

evaporate spontaneously, the residue mixed with a few cc. of water, filtered, acidulated with HCl and this solution tested with the same reagents. Very heavy precipitates were obtained in all cases.

The total quantity of acidulated aqueous solution was then treated with potassium bismuth iodide. A very heavy deep red precipitate was obtained. This was filtered out, washed with distilled water, mixed with distilled water, acidulated with HCl and H₂S passed through the mixture, the bismuth sulphide filtered off, the filtrate made alkaline with KOH and shaken out with ether and the ether allowed to evaporate spontaneously, leaving a yellow amorphous residue.

Some of this residue, dissolved in water and acidulated gave precipitates with all the reagents named above.

The amount of this residue was not sufficient for further examination.

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CANNABIS SATIVA:

IS THE MEDICINAL VALUE FOUND ONLY IN THE INDIAN GROWN DRUG?

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Not many students of the subject will to-day answer this question in the affirmative. There is too much evidence to the contrary. Some, however, have not yet been brought to the point of accepting as "Standard," an extract of Cannabis Sativa irrespective of the locality from which the crude drug was obtained if the fact is noted that it is not of Indian origin. For this undoubtedly, tradition is largely responsible. Originally only three or four provinces¹ on the west coast of India were included in the territory from which official, medicinally active hemp could be obtained. Later,² however, no limit was placed on the drug specifications except that it be from India; and as no distinguishing feature is present to assure its origin as being Indian, no doubt much material appears on the market from other sources and is accepted as "Indian."

This statement might be accepted as the cause for the uncertain action of the drug noted by many observers. What seems much more likely to be the reason for the inconstant and inconsistent results reported by some observers, is that the variable effects, both clinical and pharmacological, which are obtainable even with active material had not, at that time, been sufficiently recognized. Houghton³.

While the dog is generally accepted as the most satisfactory test animal,^{4 & 5} not every one is applicable for the purpose. Many of them must be rejected as not being sufficiently susceptible and even the susceptible ones are not uniformly so.

This being true, unless exceptional care is exercised in observing the pharmacological action of the drug extract, misleading reports are certain to follow.

It is not the intention of the writer at this time, to adduce data to prove the activity of American grown Cannabis Sativa, because it is possible to prove almost anything one wants to prove about the activity or inactivity of extracts of

hemp. The intention is rather to point out the possible reasons for such contradictory reports as have been published. These, on the other hand, are the result of incomplete or inaccurate observation, non-susceptibility of the test animal or patient, use of an extract whose activity had been destroyed or the use of extracts from inert or only slightly active drugs. On the other hand, not infrequently a patient or a test animal is highly susceptible and a particular sample of only average quality is reputed to possess exceptional activity. Many statements regarding the activity of hemp extracts are apparently colored by tradition, it being concluded without further comment that only the Indian grown drug contains the narcotic principle. Cushny⁶ states that *Cannabis Sativa* is of pharmacological interest only when grown in warm climates including Southern United States. Kobert⁷ claims that the official preparations have no action on animals and that their action on humans is inconstant. Fraenkel¹ says: "The action of haschish differs greatly according to climate, race and individuality." Bibra's book⁸ contains very interesting descriptions of experiments with haschish on humans which proved its strongly differing action on the individual. Sollmann⁹ says: "Hemp grown in western countries is generally devoid of Cannabinol and is inactive." Wood, (Geo. B.)¹⁰ noted that the European hemp appeared to have none of the exudate typical of the Indian grown drug and of that growing in the vicinity of Philadelphia. If this last statement is true, it is a logical explanation of European opinion that only the drug from India contains appreciable activity. It is probably true only in exceptional cases. Wood (H. C.)¹⁰ found that less than 1 gr. of an alcoholic extract of Kentucky grown hemp was effective on himself. This would apparently indicate exceptional activity since 1 gram of Ext. *Cannabis Indica* will not ordinarily produce so intense an action as that described. Actually, it would seem probable that he is occasionally, or generally, more susceptible than the average person.

The most recent reference of note is that by Eckler & Miller⁵ in which several series of experiments were carried out, all leading to the conclusion "that if American *Cannabis* is made official, difficulty will generally be experienced in obtaining highly active lots which will compare favorably with a good Indian drug." One statement in their summary is that "very little dependence can be placed on the estimation of the extractive matter yielded to alcohol." This, in the writer's experience, is too general a statement. The Extract is rarely inactive. When an Extract is entirely soluble in cold 95% ethyl alcohol, the yield is a fair indication of the activity of the drug¹¹. There are exceptions to this statement, however, so that it cannot be taken as true in any particular case without being verified by pharmacological assay but it may be taken as roughly indicating the value, other things being equal.

The Powdered Extract *Cannabis Sativa*, from whatever source the drug originated, very readily deteriorates. In fact, one lot came under the writer's observation in which no activity could be detected, while the extract from which it was made was of full standard activity, i. e., 10 mg. per kilo administered to a susceptible dog elicited the in-coördination characteristic of the drug's action.¹¹ Undoubtedly, a similar deterioration may take place in the drug or in an extract without any recognizable change in its physical properties.

