Reports of A. Ph. A. Committees

REPORT OF COMMITTEE OF PHYSIOLOGICAL TESTING.

The committee that you have appointed to investigate the subject of physiological testing, desires to make at this time the following report:

During the year, since the last meeting of the Association in Boston, considerable work has been done in testing the following substances:

Preparations of Cannabis Sativa.

Preparations of Suprarenal Gland.

Preparations of Ergot.

Preparations of Heart Tonics of the Digitalis Series.

Our work has progressed to a point where we feel it wise to submit specific reports on preparations of Cannabis Sativa and the Suprarenal Glands. Please note the detailed reports that follow.

Our work on Ergot has not progressed to a point where we believe it wise or desirable to report definite results. The same applies also to the heart tonics of the digitalis series. We believe that during the next year we should continue our work on these two classes of products in the most careful possible way, should take into consideration all new reports as they arise, as to method or manner of testing pharmaceutical products of these drugs and submit in due time definite reports in much the same manner as we have upon products of Cannabis Sativa and of the Suprarenal Gland.

During the course of our work the committee on physiological testing of the United States Pharmacopœial Revision Committee have suggested to us that this committee should cooperate with them. We shall attempt to do so as far as possible, in order that the combined efforts of the workers in this particular field may result in a unanimity of opinion as to the wisest course to pursue in the adoption of methods of physiological assay, standards and such, which may apply to that class of pharmaceutical and chemical products, which cannot be assayed by chemical means.

We believe it highly necessary that the association should endeavor to make arrangements with some central authority as the Bureau of Public Health and Marine Hospital Service, to keep and issue to those desiring them definite and positive standards of the preparations of these drugs, by which they can measure and standardize products as they are manufactured. We do not wish it understood that we should leave the matter to the American Public Health and Marine Hospital Service Laboratory to devise standards and such, but that we should cooperate with them. If it meets with the approval of the Association we believe it would be wise for the committee to be authorized to take this matter up in detail with the director of the American Public Health and Marine Hospital Service Laboratory, in order that it may be determined exactly what may be accomplished. Very sincerely yours,

(Signed) WORTH HALE.
CHARLES R. ECKLER.
W. A. PEARSON.
E. M. HOUGHTON,
Chairman.

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PHYSIOLOGICAL ASSAY OF PHARMACEUTICAL PREPARATIONS OF CANNABIS SATIVA.

1. The activity of pharmaceutical preparations of Cannabis Sativa depends upon one or more active substances, which produce a characteristic intoxication in animals when given internally.

Preparations of Cannabis Sativa may be tested physiologically by observing the typical intoxicating effects produced by the active substances contained in the drug when the preparations are administered to selected test animals in suitably sized doses, under proper test conditions.

2. The animal best adapted for determining the value of preparations of Cannabis Sativa is a carefully selected dog, which shows a characteristic reaction to small doses of the drug.

3. The test animals should be given a purgative twenty-four hours before the test is to be made, and allowed to fast until ready for use, plenty of water being supplied. Two

dogs, preferably four, are taken for a test. On the first day of the test two of the animals receive .005 gms. to .01 gms. per kilo body weight of the standard extract Cannabis Sativa contained in a gelatine capsule administered per os. The other two animals are each given the same quantity of the unknown preparation of Cannabis Sativa administered under the same conditions. The quality and degree of the intoxication are carefully observed in the four animals. On the second, preferably the third day, when the animals have completely recovered, the dogs are again employed for testing the activity of the drug in the same manner as before, except that the two animals that received the unknown extract of Cannabis Sativa on the first day are given the known or standard on the second administration. The tests are repeated until the amount of the unknown can be determined as accurately as possible, that will produce the same quality and degree of intoxication as the definite quantity of the known extract of Cannabis Sativa. From this data can be determined the relative activity of the two samples of the preparation of Cannabis Sativa.

4. We believe, before this method of assay is adopted in the United States Pharmacopœia, arrangements should be perfected, so that some central authority, like the Bureau of Public Health and Marine Service Laboratory at Washington, would supply a standard extract of Cannabis Sativa to be employed by various manufacturers for standardizing their pharmaceutical preparations.

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THE PHYSIOLOGICAL ASSAY OF THE BLOOD PRESSURE RAISING PRINCIPLE FOUND IN PREPARATIONS OF SUPRARENAL GLANDS.

1. The active principle of the suprarenal glands produces a characteristic quantitative rise in the blood pressure of anesthetized animals injected intravenously.

Preparations of suprarenal glands containing such active principle may be assayed quantitatively by comparing the MAXIMUM blood pressures produced by the injection of definite quantities of the preparation properly diluted into the circulatory system, with the MAXIMUM rise in blood pressure produced by the injection of definite quantities of similarly diluted active principle of the suprarenal glands UNDER THE SAME CONDITIONS.

2. The animal best adapted for the making of the blood pressure experiments for the determination of quantitative amounts of the active principle of the suprarenal glands, is the dog.

3. The test animal, the dog, should be anesthetized by some member of the fatty acid series, tri-chlor-tertiary-butyl-alcohol being especially recommended for this purpose.

4. The apparatus required is a mercury manometer with suitable connections properly arranged for making blood pressure tracings.

5. Method. The test animal is anesthetized about one-half hour before the test is to be made. When anesthesia is complete, the dog is fastened to a suitable board or warming-pan and the artery and vein chosen, a carotid artery and each femoral vein, are opened and glass cannulæ inserted, or the injections may be made into the vein through a small hypodermic needle.

6. The active principle, the standard, by which the value of the known shall be determined, should be chemically pure. This substance should be dissolved in freshly prepared physiologic salt solution, in the proportion of 0.000,01 gm. to 1 cc., or 1:100,000.

7. The unknown should be freshly prepared in physiologic SALT solution so that it will have approximately the same activity as the known. Two or more injections of the standard solution of the active principle of the suprarenal glands prepared as directed under 6 should be made into the vein chosen, and the rise in blood pressure observed in order to determine whether the animal is in a suitable condition for making a quantitative blood pressure measurement. If the animal has been found to react quantitatively to the known, then alternate injections of the solutions of the known, 6, and the unknown, 7, should be administered into the vein chosen, until the quantity of the solution of the unknown has been found, that will show the same rise in blood pressure under the same conditions as a given quantity of the standard. From this data can be figured the percentage strength of the unknown as compared with the known.

8. We believe that some central authority, like the Laboratory of the American Public Health and Marine Hospital Service should be requested to supply to such parties as wish to assay the active principles of the Suprarenal Glands, chemically pure Adrenalin or its equivalent Epinephrin as a standard.