

Cannabis

Fact Sheet

Multiple
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Cannabis

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Contents

1. Introduction	1
2. Background	2
3. Current legal position of cannabis	2
4. Current research into cannabis-based medicines	3
4.1 Completed non-commercial research trials	4
4.1.1 CAMS (Cannabis in MS trial)	
4.1.2 effects of cannabinoids on psychological factors in MS	
4.1.3 lower urinary tract symptoms in MS	
4.1.4 tremor	
4.1.5 spasticity	
4.2 Sativex	6
4.3 Ongoing non-commercial research trial	7
- CUPID trial	
5. Conclusion and Note	7
6. References	8

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. The recent approval of the cannabis-based mouth spray, Sativex, as a treatment for MS spasticity, marks a significant milestone in our understanding of the benefits people with MS may derive from such medicines.

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 classified 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 2009, the government reclassified cannabis as a Class B drug. Class B drugs are illegal and carry the following penalties: for supplying, dealing, production and trafficking the maximum penalty is 14 years imprisonment; for possession the maximum penalty increases from two years to five years imprisonment. Recent legal cases have indicated that the law makes no exception for people using or supplying cannabis to help relieve medical symptoms.

Research studies have suggested that excessive use of recreational cannabis in young people may lead to long-term mental health problems. One very small

study in people with multiple sclerosis who smoke cannabis has demonstrated a significant adverse effect on mental processes, particularly cognition¹. 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 area².

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, 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, the Cannabinoid Use in Progressive Inflammatory Brain Disease (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

4.1.1 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); or
- 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 effective³.

Extension trial

After the main 15-week trial had completed, all participants were given the option of continuing with their medication for a further 12 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 is investigating this possible effect more fully⁴.

4.1.2 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 cannabis⁵.

4.1.3 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 MS⁶.

4.1.4 Tremor

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 receiving placebo⁷.

4.1.5 Spasticity

A systematic review of randomized controlled trials reported that cannabis can reduce spasticity in people with MS.

The study reviewed six double-blind, randomized controlled trials between 2002 and 2007 where treatment involved a combination of the cannabis extracts delta-tetrahydrocannabinol (THC) and cannabidiol (CBD).

Five of the studies reported a decrease in spasticity and improved mobility. One study reported no reduction in spasticity.

All of the studies reported some adverse events, which seemed to be related to the dosage. Generally the treatment was well-tolerated⁸.

4.2 Sativex

Sativex became the first cannabis-based medicine to be licensed in the UK in June 2010. Sativex is formulated as a mouth (oromucosal) spray containing two chemical extracts derived from the cannabis plant: delta-9 tetrahydrocannabinol (THC) and cannabidiol (CBD).

It received its licence as an add-on treatment for MS-related spasticity when people have shown inadequate response to other symptomatic treatments or found their side effects intolerable.

Prior to gaining a licence for use in MS-related spasticity, Sativex had been studied for its effects on a number of MS related symptoms including: spasticity and spasms, pain, bladder symptoms, tremor, and sleep disturbance⁹⁻¹³.

In 2009, a phase III trial investigating the effects of Sativex on MS spasticity was conducted in two stages. In the first stage, 573 people received Sativex for four weeks. The 241 people who responded to the drug went into the second stage where they received either Sativex or a placebo for 12 weeks. About

three quarters of those receiving Sativex reported an improvement of greater than 30% in their spasticity score at least once during the first four weeks of treatment¹⁴. For further information about Sativex see the MS Trust Sativex factsheet.

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 493 people with primary or secondary progressive MS from around 25 hospitals across the UK. Participants' MS had worsened over the year before entering the trial and they were 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 in 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, placebo-controlled trial so people receive either the cannabis-based medicine or a placebo. 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 but results are not expected for several years.

5. Conclusion and Note

Recent developments in the area of cannabis-based medicines in MS look promising. The completion of recruitment to the CUPID study and indeed completion of the three year visit for 20 of the study participants represents significant progress in the long-term study of the effects of cannabis-based medicine in progressive MS. It is hoped that the CUPID study, alongside other research studies, will clarify whether there is a role for cannabis-based medicines in altering the long-term course of the condition.

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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