Exception may also be taken to the experiments of Eckler and Miller on account of the quality of the drug used. In no case was the quality of the crude drug, at all comparable to the quality of the Indian Cannabis with which its activity was compared. A sample of crude drug containing a large proportion of seeds, stems, and leaves, this being the description applying to most of the samples they tested, is very different from the average quality of Indian drug imported, and one should not expect equality either in yield or activity. Much better drug should be and is available on the market.

The writer¹¹ has carried out tests for the activity of samples of drug grown personally from seed collected from Indian drug, and invariably found no activity in either the stems or seed. The leaves, however, when gathered before any brown color due to decay was evident, were found to contain almost as much extractive with almost the same activity as the imported drug which meets U. S. P. requirements, while the flowering tops of the pistillate plant—the part corresponding exactly to the requirements for Indian Cannabis—were found fully equal and in some cases superior to the average good quality imported drug meeting U. S. P. requirements. This and other equally favorable results were reported in former papers.

There are occasional samples of American drug decidedly less active than standard both as regards yield of extract and its activity. These, however, can be paralleled by samples of Indian drug having no greater activity.

With the exercise of caution in selecting the drug and insistence on certain qualities essential to drug of good quality, American producers can supply material practically of equal value to that imported. It will be necessary, however, for manufacturers of extracts of this drug to recognize the economic difficulties that stand in the way of duplicating the physical qualities of the imported drug. Hand-picking is out of the question and almost of necessity the commercial drug will contain leaves, stems and seeds with some admixture of the male plant.

To obviate the difficulty of so specifying as to exclude undesirable parts, it seems advisable to specify merely as regards yield and activity of extract from the botanically correct drug. Then, no sample of hemp plant that can be economically extracted and that yields an active extract, need be rejected because of physical difference from rigid U. S. P. specifications. If the extract is active and if the yield and the cost of the drug are compensatory we then have an economic condition that should be satisfactory.

Also as Scoville¹² has pointed out, the crude drug is not used as such and really requires no specifications except botanical.

Another question has been raised relative to the comparability of therapeutic and pharmacologic activity. This point was raised by Dr. Rusby and was answered in a paper presented before this section two years ago.¹³ Experiments indicated that the dog, under rigidly prescribed conditions, is a satisfactory test animal and that lack of therapeutic results from pharmacologically active samples may safely be ascribed to individual variability. Schroof,¹⁴ moreover, has pointed out that non-susceptibility is not absolute but is merely a question of quantity.

We conclude, therefore, that, first, American hemp contains the active constituent; second, if equal care is exercised in selecting the proper part of the drug for extraction, no material difference in activity will be found between extracts of Indian and American hemp; third, apparent lack of activity and variability in

activity applies equally to both varieties of this drug; fourth, under proper direction there is no valid reason why American hemp cannot be collected to advantage to replace the imported article.

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ESTIMATION OF YELLOW PHOSPHORUS.

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At the Nashville meeting of the American Pharmaceutical Association we presented a paper on the estimation of Yellow Phosphorus. This paper was offered by us only as a preliminary one. Since then we have made numerous experiments in regard to the estimation of the metalloid and on the strength of these are now compelled in some instances to offer slightly modified methods. Since the paper did not appear in the Journal of the American Pharmaceutical Association up to May, 1914, we requested that the paper be not published prior to the meeting of the Association at Detroit when we would be in a position to give more details of the various methods applied by us in addition to a number of results obtained with pharmaceutic products of various kinds.

For the estimation of phosphorus several methods have been published. The distillation process for estimating phosphorus originated by Mitcherlich and later on modified by Dusart and Blondlot can be applied only when comparatively small quantities of phosphorus are present because the metalloid is not as volatile with steam as is generally accepted. It requires hours to distill as little as 50 mgms. of phosphorus. Neither the oxidation of the phosphorus in the distillate with nitric acid or bromine as carried out in Mitcherlich's method, nor the conversion of the phosphorus into silver phosphide and subsequent oxidation of the latter to phosphoric acid yield satisfactory results.

Various processes depending on the oxidation of phosphorus with nitric acid and simultaneously destroying any organic matter present, by this acid, by concentrated sulphuric acid or other chemicals were therefore recommended by Sayda,¹ Fry,² Vanderkleed and Turner,³ Woerner⁴ and others. These processes, however, have the disadvantage in that by them the total and not the elementary phosphorus alone is determined.

Reed⁵ determined the phosphorus by allowing a solution of bromine in acetone,

¹ Pharm. Zeitschr. f. Russl. XXXVI, 337.

² Pharm. Post, 1910, 969.

³ Proc. A. Ph. A., 1906, 395.

⁴ Pharm. Zeit., 1908, 398.

⁵ Analyst XXIV, 23.