

Regulating Cannabis for Medical Use in the UK

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Introduction

1. The medical use of cannabis has an extremely long history. In Chinese medicine, cannabis is one of the 50 'fundamental herbs' and was traditionally used to treat a number of conditions including gout and rheumatism and as a contributor to pain relief. It was widely available in the UK and cannabis tincture was prescribed to Queen Victoria for period pains and during childbirth¹. More recently the utility of cannabis and some of its derivative 'cannabinoids' is becoming established in the treatment of a range of conditions including: the symptoms of multiple sclerosis, epilepsy, various forms of chronic pain, glaucoma, nausea and loss of appetite caused by chemotherapy or radiotherapy.
2. These advances in medical knowledge have occurred in spite of the fact that the medical application of cannabis and research into it has been suppressed under the UN Convention on Drugs (1961). It was designated as a Schedule 1 drug, that is, particularly harmful and of extremely limited medicinal or therapeutic value. This is reflected in the UK where cannabis is a class B drug, determining the level of penalty that cannabis related drug offences would attract. In terms of UK medical regulation it has been classed in Schedule 1 indicating that it is perceived as having no recognised medicinal use. Although these Schedules remain in place at UN and UK level, the regulation of cannabis for medicinal purposes is starting to become established in a number of countries across the world as forward looking countries make their own decisions on the emerging evidence. For example in the USA, medicinal cannabis can now be used on doctors' recommendation in more than half of all States.
3. In the UK there is increasing acceptance within the medical profession and elsewhere of the use of cannabis and cannabis derivatives medically. However, this has been reflected only marginally in government policy and a significant number of people are not authorised to receive medication which they believe will alleviate their condition. These problems are compounded by:
 - An inflexible legal framework
 - A stranglehold on research into cannabis
 - A determination when considering medical licensing to equate cannabis, a well known substance in terms of its effects on humans and used medically for around 4000 years (Gurley et al 1998), with an entirely new chemical introduced by a pharmaceutical company.
4. What is the way forward? The mechanics of regulating medical cannabis can be relatively simple. The principle way in which access to medical marijuana could be improved is to amend its Scheduling from Schedule 1 to Schedule 2 or 3. Schedules 2 and 3 include drugs which may be illegal for recreational use but can be available via a prescription. If cannabis were to be placed in Schedule 2 it would be in the same class medically as Heroin (diamorphine). There is no evidence of significant diversion of heroin from medical supplies to the illicit recreational market. Cannabis as a Schedule 2 substance would continue to be subject to strict controls via medical regulation. Such a move would therefore be unlikely to lead to diversion of medicinal cannabis to recreational use, as is feared in some American states

¹Reynolds, J. Russell, 1890. Therapeutic Uses and Toxic Effects of Cannabis Indica, *Lancet* 1 (March 22, 1890), 637-638. Reprinted in Mikuriya, 1973, 145-149. Select Committee on Science and Technology Ninth Report (1998): <http://www.parliament.the-stationery-office.co.uk/pa/ld199798/ldselect/ldsctech/151/15101.htm> (2.15)

Evidence of the efficacy of the medical use of cannabis

Cannabis can be used medicinally in herbal form and can be taken by vapouriser, orally, as a food preparation or a tea (smoking is not encouraged because of health harms). The two major ingredients in Cannabis are the cannabinoids Δ^9 -THC (delta-9-tetrahydrocannabinol) and (CBD) cannabidiol. Herbal cannabis comes in many different strains which contain different strengths of THC and CBD. However there are least 70 other cannabinoids unique to the cannabis plant² and the medical potential of these elements of the plant are yet to be fully explored. It is known that THC and CBD have several opposing effects and there is a '... growing body of evidence that suggests a range of potential therapeutic uses of CBD, including the ability to counteract the acute memory-impairing effects of Δ^9 -THC³.

Based on a review of the research literature, the most established uses of medicinal herbal cannabis in places where it is most widely available such as in the Netherlands include:

- The relief of pain and muscle spasms or cramps associated with multiple sclerosis or spinal cord damage; chronic neuropathic pain (mainly pain associated with the nervous system, e.g. caused by a damaged nerve, phantom pain, facial neuralgia or chronic pain which remains after the recovery from shingles); nausea, loss of appetite, weight loss and debilitation due to cancer or AIDS;
- nausea and vomiting associated with chemotherapy or radiotherapy used in the treatment of cancer, hepatitis C or HIV infection and AIDS;
- Gilles de la Tourette syndrome;
- therapy-resistant glaucoma.⁴

The main active cannabinoids are also available as medicine in the form of an extract from the cannabis plant comprising equal proportions of Δ^9 -THC and CBD and marketed as Sativex in the form of a spray. Based on extensive clinical trials the use of Sativex is authorised in the UK as an extra treatment for patients with spasticity due to Multiple Sclerosis (MS).

