# THE HERB DANGEROUS

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# A PHARMACEUTICAL STUDY

## OF CANNABIS SATIVA

### (BEING A COLLATION OF FACTS AS KNOWN AT THE PRESENT DATE)

CANNABIS INDICA was introduced into England by O'Shaughnessy, and the first extract was made by the late Mr. Peter Squire, the well-known pharmacist of Oxford Street. According to the "British Pharmacopeia" the official variety may consist of the flowering or fruiting tops; and is frequently of inferior quality, seeing that the fruiting tops yield less resin.

According to the "Journal" of the Chemical Society's Transactions, the important constituent is a resin. The active principle is stated to be a red oil, Cannabinol, which is liable to become oxidised and inert.

Its medicinal properties are sedative, anodyne, hypnotic and antispasmodic. It has been used with success in migraine and delirium, neuralgia, pain of last stages of phthisis and in acute mania, also in menorrhagia and dysmenorrhœa. ("Squire's Companion," page 167, 1904 edition.)

It does not produce constipation or loss of appetite; on the contrary it restores the appetite which had been lost by chronic opium or chloral drinking. (1889, *Lancet*, vol. i. page 65.)

Dr. Martindale remarks that recently the Cannabis imported had more toxic effects than formerly (this in spite of the fact that a high export duty has been placed upon the drug); it has indeed been stated that toxic symptoms have been produced by doses of the extract within the official limits. According to the "British Pharmacopeia" the dose is ¼ to 1 grain. The *Lancet* vol. i, page 1042 (1908), records two interesting cases of toxic symptoms caused by taking over-doses of the tincture.

Antidotes for Cannabis poisoning are the stomach-pump or emetics followed by stimulating draughts of brandy and water or strong coffee, vegetable acids, such as lemon juice or vinegar.

Dr. Robert Hooper in his "Lexicon Medicum" (page 315), published in 1848, says: "Cannabis Indica is a variety of hemp much used in the East as an excitant. The Hindoos call it *Bangue*, the Arabs *Hasheesh*, the Turks *Malach*.

"The leaves are chewed or smoked like those of tobacco and an intoxicating liquor is prepared from them. This plant is also used by the Hottentots who call it *Dacha*."

The following article by Mr. David Hooper, F.C.S., F.L.S. (Curator of the Botanical Gardens at Calcutta) read at the last meeting of the British Pharmaceutical Conference at Aberdeen, throws a certain amount of light on to the commercial side of the question. At the close of the discussion Mr. D. B. Dott, an eminent Scottish Pharmacist, remarked that Professor Stockman had refused to investigate the drug, as it was useless. Mr. Edmund White, Ph.C., considered that the deterioration of the drug was due to enzymes, and suggested careful storage to preclude enzymic activity.

## A PHARMACEUTICAL STUDY

# CHARAS OF INDIAN HEMP

BY DAVID HOOPER, F.C.S., F.L.S.

Although "charas" has been properly described as "a foul and crude drug, the use of which is properly excluded from civilised medicine," it is imported into British India to the value of £120,000 per annum, a total exceeding the combined value of all the other medicinal imports, so that it is an article which deserves more than passing notice. Indian hemp (Cannabis Sativa), when grown in the East, secretes an intoxicating resinous matter on the upper leaves and flowering spikes, the exudation being marked in plants growing throughout the Western Himalayas and Turkestan, where charas is prepared as a commercial article. Formerly it was cultivated in fields in Turkestan, but now it is grown as a border around other crops (such as maize), the seeds of both being sown at the same time. A sticky exudation (white when damp and greyish when dry) is found on the upper parts of the plant before the flowers show, and in April and May, when the plants attain a height of 4 or 5 ft. and the seeds ripen, the Cannabis is gathered, after reaping the crops, and stored in a cool, dry place. When dry the powdery resinous substance can be detached by even slight shaking, the dust being collected on a cloth. In some districts the plants are cut close to the roots, suspended head downwards, and the dust or *gard* shaken from them and collected on sheets placed on the floor. The leaves, seeds, etc., are picked out, and sand, etc., separated by passing through a fine sieve, the powder being collected and stored in cloth or skin bags, when it is ready for export. In some villages the charas or

extract is made up into small balls, which are collected by the middleman.

