

CANNABIS. U. S. (Br.)

**CANNABIS Cannab. [Indian Hemp Cannabis Indica U. S. VIII, Guaza, Ganjah]**

"The dried flowering tops of the pistillate plants of *Cannabis sativa* Linne, or of the variety *indica* Lamarck (Fam. *Moraceae*), freed from the thicker stems and large foliage leaves and without the presence or admixture of more than 10 per cent. of fruits or other foreign matter. Cannabis, made into a fluidextract in which *one hundred mils* represent *one hundred grammes* of the drug, when assayed biologically, produces incoordination when administered to dogs in a dose of not more than 0.03 mil of fluidextract per kilogramme of body weight." U. S. "Indian Hemp consists of the dried flowering or fruiting tops of the pistillate plant of *Cannabis sativa*, Linn., grown in India; from which the resin has not been removed." Br.

**Cannabis Indicae**, Br.; Hemp, Indian Hemp; Herba Cannabis ludicae; Chanvre, Fr. Cod.; Chanvre de l'Inde, Fr.; Indischer Hanf, G.; Cañamo, Sp.

For many years the official cannabis was restricted to the drug which was used for centuries in India. The reason for this was that the Indian cannabis was more uniformly active. Recently the Indian Government has placed a high tax on every pound of the drug grown. The result has been that other markets have been sought and the hemp plant has been grown in other parts of Asia, Africa and America. While of course, much of this material is not equal to that grown in India yet the fact that it can be grown, as shown by experiments in the United States (see Hamilton, *J. A. Ph. A.*, 1913, ii; 1915, iv, 389) of a very high quality has caused the framers of the U. S. Pharmacopoeia to permit the use of a cannabis, no matter where it may be grown, provided it comes up to the biological standard as given in the definition. Physiologically active *cannabis* is obtained at the present time not only from India, but Africa, Turkey, Turkestan, Asia Minor, Italy, Spain and the United States.

The *Cannabis sativa*, or hemp plant, is an annual, from four to eight feet or more in height, with an erect, branching, angular stem. The leaves are alternate or opposite, and digitate, with five to seven linear-lanceolate, coarsely serrated segments. The stipules are subulate. The flowers are axillary; the staminate in long, branched, drooping racemes; the pistillate in erect, simple spikes. The stamens are five, with long pendulous anthers; the pistils two, with long, filiform, glandular stigmas. The fruit is ovate and one-

seeded. The whole plant is covered with a fine pubescence, scarcely visible to the naked eye, and somewhat viscid to the touch. The hemp plant of India has been considered by some as a distinct species, and named *Cannabis indica*; but the most observant botanists, upon comparing it without cultivated plant, have been unable to discover any specific difference. It is now, therefore, regarded merely as a variety, and is distinguished by the epithet *indica*. Pereira states that in the female plant the flowers are somewhat more crowded than in the common hemp, but that the male plants in the two varieties are in all respects the same.

*C. sativa* is a native of the Caucasus, Persia, and the hilly regions in Northern India. It is cultivated in many parts of Europe and Asia, and largely in our Western States. It is from the Indian variety exclusively that the medicine was formerly obtained, the heat of the climate in Hindostan apparently favoring the development of its active principle. H. C. Wood, many years ago, obtained a parcel of the male plant of *C. americana* (*C. sativa*) from Kentucky, made an alcoholic extract of the leaves and tops, and, upon trying it on the system, found it effective in less than a grain, and, having inadvertently taken too large a dose, experienced effects which left no doubt of the powers of the medicine, and of the identity of its influence with that of the Indian plant. (*Proc. Am. Philos. Soc.*, vol. xi, p. 226.) The results obtained by H. C. Wood have been confirmed by a number of observers.

