COMMITTEE REPORTS

THE BIOLOGIC PRODUCTS COMMITTEE REQUESTS COÖPERATION OF RETAIL PHARMACISTS.

The Biologic Products Committee of the National Retail Druggists and American Pharmaceutical Associations, mailed a few months ago a postal card to practically every druggist throughout the country. Drug publications devoted valuable space to strong propaganda requesting the readers to answer these cards. Many prominent publications gave unsolicited editorials, commending the committee's work and also urging the pharmacists to answer at once. But the replies were very disappointing.

Less than 11% took the trouble to inform the committee whether or not they carry Biologic Products. Not quite 600 of the 52,000 retail pharmacists considered it necessary to answer. Why this indifference? The committee does not attempt to force anything that is undesirable upon the profession. In fact, in its report to the N. A. R. D. Convention at Memphis it distinctly stated, "We do not advocate placing Biologicals in all drug stores, only in those having good prescription trade and with pharmacists who believe in cultivating the physician either for his prescriptions or his business. We think that no retail store should attempt to carry Biologics unless the store has mapped out a policy for building up a department."

It is imperative to know the percentage of druggists handling these products, and also, how the stores that are carrying Biologicals are distributed throughout the country.

As Chairman of this Committee, I repeat my statement—Millions of patients are treated throughout the country, with this method of medication, and there will probably be millions more in the future, as the use of this method is continually increasing.

The general public and patients are quite well acquainted now with this new "method." Therefore, there has arisen the question, "Who is the dispensing medium?"

Will you give your help to solve the question? Remember that with the steady increase in medication, with biologicals and ampuls, and the natural decrease in prescriptions for other medicines, a druggist must be on the alert to preserve the "dispensing" department for the sake of the protective legislation such as the pharmacy ownership bills, or similar regulations.

It is not too late to give the Committee a hand in solving the problem involved, by digging up the card, or answering the following questions (preferably on a post card).

1. Do you handle Biological Products?
2. Give the names of the most often prescribed Biologicals and name of manufacturer.
3. Do your physicians purchase Biological Products from retail pharmacists or from physicians' supply houses?
4. Do you keep Biologicals in a refrigerator?
5. Your suggestions for Committee to improve Biological Business.

Coöperate with a committee that is willing to work and produce desirable results.

Address
151 St. Anns Ave.,
Bronx, N. Y.

Samuel S. Dworkin, Chairman
Biologic Products Committee
National Retail Druggists and
AMERICAN PHARMACEUTICAL ASSOCIATION

REPORT OF JOINT CONTACT COMMITTEES OF THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION AND THE AMERICAN PHARMACEUTICAL MANUFACTURERS' ASSOCIATION TO THE BUREAU OF CHEMISTRY.*

We beg to submit the following report, containing recommended methods and proposed tolerances for additional hypodermic tablets, constituting a continuation of our report of November 24, 1924.

HYPODERMIC TABLETS—CODEINE PHOSPHATE.

Hypodermic tablets of codeine phosphate shall show a content of codeine alkaloid anhydrous ($C_{18}H_{21}O_3N$) not less than 61% nor greater than 73% of the labeled amount of codeine phosphate, when assayed by the method given below.

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* See also JOUR. A. PH. A., August 1925, p. 691 and January JOURNAL, p. 112.

Dissolve not less than 20 tablets in enough distilled water to make 100 cc. and take an aliquot equivalent to at least 1 grain of codeine phosphate. Add sodium hydroxide T. S. in quantity sufficient to render the solution distinctly alkaline. Shake out with 4 successive portions of 15 cc., 10 cc., and 5 cc. of chloroform, or a sufficient quantity to complete the extraction. Shake the combined chloroform solutions with 5 cc. of distilled water and completely separate the chloroform from the aqueous layer. Evaporate the chloroform almost to dryness on the water-bath, dissolve the residue by warming with 10 cc. of $N/20$ sulphuric acid, and titrate the excess of acid with $N/50$ potassium hydroxide solution, using methyl red test solution as indicator.

