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Addiction and the pharmacology of cannabis: implications for medicine and the law

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ABSTRACT

The topic of drug addiction or misuse of drugs has numerous far-reaching ramifications into areas such as neuroscience, medicine and therapeutics, toxicology, epidemiology, international economic and political policies, and the law. The last is a particular concern as drug misuse has primary legislation such as the Misuse of Drugs Act 1971 and the Drugs Act 2005, and attendant legislation such as the Drug Regulations. It elicits high media concern, not always well-informed. Medical views encompass a range of opinion from drug misuse being another form of medical disorder to a dismissal of the topic as self-inflicted damage that should not be condoned, certainly discouraged, and on which treatment facilities should not be squandered.

The general principles of drug addiction are first summarised. A recurring and intrinsic problem is lack of adequate characterisation of the independent variable, namely the drug taken. Secondly, it is not feasible to allocate subjects randomly to treatments. Thirdly, the heterogeneity of different forms of addiction precludes facile generalisations.

"A problem drug user is anyone who experiences social, psychological, physical, or legal problems related to intoxication, and/or regular excessive consumption, and/or dependence as a consequence of their use of drugs" (UK Advisory Council on Misuse of Drugs, 1982)

Cannabis is a genus of flowering plants whose products are used as recreational drugs. Claims have been made for a range of therapeutic properties, its two main active principles are Δ^9 -tetrahydrocannabinol (THC) and cannabidiol (CBD). These compounds have contrasting pharmacological properties. THC is suspected of causing psychotic phenomena, but CBD seems more sedative and may even be antipsychotic. The past use of cannabis, particularly the concentrations of THC and CBD, can be monitored with hair analysis. Recent studies involving the administration of THC and CBD to human subjects are reviewed.

Suggestions are made for further research into the pharmacology and toxicology of CBD. Such data may also point to a more rational evidence-based approach to the legal control of cannabis preparations.

INTRODUCTION

The topic of drug addiction or misuse of drugs is a complex one. Primarily a branch of pharmacology, it has numerous far-reaching

ramifications into areas such as neuroscience, medicine and therapeutics, toxicology, epidemiology, international economic and political policies, and the law. The last is a particular concern as drug misuse has primary legislation such as the Misuse of Drugs Act 1971 and the Drugs Act 2005, and attendant legislation such as the Drug Regulations. It elicits high media concern, not always well-informed. Medical views encompass a range of opinion from drug misuse being another form of medical disorder to a dismissal of the topic as self-inflicted damage that should not be condoned, certainly discouraged, and on which treatment facilities should not be squandered. In particular, its legal aspects spawn an astonishing range of lay opinions from the draconian 'lock-'em-all-up' brigade to those who advocate partial or total decriminalisation and emphasis on treatment and regard the drug regulatory legislation as being an unjustified limitation on personal liberty.

Scientific and not-so-scientific publications in this area run to many thousands, and any commentator must be selective. I have chosen to explore the pharmacology of the third most commonly used psychotropic substance, cannabis (tobacco and alcohol are the commonest). As with other aspects of drug misuse, the pharmacology can be dauntingly complex, especially with plant products. I shall concentrate on a common constituent, cannabidiol (CBD), an important substance whose study has been largely eclipsed by the main psychoactive constituent, Δ^9 -tetrahydrocannabinol (THC). The questions that I shall address

Table II. Model of general drug misuse and dependence

Social dimension
• Increasing breaking of social limits → education and occupational impairment → life revolves around subculture and procuring supply → loss of other interests
Behavioural dimension
• Impulse to use (peer pressure) → recreational use → escalation of use → impairment of behavioural control (psychological dependence) → cessation → relapse (RSM) → eventual permanent cessation
Physical dimension
• Tolerantia (depending on drugs) → physical dependence → withdrawal problems (depending on drugs) → relapse → physical harm → morbidity up, mortality up
Legal dimension
• Primary (Misuse of Drugs Act, 1971)
• Secondary – criminality → thieving, prostitution

leave the issue wide open. It is essential that each such substance is evaluated separately in its own right before commonalities across drugs are sought.