On reaching British territory all charas is weighed before the nearest magistrate, by whom it is sealed, a certificate of weight signed by the Deputy Commissioner being given to the owner. The trader, before leaving the district, obtains a permit allowing him to take the drug to a special market. The zamindars of Chinese Turkestan are the vendors of the drug, the importers being Yarkhandis or Ladakhis, who dispose of it at Hoshiapur and Amritsar principally, returning with piece-goods, or Amritsar merchants who trade with Ladakh. The drug in this way reaches the chief cities of the Punjab during September and October. Thence it is distributed over the Central and United Provinces as far as Bombay and Calcutta, and is used everywhere for smoking. Charas, though a drug, plays the part of money to a great extent in the trade that is carried on at Ladakh, the price of the drug depending on the state of the market, and any fluctuations causing a corresponding increase or decrease in the value of the goods for which it is bartered. The exchange price of charas thus gives rise to much gambling. A pony-load (two pais or three maunds) sells for Rs. 40 or Rs. 50, the cost of transport to Hoshiapur (the chief Punjab depot) is Rs. 100, and there it fetches from Rs. 30 to Rs. 100 per maund. Retail dealers sell small quantities at a price that works out at Rs. 200 to Rs. 500 per maund. Five years ago the Kashgar growers, encouraged by the high prices, sowed a large crop and reaped a bumper harvest, only to find the market already overstocked and prices on the Leh Exchange fallen from Rs. 60 to Rs. 30 per maund. The following are

the imports of charas from Ladakh and Kashmir between 1904 and 1907:

| | 1904-5 | | 1905-6 | | 1906-7 |
|---|---|---|---|---|---|
| Cwt. . . | 2818 | ... | 2446 | ... | 2883 |
| Value . . | Rs. 12,13,860 | ... | Rs. 18,39,960 | ... | Rs. 22,90,560 |

Small quantities of charas are made, chiefly for local consumption, in the Himalayan districts of Nepal, Kumaon, and Garhwal, and in Baluchistan. Samples of Baluchistan charas made in the Sarawan division of the Kalat State have been sent to the Indian Museum by Mr. Hughes-Buller.

The following is the mode of preparation:

"The female 'bhang' plants are reaped when they are waist high and charged with seed. The leaves and seeds are separated and half dried. They are then spread on a carpet made of goats' hair, another carpet is spread over them and slightly rubbed. The dust containing the narcotic principle falls off, and the leaves, etc., are removed to another carpet and again rubbed. The first dust is the best quality, and is known as *nup;* the dust from the second shaking is called *tahgalim*, and is of inferior quality. A third shaking gives *gania*, of still lower quality. Each kind of dust is made into small balls called *gabza*, and kept in cloth bags. The first quality is recognised by the ease with which it melts."

The local rates per tola are: for first quality 2a. 5p., second quality 1a. 7p., and third quality 11p. Small quantities of charas find their way from Thibet into British and Native Garhwal, and a little is prepared in Simla and Kashmir; while other sources are Nepal and the hill districts of Almora and Garhwal. In preparing Nepal charas, the ganja-plant is squeezed between the palms of the hands, and the sticky

resinous substance scraped off. *Momea*, black wax-like cakes, valued at Rs. 10 per seer, and *Shahjehani*, sticks containing portions of leaf, valued at Rs. 3 per seer, are the two kinds of Nepal charas, a few maunds being exported annually to Lucknow and Cawnpore. No charas is made in the plains of India, except a small quantity in Gwalior, the Bengal ganja yielding no charas in all the handling it undergoes in the process of preparation—thus emphasising the fact that the intoxicating secretion is developed in plants growing where the altitude and climate are suitable, as in the Himalayas and Turkestan.

