Sample.	Sold as	How prepared.	Form of malt.	Form of milk.	Source.
1	Malted milk	Mixed	Extract	Skimmed	Dairy
2	Malted milk	Mixed	Extract	Skimmed	Manufacturer
3	Malted milk	Mixed	Extract	Skimmed	Manufacturer
4	Malted milk	Mixed	Extract	Skimmed	Manufacturer
5	Malted milk	Processed	Infusion	Whole	Pharmacist
6	Malted skim milk	Processed	Infusion	Skimmed	Manufacturer
7	Malted whole milk	Processed	Infusion	Whole	Manufacturer
8	Malted milk	Mixed	Extract	Skimmed	Manufacturer
9	Malted milk	Mixed	Powdered	Whole	Manufacturer
10	Malted milk	Mixed	Extract	Skimmed	Manufacturer
11	Malted milk	Processed	Infusion	Whole	Confectioner
12	Malted milk	Mixed	Extract	Skimmed	Manufacturer
13	Malted milk	Mixed	Extract	Skimmed	Manufacturer
14	Malted milk	Mixed	Extract	Skimmed	Manufacturer
15	Malted milk	Processed	Infusion	Whole	Confectioner
16	Malted milk	Mixed	Extract	Skimmed	Dairy
17	Malted milk	Processed	Infusion	Whole	Confectioner
18	Malted milk	Processed	Infusion	Whole	Confectioner
19	Malted milk	Processed	Infusion	Whole	Confectioner
20	Malted milk	Mixed	Extract	Skimmed	Confectioner
21	Malted milk	Mixed	Extract	Skimmed	Confectioner
22	Malted milk	Mixed	Extract	Skimmed	Manufacturer
23	Malted skim milk	Mixed	Extract	Skimmed	Manufacturer
24	Substitute[1]	Mixed	Extract	Skimmed	Manufacturer

[1] Contains bread crumbs.

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THE STABILITY OF CANNABIS SATIVA AND ITS EXTRACTS.

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A recent publication by Eckler[1] regarding the deterioration of *Cannabis indica* raises a question which can be answered positively only after a long series of experiments such as Eckler himself conducted.

Over a period of five years, samples of crude drug cannabis were kept under observation, storing it under different conditions. He found that it loses from 1 to 2 percent of its activity monthly, depending apparently on the temperature of the storage room. Five years from now, however, the subject will probably have passed so completely out of general interest that there will be no incentive either to complete the experiments or to make the results public, while at the same time such an apparently authoritative statement going unchallenged may lead to a number of errors. It seems advisable, therefore, to publish some data bearing on this question even if it is not based on systematic experiments. In the course of nearly 20 years' experience in applying the physiological assay process to cannabis preparations, a number of unrelated facts are gradually collected which, taken as a whole, have a value not to be ignored.

Cannabis indica, or to use the botanical term to cover *Cannabis sativa* wherever grown, is scarcely deserving of the attention it has received from time to time in recent years. While a potent drug in many respects, its action is not specific in therapeutics and is not that of a deadly poison.

However, as a potent drug in which no active substance with well-defined chemical characteristics has been recognized, it requires standardization and sufficient investigation to insure that inert extracts be kept off the market.

Attention was first called to the variability of the drug by Houghton,[2] who found that about 50 percent of the fresh samples of crude drug were devoid of activity.

Later, Houghton and Hamilton[3] described a method by which extracts can be standardized and uniformity established in the quality of commercial extracts. It depends on the fact that dogs react to the drug in a degree proportionate to the amount of a standard product administered, and that the reaction is not only characteristic but measurable.

This method, on which all the later modifications have been based, has served as a means of eliminating most of the worthless drug from the market and of discovering evidences of deterioration. Thus it was observed that Powdered Extract Cannabis is apparently an unstable form since several samples have been found inactive. In one case[4] some step in the process of manufacture caused immediate and almost complete loss of activity.

No other evidence of deterioration has been observed, however, except that which tends to corroborate the data published by Marshall[5] and quoted by Eckler. The deterioration of the substance to which the name of cannabinol was given while easily demonstrable, does not prove anything about the drug itself or its extracts except when similar phenomena are shown to exist in each. The conclusion which Marshall drew from his observation that "There is good reason to believe that preparations of *Cannabis indica* relatively quickly deteriorate" is not based on any data submitted and is not justified by any data obtained except the two preparations already mentioned. Marshall himself did not apply it to the drug, while Eckler concludes that the crude drug alone is under suspicion, not having observed any deterioration in the fluidextract.

