

# Cannabis

# Fact Sheet

Multiple  
Sclerosis  
Trust

MS

Information

Education

Research

Support

# Cannabis

Latest revision: December 2009

## Contents

<b>Section</b>	<b>Page</b>
<b>1. Introduction</b>	<b>1</b>
<b>2. Background</b>	<b>1</b>
<b>3. Current legal position of cannabis</b>	<b>2</b>
<b>4. Current research into cannabis-based medicines</b>	<b>3</b>
<b>4.1 Completed non-commercial research trials</b>	<b>4</b>
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	
<b>4.2 Commercial cannabis-based medicine (Sativex) trials</b>	<b>7</b>
<b>4.3 Ongoing non-commercial research trial</b>	<b>8</b>
- CUPID trial	
<b>5. Conclusion and Note</b>	<b>9</b>
<b>6. References</b>	<b>10</b>

## **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 the cannabis plant is licensed for use in any condition in the UK. However, Sativex, a cannabis-based medicine, is now available on a named patient basis in the UK, and regulatory approval of the drug is a possibility in the near future. See the MS Trust factsheet on Sativex 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 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 cognition<sup>1</sup>. 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<sup>2</sup>.

It is clear that cannabis-based medicines will be licensed and available in the UK only when research trials prove that the medicines are safe and 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, 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 effective<sup>3</sup>.

### ***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 fully<sup>4</sup>.

#### **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 cannabis<sup>5</sup>.

### **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 MS<sup>6</sup>.

### **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 placebo<sup>7</sup>.

### **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-tolerated<sup>8</sup>.

## **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 in 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 results<sup>9</sup>;
- multiple symptom relief : spasticity, spasms, bladder problems, tremor and pain. Mixed results only<sup>10</sup>;
- 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 benefit<sup>11</sup>;
- 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<sup>12, 13</sup>.

Results of a further study of Sativex in people with neuropathic pain due to MS were announced in September 2008. The study demonstrated the effectiveness of Sativex in treating neuropathic pain in the long term<sup>14</sup>.

- spasticity: trial involving 189 people found patients reported statistically significant improvements but these were not replicated by the official outcome measure, the Ashworth Scale<sup>15</sup>. Following guidance from the UK regulatory authority (MHRA), a further study into the effectiveness of Sativex in spasticity due to MS was undertaken and the results announced in March 2009. These indicated a significant improvement on spasticity scores for the treatment group with 74% of participants receiving Sativex reporting an improvement greater than 30% in their spasticity score<sup>14</sup>.

In view of the positive results seen in the spasticity and neuropathic pain studies, GW Pharmaceuticals filed for regulatory approval of the drug in the UK and Spain in May 2009. It is expected that an outcome of the regulatory submission will be known early next year.

### **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**

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.

Furthermore, it is possible that the cannabis-based medicine, Sativex, will be licensed for the treatment of pain and spasticity in MS as early as 2010.