The fruits or " so-called " seeds, though not now official, have been used in medicine. They are from three to five millimeters long and about two millimeters broad, roundish-ovate, somewhat compressed, of a shining ash-gray color, and of a disagreeable, oily, sweetish taste. For a comprehensive monograph on the morphology of cannabis fruits, as well as their history and chemical composition, see Tsehirsch, "*Handbuch der Pharmakognosie*" p. 555. They yield by expression about 20 per cent. of a fixed oil, "which has the drying property, and is used in the arts. They contain also uncrystallizable sugar and albumen, and when rubbed with water form an emulsion, which may be used advantageously in inflammations of the mucous membrane, though without narcotic properties. The seeds are much used as food for birds, as they are fond of them. They are generally believed to be in no degree poisonous; but Michaud relates the case of a child in whom serious symptoms of narcotic poisoning occurred after taking a certain quantity of them. It is probable that some of the fruit eaten by the child was unripe, as in this state it would be more likely to partake of the peculiar qualities of the plant. (*Ann. Ther.*, 1860.)

In Hindostan, Persia, and other parts of the East, hemp has long been habitually employed as an intoxicating agent. The parts are the tops of the plant, and a resinous product obtained from it. *Bhang* is the selected, dried and powdered leaves. *Ganjah* or *gunjah* is the tops of cultivated female plants, cut directly after flowering, and formed into round or flat bundles from two to four feet long by three inches in diameter. It is stated that in the province of Bengal great care is taken to eradicate the male plants from the fields before fertilization of the female, and that thereby the yield and quality of the resin is greatly increased. In Bombay this matter is commonly neglected, so that Bengal ganjah is much superior to Bombay ganjah. It is recognized in India that ganjah rapidly deteriorates on keeping, that which is one year old being not more than one-quarter as potent as the fresh drug, while two-year-old ganjah is practically inert and is required by the Indian government to be burned in the presence of excise officers. It is probable, however, that much old ganjah finds its way into the markets of the world. All importations of ganjah or hemp from India should be made directly after the harvesting of the new crop in April or May, and the extract should be prepared at once and kept in hermetically sealed jars. There is on the surface of the plant a resinous exudation to which it owes its stickiness. According to Hooper (P. J., 1909, 1xxxix, 347) only small amounts of charas are raised in India, that which is being consumed there being mostly imported. The method of collection in Baluchistan is to gently rub the dried plant between carpets. The dust which comes off contains the active principle and is known as "rup." The second shaking produces an inferior variety, known as "tah-galim/" and the third shaking is known as "ganja." In Nepal the plant is squeezed between the palms of the hands, and the resin scraped off from the hands. These balls, and also masses formed out of resin mechanically separated from the hemp plant are called *charas* or *churrus*. This is the *hashish* or *hasheesh* of the Arabs.

*Hashish* is also produced in considerable quantities in Persia by rolling and rubbing the flowers, stalks and leaves of hemp on rough woolen carpets and subsequently scraping off with a knife and making into balls or sticks the adherent resinous substance. The carpets are afterwards washed with water and the extract obtained by evaporation sold at a low price. The dose for smoking of the best hashish is said to be one-fourth to one grain (0.016-0.065 Gm.). The fanatics are affirmed to be generally hashish devotees.

The dealing in hashish in India is said to be a Government monopoly, and a very heavy license is required for the right to even purchase it in quantity. The importation of it into Egypt is so strongly interdicted that the mere

possession of it is a penal offense; H. C. Wood found it, however, readily procurable. It is said to be brought into the country in pigs' bladders, in the Indo-European steamers, and thrown out at night during the passage into the Suez canal, to be picked up by the boats of confederates.

Notwithstanding the Governmental interdiction, it is largely used by smoking in Egypt, as an intoxicant. The statement of W. E. Dixon (*B. M. J.*, Nov., 1899) that the inhalations of hemp smoke produces great exhilaration and causes muscular fatigue to disappear for the time being is undoubtedly correct, but his further belief that the habit is not apt to grow upon the hemp votary is more doubtful.