Observations on the crude drug other than samples of indefinite age, are limited to two which will be described below. During a long experience in assaying samples of the crude drug before or immediately after purchase, no low activity has been observed except such as is easily referable to its physical or botanical properties. For example, low activity may be expected from samples consisting of sweepings or from those consisting largely of stems or seeds, or from those having a low yield of alcohol-soluble extractive. (NOTE: By alcohol-soluble extractive is meant the part which will redissolve in 95 percent alcohol after twice evaporating to complete dryness on the steam bath.) Low activity of crude drug other than the exceptions noted would prove nothing in itself because of having no data as to the age of the sample.

Inquiry among holders of crude drug rarely brings to light samples much over 1 year old in stock, and the standard is usually made from drug no fresher than this.

Two samples, however, have recently been obtained from shelf bottles, one 14 years on the shelf and the other at least 21 years and probably longer, 21 years being the limit of the botanist's knowledge. The results of an assay of these two samples in comparison with standard are as follows:

14-year old drug	70 percent
21-year old drug	20 percent

The first was known to the writer to be of good quality, probably fully standard. The second lot was probably also a first-class quality of *Cannabis indica* from its appearance, but there were no recorded tests in existence to prove its activity.

Exact data on old F. E. *Cannabis indica* is limited to one sample other than an occasional retest of samples not over 2 or 3 years old which are almost invariably as active as when fresh. The old sample referred to above was obtained from Hutton and Hilton, retail pharmacists of Washington, D. C. It was prepared by Squibb and had been on the shelf for 17 years. The assay showed a value equal to about 70 percent or between two-thirds and three-fourths as strong as standard. Its original value may be assumed to have been 100 percent.

Exact data on Extract *Cannabis sativa* is limited to one sample, an extract of *Cannabis Americana* first selected for a series of experiments to prove the applicability of the physiological assay to drug intended for clinical use.[6] This sample has been in constant use in our laboratory for 9 years as a standard for the selection of dogs for assaying cannabis. It is at this time as active as an extract of the best obtainable commercial lots of *Cannabis indica*. It is rare indeed when any extract exceeds it in activity. The sample is kept in a tin can with tightly fitting lid, but is opened on an average not less often than once every week.

The bottles containing the crude drug are 1-pound flint glass, glass-stoppered bottles which have never been sealed and have been kept on shelves exposed to the light and variations of temperature normal to a laboratory work room.

That the above results are not open to the suspicion of being obtained on the basis of a standard of low activity is demonstrated by the fact that comparison was made with a standard which has recently been proposed and prepared by Pearson.[7] This is in line with a similar suggestion by Lyons[8] and with that by Hamilton.[9] It eliminates the variable standard suggested in the Ninth Revision of the U. S. P., and provides identical material for comparison in the several laboratories.

The results summarized above are based on administering doses to dogs and observing the degree of the reaction, comparing the effect in each case with that of a product of known good quality. The dogs' behavior under cannabis must have been previously observed since no two react in exactly the same way. The reaction which is described as "well-marked" or "standard" refers to the incoordination and is not absolute but only relative to that produced by the Standard on that dog.

The doses used and the observed reactions are the bases of the results described in the foregoing article and are given in detail below, the work having been carried out by my colleague, L. W. Rowe:

Sample No. 1 is F. E. *Cannabis indica* from 14-year old drug.

Sample No. 2 is F. E. *Cannabis indica* from 21-year old drug.

Sample No. 3 is F. E. *Cannabis indica* from Hutton and Hilton, Washington, D. C.

Sample No. 4 is S. E. *Cannabis Americana.*

Sample No. 5 is F. E. *Cannabis indica*, mixture of 4 commercial samples supplied by Pearson.

	Dose per kilo.	Result.
Sample 1.....	0.08 mil	Slight incoördination
	0.10 mil	Distinct
	0.12 mil	Well marked
	0.14 mil	Standard
Sample 2.....	0.10 mil	No reaction
	0.20 mil	Very slight
	0.30 mil	Slight
	0.40 mil	Well marked
	0.50 mil	Standard
	0.60 mil	Very marked incoördination
Sample 3.....	0.10 mil	Distinct
	0.12 mil	Well marked
	0.15 mil	Very marked incoördination
	0.12 mil	Well marked, but scarcely standard
Sample 4.....	0.008 mil	Well marked
	0.010 mil	Standard
	0.012 mil	Very marked incoördination
Sample 5.....	0.08 mil	Well marked
	0.10 mil	Standard
	0.12 mil	Very marked incoördination
Sample 6.....	0.025 mil	No reaction
	0.03 mil*	Slight incoördination
	0.04 mil	Distinct incoördination

* This is the result using the U. S. P. dose and observing the conditions rigidly.

The above data leads to the conclusion that the rate of deterioration of *Cannabis sativa* and its official extracts is much slower than would be assumed from Eckler's work and that for practical purposes it may be ignored.

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