*Adulterations.*—Aitchison in 1874 stated that no charas of really good quality ever came to Leh, the best charas in the original balls being sent to Bokhara and Kokan. He said the chief adulterant is the mealy covering of the fruits of the wild and cultivated Trebizond date (*Elœagnus hortensis*). The impression in the United Provinces and the Punjab is that the Yarkhand drug is sophisticated, and a preference is given in some quarters to the Nepal and other Himalayan forms, which command a higher price. The Special Assistant in Kashgar declares there is no advantage in increasing the weight, as when dealers in India buy the drug they test it, otherwise they would pay a heavy duty on the adulterant as well as on the charas itself; so no exporter at present would spoil his charas by adding extraneous substances.

Mr. Hooper added descriptions of samples, namely: Kashgar charas, Yarkhand charas, Baluchistan charas, Gwalior charas, Kumaon charas, Garhwal charas, Nepal charas and Momea charas, from Simla.

*Chemical Examination.*—The table of analyses appended is taken from the author's report to the Indian Hemp Drug

Commission of 1893–4, but a few recent analyses have been added:

| Description of Charas | Extract, Alcoholic | Vegetable Matter | Ash, Soluble | Sand | Volatile Matter |
|---|---|---|---|---|---|
| Yarkhand . . . . | 40.0 | 18.2 | 23.9 | 11.4 | 6.5 |
| Amballa "Mashak" . . | 42.7 | 12.9 | 12.4 | 28.2 | 5.8 |
| Amritsar "Bhara" . . | 38.1 | 14.9 | 10.8 | 29.8 | 6.4 |
| „ "Mashak" . . | 46.5 | 12.6 | 10.0 | 27.3 | 3.6 |
| Delhi Dust, 12a. . . . | 42.4 | 17.9 | 9.8 | 25.9 | 4.0 |
| „ 1r. 1a. . . | 42.6 | 18.8 | 11.1 | 23.2 | 4.3 |
| „ "Mashak" 1r. 9a. . | 41.1 | 11.3 | 10.7 | 29.5 | 7.4 |
| Bombay . . . . | 36.1 | 20.2 | 11.8 | 27.3 | 4.6 |
| Gwalior . . . . | 43.3 | 27.7 | 8.2 | 17.7 | 3.1 |
| Kumaon (wild) . . . | 22.4 | 52.0 | 9.2 | 7.4 | 9.1 |
| „ (cult.) . . . | 34.2 | 46.3 | 9.0 | 3.0 | 7.5 |
| Garhwal . . . . | 41.9 | 37.0 | 7.9 | 5.5 | 7.7 |
| Almora . . . . | 36.9 | 40.5 | 10.5 | 4.6 | 7.5 |
| Nepal . . . . . | 44.6 | 35.1 | 8.2 | 6.5 | 5.6 |
| „ "Shahjehani" . . | 44.4 | 37.7 | 9.6 | 4.1 | 4.2 |
| Simla "Momea" . . | 37.0 | 32.0 | 12.3 | 9.3 | 9.4 |
| Baluchistan (1) 1903 . . | 22.4 | 19.9 | 14.8 | 38.6 | 4.3 |
| „ (2) „ . . | 22.0 | 35.2 | 20.8 | 15.1 | 6.9 |
| „ (3) 1905 . . | 24.2 | 16.0 | 13.3 | 39.3 | 7.2 |
| „ (4) „ . . | 26.0 | 24.1 | 9.6 | 31.0 | 9.3 |
| „ (5) „ . . | 24.9 | 27.3 | 11.5 | 25.8 | 10.5 |
| Kashgar (1) . . . . | 40.2 | 21.1 | 9.2 | 16.8 | 12.7 |
| „ (2) . . . . | 40.9 | 16.3 | 9.9 | 20.5 | 12.4 |
| „ (3) . . . . | 48.1 | 15.6 | 8.2 | 16.1 | 12.0 |

According to Fluckiger and Hanbury, charas yields one-fourth to one-third of its weight of amorphous resin, and it has been stated that good samples yield 78 per cent. of resin. It will be seen above that the average yield in the North Indian samples is 40 per cent., the highest being from Kashgar and the lowest from Baluchistan and from Kumaon wild plants, the last-named corresponding to a good sample of ganja.