Each cc. of $N/20$ sulphuric acid consumed corresponds to 0.014964 Gm. of codeine alkaloid anhydrous ($C_{18}H_{21}O_3N$).

HYPODERMIC TABLETS—PILOCARPINE HYDROCHLORIDE.

Hypodermic tablets of pilocarpine hydrochloride shall show a variation (including all tolerances) not greater than 7.5% either way from the labeled amount, when assayed by the method given below.

Dissolve not less than 20 tablets, or a sufficient number to represent not less than 1 grain of pilocarpine hydrochloride, in enough distilled water to make a clear solution, and take enough of this solution to represent at least 1 grain. Make the aqueous solution distinctly alkaline with ammonia and shake out with several portions of chloroform until tests with Mayer's reagent indicate that the aqueous solution has been completely exhausted of the alkaloid. Evaporate the combined chloroform solution to dryness on the water-bath. Dissolve the residue in a few cc. of neutral alcohol. Add 10 cc. of $N/20$ sulphuric acid and titrate the excess of acid with $N/50$ potassium hydroxide solution, using methyl red indicator.

Each cc. of $N/20$ sulphuric acid consumed corresponds to 0.012234 Gm. of pilocarpine hydrochloride ($C_{11}H_{16}O_2N_2HCl$).

HYPODERMIC TABLETS—CAFFEINE AND SODIUM BENZOATE.

Hypodermic tablets of caffeine and sodium benzoate shall show a content of caffeine alkaloid anhydrous ($C_8H_{10}O_2N_4$) not less than 43.5% nor greater than 53.7% of the labeled amount of caffeine and sodium benzoate, when assayed by the method given below.

Dissolve not less than 20 tablets in a minimum amount of distilled water in a separatory funnel. Add 3.5 cc. sodium hydroxide T. S. and shake the mixture with 4 successive portions of 20 cc., 10 cc., 10 cc., and 5 cc. of chloroform. Pass the chloroform solutions through a filter which has been previously moistened with chloroform, and wash the stem of the funnel and filter with a few cc. of hot chloroform to remove any adhering caffeine. Evaporate the combined chloroform solutions on a water-bath and dry the residue, consisting of anhydrous caffeine ($C_8H_{10}O_2N_4$) to constant weight at 80° C.

HYPODERMIC TABLETS—CAFFEINE

Hypodermic tablets of caffeine shall show a variation (including all tolerances) not greater than 7.5% either way from the labeled amount, when assayed by the method given below.

Dissolve not less than 20 tablets in a minimum amount of distilled water in a separatory funnel. Add 3.5 cc. of sodium hydroxide test solution and shake the mixture with 4 successive portions of 20 cc., 10 cc., 10 cc., and 5 cc. of chloroform.

Pass the chloroform solution through a filter which has been previously moistened with chloroform, and wash the stem of the funnel and filter with a few cc. of hot chloroform to remove any adhering caffeine. Evaporate the combined chloroform solutions on a water-bath and dry the residue, consisting of anhydrous caffeine ($C_8H_{10}O_2N_4$), to constant weight at 80° C.

Multiply the weight of this residue by 1.093 to obtain the weight of caffeine in the sample examined.

HYPODERMIC TABLETS—APOMORPHINE HYDROCHLORIDE.

Hypodermic tablets of apomorphine hydrochloride shall show a variation (including all tolerances) not greater than 9% either way from the labeled amount, when assayed by the method given below.

Dissolve not less than 20 tablets in enough distilled water to make 100 cc. and take an aliquot equivalent to at least 1 grain of apomorphine hydrochloride. To the aqueous solution

add 0.5 Gm. of sodium bicarbonate and shake out with several portions of ether, until the aqueous layer is shown to be completely exhausted of alkaloid, using Mayer's reagent for the test. Combine the ether extracts in a separatory funnel, and wash out three times with 5 cc. of distilled water, separating the water carefully and completely after each shaking and collecting it in a second separatory funnel. Shake out the united water washings once with a small portion of ether. Separate completely and add the ether washings to the combined ether extracts. To the ethereal solution add a measured excess (10 cc.) of $N/20$ sulphuric acid. Shake the mixture thoroughly and draw off the aqueous layer into a small flask or beaker. Wash the ethereal solution twice more with small portions of distilled water and add to the acid liquid. Finally, titrate the excess of acid with $N/50$ potassium hydroxide, using methyl red indicator.