*Momea* or *mimea* is a hemp preparation said to be made in Thibet with human fat. From ganjah the Messrs. Smith, of Edinburgh, obtained a purer resin by the following process: Bruised ganjah is digested, first in successive portions of warm water, until the expressed liquid comes away colorless; and afterwards for two days, with a moderate heat, in a solution of sodium carbonate, containing one part of the salt for two of the dried herb. It is then expressed, washed, dried, and exhausted by percolation with alcohol. The tincture, after being agitated with milk of lime containing one part of the earth for twelve of the ganjah used, is filtered; the lime is precipitated by sulphuric acid; the filtered liquor is agitated with animal charcoal, and again filtered; most of the alcohol is distilled off, and to the residue twice its weight of water is added; the liquor is then allowed to evaporate gradually; and, finally, the resin is washed with fresh water until it ceases to impart a sour or bitter taste to the liquid, and is then dried in thin layers. Thus obtained, it retains the odor and taste of ganjah, which yields from 6 to 7 per cent. of it.

**Properties.**—**Fresh** hemp has a peculiar narcotic odor, which is said to be capable of producing vertigo, headache, and a species of intoxication. It is much less in the dried tops, which have a feeble bitterish taste. According to Royle, *churrus* is, when pure, of a blackish-gray, blackish-green, or dirty olive color, of a fragrant and narcotic odor, and a slightly warm, bitterish, and acrid taste. Cannabis is officially described as "in dark green or greenish-brown and more or less agglutinated fragments, consisting of the short stems with their leaf-like bracts and pistillate flowers, some of the latter being replaced with more or less developed fruits; stems cylindrical, of varying length, not more than 3 mm. in diameter, longitudinally furrowed, light green to light brown, strigose-pubescent; leaves digitately compound; leaflets, when soaked in water and spread out, linear-lanceolate, nearly sessile, margin deeply serrate, bracts ovate, pubescent, each enclosing one or

two pistillate flowers, or more or less developed fruits; calyx dark green, pubescent and somewhat folded around the ovary or fruit; styles two, filiform and pubescent; ovary with a single campylotropous ovule; fruit light green to light brown, broadly ellipsoidal, about 3.5 mm. in length, finely wrinkled and slightly reticulated; odor agreeably aromatic; taste characteristic. The powder is dark green, giving a strong effervescence on the addition of dilute hydrochloric acid; numerous sharp pointed fragments of upper portion of non-glandular hairs and fragments of bracts and leaves showing yellowish-brown laticiferous vessels, rosette aggregates of calcium oxalate from 0.005 to 0.025 mm. in diameter; non-glandular hairs unicellular, with a very slender pointed apex and a considerably enlarged base containing, usually in the lumen, some calcium carbonate; glandular hairs of two kinds, one with a short, one-celled stalk and the other with a multicellular, long, tongue-shaped stalk, the glandular portion being globular and consisting of from 8 to 16 cells, fragments of fruits with palisade-like, non-lignified sclerenchymatous cells, walls yellowish-brown, finely porous, the lumina usually containing air; tissues of embryo and endosperm with numerous oil globules and aleurone grains, the latter from 0.005 to 0.01 mm. in diameter and consisting of large crystalloids and globoids. The yield of alcohol extractive is not less than 8 per cent. and the alcoholic solution is of a bright green color. Cannabis yields not more than 15 per cent of ash." *U. S.*

"In compressed, rough, dusky-green masses, consisting of the branched upper part of the stem, bearing leaves and pistillate flowers or fruits, matted together by a resinous secretion. Upper leaves simple, alternate, 1-3 partite; lower leaves opposite and digitate, consisting of five to seven linear-lanceolate leaflets with distantly serrate margins. Fruit one-seeded and supported by an ovate-lanceolate bract. Both leaves and bracts bear external oleo-resin glands and one-celled curved hairs, the bases of which are enlarged and contain cystoliths. Strong, characteristic odor; taste slight. When a mixture of 10 grammes of finely powdered Indian Hemp and 100 millilitres of *alcohol* (90 per cent.) is shaken occasionally during twenty-four hours and then filtered, 20 millilitres of the filtrate, evaporated in a flat-bottomed dish, yield a residue weighing, when dried at 100° C. (212° F.), not less than 0.250 gramme. Ash not more than 15 per cent." *Br.*

For a histological description of the leaf by A. R. L. Dohme, see *Proc. A. Ph. A.*, 1897, 569. The Cannabis of the market may consist of fruiting tops and stems and occasionally the staminate tops are admixed with it.

