J. Pharm. Pharmac., 1976, **28**, 1–7 *Received July* 28, 1975

The stability of cannabis and its preparations on storage

J. W. FAIRBAIRN, J. A. LIEBMANN AND M. G. ROWAN

Department of Pharmacognosy, The School of Pharmacy, University of London, 29/39, Brunswick Square, London WC1N 1AX, U.K.

Solutions of pure cannabinoids, nine samples of herbal and two of resin cannabis (one freshly prepared) were stored in varying conditions for up to 2 years. Exposure to light (not direct sunlight) was shown to be the greatest single factor in loss of cannabinoids especially in solutions, which should therefore be protected from light during analytical and phytochemical operations. Previous claims that solutions in ethanol were stable have not been substantiated. The effect of temperature, up to 20°, was insignificant but air oxidation did lead to significant losses. These could be reduced if care was taken to minimize damage to the glands which act as "well filled, well closed containers". Loss of tetrahydrocannabinol after exposure to light does not lead to an increase in cannabinol, but air oxidation in the dark does. It is concluded that carefully prepared herbal or resin cannabis or extracts are reasonably stable for 1 to 2 years if stored in the dark at room temperature.

It has long been recognized that cannabis resin and herbal cannabis lose potency on storage and this instability is said to be one reason against the use of cannabis in medicine in the past. Since the recognition that potency is mainly due to the content of Δ^1-*trans*-tetrahydrocannabinol (THC) some work on resin and herb has indeed confirmed that the THC content falls on storage (Lerner, 1969; Maunder, 1970; Mechoulam, 1970; Schou & Nielsen, 1970). Three reports indicate that ethanol may exert a marked stabilizing effect (Eckler & Miller, 1917; Kubena, Barry & others, 1972; Razdan, Puttick & others, 1972). Little of the earlier work was done on carefully dated samples, with adequate methods of analysis, nor were varying conditions of storage examined in detail. In 1971 we therefore began experiments designed to test the effect of the obvious factors of light, oxygen and temperature and to include in our consideration the fact that in the plant the active resin is stored in glands which are virtually "well-filled, well-closed containers". When preparing resin cannabis and some forms of herbal cannabis, such as ganja, many of these glands will be burst and the released resin will be exposed to air oxidation. Extracts and solutions in various solvents were also examined as these preparations are likely to be handled during phytochemical work.

Since commencing our work Turner, Hadley & others (1973a) published results of experiments covering 1970–72; they used a wider range of temperature than we did but did not study the effect of light in detail: also their results were based on one sample of herb only. Work has also been carried out on short exposure of cannabis leaf to relatively high temperatures (Coffman & Gentner, 1974) and the stability of extracts and pure cannabinoids in solvents (Turner, Hadley & Davis, 1973b; Parker, Borke & others, 1974; Turner & Henry, 1975). Garrett & Tsau (1974) reported on the effect of pH during storage; however, they used extremely dilute solutions of THC in water (0·5 ppm) and do not seem to have considered the effect of light.

MATERIALS AND METHODS

Herbal cannabis. Samples were prepared from our own plants grown in England: those labelled "UN etc." were from seeds supplied by the UN Division of Narcotics, Geneva; SP1 was from seeds purchased in Merzifon, Turkey, 1969; SP4, a Nepalese variety; SP5, from a police seizure in London, 1971; SP10, a Mexican strain and SP11, seeds from the Cameroons, 1972. The leaves and tops, freed from stems more than 2 mm in diameter, were dried in the shade in a current of air at about 20°. For analytical purposes it was not possible to sample adequately without powdering the heterogeneous material; unfortunately this obviously burst some of the glands. To get some idea therefore of this effect, coarsely and finely powdered samples from the same material were stored separately.

Cannabis resin. One batch of Pakistani resin which had been seized by the police in August 1968 was used. In addition we prepared a sample from the dried tops of one of our varieties (South African, UNC 335, collected in November, 1973). The tops which contained 3·64% THC were frozen to make the glands hard and brittle and then coarsely powdered. This powder was rapidly sieved through sieves of varying fineness. Those fractions coarser than 180 μm mesh aperture width contained 1·9 to 3·7% THC; that fraction passing completely through 125 μm mesh contained 11·6% THC. Microscopical examination showed the presence of numerous cystolith and covering trichomes as well as glands, most of which were intact. Some of this fine powder was stored loose with occasional shaking to keep the powder from clumping; another part was compressed into blocks to simulate the method used for making "commercial" resin.