Clinical trials have also established the medicinal benefits of synthetic forms of THC: Dronabinol and Nabilone. The US Food and Drugs Administration advise that the use of Dronabinol (in the form of capsules where synthetic Δ^9 -THC is formulated in sesame oil) is indicated for:

1. 'anorexia associated with weight loss in patients with AIDS; and
2. nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.'⁵

² Celia J. A. Morgan , Gráinne Schafer , Tom P. Freeman , H. Valerie Curran (2010): *Impact of cannabidiol on the acute memory and psychotomimetic effects of smoked cannabis: naturalistic study*:

10.1192/bjp.bp.110.077503 Published 30 September 2010 <http://bjp.rcpsych.org/content/197/4/285> (2.1)

³Op cit 1

⁴Op cit 1

They also advise that the use of Nabilone is indicated for the ‘treatment of the nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.’⁶

Although not as well advanced there are emerging mental health indications of use of CBD⁷. Several studies have demonstrated a positive impact of CBD alone on anxiety in patients with social anxiety disorder.⁸ A further intriguing, potentially highly desirable, property of CBD appears to be the capacity to reduce psychotic symptoms in schizophrenia⁹ although this work needs replication.

Recent evidence also suggests that CBD may have a use as a treatment to modulate memory, by either enhancing fear extinction learning¹⁰ or blocking ‘reconsolidation’: the process by which memories are made labile to allow them to be strengthened or updated or disrupted¹¹. Either of these approaches makes CBD a candidate treatment for disorders of pathological fear memory, such as post-traumatic stress disorder and phobias. We have preliminary data that suggests that CBD reduces cigarette smoking¹² therefore this constituent of cannabis may help treat addiction. Five clinical trials in the USA and one in the UK are currently ongoing using CBD to treat certain forms of severe childhood epilepsy (e.g. Dravet’s syndrome); very positive early results have led to CBD being given orphan drug status in the US.

Recent reviews have addressed the broad spectrum of potential therapeutic uses of CBD, attributing them to a range of neurotransmitter actions¹³.

Countries which regulate the medical use of cannabis and cannabis derivatives

Summary

Currently, herbal cannabis for medical use can be grown under licensed conditions in Canada, the Netherlands, Israel and over 20 states in the US. It can be imported from the Netherlands to a number of other European states including Germany and Switzerland. Sativex is not only authorised in the UK but in an increasing number of other European countries as well. Dronabinol and Nabilone are authorised at federal level in the US, and in a few European countries, are licensed for ‘Compassionate Use’. Examples where cannabis is more freely available than in the UK include:

⁵ <http://www.fda.gov/ohrms/dockets/dockets/05n0479/05N-0479-emc0004-04.pdf>

⁶ <http://www.drugs.com/pro/cesamet.html>

⁷ Campos et al. 2012

⁸ Schier 2012; Guimares et al.1990; Bergamaschi et al. 2011

⁹ Leweke et al. 2012

¹⁰ Das et al. 2013

¹¹ Stern et al. 2012

¹² Morgan et al., 2013

^{12a} Russo EB ‘Medicinal cannabis and cannabinoids: clinical data’ pages 319-434 in Pertwee R (Ed) The Handbook of Cannabis. OUP 2014.

¹³Russo EB ‘Medicinal cannabis and cannabinoids: clinical data’ pages 319-434 in Pertwee R (Ed) The Handbook of Cannabis. OUP 2014.

Canada

Between 2001 and 2013 medical cannabis has been available for patients understood to require compassionate end of life care, relief from severe pain or seizures or relief from debilitating symptoms. Sufferers had to apply to Health Canada under the Marijuana Medical Access Regulations (MMAR). Since 2014 those needing medical marijuana can apply to authorised suppliers direct using a standard form authorised by a doctor with none of the above conditions having to apply. The status of authorised suppliers is being tested in law this year¹⁴.

The Netherlands

Medicinal cannabis in the form of florets or powder has been available since 2001 on prescription from pharmacies. Its production is controlled by the Office for Medicinal Cannabis which is responsible for ensuring supply and quality control. It supplies a variety of strains of cannabis as below¹⁵

Variety	THC content	CBD content
Bedrocan	About 19%	< 1%
Bedrobinol	About 12%	< 1%
Bediol	About 6%	About 7.5%

The Dutch Health authorities have carried out an extensive review of the scientific literature and consequently made a limited list of the conditions where the use of medicinal cannabis can be indicated (see above). The reason for this limited list of indications is that the efficacy of medicinal cannabis use for other medical conditions has not yet been properly studied in convincing clinical trials. The list is subject to change based on findings of new studies.

