MONDAY, AUGUST 28TH, AT 6:00 P.M.—*N. A. B. P. Banquet.*

TUESDAY, AUGUST 29TH, 9:00 A.M.—*Joint Session with American Association of Colleges of Pharmacy.*

1. Report of Fairchild Scholarship Committee, E. G. Eberle, *Chairman.*
2. Paper: "Is Compulsory Apprenticeship Registration Working a Hardship on Young Men Entering Pharmacy?" C. B. Jordan, R. W. Sterling.
3. Resolutions from District Meetings, A. F. Schlichting, A. C. Taylor.

TUESDAY, AUGUST 29TH, 2:30 P.M.—*Final Session.*

1. Report of Department of Education, R. L. Swain, *Director.*
2. Report of Committee on President's Address.
3. Report of Publicity Committee, F. D. Pierce, *Chairman.*
4. Report of Committee on Prerequisite Legislation, W. R. Acheson, *Chairman.*
5. Report of Grievance Committee, A. H. King, *Chairman.*
6. Final Report of Credentials Committee.
7. Report of Resolutions Committee, A. C. Taylor, *Chairman.*
8. Report of Committee on Constitution and By-Laws, Duncan Weaver, *Chairman.*
9. Reports of Special Committees.
10. Unfinished Business.
11. New Business.
12. Report of Nominating Committee.
13. Election and Installation of Officers.
14. Adjournment.

COMMITTEE REPORTS

REPORT OF SUB-COMMITTEE ON DIGESTIVE FERMENTS AND GLANDULAR PRODUCTS.*

Three subjects were studied during the past year, whole pituitary substance, trypsin and rennin.

WHOLE PITUITARY POWDER.

It will be recalled that at last year's meeting, a report was made on the oxytocic activity of whole pituitary powder, and that it was voted to re-assay the composite sample this year as well as to prepare and assay a new composite.

This has been done. The composite was prepared, as was last year's, by thoroughly mixing equal weights of whole pituitary powder donated by Armour & Co., Digestive Ferments Co., Eli Lilly & Co., Parke, Davis & Co. and The Wilson Laboratories.

The method of preparing the solution for assay by the collaborators was the same as that used last year.

It was requested that last year's composite sample be re-assayed to ascertain if it had lost any activity.

The results are as follows:

WHOLE PITUITARY POWDER.

Lab.	1933 Sample.	1932 Sample Assayed 1932.	1932 Sample Assayed 1933.
1	160	90	90
2	125	89	87
3	120	80	80
4	125	...	80
5	...	65	65
6	150	100	80
Average	136	85	80

All figures are expressed in international units per Gm.

* Presented at the Twenty-Second Annual Meeting of the American Drug Manufacturers' Association held at Hot Springs, Virginia, May 8–11, 1933.

From the table, it will be seen that the 1933 composite is considerably stronger than the 1932, the average being 136 international units per Gm. as against 85 units for the 1932 composite, as reported last year.

The average of the 1932 composite assayed in 1933 was 80 units as against 85 units last year. Four laboratories report practically identical results for the two years, and the only large variation was that of Laboratory 6. From this, it may be concluded that the 1932 composite has not lost any oxytocic activity in one year.

Why the 1933 composite should be so much stronger than the 1932 is not apparent. Last year, it was agreed to adopt tentatively a value of 75 international units per Gm. In the light of this year's work, it may be desirable to revise this figure. Furthermore, a 1934 composite would add valuable information, as to the variations in strength that could be expected.

The values found by the different laboratories are in excellent agreement considering the nature and limitations of the method. This agreement is due, for the most part, to the use of a standard pituitary powder as a basis of comparison. Without such a standard, it is doubtful if the results would agree so closely. This is an example of the utility of a standard sample, where the method of assay *per se* is subject to wide variations.

It is recommended that

1. A 1934 composite whole pituitary powder be prepared and assayed.
2. The 1932 composite be re-assayed to determine its further keeping qualities.
3. The definition for whole putuitary powder adopted last year be tentatively changed to read as follows:

> Whole pituitary powder, derived from cattle, swine or sheep, shall contain not less than 100 international units per Gm.

TRYPSIN.

Last year, an A. D. M. A. reference trypsin was adopted tentatively, with the recommendation that it be re-assayed this year. Eight laboratories collaborated.

The methods of assay were the same as employed last year, *viz.*, the U. S. P. X method and the Smith-Sorensen method. The results are shown in the following table:

TRYPSIN.