Pure cannabinoids were obtained from Professor R. Mechoulam or from Makor Chemicals, Jerusalem. The $\Delta^{1(6)}$-THC showed a single peak on the g.l.c. system used; the Δ^{1}-THC showed some impurities representing about 10% of the area of the major peak. The cannabinol (CBN) and cannabidiol (CBD) were pure to g.l.c.

Analysis was carried out by the method of Fairbairn & Liebmann (1973). However, for the work on the effect of light on pure THC, triacontane was used as internal standard because it is more stable than the steroid normally used. The problem of sampling resin has been discussed earlier (Fairbairn & Liebmann 1973); for our present purpose samples 5 × 3 × 3 mm were cut from the block on each occasion. Each piece was then cut into three equal parts by slicing parallel to the original surfaces of the entire block so that two segments contained the outer part and the third the interior of the block only.

Storage conditions

Samples were stored in transparent glass bottles at 5° in the dark (refrigerator) at room temperature (about 20°) in a dark cupboard and at room temperature behind a north-facing window. The samples were kept well mixed and portions were removed periodically for analysis.

RESULTS

The results for cannabinoids in solution are given in Table 1 and Figs 1A and 1B. One striking feature not recorded in Table 1 is the absence of any evidence for the production of cannabinol (CBN). The results for herbal cannabis are given in Tables 2 and 3 and for our own prepared cannabis resin in Table 4. For the commercial

Table 1. *Cannabinoids in solution; loss during different conditions of storage.* Figures are the percentages of the main cannabinoid retained; absolute values, at the commencement (t_0) are given in brackets, as mg ml^{-1}.

	5° in dark	20° in dark	20° in light
1. Δ^1-THC in petroleum t_o—(0·08)			
t_o + 2 days	94	95	80
t_o + 6 days	92	94	9
2. $\Delta^1(^6)$-THC in petroleum t_o—(0·15)			
t_o + 2 days	100	100	51
t_o + 6 days	99	101	1
3. THC in $CHCl_3$ t_o—(1·30)			
t_o + 2 days		99	92
t_o + 6 days		105	65
t_o + 20 days		95	9
4. CBD in $CHCl_3$ t_o—(1·0)			
t_o + 2 days		69	47
t_o + 6 days		32	5
t_o + 20 days		traces	none
5. CBN in $CHCl_3$ t_o—(1·32)			
t_o + 2 days		95	99
t_o + 6 days		87	67
t_o + 20 days		87	48
6. $CHCl_3$ extract of UNC 255 t_o—(THC 1·52)			
t_o + 2 days		103[a]	67[b]
t_o + 6 days		103	15
t_o + 20 days		101	none
7. $CHCl_3$ extract of SP1 t_o—(CBD 0·38)			
t_o + 2 days		100	92
t_o + 6 days		95	61
t_o + 20 days		103	8

(a) CBN remained at 0·12, 0·12 and 0·09 respectively.
(b) CBN concentration at t_o was 0·12 mg ml^{-1} and rose to 0·22, 0·39 and 0·31 respectively.

sample of resin the sampling difficulties already referred to made it impossible to carry out adequate storage tests. In general however, (a) the inner layers contained more THC than the surface layers; (b) in any given piece a low THC content corresponded to a high CBN and vice versa; (c) in the inner layers the total THC + CBN was higher than in the surface layers. Thus for the inner layers the average THC and CBN contents were 4·5 and 2·4% respectively giving a total of 6·9%; in the surface layers the corresponding figures were 2·5, 3·4, with a total of 5·9%. In contrast to these fluctuations, the CBD content was surprisingly stable giving the same average of 4·1% for the inner and surface layers.

