

A sample of German oil of coriander just received from a prominent importer of essential oils is also submitted. This does not comply with the requirements of the United States Pharmacopœia in respect to being entirely soluble in three volumes of 70 per cent. alcohol at a temperature of 77° F. Only about 25 per cent. of the oil will dissolve at this temperature. It does, however dissolve, in this menstruum, when the temperature is raised to 80° F. It is also soluble in all proportions of 80 and 90 per cent. alcohol. Its specific gravity is 0.866 at 77° F., being still within the limits of the U.S.P. of 0.863 to 0.878.

As linalool is a normal constituent of oil of coriander, this substance has been sometimes used as an adulterant of the oil, as well as oil of cedarwood and oil of sweet orange.

Samples of oil of linaloe, composed in the main of linalool, and of pure oil of coriander, to which 25 per cent., respectively of oil of sweet orange, and oil of red juniper wood (the so-called oil of cedarwood of commerce) have been purposely added, are submitted. Both of these adulterations are noted in the text-books.

The distillation of the oil, and the chemical and physical examination of the specimens submitted, were conducted by Mr. Ralph R. Opie.

A PHARMACOLOGICAL STUDY OF CANNABIS AMERICANA (CANNABIS SATIVA).¹

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Much has been said and written by physicians and pharmacists relative to the activity of *Cannabis Sativa* (*Cannabis Indica* and *Americana*). It is generally believed that the American grown drug is practically worthless for therapeutic purposes, and that one must employ the true cannabis from India, in order to obtain physiological activity. The best quality of Indian drug, it is claimed, is that grown especially for medicinal purposes and consists of the flowering tops of the unfertilized female plants, care being taken

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during the growing of the drug to weed out the male plants. This notion, according to our experience, is based largely upon error, as we have found repeatedly that the Indian drug which contains large quantities of seed is fully as active as the drug which does not contain the seed, provided the seed is removed before it is percolated, and the experiments are based upon a fluid extract or other pharmaceutical product obtained from an equal weight of drug minus the seeds. The seeds themselves do not contain the active principle upon which the therapeutic properties of the plant depend, but may make up a very large percentage of the weight of the drug as it appears on the market.

Several years ago we began a systematic investigation of American grown hemp. Samples were obtained from the following localities and studied:

(1) August, 1905, Mr. Gaumnitz, of the Department of Agriculture, of the University of Minnesota, sent us samples of hemp grown on the college grounds.

(2) 1906. Also supplied by Mr. Gaumnitz.

(3) Grown in Mexico, 1903. Sent in for examination.

(4) " " " 1904.

(5) " " " 1906.

(6) " " Kentucky, 1905.

(7) " " " 1906.

(8) " near Detroit, Mich., 1907.

From these several samples of *Cannabis Americana*, were prepared fluid extracts and solid extracts according to the U.S.P., which 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 of the careful observation of the physiological effects produced upon dogs from the internal administration of the preparation of the drug under test, compared with the physiological effects produced by definite doses of a standard preparation of the drug, according to the following method. It is necessary in selecting the test animals to pick out those that are easily susceptible to the action of 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 pur-

poses, 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, .010 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 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 swallowed with ease. In order that the drug may be rapidly absorbed, food should be withheld twenty-four hours before the test and an efficient cathartic given, if needed.

Within a comparatively short time, one to two hours, the dog begins to show the characteristic effects of the drug: First a stage of excitability is noticed, followed sooner or later by a condition of incoordination; the animal behaving as though intoxicated. Experience is necessary on the part of the observer to determine just when the physiological effects of the drug begin to manifest themselves, as there is always, as in the case of many chemical tests, a personal factor to be guarded against. The dogs must be kept perfectly quiet and watched without attracting their attention. The influence of the test dose of the unknown drug is carefully compared with the same dose of the standard preparation administered to another test dog at the same time, under the same conditions. Finally, the dogs become sleepy, the observations are recorded and the animals returned to their quarters.

The second day following, the two dogs are reversed, *i. e.*, the animal receiving the test dose of the unknown receives the test dose of the known, and vice versa, and a second observation made. If one desires to make a very accurate quantitative determination, it is advisable to use not two dogs but four or five, and study the effects of the test dose of the unknown in comparison with the test dose of the known upon each. If the unknown is below standard activity, the amount should be increased until the effect produced is the same as for test dose of 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 and care exercised by the observer.

It is best to use the dogs on alternate days, in order that they may completely recover from the influence of the drug. Another point to be noted in the use of dogs for standardizing cannabis is that, although they never appear to lose their susceptibility to the drug, the same dogs cannot be used indefinitely for accurate testing. After a time they become so accustomed to the effects of the drug that they refuse to stand on their feet, and so do not show the typical incoordination which is the most characteristic and constant action.

We have never been able to give an animal a sufficient quantity of a U.S.P. or other preparation of the drug to produce death. When study of the drug was first commenced, careful search of the literature on the subject was made to determine its toxicity. Not a single case of fatal poisoning have we been able to find reported although often alarming symptoms may occur. A dog weighing about 25 pounds received an injection of 2 ounces of an active U.S.P. fluid extract in the jugular vein with the expectation that it would certainly be sufficient to kill the animal. 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 S. E. Cannabis with the same result.

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 has been a certain amount of variation in the physiological action, but in every case there has been elicited the characteristic symptoms from the administration of .010 grammes, per kilo body weight, of the extract.

The repeated tests that we have made have convinced us that the drug, properly grown and cured, is fully as active as the best Indian Cannabis, which we have sometimes found to be practically inert. 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 single report of inactivity, although many tons of the various preparations of *Cannabis Indica* have been tested and supplied for medicinal purposes.

Furthermore, we have placed out 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*. We are of the opinion that *Cannabis Americana* will be found equally as good, and perhaps better, than that obtained from foreign sources, as proper directions can be given to the grower, in order to produce a drug of the greatest value. We expect to give this phase of the subject especial attention during the next few years, and see what improvements may be effected.

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, .010 per kilo body weight, is tested in comparison with the same quantity of a standard preparation of known strength.

(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*.