General principles influencing management

A general schema regarding the various components of the natural history of drug abuse is set out in Table II. Again, it is important to recognise that the various elements of this multi-dimensional pattern vary greatly from drug to drug, in the usage of the drug, and the type of misuser. Possible points of intervention and criticism of their effectiveness are set out in Table III. These will be discussed further in relation to cannabis.

What is cannabis?

Cannabis is a genus of flowering plants of which the two main species are *cannabis sativa* (Linnaeus) and *cannabis indica* (Lamarck). The exact taxonomy is still being worked out using genetic typing techniques. *Cannabis indica* is Indian hemp which has a high fibre content and low concentration of psychoactive substances. *Cannabis sativa* is an annual flowering herb with attractive serrate leaves. It grows freely in many parts of the world, the content of its psychoactive substances varying

Table III. Tactical interventional options

- Reducing supply.** No evidence for effectiveness – cost on the street of many addictive drugs is historically low
- Reducing demand.** Mainly an educational exercise – not much evidence for effectiveness unless intense personalised treatment, initially within the prison system
- Withdrawal problems.** A medical problem, usually exaggerated e.g. cold turkey, benzodiazepine withdrawal more hazardous than heroin cessation, but generally accepted that treatment starts with detoxification, addicts often ambivalent about discontinuation, too often no further treatment – inadequacy of resources
- Reducing harm.** Slogan – Harm minimisation, HIV and injecting – changed regulatory and medical attitudes but not enough; use of oral or smoked preparations e.g. methadone for heroin, ‘cheating the dragon’ driven by medical not legal requirements – criticism of methadone regimen, overdose – reflects street provenance
- Primary (Misuse of Drugs Act, 1971 and associated schedules).** Does scheduling have any effect? Symbolic implications – users’ knowledge is sketchy but they are aware of distinction between possession and dealing, practice among law enforcement agencies is interpreted differently according to place and time. Relationship between level of scheduling and illicit usage is complex

widely according to climate, weather and soil conditions. It can be grown indoors using hydroponics and artificial light; high cannabinoid contents can be achieved (up to 15%). Indeed most cannabis found in the UK is home-grown and attempts to prevent its cultivation are largely ineffectual as deep cellars can be utilised and are almost impossible to detect. As a drug it can be in the form of

- Dried plant – Floral and foliar material from outdoor-grown female plants (herbal in UK, marijuana in USA)
- Sinsemilla (without seeds) indoor-grown female plants (‘skunk’)
- Resin (Hashish in USA)
- Hash oil
- Powder
- Cannabis/tobacco mixtures

Table IV. History of cannabis use

BCE 2800 Use in China as a medicine (Emperor Shen Nung)
BCE 1000 Bhang used as an anaesthetic in India
CE 500 Use spreads in Middle East
1800 Used in Western Europe
1900 Viewed as a dangerous intoxicant
1928 Made illegal in UK
1937 Made illegal throughout USA
1992 Synthetic compound licensed for nausea of HIV patients

There are many strains of cannabis, each with its putative attributes. These include Acapulco Gold, BC Bud, Panama Red, Kush, Northern Lights, Purple Haze and White Widow. Cannabis was known to ancient civilisations such as the Chinese and Hindu, and the history of its usage in various societies has been regularly reviewed (e.g. Russo, 2007) (Table IV).

Cannabinoids and their receptors

In 1964, the main psychoactive constituent of *cannabis sativa*, namely, Δ⁹-tetrahydrocannabinol (THC) was isolated in pure form and its structure determined (Mechoulam and Hanus, 2000). It exerts its effects by acting as an agonist at the cannabinoid 1 receptor (Mackie, 2007). This was discovered in 1988 (Guestis et al., 1988), and cloned two years later (Devane et al., 1990). It is a common G-protein-coupled receptor in the brain, and is found especially in the cerebellum, basal ganglia, hippocampus, and the neocortex. This localisation appears consistent with the motor and psychological effects of THC. CB1 receptors are also high in density in the dorsal root ganglion, the spinal dorsal horn and the periaqueductal grey matter, consistent with the analgesic properties of THC (Calignano et al., 1998). More recently a second receptor (CB2) has been identified which is also found in the brain but at lower concentrations than those of CB1, and may be largely involved in the immune system (Munro et al., 1993).