DISCUSSION

The most important result of this work has been to emphasise the deleterious *effect of exposure to light*, a point not sufficiently stressed previously. The effect on solutions of cannabinoids is dramatic. Pure THC in light petroleum is almost completely decomposed in 6 days at room temperature, whereas in the dark there is

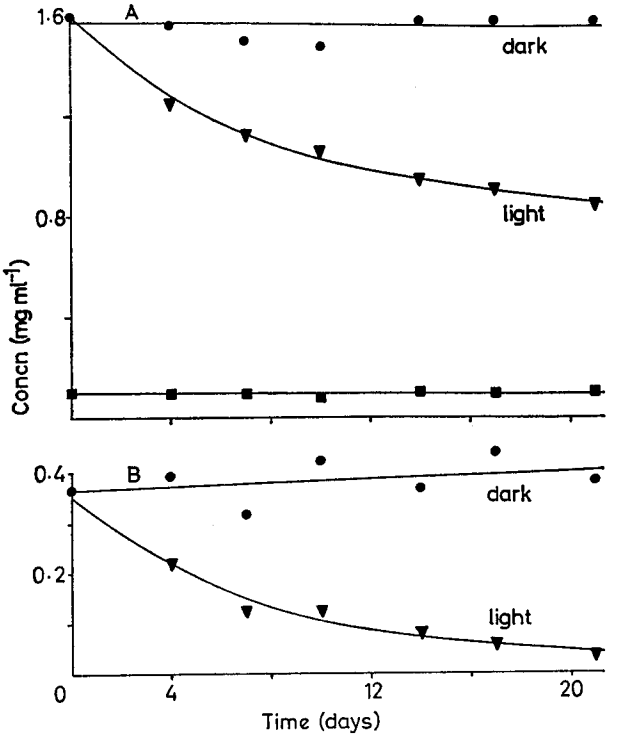

FIG. 1.A. Ethanolic extract of UNC 255; effect on THC content of storage in the dark (●) and in the light (▼). CBN content, in dark and light (■). B. Ethanolic extract of SP1; effect on CBD content of storage in the dark (●) and in the light (▼).

practically no loss (Table 1, samples 1 and 2). In $CHCl_3$ solutions decomposition is less marked (sample 3) but the presence of pigments in crude extracts does not seem to have any protective effect against light (sample 6). CBD in $CHCl_3$ is markedly less stable even in the dark (sample 4), and this confirms the results of Parker & others (1974) which showed significant loss in 1 day and almost total loss in 8 days in the dark. However, in crude samples CBD is very stable in the dark, but once more the pigments present do not protect from the deleterious effect of light (sample 7). This stability in crude extracts in the dark is confirmed by our previous work on commercial resin. Turner & others (1973b) report that THC and CBD in crude extracts in $CHCl_3$ are stable for 6 days, but unfortunately they do not state whether storage was

Table 2. *Herbal cannabis: effect of temperature and light on one sample (SP4).* Figures are % remaining in each sample (100 = 1·37% THC).

Storage time	5° in dark	20° in dark	20° in light
t_o	100	100	100
t_o + 31 weeks	92	88	65
t_o + 47 „	93	87	64
t_o + 73 „	89	80	50
t_o + 98 „	91	75	37

Table 3. *Herbal cannabis: effect of storage at 20° in the dark of eight varieties.* Figures are % of the main cannabinoid retained, absolute values at the commencement (t_0) are given in brackets.

Variety	Time	Coarse powder (about 1 mm mesh)	Fine powder (about 0·33 mm mesh)
SP5	t_0 (2·65% THC)		
	t_0 + 1 year	83	74
SP10	t_0 (1·46% THC)		
	t_0 + 1 year	92	80
SP11	t_0 (2·01% THC)		
	t_0 + 1 year	74	68
UNS1	t_0 (3·43% THC)		
	t_0 + 1 year	91	84
UNC255			
Sample (a)	t_0 (1·90% THC)		
	t_0 + 2 years	n.d.	52
Sample (b)	t_0 (4·60%)		
	t_0 + 1 year	n.d.	57
UNC254	t_0 (1·05% THC)		
	t_0 + 2 years	n.d.	54
UNC335	t_0 (4·50%)	n.d.	69
UNC258			
Sample (a)	t_0 (1·37% CBD)		
	t_0 + 1 year	86	78
Sample (b)	t_0 (1·55% CBD)		
	t_0 + 1 year	87	73
Sample (c)	t_0 (0·21% CBD)		
	t_0 + 2 years	n.d.	76

n.d. Not determined.