*Physiological Values.*—Captain J. F. Evans, I.M.S., Chemical Examiner to the Government of Bengal, also gave results of his physiological tests in the Indian Hemp Drug Commission's Proceedings for 1893–4. His experiments were made with alcoholic extracts, and only one sample—Amritsar best charas—approached in definite physiological effects the extract, taken as a standard, prepared from Bengal ganja. The following are the values compared with that of Amritsar mashak, designated as 32:

| | | | |
|---|---|---|---|
| Amritsar Mashak . | 32 | Bombay . . . | 4 |
| Delhi Mashak . . | 24 | Amballa Mashak . . | 2 |
| Amballa Mashak . . | 23 | Delhi dust . . . | 2 |
| Garhwal . . . | 21 | Kumaon wild . . | 1 |
| Delhi dust (2nd) . . | 20 | Kumaon cultivated . | 1 |
| Amritsar Bhara . . | 19 | Gwalior . . . . | 1 |

so that the best Amritsar charas is thirty-two times as potent as the Gwalior product, the latter from plants grown in the plains, while the amount of alcoholic extract bears no relation to the physiological activity of the drug.

Professor Greenish in his well-known work on *Materia Medica* says that Cannabis Indica is an annual dicœcious herb indigenous to Central and Western Asia, but largely cultivated in temperate countries for its strong fibres (hemp) and its oily seed (hemp-seed) and in tropical countries also for the resinous secretions which it there produces. The secretion possesses very valuable and powerful medicinal properties; but it is not produced in the plant when grown in temperate climates; on the other hand the fibre of the plant under the latter condition is much stronger than that of the tropical plant.

The hemp plant grown in India differs, however, in certain

particulars from that grown in Europe; and the plant was formerly considered a distinct species and named Cannabis Indica, but this opinion is now abandoned.

The cultivation of hemp for its seed and fibre dates from very remote periods. It was used as an intoxicant by the Persians and Arabians in the eleventh and twelfth centuries and probably much earlier, but was not introduced into European medicine until the year 1838. For medicinal use it is grown in the districts of Bogra and Rajshaki to the North of Calcutta and westward, thence through Central India to Gujerat. Very good qualities of the drug are purchased in Madras, but the European market is chiefly supplied with inferior grades from Ghalapur.

The pistillate plants by which alone the resin is secreted in any quantity are pruned to produce flowering branches, the tops of these flowering branches are collected, allowed to wilt, and then pressed by treading them under the feet into more or less compact masses. This forms the drug known as "ganjah," or (on the London market) Guaza.

The larger leaves are collected separately; when dried they are known as "bhang."

During the manipulations to which the plant is subjected in preparing the drug, a certain quantity of the resin is separated; it is collected and forms the drug known as "charas" (Churrus). Charas is also prepared by rubbing ganjah between the hands or by men in leather garments brushing against the growing plants, in any case separating part of the active adhesive resin; hence the official description limits the drug to that from which the resin has not been removed.

All these forms of the drug are largely used in India for producing an agreeable form of intoxication; ganjah and charas are smoked, while bhang is used to prepare a drink or sweetmeat.

The drug has a powerful odour, but is almost devoid of taste.

Numerous attempts have been made to isolate the active constituent of Indian hemp; it is not possible here to do more than allude to the chief later ones.

In 1881 Siebold and Bradbury isolated a thick yellowish oily liquid which they termed *Cannabinine* and their results were confirmed in 1884 by Warden and Waddell.

In 1894 Robert separated a dark red syrupy mass possessing intoxicating properties and in 1896 Wood, Spivey, and Easterfield obtained from charas under reduced pressure certain inactive terpenes and a viscous resin *Cannabinol* which when warmed melts to an oily liquid. Cannabinol when taken internally induces delirium and sleep, and, as far as at present known, is the intoxicating constituent of Indian hemp.

In addition to this principle Matthew Hay in 1883 obtained colourless crystals of an alkaloid *tetano-cannabine* which in physiological action resembled strychnine.

Cannabis Indica was formerly used as a hypnotic and anodyne but is uncertain in its action.

