

THE PHYSIOLOGICAL STANDARDIZATION OF CANNABIS.*

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The inclusion of Biological Assays in The United States Pharmacopœia IX is an important step in the right direction, the wisdom of the Committee cannot be questioned and in fact deserves a great amount of credit for being progressive.

The physiological standardization of Cannabis is unfortunately the only biological assay that is actually compulsory. The biological standardization of Aconite, Digitalis, Strophanthus, Squill and Suprarenal Gland is optional, as may be seen by consulting the text of the new Pharmacopœia. No biological assay has been even recommended for the standardization of Ergot.

The object of this paper is to give my experience in regard to the difference in the susceptibility of dogs, which fact is recognized in the Pharmacopœia, and also to propose an arbitrary standard.

In the first place, all dogs do not prominently show the three stages of action which have been described in most reliable text-books. Restlessness, muscular incoördination and drowsiness are not even seen in all cases, but the same dog usually develops most prominently a single one of these three characteristic symptoms, providing that the dose is not excessive, when nausea and vomiting may be seen.

In my experience bull terriers develop most prominently muscular incoördination while other dogs have shown a distinct propensity to drowsiness without much muscular incoördination. Other dogs have shown more prominently the stage of excitement with little muscular incoördination and with marked stupor later.

The most susceptible dog I have even seen is a male fox terrier which has been in the employ of the Smith, Kline & French Co. for the last five years. He seems to be just as sensitive to the action of cannabis now as he was five years ago. He weighs 21 pounds and develops marked muscular incoördination when fed 0.6 mil of my standard fluidextract of cannabis. Let me state that I believe my standard fluidextract of cannabis is as active or even more active than the standard used by other men doing this work. Recently Dr. Pittenger and I made physiological tests on the same unknown sample of cannabis and he reported the unknown sample as being 90 percent as strong as his standard and I considered the unknown only 80 percent as strong as my standard.

Every dog that is used for blood-pressure work is first fed my standard sample of cannabis in order to select the most susceptible dogs for the "poison squad" and save for testing cannabis. Very few dogs have been found which would develop noticeable muscular incoördination when fed 0.03 mil of my standard fluidextract of cannabis per kilo weight of dog. In other words the standard set by the new Pharmacopœia seems to be higher than it should be unless other men have found more susceptible dogs than those brought to my laboratory.

Since I have had so much difficulty in obtaining dogs highly susceptible to cannabis I have tried to breed them from my highly susceptible male dog. A female short haired mongrel weighing 26 pounds was bred. This female was not very sensitive to the action of cannabis, as about 0.05 mil per kilo was required to produce noticeable incoördination and even this amount produced proportionally little drowsiness. Four pups were born but only one (a female) which resembled the sire in other ways was very sensitive to the action of cannabis. Unfortunately this young female lost her life in defending her ideas of woman's

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suffrage or some other subject. The details of the conflict were never made public and are still a secret which her associates have never divulged even to me, their chief counsel.

Failing to raise the most promising young female the two other females were bred to the same sire (their father). I now have four young pups three of which are males and of which much is expected. I will try to raise these pups under proper influences and in this way meet the requirements of the new Pharmacopœia.

The fact that cannabis must now be legally standardized physiologically would seem sufficient reason why a standard fluidextract should be prepared similar to the standard antidiphtheritic serum that was prepared by Dr. Anderson and is kept in Washington for the use of all who may wish to test the strength of antidiphtheritic serum.

I would suggest that the Committee on Physiological Testing, of which Dr. Houghton is chairman, prepare a composite standard fluidextract of cannabis which has been obtained from several sources and that portions of this standard fluidextract be sent in ampoules to the various laboratories where physiological standardization is done. There is not much question about fluidextract of cannabis retaining its full activity for a number of years possibly till the United States Pharmacopœia X is ready for distribution.

LABORATORY OF SMITH, KLINE & FRENCH CO.

CARREL'S SOLUTION.

The *California State Journal of Medicine* (November, 1916, 429) states, with reference to this solution, which is now largely used in the European hospitals for the antiseptic treatment of wounds:

"Several inquiries have come to this office for the formula of the antiseptic solution which developed as one of the innumerable by-products of the European War. This solution is generally referred to under the name of Carrel's solution, and is made as follows:

"Dissolve in a large bottle 140 grammes of dry sodium carbonate with 10 liters of sterile water. Add to this 200 grammes of chloride of lime (bleaching powder), and shake well. After half an hour siphon off the clear fluid into another bottle through a cotton plug or filter paper and then add 40 grammes boric acid to the clear fluid."

This solution is simply a solution of boric acid in Solution of Chlorinated Soda (Labarraque's solution) and water. It can be made much more expeditiously by the following formula:

Solution of Chlorinated Soda (U. S. P. IX)	200 Gm. (practically 50 mils or Cc.)
Sterile Water	800 mils
Boric Acid	4 Gm.

Dissolve. Keep in well-stoppered bottles, in a cool place, protected from the light.