The characterisation of these receptors naturally led to the search for the endogenous

ligands (Lambert, 2007). The first one to be described was arachidonyl ethanolamide called anandamide, after the Sanskrit word ‘ananda’ meaning bliss (Mechoulam et al., 1995). It was classified as an endocannabinoid. Others have followed. The function of these endocannabinoids is to inhibit the release of fast-acting amino-acid neurotransmitters, such as GABA and glutamate, by acting pre-synaptically. An important function is to mediate transient and long-term plasticity in the cortex, the limbic system, the basal ganglia, and the cerebellum (Mechoulam and Hanus, 2000). More recently, it has become apparent that the pharmacology of the endocannabinoid system is complex and it is implicated in many brain-behaviour relationships that are modulated by the functions of several different neurotransmitter functions (Deadwyler, 2008). Indeed, this topic formed a special issue of the specialist journal, *Psychopharmacology* (2008, vol. 198).

Although THC has excited the greatest interest, at least 60 other psychoactive constituents of *cannabis sativa* are known. The phytochemistry of these compounds is complex, as is their synthesis and breakdown (Taura et al., 2007). Of these cannabis constituents, cannabidiol (CBD) has been evincing the most interest. It has been known for some time to be present in high concentrations in *cannabis indica* (Waller, 1971). It can constitute up to 40% of the cannabinoids in cannabis preparations. It does not, however, bind to either CB1 or CB2 receptors (Straus, 2000).

Contrasts between THC and DMC are clear and have profound implications for the pharmacology, possible clinical uses, toxicology and legal control of cannabis (Mechoulam et al., 2007). The chemical formulae for THC and DMC are displayed in Figure 1. It can be seen that DMC has an open cycle as compared with THC. However, under certain conditions DMC can form THC by a process of cyclisation, so the distinction between the compounds is not always clear-cut.

Psychopharmacology of cannabis

Cannabis has numerous actions including anti-inflammatory effects, neuro-protection against degenerative diseases, anti-tumour

(Manshouwer et al., 2005). The United Nations report estimated that 40% of adolescents had tried cannabis by the age of sixteen.

Another worrying trend, if it is confirmed, is for increasing the potency of the available cannabis. Claims have been made that the concentration of THC has risen in various cannabis preparations, particularly sinsemilla (skunk). It has doubled from 8 to 12% and has even reached 20% in some Dutch samples (UNODC, 2006). A careful analysis of samples from five sites of police seizure in the UK revealed that the content of THC varied widely, ranging from 2.1% in the herbal preparation to 14% in sinsemilla (Poitard et al., 2008). The latter figure represented a definite increase over ten years. In sinsemilla and unreported herbal cannabis, the concentration of CBD was very low but much higher in resin. It was concluded that the increases in average THC content of sinsemilla, coupled with the absence of CBD, posed an increased risk to susceptible users.

On the international scene, the potency and contamination of cannabis has been reviewed (McLaren et al., 2008). Over the past ten years tested samples of cannabis have increased in potency in the USA, the Netherlands, the UK and Italy, but not in other places. There was great variation between samples and over time. Contamination can occur with both fungal and bacterial agents. Storage conditions are important. Suppliers have added tiny glass beads to marijuana to simulate the crystalline appearance of resin. The UK Dept of Health issued warnings about inhaling these beads (Dept of Health, 2007).