It is administered in mania and hysteria as an anodyne and antispasmodic.

Mr. E. M. Holmes, F.L.S., Curator of the Pharmaceutical Society's Museum, writing on the subject of Cannabis Indica says "The Dervishes make a preparation by macerating the resinous type in almond oil and give a small quantity of it in soup to produce prolonged sleep."

## A PHARMACEUTICAL STUDY

A strong dose of Cannabis produces curious hallucinations abolishing temporarily the ideas of time and distance; but the ordinary drug as imported is never the current crop, which the Hindoos keep for their own use. The active principle Cannabinol (as far as is known) rapidily oxidises and loses its properties so that if a really active preparation is required, it is best to get it made in India, using absolute alcohol and the fresh tops, or recently made charas, which, being a solid mass, does not readily oxidise.

Before closing it might be well to notice in detail the final investigations made by Messrs. Wood, Spivey, and Easterfield.

The following is re-printed from the "Proceedings of the Chemical Society" for 1897–8, and is to be found on page 66.

## CANNABINOL

"The Authors have continued their examination of Cannabinol, the toxic resinous constituent of Indian Hemp (Trans. 1896, *69*, 539).

"The substance boils with slight decomposition at about 400° its absorption spectrum shows no characteristic bands, its vapour-density at the temperature of boiling Sulphur corresponds with the formula $C_{18}H_{24}O_2$ already assigned to the compound.

"An account is given of the reaction of Cannabinol with Acetic Anhydride, benzoyl Chloride and phosphoric Anhydride; the results indicate that one hydroxyl group is present. In the case of Acetic Anhydride or Acetyl chloride, however, a crystalline compound melting at 75° is one of the products of the

reaction. The Authors assign the formula $C_{15}H_{18}O_2$ to this compound. The same compound has recently been described by Dunstan and Henry (Proc. 1898, 14, 44, Feb. 17), who ascribe the formula $C_{18}H_{22}OAc$ to it, fuming hydriodic Acid gives no methyl or ethyl iodide when boiled with Cannabinol. Reduction with hydriodic Acid in sealed tubes produces a hydro-carbon, $C_{10}H_{20}$.

"By long boiling with or without dehydrating agents a hydro-carbon $C_{10}H_{16}$ is formed.

"Oxidation with aqueous chromic acid, alkaline or acid permanganate or dilute nitric acid is accompanied by the production of a caproic acid, lower fatty acids being probably produced at the same time. The action of fuming nitric acid upon cannabinol dissolved in cold glacial acetic acid removes one carbon atom as carbonic anhydride, and produces a red amorphous substance which gives numbers on analysis agreeing with the formula $C_{17}H_{20}N_2O_6$.

"This substance when boiled with nitric acid yields a light-red substance $C_{17}H_{20}N_2O_8$ which upon further oxidation yields among other substances a yellow acid crystalline compound $C_{13}H_{15}N_2O_5$, which forms sparingly soluble crystalline sodium, ammonium and silver salts and is probably a dinitrophenol, and a compound $C_{11}H_{11}NO_4$, the properties of which agree closely with those of the oxycannabin of Bolas and Francis (*Chemical News* 1871, 24, 77).

"This compound has the properties of a nitro-lactone, as has already been shown by Dunstan and Henry.

"Corresponding crystalline potassium and silver Salts have been prepared and analysed. The name Cannabinic Acid is proposed for the unnitrated parent oxy-acid.

"Amido-Cannabinolactone, $C_{11}H_{11}O_2NH_2$ is obtained in colourless crystals melting at 119° when the nitro-lactone is reduced either by hydriodic acid, or by tin and hydrochloric acid.

"The base is readily re-crystallised from hot water, its salts cannot be re-crystallised from water without decomposition; the hydriodide and the platinochloride have been analysed."

In a later paper read before the Chemical Society Messrs. Wood, Spivey, and Easterfield (Proc. Chem. Soc. 1897–8, page 184) say:

"The oily lactone prepared from nitrocannabinolactone (oxycannabin) is shown to be a metatolybutyrlactone, oxycannabin being the corresponding nitroderivative.

