter *Open Door*, which provides an update on research and latest developments. Our website is regularly updated www.mstrust.org.uk

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