Long term outcomes

Two recent studies have explored the natural course of cannabis use. The first was a prospective longitudinal epidemiological study conducted in Germany (Perkonig et al., 2008). A community sample of about 1,000 14-24 year-old general population youngsters was followed up for four and ten years. At baseline, a third of the sample had used cannabis at least once, the cumulative incidence of usage at four-year follow-up was 56% and had dropped only slightly to 46% seven years later.

Repeated users were more likely to persist than occasional users.

The second study was based in New Zealand (Fergusson and Boden, 2008). A birth cohort was followed up to age twenty-five. Measures of cannabis use aged 14-25 were correlated with various social, educational and occupational variables at age twenty-five. Increased use was associated with later lower degrees of educational attainment, lower incomes, higher levels of welfare dependency and lower levels of social and life satisfaction. Both these studies are subject to the problem of interpreting group differences where allocation to a group is self-determined.

Cannabis and psychosis

This area of concern has proved to be a major issue of contention between experts who regard the risk as low and those who think it so important that it should strongly influence legal policies. It is well-known that large doses of THC can produce transient psychotic episodes (Mathers and Ghodse, 1992). Symptoms include anxiety, agitation, confusion, delusions and hallucinations. There is often amnesia for the episode. These effects are not specific to THC *overus* but occur with a range of illicit drugs. Some individuals appear to be particularly liable to respond adversely. However, the psychotic episodes are generally short-lived and there is little evidence that longer-term psychoses persist in the majority of individuals (Ury et al., 1999).

Continuing cannabis use is associated with a worse prognosis in patients with an established psychosis. In one study in the Netherlands (Linszen et al., 1994), psychotic cannabis users had earlier relapses than non-users, an effect that was dose-related. In another Dutch study that involved a three-year follow-up of psychotic and non-psychotic patients in the community (Van Os et al., 2002), those diagnosed as psychotic at inception showed more adverse effects from smoking cannabis than those not so diagnosed. An in-patient study (Hides et al., 2006) showed an increased risk of relapse in psychotic patients, whereas somewhat paradoxically a Canadian study on out-patients showed the opposite (Marquis et al., 2006).

An imaging study provided some anatomical correlates for the worse prognosis in cannabis users (Raisz et al., 2008). Schizophrenic patients with a recent onset (N=19) who had regularly smoked cannabis were compared over five years with those who had not (N=32) and with normal individuals (N=53). A measure of grey matter volume decreased more over time in the schizophrenics than the normal subjects. They also showed larger increases in cerebral ventricular volumes. These changes were significantly more pronounced in those who had used cannabis than in those who had not. No confounding factors were discerned either at baseline or at the follow-up.

In general, national surveys in the USA, the Netherlands, and Australia have shown higher rates of cannabis use in patients diagnosed with schizophrenia than in the background population, e.g. Robins and Regier (1991). Thus, their US ECA study cited earlier found that half of schizophrenic patients also abused drugs (so-called dual diagnosis) as compared with 17% in the general population (Regier et al., 1990).

The relationship between cannabis use and psychotic illness remains contentious – four main explanations for the association have been proposed.

1. Social, economic or genetic factors may be common to both cannabis use and schizophrenia.
2. Schizophrenic patients may find the effects of cannabis helpful so that they self-treat their symptoms.
3. Cannabis directly causes psychosis – a hypothesis that parallels the effects of amphetamine in precipitating psychosis.
4. Some people are particularly vulnerable to develop or worsen schizophrenia if they use cannabis.

To address these various alternatives, prospective studies are needed. But first a word of caution – even prospective studies cannot escape the limitation that allocation of individuals to cannabis and non-cannabis using groups is self-determined. Randomised clinical trials are not feasible or ethical. Nor is it usually possible to quantify the type and extent of the cannabis.

The findings of these studies have been summarised in several excellent recent reviews (Arsenault et al., 2004; Smith et al., 2004; Degenhardt and Hall, 2006; Murray et al., 2007; European Monitoring Centre for Drugs and Drug Addiction, 2008). Other useful references include Henquet et al. (2005b), Semple et al. (2005) and Moore et al. (2007). Some of the key studies will be briefly reviewed.