in the light or in the dark. Later Turner & Henry (1975) reported that THC and CBD, either in solution or in crude extract form, are stable for 6 days in both natural and artificial light. They suggest that the instability reported by Parker & others (1974) may be due to their having used impure $CHCl_3$. We have used varying qualities of chloroform, including spectrograde used by Parker & Turner and their colleagues and found in all cases decomposition is rapid in the light. The main problem raised by our results and those of Parker and others is the use of $CHCl_3$ in the assay of cannabis (e.g., Fairbairn & Liebmann, 1973). Fortunately the extraction procedure is short (about 1 h at the most) so that little decomposition will take place, but obviously $CHCl_3$ extracts or solutions should not be left standing for long before completing the assay, nor should they be exposed to strong light.

Ethanolic extracts are also quite stable in the dark but exposure to light leads to fairly rapid loss of cannabinoids (Figs 1 and 2). These results agree with those for other solvents but do not support the claim made by Kubena & others (1972) that an ethanolic extract (Fluid extract of Cannabis U.S.P.X) had lost little or any of its original activity after 43 years storage in amber bottles with temperatures ranging up to 38°. Obviously no figures for the original THC concentration are available but reference to the U.S.P. X shows that the fluid extract is prepared from the "dried flowering tops of pistillate plants" and that 1 ml should represent 1 g of the drug. In view of the fact that flowering tops produced in England contained 2 to 7% THC (Fairbairn & Liebmann, 1974), it would be reasonable to assume that the USP cannabis (probably from India) would contain at least 4% THC. The authors reported that the

Table 4. *Cannabis resin (freshly prepared); changes in cannabinoid content (%) in different conditions of storage for 1 year at room temperature (20°).*

Conditions	THC	CBN
Freshly prepared (t_0)	11·6	traces
Light and air		
1. Loose powder	7·3	1·8
2. Compressed powder but mass broken up	5·2	2·4
3. Compressed, unbroken lump		
(a) Surface layer (0·2 mm)	5·2	2·3
(b) Next 2 mm layer	10·7	1·8
(c) Centre	11·4	1·6
Darkness and air		
4. Loose powder	12·0	0·65
5. Compressed but broken up	10·1	1·0
6. Compressed, unbroken lump		
(a) Surface layer	11·1	1·86
(b) Next 2 mm layer	10·3	1·04
(c) Centre	11·0	1·47

fluid extract only contained 0·4% THC, indicating that only about 10% of the original amount remained, a value which would be consistent with our own experience.

The effect of light on one sample of *herbal cannabis* (Table 2) shows once more its deleterious effect. The results in Table 3 on a further 8 samples confirm that in the absence of light carefully dried herbal cannabis is quite stable; in fact more so than previously thought. Thus Lerner (1969) surmised a rate of loss of THC of 3 to 5% per month at room temperature, corresponding approximately to 31 to 46% per year. Assuming a linear rate of decomposition Turner & others (1973a) found a loss of THC of 7% per year at room temperature when stored in amber bottles either in the dark or with limited exposure to light. Our seven samples of coarse powder in Tables 2 and 3 give corresponding values ranging from 5 to 26% with a mean of 13%. The results on *cannabis resin* (Table 4) also show the deleterious effects of light but in addition they illustrate other effects which are discussed below.

Although in our experiments the *effect of temperature* (5° and 20°) was not marked (Tables 1, 2) Turner & others (1973a) showed that at 37 and 50° significant losses occurred. As their experiments were carried out in ovens, presumably light played no part in the deterioration. Coffman & Gentner (1974) also studied the effect of higher temperatures for periods up to 64 h. Little decomposition took place at 65° but considerable losses occurred at 85 and 100°.