Lab.	U. S. P. Method, 1933.	Smith-Sorensen, 1933.	U. S. P. Method, 1932.	Smith-Sorensen, 1932.
1	20.0	23.6	25.0	25.0
2	32.0	26.8	35.0	23.5
3	26.3	28.0	37.5	35.8
4	25.0	26.3	25.0	26.3
5	23.8	23.9	25.0	25.6
6	30.0	31.8	25.0	25.8
7	25.0	34.0	25.0	26.9
8	33.0	36.3	33.3	37.5
Average	26.9	28.8	28.8	28.3

The figures mean the number of parts of casein digested by one part of the trypsin.

It will be noted that the average strength by the U. S. P. method in 1932 was 28.8, whereas this year it is 26.9; by the Smith-Sorensen method 28.3 in 1932 and 28.8 in 1933. This would indicate that the reference trypsin had not undergone any serious deterioration, if any, during the past year.

Comments by various laboratories are worthy of mention.

Laboratory 1.

> "It will be noted that the reference sample has shown deterioration and that the U. S. P. X method indicates a greater loss in potency than does the modified Smith-Sorensen method.
>
> "Our experience leads us to believe that trypsin is distinctly unstable.

"We believe that the modified Smith-Sorensen method appears the means of providing a standard assay procedure, at least until something better is proposed. For instance a sample of trypsin requiring not less than 2 cc. of exactly $N/20$ sodium hydroxide solution would be considered to meet the U. S. P. requirement."

Laboratory 3.

"We re-assayed the six samples that had been used to make up this reference standard, and I give you below the comparative tests on all six as made in 1931 and again as recently retested.

	U. S. P. Method.		Smith-Sorensen Method.	
	(1931) Per Cent.	(1933) Per Cent.	(1931) Per Cent.	(1933) Per Cent.
No. 1	120	110	112	122
No. 2	100	85	123	112
No. 3	105	90	100	86
No. 4	110	105	98	101
No. 5	105	110	128	127
No. 6	100	90	100	91

"From these results it will be observed that the two methods check very closely in regard to deterioration of samples with the exception of No. 2. In samples Nos. 3 and 6 there appears to be about a 10 per cent loss in activity."

Mr. Taylor calls attention to a lack of preciseness in the directions of the U. S. P. method, with regard to the time that should elapse between the removing of the tubes from the bath and the adding of the acetic acid-alcohol mixture. Also, that there is no specification of temperature to which the tubes should be cooled before adding the acid-alcohol mixture. Both of these factors affect the accuracy of the end-point.

"There is a point to be observed in regard to the Smith-Sorensen method that has to do with adjustment of the hydrogen-ion concentration. From our experience we do not believe phenol red a satisfactory indicator for adjustment of casein solutions. In the work we did on this particular method several years ago we tried phenol red and could not obtain satisfactory results, so we carried out our adjustments using brom thymol blue and thymol blue as indicators. We were able in this way to adjust solutions to a definite p_H colorimetrically which we were able to check almost perfectly by potentiometric means."

Mr. Willson, of Parke, Davis & Co., is working on the details of a revised simplified method of preparing the casein solution. This would be a big advantage, since the present method of making the casein solution for the Smith-Sorensen method is time-consuming, and is the main objection to the method.

Mr. W. H. Blome called attention to an uncertainty in the directions for making up the casein solution for the Smith-Sorensen method, in that a 4 per cent solution could not be obtained if the final volume was as directed and no allowance made for the portions of the solution used to determine the p_H. Inquiry among the collaborators disclosed that practically all of them had recognized the discrepancy and had made up the final solution on a 4 per cent basis.

The Smith-Sorensen method appears to be gaining favor among the collaborators. It has the advantage over the present U. S. P. method of greater preciseness of end-point, and would not require a standard reference trypsin.

RECOMMENDATIONS.

It is recommended that

1. The present study of the A. D. M. A. reference trypsin be continued.
2. The Smith-Sorensen method be studied more critically with a view to simplifying it, and ascertaining its accuracy.
3. The U. S. P. Revision Committee be asked to postpone final action on pancreatin as long as possible, so that the A. D. M. A. may study certain improvements in the methods of assay.

RENNIN.

This year's work consisted of a further study of the keeping qualities of the A. D. M. A. reference rennin. The collaborators were asked to test the rennin by the National Formulary Fifth Edition Method.

The results are contained in the following table:

RENNIN.

Lab.	Time of Coagulation (Minutes).	Milk.	Acidity before Adjustment (Per Cent).	Acidity after Adjustment.
1	9.5	Certified	0.144	Not adjusted
1	10.0	Pasteurized	0.140	Not adjusted
2	9.5	Pasteurized	0.140	0.146
3	11.75	Pasteurized	0.142	Not adjusted
4	11.16	Pasteurized	0.145	Not adjusted*
4	11.75	Pasteurized	0.145	Not adjusted†
4	10.42	Pasteurized	0.145	Not adjusted‡
5	10.5	Grade A Raw	0.144	Not adjusted
6	10.25	Pasteurized	0.144	Not adjusted
7	11.5			0.147
8	12.25	Grade A	0.165	Not adjusted
8	22.0	Grade A	0.165	0.150

*Milk two days old. † Milk one day old. ‡ Milk four hours old.