Hooper (*P. J.*, lxxxii, p. 80) describes a method for the chemical standardization of *cannabis indica* based upon its iodine value. He finds that the alcoholic extract of old samples has a lower iodine value than that from recent specimens, and there is more or less constancy of relation between the age and the iodine value.

*Indian churrus* or hasheesh is a hard resinous mass of a greenish-gray color, containing much gritty earth, and, as it occurs in Egypt, of a feeble, hemp-like odor and taste. Schlesinger found in the leaves a bitter substance, chlorophyll, green resinous extractive, coloring matter, gummy extract, extractive, albumen, lignin, and salts. The plant also contains volatile oil in very small proportion, which probably has narcotic properties. The resin obtained by T. & H. Smith of Edinburgh, in 1846, has been thought to be the active principle, and received the name of *cannabin*. By repeated distillation of the same portion of water from relatively large quantities of hemp renewed at each distillation, M. J. Personne obtained a volatile oil, of a stupefying odor, and an action on the system such as to dispose him to think that it was the active principle of the plant. As the water distilled was strongly alkaline, he supposed that his volatile principle might be a new alkaloid; but the alkaline reaction was found to depend on ammonia; and the liquid obtained proved to be a volatile oil, lighter than water, of a deep amber color, a strong odor of hemp, and composed of two distinct oils, one colorless, with the formula  $C_{18}H_{22}$ , the other a hydride of the first,

$C_{18}H_{22}$ , which was solid, and separates from alcohol in plate-like crystals. For the former Personne proposes the name of *cannabene*. It is affirmed that when this is inhaled, or taken into the stomach, a singular excitement is felt throughout the system, followed by a depression, sometimes amounting to syncope, with hallucinations which are generally disagreeable, but an action on the whole slighter and more fugitive than that of the resin. The various substances of alkaloidal nature that have been described by different investigators as found in Indian hemp are now recognized as due to decomposition products of *choline*, which was identified as present by Jahns. (*P. J.*, 1887, xvii, 1049.) Cannabindon,  $C_8H_{12}O$ , is a dark red syrupy liquid obtained by

Kobert (*Chem. Ztg.*, 1894, 741) from *Cannabis Indica*; it is soluble in alcohol, ether and oils; it is affirmed to be narcotic in doses of from half a grain to two grains (0.032-0.13 Gm.). As a result of a reinvestigation of charras (*churrus*) from Indian hemp, Wood, Spivey, and Easterfield (*J. Chem. S.*, vol. Ixix, 539) have found the following principles: 1, a terpene, boiling between

150° and 180° C. (302° and 356° F.); 2, a sesquiterpene, boiling at 258° to 259° C. (496.4°-498.2° F.); 3, a crystalline paraffin of probable formula  $C_{22}H_{38}$ , melting at 63.5° C. (146.3° F.); and 4, a red oil, boiling at 265° to 270° C. (509°-518° F.) under a pressure of 20 mm., to which they give the name *cannabinol*, and the formula  $C_{18}H_{24}O_2$ . This latter constituent they consider the

