in the extraction and the percentage of alkaloids found in a sample of Belladonna leaves and a sample *Datura Tatula* leaves.

DRUG.	Weight of Sample (grams).	Amount of Menstruum (c.c.)		Amount of Ammonia Water (cc.)	Percentage Total Alkaloids.
		Maceration.	Percolation.		
Belladonna Leaves	5	50	60	5	0.623
	4	50	60	4	0.621
	3	50	60	3	0.618
	2	50	60	2	0.621
Datura Tatula Leaves	5	50	60	5	0.481
	4	50	60	4	0.481
	3	50	60	3	0.490
	2	50	60	2	0.488

The above table shows that the method as modified is well adapted to assaying small samples. While the amount of menstruum used is probably considerably larger than actually necessary to insure complete exhaustion there is no harm in such excess and it is a very convenient quantity to work with. The menstruum can readily be recovered and by means of its specific gravity adjusted to its proper proportion of ether and chloroform so that it may be used indefinitely.

The method described has been used with equal success on Belladonna Root and Stramonium Leaves. When used on Hyoscyamus Herb, the proportion of ammonia water could no doubt be reduced considerably although the method has given very good and concordant results without any modification.

In view of what has been written it would seem then that the official process could be improved by the following several changes:

1. The introduction of a suitable vessel or apparatus such as a Squibb separatory funnel for the combined maceration and percolation. This would save time and insure against loss of material through transference to a percolator.

2. An increase in the quantity of menstruum both for maceration and percolation. This would insure a more thorough exhaustion.

3. An increase in the quantity of ammonia water used, when extracting the drug. This would aid in the complete liberation of the alkaloids from their salts.

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THE PHARMACOPŒIAL REQUIREMENTS FOR CANNABIS SATIVA.*

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The United States Pharmacopœia, Eighth Revision, specifies that "*Cannabis Indica* shall consist of the dried prepared tops of the pistillate plant of *Cannabis sativa*, grown in the East Indies and gathered while the fruits are yet undeveloped,

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and carrying the whole of their natural resin." Cannabis Indica, that is, Indian grown *Cannabis sativa,* has been considered to be a distinct variety, or to owe its activity to differences in the soil and climate of India, from that of other localities. A statement in the National Standard Dispensatory, under the head of Cannabis Indica, is as follows: "The rich soil, and cool climate, suitable for the production of hemp fibre, will not develop the medicinal properties, which, moreover, are largely sacrificed by allowing the male plant to grow near as a requisite for the production of hemp seed. Notwithstanding this fact, large quantities of tops of such plants are marketed for medicinal use, this to a great extent explaining the weak action of much of the medicine."

Various investigators have examined American hemp, which is grown almost entirely for its fibre and seed, and obtained results which indicate that the influence of soil and climate does not affect the quality of the extract. The results obtained by H. C. Wood (Proc. Am. Phil. Soc., Vol. XI, p. 226) are responsible for its having been made official in the Pharmacopœia of 1880. *Cannabis Americana* appears in this Sixth Revision with the description *"Cannabis sativa,* grown in the Southern States and collected while flowering." Wood examined the leaves and tops of the staminate plant and found the extract to possess a high degree of activity. The American variety, however, was dropped from the Seventh Edition of the U. S. P. and does not appear in the Eighth.

Later a more exhaustive investigation was made by Houghton and Hamilton (Am. Jour. of Pharmacy, Jan., 1908). The authors described in detail, the method employed to standardize these extracts and gave the results obtained from tests of eight samples grown in various localities in America. It was concluded from these experiments that *"Cannabis sativa,* when grown in various localities of the U. S. and Mexico is found to be fully as active as the best imported Indian grown *Cannabis sativa."* No part of the plant, of either the pistillate or staminate, was found inactive, except the stems and seeds and at no stage in its growth, from the flowering to the fruiting, was there any difference in the quality of the extract. It was determined, however, that the flowering top of the pistillate plant contained the highest percentage of active extractive matter.

The acivity of American grown hemp has been noted also by True and Klugh (Proc. A. Ph. A., 1909). (See also Am. Jour. Pharm., Jan., 1912, page 31.) Their work, however, was more in the direction of obtaining a drug duplicating in appearance the imported article although they record the fact that the physiological effect on dogs was fully equal to that of the latter.

From time to time there has been obtained further evidence pointing to the necessity for specifications, which would insure that the drug so characterized is active and also that no drug having physiological activity should be rejected because of non-essential characteristics. Among these may be noted a few which suffice for illustration. From a sample of American hemp from the Continental Fibre Company of Kentucky the following data was obtained: The sample consisted largely of leaves with approximately 10% of tops. The yield of active extract soluble in cold alcohol was 8 per cent. From 15 grams of the selected fruiting or flowering tops there was separated 5½ grams or over 30 per cent of seeds. The yield of active extract from these tops deprived of their seeds was 13 per cent.

Two samples of hemp from another locality in Kentucky were examined and found to have 3½ and 8 per cent respectively, of active extract. The low yield of the former was on account of its high content of stems and the small percentage of flowering tops.