Laboratory No. 1 comments,

"Two reference samples submitted to us in October of 1928, have also been re-assayed at this time and have shown no appreciable deterioration.

"Our experience indicates that rennin is stable over a period of years. We would recommend that a standard rennin be adopted."

Laboratory No. 3 states,

"We have had a peculiar experience in retesting the A. D. M. A. reference rennin according to the National Formulary 5th Edition Method. Our first test was as follows:

Curdling time: 17 minutes 5 seconds.
Kind of milk: Pasteurized.
Acidity: 0.141 per cent lactic acid (no adjustment).

"This result on curdling time is much different from results obtained during the past several years using this same sample. The curd obtained instead of being firm as it usually is, was stringy. We attributed this slowness in curdling to the sample of milk used although its acidity was almost exactly that which is desired and there was no adjustment of acidity by addition of alkali. Subsequently we obtained another quantity of milk from the same dairy and the test on the standard rennin results as follows:

Curdling time: 11 minutes 45 seconds.
Kind of milk: Pasteurized.
Acidity of milk: 0.142 per cent lactic acid (unadjusted).

"The first test above is the first one in several years of testing that has been outside the limits of 9 minutes to 13 minutes curdling time. Usually we have been able to blame variations of curdling time upon variations in acidity and especially attempts to adjust the acidity artificially. In this case these factors are not involved but it appears that this is one more fact indicating that variation in milk supplies sometimes unknown may very materially affect the result of the rennin test.

"We have made it a rule not to use for the test any milk that exceeded an acidity of 0.15 per cent calculated as lactic acid and we have abandoned altogether any idea of adjusting milk that is more acid by adding sufficient alkali. If the milk is not naturally at the proper acidity, we do not use it.

"I am decidedly of the opinion that in the next revision of the National Formulary adjustment of the milk by the addition of alkali should be omitted but that preferably a test for acidity should be included and milk that runs more than 0.15 per cent acidity as lactic acid should not be used.

"Of course, with a reference standard for direct comparison it does not make so much difference if the acidity varies somewhat and the adoption of such a standard would help to eliminate the errors that may occur due to variations in sources of supply of milk."

Laboratory No. 4 states,

"These tests indicate that, compared with the laboratory test last year, this rennin standard has decreased slightly in activity."

Laboratory No. 5 concludes that the standard rennin "curdles the milk in slightly less time than we reported last year." This laboratory also makes the suggestion that the titration for acidity can be made more sensitive, if five drops of the milk being titrated be added to 5 cc. of water. The pink color shows up better. It is customary to use 50 cc. of the milk, to which 0.5 cc. of phenolphthalein solution has been added. After the preliminary titration a second one should be made using just a little less than expected amount of alkali.

Laboratory No. 6 remarks that this year's results "are very close to those which we reported last year."

This year's work confirms the previous conclusion that the National Formulary Fifth Edition Method is unsatisfactory and unreliable, and that a standard rennin would overcome the difficulties inherent in the present method. The work adds another year's cumulative evidence for the excellent keeping quality of the A. D. M. A. reference rennin and its suitability as a standard in case a method based upon the use of a standard is adopted in the National Formulary Sixth Edition.

RECOMMENDATIONS.

It is recommended that,

1. The study of the keeping quality of the A. D. M. A. reference rennin be continued.
2. On behalf of the American Drug Manufacturers' Association, a revised method for the assay of rennin be submitted to the National Formulary Sixth Edition Revision Committee. Such method will make use of a standard rennin and will omit adjustment of the acidity of the milk.

In conclusion, I want to express my very sincere appreciation to the members of the committee for their splendid collaboration during these many years. It is hoped that their efforts will result in improved methods of assay in the forthcoming editions of the United States Pharmacopœia and of the National Formulary.

DAVID KLEIN, *Chairman*,	HOWARD T. GRABER,
W. H. BLOME,	F. W. HEYL,
H. A. B. DUNNING,	H. W. RHODEHAMEL,
B. TAPPEN FAIRCHILD,	F. O. TAYLOR,
FREDERIC FENGER,	D. M. FINDLAY.

DETERMINATION OF TAUROCHOLIC ACID IN BILE SALTS.*

F. E. WILLSON.

The bile contains as its chief constituents, taurocholic acid and glycocholic acid. These generally occur as the sodium salts and are not to be found in the pancreatic juice or in any of

* Presented at the Twenty-Second Annual Meeting of the American Drug Manufacturers' Association held at Hot Springs, Virginia, May 8–11, 1933.