A prospective study in over 50,000 Swedish military conscripts followed them up from 1969 (Andreasson and Allebeck, 1990). Those found to have been hospitalised for schizophrenia had their records scrutinised for self-reported cannabis use at recruitment. The relative risk for schizophrenia increased with extent of early cannabis use. The relative risk was about 2-3. A later follow-up showed heavy cannabis users to have a threefold risk of developing schizophrenia (Zammit et al., 2002).

A study in Dunedin, New Zealand, utilised a birth cohort of 1,034 children, born in 1973-4, who were asked about their drug usage at the ages of 15 and 18 (Arsenault et al., 2002). At age 26 the sample was evaluated using a standardised psychiatric interview. Those who had used cannabis by the ages of 15 or 16 had four times the risk of being given a diagnosis of a schizophrenia-like syndrome than non-users. Cannabis use did not predict a diagnosis of depression.

A similar birth cohort study of 1,265 people in Christchurch, New Zealand, took into account various possibilities linking cannabis and psychosis (Fergusson et al., 2005). Again, the data indicated a risk between 2.3 and 3.3 times higher for psychotic symptoms for daily users of cannabis, as compared with non-users. Even after adjusting for possible confounding factors such as family functioning, educational achievement and earlier psychotic symptoms, the relative risk remained at 1.6 – 1.8 times. Increased cannabis use did not relate to increases in psychotic symptoms, thus casting doubt on the self-medication hypothesis.

A study in the Netherlands followed over 7,000 randomly selected adults, who were evaluated in the late 1990s (van Os et al., 2002). At the three-year follow-up point, those

who had reported using cannabis at baseline had three times the risk of showing psychotic symptoms than non-users. Possible confounding factors did not remove this relationship. In this study a dose-response relationship was found, high users at baseline being at higher risk.

A study in Germany attempted to assess predisposition for risk of psychosis in a 121 participant sample (Henquet et al. 2005b). In this study the use of cannabis at baseline modestly increased the risk, particularly in those individuals who were homozygous for the allele that resulted in rapid dopamine breakdown, carried no increased risk of cannabis-associated psychotic breakdown. By contrast, those with the other gene coding for COMT and slow breakdown of dopamine were five times more likely to develop a schizophreniform psychosis if they took cannabis than non-users. However, the finding was not replicated in another sample (Lammuz et al. 2007).

In an experimental study, administration of 500 micrograms of THC to healthy volunteers produced more symptoms in the allele carriers for slow dopamine breakdown than in those coded for rapid breakdown (Henquet et al. 2005).

The problem of what the cannabis users actually used has been ingeniously addressed by two analysts (Morgan and Curran 2006). A sample of volunteers from another study gave samples of hair that were analysed for THC and CBD content. The volunteers completed a questionnaire designed to assess for schizophrenic proneness. The subjects with a predisposition of THC developed a higher incidence of schizophrenic-like features such as unusual experiences and abnormal cognitions (than did those with a mixture of the THC and CBD) in their hair samples, who in turn were more symptomatic than those with neither clearly a combination of the study with genetic analysis would lead to even more clarification of the relationship between cannabis use and psychosis.

The practical implications are that education and advice concerning cannabis use should focus on those with established psychosis and those with pre-psychotic features who carry an especial risk and could be

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The practical implications are that education and advice concerning cannabis use should focus on those with established psychosis and those with pre-psychotic features who carry an especial risk and could be

Whether genetic typing for the COMT enzyme is a fruitful strategy awaits further studies. Current group in Israel showed that CBD has specific redemptive effects (Gertin et al. 1981). The use of CBD alone in various therapeutic contexts has been explored. More specifically, it is possible to use an antidepressant, has been evaluated in animal models, and in a few schizophrenic patients (Gruart et al. 2006). The same preliminary data indicated similarities with atypical antipsychotics. Further trials are in progress.