From the flowering tops, stems and leaves of the pistillate plant of some hemp grown experimentally in Michigan, a yield of 10 per cent of active extract was obtained. This sample, carefully separated into its component parts, was extracted and tested physiologically. From the tops a yield of 12 per cent active extract was obtained while from the leaves the yield was 10 per cent of an extract equally active. The higher yield from the tops was sufficient to compensate for the presence of the short stems which contain no extractive.

The American grown hemp is not alone in being gathered in the fruiting instead of the flowering stage. A sample of *Gauza Tops* from India recently submitted by a German importer contained 50 per cent of seeds. The tops entirely freed from seeds contained 16 per cent of active extractive, but the net yield from the sample as submitted was considerably below the average. Samples containing 25 per cent of seeds are very common.

A further statement is made in the N. S. Dispensatory of 1900, that "it is most unfortunate, in the case of such a drug, that we have no means of establishing a chemical standard, since the active constituent is not known. Large manufacturing houses are able to improve the standard very greatly by employing physiological examination." It is a well known fact that much of the *Cannabis Indica* which is sold on the market does not meet the requirements of the Pharmacopœia, because it contains too large a proportion of ripe, or well developed seed. For that reason it is almost impossible for manufacturers to obtain any considerable quantity of crude drug, which meets the requirements of the Pharmacopœia. It therefore seems advisable that some means be taken to establish a standard, either chemical or physiological, which shall specify in no uncertain terms, what quality of *Cannabis sativa* will meet the requirements and make a physiologically active extract. The specifications should be of such a character that no drug containing a fair percentage of active extract need be rejected because of not meeting the U. S. P. requirements.

Since *Cannabis sativa,* grown in different localities, differs not at all in the quality of its active extract and since the leaves and the fruiting, as well as the flowering tops contain this active extract, there seems to be a physical basis on which, along with a physiological test, such a specification can be made.

The fact that little, if any, truly pharmacopœial hemp appears on the market was noted by Pearson (Bull. Am. Pharm. Assn., October, 1910). Various opinions were received from prominent pharmacists and teachers of pharmacy in response to a request from him with no considerable agreement among themselves. This lack of agreement made it more than ever evident that a reform in this particular is very desirable. The subject was referred to the writer, who in response to a request for a statement which would, in his opinion, cover the points in question, gave the following, which was published in the Bulletin of the American Pharmaceutical Association of January, 1911:

"Since almost every sample of *Cannabis sativa,* whether grown in India, the United States, or any other country, almost invariably contains seeds, and since

these samples vary greatly in the amount of alcohol soluble extractive matter contained, the following specifications seem to be that which would insure a drug of standard quality.

"That the yield of solid extract *Cannabis sativa* be not less than 9 per cent and that this solid extract be entirely soluble in cold alcohol. 0.1 gram of this extract should produce the typical effect of the drug on a 10 kilo dog. The dog should be one which reacts to this drug and the effect noted is that of incoördination in its movements.

"The reasons for this specification are that almost any part, either the flowering top, the fruiting top or the leaf and either the male or the female plant, contains the active extract, but in quantities considerably different from the percentage found in that specified by the Pharmacopœia. When the top of the female plant contains a considerable quantity of seeds the percentage of extractive matter is lowered, but the activity of that extract is no less than from tops which have been gathered earlier in the season.

"The yield of extractive answering the above requirements is greater, usually, in the drug imported from India than from American grown hemp, and should be valued higher on that account. Occasionally drug which has been improperly dried or stored will be found inactive, although the percentage of extractive matter and its appearance may be no different from that which has its full activity."

The foregoing was written hastily and largely from the point of view of a pharmacologist. However, the extract, soluble in cold 95% alcohol, rarely fails to produce its typical effect on dogs. A pharmacist can readily make such an extract and thus be in a position to assay his own drug. With the additional knowledge regarding the relative amounts of extract contained in different parts of the plant, he is then in a position to make a rough choice among the samples submitted.

To the manufacturer the specification is even more satisfactory. He can purchase his drug on the basis of its yield of extract of standard quality regardless of the presence of parts which contain no activity.

If the drug contains an average of ten to twelve per cent of extractive matter of the desired quality, it then meets the specifications, while if the yield is low a proportionately larger amount of drug must be used to make a galenical preparation of standard quality.

Such a specification also opens the door to *Cannabis Americana* or in general to *Cannabis sativa,* since yield and activity are the essential features of the specification.

With further reference to the statement in the Dispensatory, relative to our inability to establish a chemical standard, it may be said, that although no well defined compound has been isolated, an extract has been prepared which represents apparently the nearest approach to such a constituent. There is reason to believe that the active constituent is of such a nature as to resist combination with reagents, and so to obtain crystalline compounds of a definite character.

Experiments along these lines will form the basis for a further contribution on the chemistry of *Cannabis sativa.*—(From the Research Laboratory of Parke, Davis & Co., Detroit, Mich.)