The *effect of oxygen* on herbal cannabis seems much less significant than that of light or higher temperatures. This may be due to the fact that, in the carefully dried plant, the cannabinoids are stored in "well-closed containers", the glands. If these are burst by careless preparation or in the making of resin, then loss by oxidation is more likely. The results for herbal cannabis in Table 3 are consistent with this suggestion: losses in the fine powder, where more glands will be damaged, are consistently greater than in the coarse powder. On average the 6 samples of fine powder contained 11% less cannabinoids than the coarse powder after 1 year storage. The results of a more ambitious experiment on specially prepared resin are given in Table 4. The loose powder showed less loss in THC after 1 year than compressed powder in which many glands would be burst. However, if the compressed powder was

retained as one lump this loss was mainly confined to the surface layer which clearly protected the inner layers from breakdown. This is also shown in our work on the Pakistani resin sample (see Results) in which the inner layers always contained more THC than the outer. The results (Table 4), do show that the effect of oxygen is much less significant than that of light, in the material we used. Thus in the light there was a loss, for the loose powder, of 37% of the original activity and for the compressed material (more glands broken) of 55% (samples 1 and 2). In the dark the losses in comparable samples 4 and 5, are only zero and 13% respectively. Razdan & others (1972), however, deliberately increased the possible effect of oxygen by spreading THC on filter paper (in the dark at 25°); in these circumstances they report a loss of 75% in 10 months. It can be concluded, that cannabis resin is quite stable if stored in the dark in large lumps which prevent access of air to the interior.

We have already referred to the fact that decomposition of THC in the light does not lead to an increase of CBN, although the latter is not markedly unstable in the light (Table 1, sample 5, and Fig. 1). Conversion to CBN however seems to occur in the resin stored in the dark as well as in the light (Table 4). Levine (1944) also reported a significant conversion of THC to CBN in resin stored in the dark for 3 years. Our results on the Pakistani resin also showed that a low THC content corresponded to a high CBN and vice versa. We make the tentative suggestion therefore that the effect of light may be to convert THC rapidly to polymers which would not be detected by the usual g.l.c. and t.l.c. methods and of oxygen to convert the THC to CBN, some of which will polymerize especially in the light. It would be intriguing to know however how the cannabinoids in the living plant are preserved in the transparent glands which are often exposed for long periods to brilliant sunshine.

Acknowledgements

We would like to thank the Medical Research Council for a grant towards the cost of this work, and Professor F. Sandberg for the Cameroon seed.

REFERENCES

COFFMAN, C. B. & GENTNER, W. A. (1974). *Bull. Narcotics*, **26** (1), 67–70.

ECKLER, C. R. & MILLER, F. A. (1917). *J. Am. pharm. Ass. Sci. Ed.*, **6**, 872.

FAIRBAIRN, J. W. & LIEBMANN, J. A. (1973). *J. Pharm. Pharmac.*, **25**, 150–155.

FAIRBAIRN, J. W. & LIEBMANN, J. A. (1974). *Ibid.*, **26**, 413–419.

GARRETT, E. R. & TSAU, J. (1974). *J. pharm. Sci.*, **63**, 1563–1574.

KUBENA, R. K., BARRY, H., SEGELMAN, A. B., THEINER, M. & FARNSWORTH, N. R. (1972). *Ibid.*, **61**, 144–145.

LERNER, P. (1969). *Bull. Narcotics*, **21**, (3), 39–42.

LEVINE, J. (1944). *J. Am. chem. Soc.*, **66**, 1868–1870.

MAUNDER, M. J. DE FAUBERT (1970). *J. Assoc. Publ. Analysts*, **8**, 42–47.

MECHOULAM, R. (1970). *Science*, **168**, 1159–1166.

PARKER, J. M., BORKE, M. L., BLOCK, L. H. & COCHRAN, T. G. (1974). *J. pharm. Sci.*, **63**, 970–971.

RAZDAN, R. K., PUTTICK, A. J., ZIKTO, B. A. & HANDRICK, G. R. (1972). *Experientia*, **28**, 121–122.

SCHOU, J. & NIELSEN, E. (1970). *Dansk. Tidsskr. Farm.*, **44**, 359–364.

TURNER, C. E., HADLEY, K. W., FETTERMAN, P. S., DOORENBOS, N. J., QUIMBY, M. W. & WALLER C. (1973a). *J. pharm. Sci.*, **62**, 1601–1605.

TURNER, C. E., HADLEY, K. W. & DAVIS, K. H. (1973b). *Acta Pharm. Jugoslav.*, **23**, 89–94.

TURNER, C. E. & HENRY, J. T. (1975). *J. pharm. Sci.*, **64**, 357–359.