COMMITTEE REPORTS

REPORT OF COMMITTEE ON PHYSIOLOGIC ASSAYING, AMERICAN PHARMACEUTICAL ASSOCIATION, 1922.*

BY PAUL S. PITTENGER, CHAIRMAN.

In order to determine which of the various biologic methods of testing digitalis was being employed by the various workers throughout the country, your chairman last year addressed to practically all of the experts throughout the country, the following questionnaire on digitalis.

Last Year's Biological Assay Questionnaire.

1. What biologic method do you use in standardizing the Digitalis Series?
2. Give detailed outline of technique employed.
3. What do you consider the principal advantages of the method which you use as compared with other commonly used methods?
4. What method do you prefer?
5. Would you consider it a practical plan not to make any method of assay official, but simply to state the U. S. P. standard in terms of the most commonly used methods and thus permit the use of any recognized method as a means of standardization.
6. In case this scheme is favored it would be necessary to coördinate the different methods of technique so that whatever one is followed, the standard by that method would be equivalent to the standard by any other one.

ASSAY METHODS EMPLOYED BY DIFFERENT WORKERS.

The replies received showed that of the various biologic methods employed for testing digitalis preparations, 16 workers employed the "One-Hour Frog Heart Method," 5 the "M. L. D. Guinea Pig Method," 2 the "M. L. D. Frog Method," and 2 the "Hatcher Cat Method."

The number of workers using a method, however, is not necessarily an index to its relative accuracy. It was thought advisable, therefore, that this year our committee do some coöperative laboratory work in order to see if results could be obtained showing the comparative accuracy of the various methods employed.

In coöperative tests which have been made by our committee heretofore, each worker was asked to assay the samples submitted by several different methods. A large variation was usually found in the results obtained.

We are of the opinion that a great deal of this variation has been due to the fact that the individual worker was asked to carry out tests, using methods not employed in his routine work.

TESTS BY REGULAR METHOD OF EACH WORKER.

It is natural that each worker obtains the best results with the method with which he is most familiar and uses daily in his laboratory.

In order to obtain additional information as to the relative accuracy of the proposed methods, the chairman accordingly sent a set of 3 samples of Tincture Digitalis to each member of this Committee, to the members of the "Sub-committee on Digitalis" of the American Drug Manufacturers' Association, and to a number of other workers interested in physiologic assaying.

Each was requested to assay the samples according *to the method or methods with which he is most familiar and uses in his routine work.* The results obtained follow:

Sample no.	Actual strength.	"M. L. D. Guinea Pig" (Quici).	"M. L. D. Guinea Pig" (Harvey).	"M. L. D. Guinea Pig" (Butts).	"One-Hr. Frog Heart" (Rowe).	"One-Hr. Frog Heart" (Hunt).	"One-Hr. Frog Heart" (Walters).	"M. L. D. Frog" (Rowe).
1	100	100	100	100	100	100	100	100
2	80	77.2	85	75	67	50	96.4	89
3	60	65.5	75	55	57	45–55	81.8	64

Sample no.	Actual strength.	"Cat" (Hatcher).	"Cat" (Rowe).	"Cat" (modified) (Newcomb).	? (Fiske).
1	100	100	100	100	100
2	80	72.9	93	74.9	93
3	60	84.2–92.6	76	54.3	70

* Received at Cleveland meeting, A. Ph. A., 1922.

You will note from the table that differences between results obtained and the actual strength of the samples are as follows:

Method employed.	Sample No. 2.	Sample No. 3.
M. L. D. guinea pig method.....	2.8 to 5.0%	5.0 to 5.5%
M. L. D. frog method.....	9.0%	4.0%
One-hr. frog method.....	13.0 to 30.0%	3.0 to 21.8%
Cat method.....	5.1 to 13.0%	5.7 to 32.6%

The relative strength of the 3 samples was to be determined by comparing samples No. 2 and No. 3 with sample No. 1 which was called 100%.

Samples No. 2 and No. 3 were dilutions of No. 1 prepared so that No. 2 was 80 percent of the strength of No. 1, and No. 3 was 60 percent of the strength of No. 1. Each set of samples, however, was simply labeled No. 1, 2 and 3, the members of the committee having no knowledge of their relative activity.

RELATIVE MERITS OF THE DIFFERENT METHODS.

The above results would indicate, therefore, that the "M. L. D. Guinea Pig Method" and the "M. L. D. Frog Method" are about equally accurate, that both are more accurate than either the "One-Hour Frog Heart Method" or the "Cat Method," and that the "One-Hour Frog Heart Method" is more accurate than the "Cat Method."

In addition to giving data as to the relative accuracy of the various methods, the above experiments bring out another important point, *i. e.*, that the greatest variation between the results obtained and the actual strength of the preparation was only 32.6 percent.

When we consider the fact that tinctures of digitalis vary 300 to 400 percent in activity it is apparent that if properly conducted, digitalis and its allies can be satisfactorily assayed and standardized by either the "M. L. D. Guinea Pig or Frog Method," the "One-Hour Frog Method," or the "Cat Method."

In conclusion, your Committee would recommend that a copy of this report be forwarded to the chairman of the U. S. P. Revision Committee for consideration in connection with preparing the chapter on "Biologic Assays."

Your chairman would also recommend that, in view of the increase in the number of laboratories engaged in routine biologic assaying and the increased importance of this work, the membership of this Committee be increased from five to seven members.

Respectfully submitted,

PAUL S. PITTENGER, *Chairman.*

REPORT OF COMMITTEE ON U. S. PHARMACOPOEIA, AMERICAN PHARMACEUTICAL ASSOCIATION.*

BY L. F. KEBLER, CHAIRMAN.

Most of the members of this committee have made suggestions bearing on pharmacopoeial revision and feel that pending action by the Revision Committee they do not consider it desirable to discuss such matters publicly, which accounts for this brief report. The chairman believes, however, that attention might be directed to the advantage of a uniform general working temperature even though the U. S. Pharmacopoeial Convention adopted a recommendation of temperatures to be used by the Committee of Revision.

Those engaged in regulatory work, federal, state and municipal, as well as manufacturers are desirous of having written into the Pharmacopoeia the best available methods and up-to-date standards but what is wanted more are uniform methods of analysis so far as practicable. It is believed that a little thought and concession on the part of all concerned will make this possible. Simply because a certain temperature and routine has prevailed in a given industry for years ought not to stand in the way of yielding certain points for the common good. It may mean some inconvenience, confusion and money outlay, in the beginning for many, but in the end all will be benefited. At the 1921 meeting of the Association of Official Agricultural Chemists, some of these features were discussed and a committee appointed. In order to obtain the views of the association members the following questionnaire was sent out:

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* Presented at the Cleveland meeting of the American Pharmaceutical Association, 1922.