only active ingredient. It is probably the same substance as the dark red syrup of Kobert, mentioned above under the name *cannabindon*. The authors found that *cannabinol* readily underwent superficial oxidation, at the same time losing its toxic activity. Famulener and Lyons (*A. Pharm.*, 1904) believe that the only reliable preparation of cannabis is a fluidextract made from the *fresh* drug. I. Roux (*A. Pharm.*, 1887) has experimented upon extracts made by treating purified extract of hemp with petroleum benzin and ether. The ether extract produced insignificant results. The petroleum extract was excitant and convulsant. The alcoholic extract was a feeble narcotic. The resin "cannabin" of which *cannabinol* is the chief constituent, appears to be active. Frankel (*A. E. P. P.*, 1903, p. 266) claims to have isolated the active principle of hashish as a pure and chemically well defined body. It has the formula  $C_{21}H_{30}O_2$ , and is a phenol-aldehyde. It is of a pale

yellow color and of a thick consistency. When heated it becomes quite fluid and distils at 215° C. (419° F.), under a pressure of 0.5 mm. It oxidizes in the air, acquiring a brown tint. It responds to Millon's reaction, and can be acetylated, showing thus its phenol character. Frankel proposes that the name *cannabinol* be given to it and that the term *pseudo-cannabinol* be given to the inactive substance of Wood, Spivey and Easterfield.

Assay.—"Prepare a fluidextract and proceed as directed below." *U. S.*

Attempts have been made to apply physiological tests to the standardization of cannabis indica. Up to the present no means have been suggested for determining the relative potency of different samples of cannabis indica, the physiological test simply demonstrating that the drug possesses a certain indefinite amount of physiological action. This test is carried out upon dogs in the following manner: It is advisable to use the same animal for repeated tests, because the individual susceptibility of the dog varies so greatly, and the experimenter gradually learns the degree of reaction to be expected from a certain dog. A tincture of the specimen to be tested is either evaporated into a soft extract and given in the form of a pill or mixed with an inert absorbing powder and enclosed in a capsule; it must not be given hypodermically. The symptoms caused by cannabis indica in the dog recall

those of alcoholism in the human being. There is at first a slight loss of control in the hind legs so that the animal staggers as he walks, later the ataxia becomes so marked that the dog is unable to stand up without leaning against some object, and about this time begins to show distinct drowsiness, and may eventually pass into a heavy sleep.

The details of assay as directed by the U.S. are as follows: " The assay of Cannabis and its preparations has been made a requirement and is based upon the fact that this drug produces certain symptoms of muscular incoordination. The method consists of ascertaining the dose of the preparation to be tested which will produce these symptoms of incoordination in dogs and then adjusting its strength by comparison with a standard preparation.

"Dogs.—The animals differ considerably in susceptibility to the drug and therefore it is best to make preliminary tests upon several dogs with average-sized doses and select from among them the animals which react easily to the drug. As a rule, fox terriers serve very-well for the purpose, but any dog may prove satisfactory. It is best to provide at least two dogs for each assay, but if many samples are to be examined more dog's will be needed. The dogs should be at least one year old and in normal health and must be kept under the best sanitary conditions. They may be used repeatedly for the purpose but not at shorter intervals than three days. Each series of tests should be conducted by the same person, who should be perfectly familiar with the peculiarities of each animal in order that he may recognize more certainly deviations from the normal. While the tests are being made the animals should be kept in a perfectly quiet room, free from disturbance and separated so that they cannot see each other.

"Preparation of the Drug.—*The* drug may be given most conveniently in the form of the fluidextract which is administered in gelatin capsules, or the extract made into soft pills may be used; but whichever form is chosen the same should be used for both the standard and the preparation that is to be tested.

“Before administration the animal should not be fed for twenty-four hours in order to hasten absorption. The head of the animal being held, its mouth is opened and the capsule or pill is placed upon the back of the tongue. Usually the drug is easily swallowed when given in this way, but this may be facilitated by giving the animal a small amount of water to drink.

"Assay.—An average dose of the known or standard preparation is given to one of the dogs and a like dose of the preparation to be standardized is given

the second dog. After one hour both dogs are observed very carefully for symptoms of muscular incoordination. The incoordination is manifested differently in different animals, but in small doses it shows itself most frequently in slight swaying, when the animal is standing quietly, or in some ataxia when it runs about. The observation should be made frequently during the second hour following the administration of the drug.