### **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.

## 6. References

1. Ghaffar O, Feinstein A.  
Multiple sclerosis and cannabis. A cognitive and psychiatric study.  
*Neurology* 2008;71:64-169.
2. Papathansopoulos P, Messinis L, Lyros E, et al.  
Multiple sclerosis, cannabinoids and cognition.  
*Journal of Neuropsychiatry and Clinical Neuroscience* 2008;20(1):36-51.
3. Zajicek J, Fox P, Sanders H, et al; UK MS Research Group.  
Cannabinoids for treatment of spasticity and other symptoms related to multiple sclerosis (CAMS study): multicentre randomised placebo-controlled trial.  
*Lancet* 2003;362(9395):1517-1526.
4. Zajicek JP, Sanders HP, Wright DE, et al.  
Cannabinoids in multiple sclerosis (CAMS) study: safety and efficacy data for 12 months follow up.  
*Journal of Neurology, Neurosurgery & Psychiatry* 2005;76(12):1664-1669.
5. Langdon D.  
The effect of cannabinoids on psychological factors in MS.  
RIMS- Rehabilitation in Multiple Sclerosis 8<sup>th</sup> Annual Meeting, 22-25 May 2003.
6. Freeman R, Adekanmi O, Waterfield M, et al.  
The effect of cannabis on urge incontinence in patients with multiple sclerosis: a multicentre, randomised placebo-controlled trial (CAMS-LUTS).  
*International Urogynecology Journal and Pelvic Floor Dysfunction* 2006;17(6):636-641.
7. Fox P, Bain PG, Glickman S, et al.  
The effect of cannabis on tremor in participants with multiple sclerosis.  
*Neurology* 2004;62(7):105-1109.
8. Shaheen E Lakhani SE, Rowland M.  
Whole plant cannabis extracts in the treatment of spasticity in multiple sclerosis: a systematic review.  
*BMC Neurology* 2009;9:59.
9. Wade DT, Makela P, Robson P, et al.  
Do cannabis-based medicinal extracts have general or specific effects on symptoms in multiple sclerosis? A double-blind, randomised, placebo-controlled study on 160 participants.  
*Multiple Sclerosis* 2004;10(4):434-441.
10. Wade DT, Makela P, House H, et al.  
Long-term use of a cannabis-based medicine in the treatment of spasticity and other symptoms in multiple sclerosis.  
*Multiple Sclerosis* 2006;12(5):523-525.
11. Rog DJ, Nurmikko TJ, Friede T, Young CA.  
Randomized, controlled trial of cannabis-based medicine in central pain in multiple sclerosis.  
*Neurology* 2005;65(6):812-819.
12. Rog DJ, Nurmikko TJ, Young CA.  
Oromucosal delta9-tetrahydrocannabinol/cannabidiol for neuropathic pain associated with multiple sclerosis: an uncontrolled, open-label, 2-year extension trial.  
*Clinical Therapeutics* 2007;29(9):2068-2079.
13. GW Pharmaceuticals.  
Press releases. [cited 2009; September 3]. Available from URL: [www.gwpharma.com](http://www.gwpharma.com)
14. Collin C, Davies P, Mutiboko IK, Ratcliffe S; Sativex Spasticity in MS Study Group.  
Randomized controlled trial of cannabis-based medicine in spasticity caused by multiple sclerosis.  
*European Journal of Neurology* 2007;14(3):290-296.

## 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](http://www.mstrust.org.uk)

**Contact us to receive our newsletter or to request another publication.  
All our services are free within the UK, but your donation  
allows us to continue our work.**

## MS Trust Information Service

The MS Trust Information Service is here to answer YOUR questions about MS. To contact us you can:

**phone** 01462 476700 (Lines are open Monday - Friday 9am-5pm)

**email** [infoteam@mstrust.org.uk](mailto:infoteam@mstrust.org.uk)

**write** MS Trust  
Spirella Building, Letchworth Garden City, SG6 4ET

---

## Can you help us to help others?

Each year we send out more than 50,000 booklets and answer more than 1,500 personal enquiries. We depend on voluntary donations to help fund this unique service and we would not be able to continue our work without the generosity of our supporters.

Please use this form to make a donation and/or to receive more information about the MS Trust

Name (Mr/Mrs/Ms/Other) \_\_\_\_\_

Address \_\_\_\_\_

Telephone number \_\_\_\_\_

Email \_\_\_\_\_

- Please add me to your mailing list to receive Open Door, your quarterly newsletter
- Please send me a publication list
  
- I would like to make a donation to support the charity's work and enclose a cheque payable to the MS Trust.

Credit or debit card donations can be made via our secure website or by telephoning 01462 476700.

### If you Gift Aid your donation we can claim the tax back from the money you give

- I would like the MS Trust to treat this donation and all donations I have made for the four years prior to this year and all donations I make from the date of this declaration until I notify you otherwise, as Gift Aid donations. Date: \_\_\_/\_\_\_/\_\_\_\_\_ Signed: \_\_\_\_\_

You must pay an amount of Income Tax and/or Capital Gains Tax in each tax year (6<sup>th</sup> April 2009 to 5<sup>th</sup> April 2010) at least equal to the tax that the MS Trust will claim from HM Revenue and Customs on your Gift Aid donation(s) for that tax year. Please notify us if you change your name or address.

The MS Trust will use your details to keep you informed about our work, including our fundraising and to pass to our wholly owned subsidiary companies MS Trust (Education) Ltd and MS Trust (Trading) Ltd which exist only to carry out our educational objectives and to raise funds for the MS Trust.

We will not sell or pass your details to anyone else (unless we are required to by law).

**If you object to either use of your details, please let us know.**