LEGAL ASPECTS

Legal policies vary widely throughout the world ranging from Sweden's restrictive policy and low cannabis use to the liberal approach in the Netherlands with average cannabis consumption. France, Spain and the United Kingdom have higher levels as does the United States.

In the UK, legal policies towards drugs have resulted in complex laws. The primary legislation is the Misuse of Drugs Act 1971 which prohibits certain activities in relation to controlled drugs in particular their manufacture, supply and possession (British National Formulary 2006). The drugs are classified according to the perceived harmfulness of a drug when it is misused. Class B contains cannabis and cannabis resin. The various classes of person who can supply and possess controlled drugs are defined into five schedules. Schedule 1 includes cannabis and lysergic acid diethylamide (LSD) and other controlled drugs, e.g. doctors and vets. The Misuse of Drugs Regulations 2001 and 2004 set out the various sanctions and penalties for transgressing these laws.

However, the basis for these perceptions has been challenged and an alternative consensus proposed (Kun et al. 2007). A standardised rating system of physical harm, dependence and social harms was applied. Cannabis was ranked 11th out of 20 substances with heroin ranked highest. Large scale trials are being carried out or planned in many other countries including the USA. Data so far are encouraging (Ward et al. 2004, 2006). Both these drugs need further investigation as therapeutic agents but also provide a standardised form. Each spray delivers 2.7 mg of a mixture of THC and CBD in a standardised form. Each spray delivers 2.7 mg of a mixture of THC and CBD in a standardised form. Each spray delivers 2.7 mg of a mixture of THC and CBD in a standardised form. Each spray delivers 2.7 mg of a mixture of THC and CBD in a standardised form.

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use in treatment in the States, and a lack of accepted safety (US DEA, 2008).

The situation in the UK over the past decade or so has been characterised by a flurry of claims and counter-claims concerning the safety and medical utility of cannabis preparations. Eventually the pro-cannabis lobby prevailed and, on the advice of the statutory Advisory Council on Misuse of Drugs, the UK government decided in 2002 to reschedule cannabis from B to C (ACMD, 2002). The practical implications of this measure, when executed, were not to legalise or even de-criminalise cannabis, but to ease the penalties for manufacture, supply and possession. Possession would become a non-arrestable offence.

The effect of this change in scheduling was to introduce much ambiguity and variation in the enforcement of the relaxed regime (Pearson, 2007). A survey of police officers suggested that the majority wanted retention of the power to arrest (May et al., 2002). Overall, re-scheduling had little overall impact.

Soon after the link between cannabis and schizophrenia, or at the least schizophrenic relapse, became better documented, Cassandrian predictions were made that increased use of cannabis would inevitably increase psychotic problems (Hickman et al., 2007). Data from the last third of the 1980s concerning the incidence of schizophrenia was adduced to reinforce these warnings: the incidence had doubled in some areas and there was a large increase in those using cannabis (Boydell et al., 2003, 2008).

Despite data suggesting that the re-scheduling of cannabis had not increased the usage of cannabis, the propaganda machine went into reverse and the media agitated for a reversion to Schedule B. The UK government have agreed to this against the advice of the ACMD, some of whose members threatened to resign in high dudgeon.

DISCUSSION

Numerous issues are raised in this overview from a standard pharmacological viewpoint. Cannabis, albeit a plant product and very complex, has a definable pharmacology that is often overlooked in the welter of sociological, economic and political discussion. Although

cannabis contains over 50 active principles, the emphasis for the past 40 years or so has been on THC. Recent developments now provide us with the opportunity to look also at CBD. This is turning out pharmacologically to have a profoundly dissimilar spectrum of properties. Thus, there is preliminary evidence that it may be antipsychotic rather than psychotogenic like THC.

This development has profound research implications. Hair analysis, despite its technological complexity, should provide us with some important information about the recent usage of cannabis by a subject. Furthermore, it can give an integrated picture of the relative concentrations of THC and CBD. Such analyses have proved invaluable in other areas of illicit drug use, extending into forensic applications. Much of the epidemiology of cannabis use will need re-working. It is no longer sufficient to rely on a retrospective self-report. However, hair analysis has its limitations, as it provides only a broad-brush approach.