"By the oxidation of Cannabinolactone a lactonic acid is produced which on fusion with potash yields isophthalic acid. Nitrocannabinolactonic acid is obtained by oxidising oxycannabin either by nitric acid in sealed tubes or by potassium permanganate. The volatile fatty acids produced on oxidising Cannabinol by nitric acid are shown to be normal butyric (Dunstan and Henry, Proc. Chem. Soc. 1898, *14*, 44), normal valeric and normal caproic acids, Valeric acid being formed in largest amount."

Through the courtesy of Messrs. Parke, Davis and Co., manufacturing chemists of London and Detroit, Michigan, U.S.A., we are enabled to reproduce a clear pharmacological study of the drug by E. M. Houghton, Ph.C., M.D.; and H. C. Hamilton, M.S. (Excerpt from an article in the *American Journal of Pharmacy* for January 1908.)

From several samples of Cannabis Americana fluid

extracts and solid extracts were prepared according to the U.S.P., and were tested upon animals for physiological activity.

The method of assay, which has previously been called to the attention of this Society, is that which one of us (Houghton) devised and has employed for the past twelve years. This method consists essentially in the careful observation of the physiological effects produced upon dogs from the internal administration of the preparation of the drug under test. It is necessary in selecting the test animals to pick out those that are easily susceptible to the action of the Cannabis, since dogs as well as human beings vary considerably in their reaction to the drug. Also, preliminary tests should be made upon the animals before they are finally selected for test purposes, in order that we may know exactly how they behave under given conditions. After the animals have been finally selected and found to respond to the standard test dose, 0.01 Gm. per kilo, they are set aside for this particular work, care being taken to have them well fed, well housed, and in every way kept under the best sanitary conditions. Usually we have found it desirable to keep two or more of the approved animals on hand at all times, so there may not be delay in testing samples as they come in.

In applying the test, the standard dose (in form of solid extract for convenience) is administered internally in a small capsule. The dog's tongue is drawn forward between the teeth with the left hand and the capsule placed on the back part of the tongue with the right hand. The tongue is then quickly released and the capsule is swallowed with ease. In order that the drug may be rapidly absorbed, food should be

withheld for twenty-four hours before the test and an efficient cathartic given if needed.

Within a comparatively short time the dog begins to show the characteristic action of the drug. There are three typical effects to be noticed from active extracts on susceptible animals: first a stage of excitability, then a stage of inco-ordination, followed by a period of drowsiness. The first of these is so dependent on the characteristics of the dog used that it is of little value for judging the activity of the drug, while with only a few exceptions the second, or the stage of inco-ordination, invariably follows in one or two hours; the dog loses control of its legs and of the muscles supporting its head, so that when nothing occurs to attract its attention its head will droop, its body sway, and, when severely affected, the animal will stagger and fall, the intoxication being peculiarly suggestive and striking.

Experience is necessary on the part of the observer to determine just when the physiological effects of the drug begin to manifest themselves, since there is always, as in the case of many chemical tests, a personal factor to be guarded against. When an active extract is given to a susceptible animal, in the smallest dose that will produce any perceptible effect, one must watch closely for the slightest trace of inco-ordination, lack of attention, or drowsiness. It is particularly necessary for the animals to be confined in a room where nothing will excite them, since when their attention is drawn to anything of interest the typical effect of the drug may disappear.

The influence of the test dose of the unknown drug is carefully compared with that of the same dose of the standard

preparation administered to another test dog at the same time and under the same conditions.

Finally, when the animals become drowsy, the observations are recorded and the animals are returned to their quarters.

The second day following, the observations upon the two dogs are reversed, *i.e.*, the animal receiving the test dose of the unknown receives a test dose of the known, and *vice versâ*, and a second observation is made. If one desires to make a very accurate quantitative determination, it is advisable to use, not two dogs, but four or five, and to study the effects of the test dose of the unknown specimen in comparison with the test dose of the known, making several observations on alternate days. If the unknown is below standard activity, the amount should be increased until the effect produced is the same as for the test dose of the standard. If the unknown is above strength, the test dose is diminished accordingly. From the dose of the unknown selected as producing the same action as the test dose of the standard, the amount of dilution or concentration necessary is determined. The degree of accuracy with which the test is carried out will depend largely upon the experience of the observer and the care he exercises.