"The results obtained from the first test should be confirmed after an interval of not less than three days by repeating the administration, but reversing the order, that is, giving the known strength drug to the dog which received that of unknown strength before and vice versa.

"In subsequent tests which are carried out, the dose of the preparation of unknown strength is modified so as to produce similar symptoms to those produced by the standard. If the preparation to be tested is below the standard in strength, its dose must be increased, or if it is above strength its dose is lessened until equivalent doses of the two are found. Dogs may be used over long periods of time, even for some years, but occasionally they have to be discarded, as in some cases they seem to learn the effects of the drug and so refuse to stand up. A certain degree of tolerance is sometimes gained which necessitates larger doses.

"Standard.—As there is no chemical substance of definite composition which can be adopted as a standard, a Fluidextract of Cannabis or an extract which has been carefully prepared and suitably preserved may be utilized for this purpose. A standard Fluidextract will produce incoordination when administered to dogs in the dose of 0.03 mil for each kilogramme of body weight of dog. When administered in the form of the Extract a dose of 0.004 Gm. for each kilogramme of body weight of dog should produce similar symptoms, and the requirement for a standard tincture is a dose of 0.3 mil for each kilogramme of body weight of dog." *U. S. IX.*

**Uses.**—**Aside** from a slight local irritant effect the action of cannabis seems to be limited almost exclusively to the higher nerve centers. In man this is first manifested by a peculiar delirium which is accompanied with exaltation of the imaginative function and later by a remarkable loss of the sense of time. The delirium is often accompanied with motor weakness and diminished reflexes and generally followed by drowsiness. In the dog the earliest manifestation of the drug's action is a slight degree of restlessness which is soon followed by disturbances of equilibrium and later weakness of the legs and drowsiness.

Cannabis is used in medicine to relieve pain, to encourage sleep, and to

soothe restlessness. Its action upon the nerve centers resembles opium, although much less certain, but it does not have the deleterious effect on the secretions. As a somnifacient it is rarely sufficient by itself, but may at times aid the hypnotic effect of other drugs. For its analgesic action it is used especially in pains of neuralgic origin, such as migraine, but is occasionally of service in other types. As a general nerve sedative it is used in *hysteria*, *mental depression*, *neurasthenia*, and the like. It has also been used in a number of other conditions, such as *tetanus* and *uterine hemorrhage*, but with less evidence of benefit. One of the great hindrances to the wider use of this drug is its extreme variability. Formerly many of the preparations of cannabis were inert before they left the manufacturers' hands, and the present requirements of the U. S. P. that the drug be tested upon dogs to insure its activity is an important step in the right direction. But even granted an active preparation when manufactured, so rapidly does the drug deteriorate that by the time the drug reaches the patient it has lost a large proportion of its activity. The only way of determining the dose of an individual preparation is to give it in ascending quantities until some effect is produced. The fluid extract is perhaps as useful a preparation as any; one may start with two or three minims of this three times a day, increasing one minim every dose until some effect is produced. According to C. R. Marshall (*L. L.*, 1897, i, also *J. A. M. A.*, Oct., 1898) the deterioration of cannabis is due to the oxidation of cannabinal, which he has found to act upon dogs and cats as the crude drug.

*Dose*, of cannabis, one to three grains (0.065-0.2 Gm.).

**Off. Prep.**—**Extractum Cannabis**, *U. S. (Br.)*; **Fluidextractum Cannabis**, *U. S.*; **Tinctura Cannabis** (from Extract), *U. S. (Br.)*; **Collodium Salicylici Composita** (from Fluidextract), *N. F.*; **Mistura Chlorali et Potassii Bromidi Composita** (from Extract), *N. F.*; **Mistura Chloroforma et Morphinae Composita** (from Tincture), *N. F.*