Other studies should involve the administration of THC, CBD and their combination, compared with a placebo to volunteer subjects. This can become very complex as an infinite variety of combinations and doses can be drawn up. However, analyses indicate that the relative quantities can be limited to a few combinations and doses. In particular, the provocation of psychotic problems and possible protection need exploration.

The therapeutic potential of CBD needs formal evaluation in randomised clinical trials. This will need to be done in conjunction with THC as a protection against THC-induced psychosis, but also CBD could be evaluated as a stand-alone antipsychotic. Pilot data are promising.

The regular monitoring of cannabis preparations on the street is important in order to inform experts and politicians. Together with hair analyses, these should provide a much more comprehensive and integrated view of actual cannabis use.

A basic principle in clinical pharmacology is assessment of the risk/benefit ratio, set against the severity of the indication. Cannabis may yet be shown to have useful therapeutic in-

dications but the vast preponderance of cannabis use will remain for recreational purposes. Therefore the 'benefits' are non-medical. Nevertheless, they are real as so many young people use the drug on at least a sporadic basis. That is going to be very difficult to prevent and it remains entirely unrealistic to expect attempts to interrupt the supply to have more than a marginal effect. The logical step is to minimise harm. The main areas are of respiratory pathology that may be accruing and an increased risk of psychotic breakdown. The latter is not a factor in the general users of cannabis but is probably important in the psychotic patients who have succumbed, and perhaps in the pre-psychotic individuals if they can be identified.

The respiratory risk can be obviated by dissuading the smoking of cannabis and suggesting that users switch to oral use. The second is to try and ensure that cannabis preparations of whatever modality contain CBD as well as THC. This development is a radical suggestion and the relevant research must be completed first and its implications digested.

The institution of adequate risk prevention measures would be facilitated by closer control by the medical and legal authorities of the preparations available to the users. Tablets are acceptable to illicit drug users, as the widespread use of MDMA (Ecstasy) and amphetamines show. But that would not guarantee an optimum cannabinoid content. The radical solution is for the Government to legalise cannabis and remove it from the ambit of the Misuse of Drugs Act 1971. It should then come under the Medicines Act 1968. Producers of cannabis would be licensed as drug manufacturers as with other medications. The appropriate licensing authority would evaluate the risk/benefit ratio of various preparations in the usual way and license the most appropriate. Cannabis tablets would be sold as medicines, on prescription. The price could be set fairly low, thus undercutting the dealers and driving them out of the cannabis business. If cannabis use is indeed a gateway to hard drug use, this link would also be severed.

The police forces would no longer have some of their resources used in cannabis vigilance

and could concentrate on more pressing and hazardous illicit drug practices.

Furthermore, government control of cannabis tablet use would enable the product to be taxed as are tobacco and alcohol. The level of taxation would need some careful consideration. But the overall harm associated with cannabis use is probably less than those associated with the other two taxed substances.

This regimen could lead to useful sums of money. They should be ring-fenced and the money applied to medical and educational programmes, particularly directed to the psychosis-inducing effects. This educational approach could be carefully focused on those schizophrenic patients who have continued to smoke cannabis and those at risk of breaking down.

With modern industrial horticultural techniques, we cannot prevent the widespread availability of cannabis preparations, typically with a high THC content. By legalising, nationalising, and regulating the cannabis industry, we may have a reasonable chance of minimising the very real harms associated with this habit. We need to carry out the appropriate studies using modern techniques, evaluate the results and their implications dispassionately and disinterestedly. We must avoid sentiment and moralistic posturing.

(This paper is based on a presentation in the Symposium entitled Science and Justice: Detection, Prevention and Prosecution: A Commemoration of the centenary of the death of Sir Thomas Stevenson (1836-1908), held at Guy's Hospital, 6 September 2008).

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