Another point to be noted in the use of dogs for standardising Cannabis is that, although they never appear to lose their susceptibility, the same dogs cannot be used indefinitely for accurate testing. After a time they become so accustomed to the effects of the drug they refuse to stand on their feet, and so do not show the typical inco-ordination which is its most characteristic and constant action.

Previous to the adoption of the physiological test over twelve years ago, we were often annoyed by complaints of

physicians that certain lots of drugs were inert; in fact some hospitals, before accepting their supplies of hemp preparations, asked for samples in order to make rough tests upon their patients before ordering. Since the adoption of the test we have not had a well-authenticated report of inactivity, although many tons of the various preparations of Cannabis Indica have been tested and supplied for medicinal purposes.

At the beginning of our observations careful search of the literature on the subject was made to determine the toxicity of the hemp. Not a single case of fatal poisoning have we been able to find reported, although often alarming symptoms may occur. A dog weighing 25 pounds received an injection of two ounces of an active U. S. P. fluid extract in the jugular vein with the expectation that it would certainly be sufficient to produce death. To our surprise the animal, after being unconscious for about a day and a half, recovered completely. This dog received, not alone the active constituents of the drug, but also the amount of alcohol contained in the fluid extract. Another dog received about 7 grammes of Solid Extract Cannabis with the same result. We have never been able to give an animal a sufficient quantity of a U. S. P. or other preparation of the Cannabis (Indica Americana) to produce death.

There is some variation in the amount of extractive obtained, as would be expected from the varying amount of stems, seeds, etc., in the different samples. Likewise there is a certain amount of variation in the physiological action, but in every case the administration of 0.01 gramme of the extract per kilo body weight, has elicited the characteristic symptoms in properly selected animals.

The repeated tests we have made convince us that Cannabis Americana properly grown and cured is fully as active as the best Indian drug.

Furthermore, we have placed our quantities of fluid extract and solid extract of Cannabis Americana in the hands of experienced clinicians, and from eight of these men, who are all large users of the drug, we have received reports which state that they are unable to determine any therapeutic difference between the Cannabis Americana and the Cannabis Indica.

## CONCLUSIONS

1. The method, outlined in the paper, for determining the physiological activity of Cannabis Sativa by internal administration to especially selected dogs, has been found reliable when the standard dose of extract 0.01 gramme per kilo body weight, is tested on animals, the effects being noted by an experienced observer in comparison with the effects of the same quantity of a standard preparation.

2. Cannabis Sativa, when grown in various localities of the United States and Mexico, is found to be fully as active as the best imported Indian-grown Cannabis Sativa, as shown by laboratory and clinical tests.

Much has been written relative to the comparative activity of Cannabis Sativa grown in different climates (Cannabis Indica, Mexicana and Americana). It has been generally assumed that the American-grown drug was practically worthless therapeutically, and that Cannabis Sativa grown in India must be used if one would obtain physiologically active preparations.

Furthermore, it has been claimed that the best Indian drug is that grown especially for medicinal purposes, the part used consisting of the flowering tops of the unfertilised female plants, care being taken during the growing of the drug to weed out the male plants. According to our experience, this is an erroneous notion, as we have repeatedly found that the Indian drug which contains large quantities of seed is fully as active as the drug which consists of the flowering tops only, provided the seed be removed before percolation.

Several years ago we began a systematic investigation of American-grown Cannabis Sativa. Samples from a number of localities were obtained and carefully investigated. From these samples fluid and solid extracts were prepared according to the Pharmacopœial method, and carefully tested upon animals for physiological activity, and eventually they were standardised by physiological methods. Repeated tests have convinced us that Cannabis Americana properly grown and cured is fully as active as the best Indian drug, while on the other hand we have frequently found Indian Cannabis to be practically inert.