Each cc. of $N/20$ sulphuric acid corresponds to 0.015636 Gm. of apomorphine hydrochloride ($C_{17}H_{17}O_2NHCl.{}^1/_2H_2O$).

HYPODERMIC TABLETS—HYOSCINE HYDROBROMIDE.

Hypodermic tablets of hyoscine hydrobromide containing small grainages ($^1/_{60}$ gr. or less) may show the same variation (including all tolerances) finally allowed for atropine sulphate tablets of like grainage, when assayed by the method given below.

Dissolve a sufficient number of tablets to represent at least 1 grain of hyoscine hydrobromide in enough distilled water to make a clear solution.

Make the aqueous solution distinctly alkaline with ammonia and shake out with several portions of chloroform, until tests with Mayer's reagent indicate that the aqueous solution has been completely exhausted of the alkaloid. Evaporate the combined chloroform solutions to dryness on the water-bath. Dissolve the residue in a few cc. of neutral alcohol. Add 10 cc. of $N/20$ sulphuric acid and titrate the excess of acid with $N/50$ potassium hydroxide, using methyl red for the indicator.

Each cc. of $N/20$ sulphuric acid consumed corresponds to 0.021912 Gm. of hyoscine hydrobromide ($C_{17}H_{21}O_4N.HBr.3H_2O$).

HYPODERMIC TABLETS—PROCAINE.

Hypodermic tablets of procaine shall show a variation (including all tolerances) not greater than 7.5% either way from the labeled amount, when assayed by the method given below.

Dissolve not less than 20 tablets in enough distilled water to make 100 cc. and take an aliquot equivalent to at least 3 grains of procaine.

Make the solution strongly alkaline by the addition of 3 cc. of strong ammonium hydroxide. Extract the ammoniacal solution four or five times with chloroform, using 15 cc. of chloroform for the first extraction and 10 cc. for the subsequent extractions. Filter into a weighed beaker and evaporate the chloroform by means of an electric fan, preferably at room temperature. (Avoid prolonged heating of the procaine base, as it appears to be slightly volatile at 100° C.).

Calculate the quantity of procaine in the sample by multiplying the weight of extracted residue by the factor 1.1545.

Take up the residue with a slight excess of $N/20$ sulphuric acid. Titrate the excess of acid with $N/50$ sodium hydroxide, using methyl red indicator. One cc. of $N/20$ sulphuric acid is equivalent to 13.63 mgms. of procaine ($C_{13}H_{20}O_2N_2HCl$).

This method is the official method of the A. O. A. C., 1925 edition, page 403.

HYPODERMIC TABLETS—MORPHINE AND ATROPINE.

Hypodermic tablets of morphine and atropine shall show a variation in content of morphine sulphate (including all tolerances) not greater than 9% either way from the labeled amount, when assayed by the method given below. The tablets shall also show the presence of atropine when subjected to a physiological test.

Take a sufficient number of tablets to represent about 8 grains of morphine sulphate, place in 100-cc. Erlenmeyer flask, and dissolve in 12 cc. of morphinated water. Add, drop by drop, 10% ammonia water, until the solution positively smells of ammonia. Shake thoroughly, and let the flask stand aside in a cool place over night. Filter off on paper the crystals of morphine alkaloid, and wash the crystals with morphinated water. Wash the crystals once with a little distilled water to replace the morphinated water. Then place filter paper and contents in the

Erlenmeyer flask and add 20 cc. of $N/10$ sulphuric acid. Break up the filter paper with a glass rod. Heat for about 1 hour, until the filter paper contents are completely dissolved, and then titrate with $N/50$ potassium hydroxide, using methyl red as indicator.