A number of neighbouring countries, whilst not permitting the production of herbal cannabis in their country, allow the import of Bedrocan from the Netherlands for medical use on application from a physician.

¹⁴ Health Canada: <http://www.hc-sc.gc.ca/dhp-mps/marihuana/index-eng.php> (2.15)

¹⁵ Institute of Responsible Medicine Use and the Office of Medicinal Cannabis of the CIBG, Ministry of Health, Welfare and Sport, the Netherlands (2011): *Medicinal Cannabis – Information for Patients*: http://www.cannabisbureau.nl/en/doc/pdf/5089-A5-BMC-Pat-ENG-web_35842.pdf (2.15)

Israel

Medicinal use has been permitted since the early 1990s. In 2013, 13,000 patients had been given a state licence to use cannabis for medical purposes.¹⁶ It is currently being used to treat the following conditions: -

- Parkinson's Disease;
- Multiple Sclerosis;
- Crohn's disease;
- other chronic illnesses; and
- Post-traumatic Stress Disorder.

Methods of delivery. Israel not only has the usual methods of delivery – inhalation, ingesting in liquid form but cannabis is also available as a balm which can be rubbed into the skin. Israel, like the Netherlands, is in the forefront of developing technology such as a marijuana inhaler which can precisely calibrate dosage and help to minimise the drug's better known side effects.

20 + States within the USA

In those States where medicinal cannabis is available there are variations in the systems employed but the common elements between them include:

1. Physicians can recommend rather than prescribe cannabis if they think it will be beneficial.
2. An identity card is issued to the patient and/or the carer
3. Most states allow for private growing of cannabis plants but there are varying rules between states as to what extent patients and/or carers are allowed to grow their own cannabis.

Spain

A limited amount of cannabis which is used for therapeutic purposes is available via Spain's cannabis social clubs. These operate in a legal grey area. The Organisation of Cannabis Social Clubs would welcome regulation.

Uruguay

Uruguay has regulated the supply of cannabis in the country. It has argued that one of the reasons for this policy is to ensure its compliance with human rights conventions and an aim of the regulation of supply of cannabis is to enable research into its medicinal use.

The Current situation in the UK

Although, in the UK, Nabilone has been licensed since 1982 for prescription-only hospital-only use against nausea arising from chemotherapy and unresponsive to other treatment, it has been very

¹⁶ Danish Health and Medicines Authority (2014): *Medicinal Use of Cannabis 2nd Edition*:
http://sundhedsstyrelsen.dk/en/news/2014/~/_media/57439DD97F054C60AE9B6A7FFC68F3BC.ashx

rarely used. In 2010 the Medicines and Healthcare Products Regulatory Agency (MHRA) authorised Sativex as an extra treatment for patients with spasticity due to Multiple Sclerosis (MS). In 1997 the British Medical Association (BMA) called for more trials into medicinal use of cannabis and advised that there was a case for the use of Dronabinol¹⁷ in the treatment of multiple sclerosis and other chronic spastic disorders unresponsive to other drugs.¹⁸ Dronabinol is a Schedule 2 drug which means that it has a recognised medical use and can be prescribed on a named patient basis but it has never been licensed.

Cannabis remains within Schedule 1. Thus its medicinal use is not officially recognised. However all the products above contain in pharmaceutical terms the same constituent elements which are included in Schedule 1.

Overall in the UK there is extremely limited availability of Sativex, no access to other forms of cannabis based treatment and no access to herbal cannabis. The result is that many people with chronic medical conditions are denied medicinal cannabis. If the drug were re-scheduled it could be delivered in different ways and could be available in different strains where the balance between the main constituent cannabinoids (Δ^9 -THC, CBD) can be controlled. For these people cannabis can offer the best medication with relatively mild side effects. At present they are being denied the treatment that they find works best for them. It is estimated that 30,000 people in the UK are risking breaking the law by using cannabis medicinally¹⁹. Further, because 80% of street cannabis in the UK is now 'skunk' – a high Δ^9 -THC content with virtually no CBD – these people risk more severe side effects and greater potential harms than if they were able to obtain a more balanced variety.

Other issues restricting the potential applications of cannabis medicinally include:

Cost

The main cannabis derivative available legally in the UK, Sativex, is expensive. The cost of Sativex can vary between £150 per week or £7,800 per annum²⁰ and £225 per week or £11,700 per annum. Based on the same dosage Bediol (high CBD content medicinal cannabis) would cost £20.43 per week / £1,062.15 per annum.