Before marketing preparations of Cannabis Americana, however, we placed specimens of the fluid and solid extracts in the hands of experienced clinicians for practical test; and from these men, all of whom had used large quantities of Cannabis Indica in practice, we have received reports which affirm that they have been unable to determine any therapeutic difference between Cannabis Americana and Cannabis Indica. We are, therefore, of the opinion that Cannabis Americana, will be found equally as efficient as, and perhaps more uniformly reliable than Cannabis Indica obtained from abroad,

since it is evident that with a source of supply at our very doors proper precautions can be taken to obtain crude drug of the best quality.

The proper botanical name of the drug under consideration is Cannabis Sativa. The Indian plant was formerly supposed to be a distinct species *per se*, but botanists now consider the two plants to be identical. The old name of Cannabis Indica, however, has been retained in medicine. Cannabis Indica simply means Cannabis Sativa grown in the Indies, and Cannabis Americana means Cannabis Sativa grown in America. Its introduction into Western medicine dates from the beginning of the last century, but it has been used as an intoxicant in Asiatic countries from time immemorial, and under the name of "hashish," "bhang," "ganja," or "charas," is habitually consumed by upwards of two hundred millions of human beings.

The physiological action of Cannabis Americana is precisely the same as that of Cannabis Indica. The effects of this drug are said to be due chiefly to its action upon the central nervous system. It first produces a state of excitement similar to that of the initial stage of acute alcoholism. This excitement of the motor areas and other lower centres in the brain, according to W. E. Dixon, of the University of Cambridge, "is not the result of direct stimulation of these, but is due to depression of the highest and controlling centres. At all events there is a depression of the highest centres, and this is shown by diminished efficiency in the performance of mental work, by inability to concentrate attention, and by feeble judgment." In lower animals the effects of Cannabis Indica resemble those in man, and present the

same variations. A stage of exaltation with increased movements is sometimes present, and is followed by depression, lassitude and sleep. Reflex excitability is first increased and then diminished. Cannabis Indica differs from opium in producing no disturbance of digestion and no constipation. The heart is generally accelerated in man when the drug is smoked. Its intravenous injection into animals slows the pulse, partly through inhibitory stimulation and partly through direct action upon the heart muscle. The pupil is generally somewhat dilated. Death from acute poisoning is extremely rare, and recovery has occurred after enormous doses. The continued abuse of hashish by natives of the East sometimes leads to mania and dementia, but does not cause the same disturbance of nutrition that opium does; and the habitual use of small quantities, which is almost universal in some Eastern countries, does not appear to be detrimental to health.

Cannabis Americana is employed for the same medicinal purposes as Cannabis Indica, which is frequently used as a hypnotic in cases of sleeplessness, in nervous exhaustion, and as a sedative in patients suffering from pain. Its greatest use has perhaps been in the treatment of various nervous and mental diseases, although it is found as an ingredient in many cough mixtures. In general, Cannabis Americana can be used when a mild hypnotic or sedative is indicated, as it is said not to disturb digestion, and it produces no subsequent nausea and depression. It is of use in cases of migraine, particularly when opium is contra-indicated. It is recommended in paralysis agitans to quiet the tremors, in spasm of the bladder, and in sexual impotence not the result of organic disease, especially in combinations with nux vomica and ergot.

The ordinary dosage is:

Extractum Cannabis Americanæ, 0.01 gramme (1.5 grain).

Fluidextractum Cannabis Americanæ, 0.05 cc. (1 minim).

The dosage of Cannabis Americana is the same as that of Cannabis Indica, as from our experiments we find there is no therapeutic difference in the physiological action of the two drugs.

Cannabis Sativa, when grown in the United States (Cannabis Americana) under careful precautions, is found to be fully as active as the best imported Indian-grown Cannabis Sativa, as shown by the laboratory and clinical tests. The advantages of using carefully prepared solid and fluid extracts of the home-grown drug are apparent when it is considered that every step of the process, from the planting of the drug to the final marketing of the finished product, is under the supervision of experts. The imported drug varies extremely in activity and much of it is practically inert or flagrantly adulterated.

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