Each cc. of $N/10$ sulphuric acid consumed corresponds to 0.037932 Gm. of morphine sulphate U. S. P. $(C_{17}H_{19}O_3N)_2H_2SO_4.5H_2O$.

HYPODERMIC TABLETS—PHYSOSTIGMINE SULPHATE, HYPODERMIC TABLETS—PHYSOSTIGMINE SALICYLATE.

Hypodermic tablets of physostigmine sulphate shall show a variation (including all tolerances) not greater than 10% either way from the labeled amount, when assayed by the method given below.

Hypodermic tablets of physostigmine salicylate shall show a variation (including all tolerances) not greater than 9% either way from the labeled amount, when assayed by the method given below.

In case of tablets containing $^1/_{20}$ grain of physostigmine sulphate (or physostigmine salicylate) dissolve at least 20 tablets in enough distilled water to make 100 cc. and take an aliquot equal to at least 1 grain of physostigmine sulphate (or physostigmine salicylate).

In case of tablets containing less than $^1/_{20}$ grain of physostigmine sulphate (or physostigmine salicylate) dissolve a sufficient number to represent at least 1 grain of physostigmine sulphate (or physostigmine salicylate) in enough distilled water to make a clear solution.

In either case make the aqueous solution alkaline with sodium bicarbonate, and shake out with several portions of ether, until the aqueous layer is shown to be completely free of alkaloid, using Mayer's reagent for the test. Combine the ether extracts and wash with several portions of distilled water until the ether extracts are free from alkali. Evaporate the major portion of the ether on the steam-bath, finally allowing the remainder to be dissipated at room temperature. Dissolve the residue in a few cc. of neutral alcohol. Add 10 cc. of $N/20$ sulphuric acid, and titrate the excess of acid with $N/50$ potassium hydroxide, using methyl red as indicator. Each cc. of $N/20$ sulphuric acid corresponds to 0.016215 Gm. of physostigmine sulphate $(C_{15}H_{21}O_2N_3)_2$-H_2SO_4 or 0.020667 Gm. of physostigmine salicylate $(C_{15}H_{21}O_2N_3C_7H_6O_3)$.

HYPODERMIC TABLETS—CORROSIVE SUBLIMATE.

Hypodermic tablets of corrosive sublimate shall show a variation (including all tolerances) not greater than 9% either way from the labeled amount, when assayed by either of the methods given below.

In case of tablets containing $^1/_{20}$ grain of corrosive sublimate, or more, dissolve at least 20 tablets in enough distilled water to make 100 cc., and take an aliquot equal to at least 1 grain of corrosive sublimate.

In case of tablets containing less than $^1/_{20}$ grain of corrosive sublimate, dissolve a sufficient number to represent at least 1 grain of corrosive sublimate in enough distilled water to make a clear solution. For determination of the mercury use the electrolytic method described in U. S. P. X, or, as an alternative, the hydrogen sulphide method of the U. S. P. X. The weight of mercury in the electrolytic process multiplied by 1.353 represents the weight of corrosive sublimate.

The weight of the mercuric sulphide obtained in the hydrogen sulphide method multiplied by 1.167 represents the weight of corrosive sublimate.

HYPODERMIC TABLETS—EMETINE HYDROCHLORIDE.

While recognizing that the legal standard for emetine hydrochloride as given in the U. S. P. X permits as much as 19% of moisture on drying, nearly twice as much moisture as is suggested in this recommendation, the Committees offer this method and tolerance as consistent with the best production practices now prevailing, and believe that this action will be a guide for the commercial production of these hypodermic tablets in the future.

In accordance with this plan, hypodermic tablets of emetine hydrochloride shall show a variation (including all tolerances) in content of emetine hydrochloride containing 10% of water not greater than 7.5% either way from the labeled amount, when assayed by the method given below.