Post-code lottery

The National Institute of Clinical Excellence (NICE) recommendation is: "Do not offer Sativex to treat spasticity in people with MS because it is not a cost effective treatment". NICE Guidelines apply to NHS care in England. Specialist prescribers may make individual funding requests for Sativex if they feel that it would help the patient. This has led to wide variations in availability across England as it

¹⁷ Dronabinol is a synthetic version of δ^9 -Tetrahydrocannabinol, an isomer of THC which is delivered in sesame oil contained in gelatine capsules

¹⁸ British Medical Association (1997): *Therapeutic Uses of Cannabis*: http://books.google.at/books?id=vsMYE186qiUC&printsec=frontcover&hl=de&source=gbs_ge_summary_r&cad=0#v=onepage&q&f=false (2.15)

¹⁹ David Nutt (2014): *Medicinal Cannabis Time for a Comeback*: The Pharmaceutical Journal, 19th November 2014 http://www.pharmaceutical-journal.com/opinion/comment/medicinal-cannabis-time-for-a-comeback/20067185.article#fn_5 (2.15)

²⁰ Comparison calculated by a member of CLEAR (2.15)

depends on the preparedness of prescribers to test the system. This is not the case in Wales where the use of the drug is approved.

Inflexible legal system

Cannabis possession is routinely prosecuted in the UK and the legal system is determined to go after those who are sick or in pain who believe cannabis offers them the best chance of relief. Before 2005 the defence of 'necessity' was employed where defendants using cannabis medicinally argued that only cannabis worked for their condition. In 2005 the UK Court of Appeal (Criminal Division) ruled that 'necessity' could not be used as a defence as that would challenge the very basis of current law that cannabis is a controlled substance of no medical benefit and possession is illegal.²¹

Stranglehold on research

Carrying out research into cannabis in the UK is a costly obstacle course. It involves a minimum outlay of £5,000 to cover licensing and security; licence applications take about a year.

As a result of its Schedule 1 status in the UK only four hospitals have been granted a licence to hold stocks of cannabis although all of them are able to hold heroin.²² Only a handful of UK universities hold a Home Office Licence to do research on cannabis. Researchers generally need to import cannabis for their research. Import licences are only granted for 12 weeks by the Home Office and can expire before all the arrangements (e.g. export licence from the Netherlands and approval by the Dutch Medical Cannabis Office) are made. As a result of these restrictions it has been calculated that research involving Schedule 1 drugs takes significantly longer and costs about 10 times that of research into other drugs.²³ This means that UK research on the medical properties of cannabis and its 80-odd constituent cannabinoids is a massive uphill struggle.

Inflexible licencing system

A particular obstacle for the licensing of herbal cannabis preparations such as Bedrocan is that they need to be put forward to the MHRA for marketing authorisation. This will almost certainly come up with the problem that the preparation has not been subject to full clinical trials conducted as double blind, placebo controlled trials. These are principally designed to test both efficacy and safety for new and unknown drugs. However, as far as the safety of cannabis is concerned, its side effects have been well established and on a scale of harms it has been assessed as of less harm than alcohol. While it has harms that should not be ignored these are mild compared with many widely used drugs, for example in, pain management.

²¹ David Nutt (2010): *Necessity or Nastiness: The hidden law denying cannabis for medical use*: David Nutt's Blog, December 13 (2010) <https://profdavidnutt.wordpress.com/2010/12/13/necessity-or-nastiness-the-hidden-law-denying-cannabis-for-medicinal-use/> (2.15)

²² David Nutt (2015): *Illegal Drug Laws: Clearing a 50 year old obstacle to research*: PLOS Biology DOI:10.1371/journal.pbio.1002047 January 27, 2015

²³ Op cit 7

The Way Forward

A logical first step in policy change would be to take cannabis out of schedule 1 and place it in schedule 2. This would have several benefits:

1. People would be prescribed medicinal cannabis by a doctor. Medicinal cannabis could be imported from Bedrocan (Holland's single approved medicinal supplier). They would therefore no longer have to break the law by using an illicit substance or go to Holland to buy the drug. This would enhance the human rights of those who find the drug helpful e.g. for the relief of chronic pain.
2. Schedule 2 status would greatly facilitate research on the medical uses of cannabis, thus stimulating UK medical research into the drug and its constituents.

Will the availability of medicinal cannabis lead to increased recreational use?

Cannabis use increased exponentially and, more recently, decreased modestly under prohibition in the UK. The recent Home Office report 'Drugs - International Comparators' suggests that the severity of the drug control regime has little impact on the prevalence of drug use. An adjustment to the current UK control regime to give patients the right to medication that they believe works for them is unlikely to have any wider impact on the level of recreational cannabis use.