Dissolve not less than 20 tablets in enough distilled water to make 100 cc., and take an aliquot equivalent to at least 1 grain of emetine hydrochloride. Make the aqueous solution alka-

line with sodium hydroxide, and shake out with several portions of ether, until the aqueous layer is shown to be completely exhausted of alkaloid, using Mayer's reagent for the test. Combine the ether extracts and wash with several portions of distilled water, until the ether extracts are free from alkali. Evaporate the major portion of the ether on a steam-bath, allowing a small portion of ether to remain to prevent complete dryness. Add a few cc. of neutral alcohol, Add 10 cc. of $N/20$ sulphuric acid and titrate the excess of acid with $N/50$ potassium hydroxide, using methyl red as indicator. Each cc. of $N/20$ sulphuric acid corresponds to 0.015818 Gm. of emetine hydrochloride containing 10% of water ($C_{15}H_{22}O_2N.HCl$ (90%) + H_2O(10%)).

HYPODERMIC TABLETS—ARECOLINE HYDROBROMIDE.

Hypodermic tablets of arecoline hydrobromide shall show a variation (including all tolerances) not greater than 7.5% either way from the labeled amount, when assayed by the method given below.

Dissolve not less than 20 tablets in enough distilled water to make 100 cc. and take an aliquot equivalent to at least 4 grains of arecoline hydrobromide. Add an excess of $N/10$ silver nitrate, 3 cc. of 10% nitric acid, and 3 cc. of ferric ammonium sulphate test solution. Allow to stand about 5 minutes, and titrate the excess of silver nitrate with $N/10$ potassium thiocyanate until a faint brown color persists after shaking. Each cc. of $N/10$ silver nitrate corresponds to 0.02359 Gm. of arecoline hydrobromide.

This report, like the preceding recommendations made to the Bureau, is based upon such information as was at hand and which seemed applicable to the problem. The Committees do not feel, however, that all sources of information have been exhausted. Hypodermic tablet control, viewed in the light of the Committee recommendations, remains an open question as present day experience accumulates. The Committees hold themselves ready to receive information on all of these matters and regard all their recommendations as subject to future review and revision. As occasion arises, they will ask for such changes as experience may show to be advisable.

Respectfully submitted,

Contact Committee of the American Drug Manufacturers' Association,
J. P. SNYDER, *Chairman.*
December 9, 1925.

Contact Committee of the American Pharmaceutical Manufacturers' Association,
R. LINCOLN MCNEIL, *Chairman.*

EXHIBIT SHOWS HOOKWORM CONTROL FOR DOGS, CATS AND MAN.

"Carbon Tetrachloride" is the title of an illustrated, three-section exhibit prepared by the United States Department of Agriculture. Carbon tetrachloride, a well-known chemical, was proposed in 1921 by the Bureau of Animal Industry, of the Department, as a drug for the treatment of hookworm disease and is now in general use the world over for this disease in man and in dogs, cats and foxes. More than 1,500,000 human hookworm cases have been treated with the chemical.

One panel shows a photograph of two brothers, one 21 years old weighing only 66 pounds, a hookworm victim, while his brother who was only 17 years old and not infected with hookworms weighed 126 pounds. Another panel illustrates hookworms and gives information concerning the animals they affect. A third points out that carbon tetrachloride has saved the lives of thousands of dogs, especially of pups and hunting dogs in the South.

The exhibit is 30 inches high and when packed for shipment weighs approximately 75 pounds. A table 2 by 4 feet is suitable for displaying it. The exhibit will be loaned for a period not to exceed 30 days to responsible persons requesting it and agreeing to pay transportation charges. Applications will be filled in the order received and should be addressed to the Bureau of Animal Industry, United States Department of Agriculture, Washington, D. C.

The following has no reference to the foregoing paragraphs. Magazine sections of Sunday papers have recently had pages on the cruelty of "de-barking" dogs. When man's friend is serving for experimental work this operation may be necessary, but, with that exception, we are in agreement with those who register their opposition to the method which deprives a dog of his bark.