Tin: Stannous and stannic bromides and chlorides in concentrations of 5%. Red label.
Trinitrophenol: See Picric Acid.
Uranium: Acetate, nitrate, sulphate, in concentrations of 5%. Red label.
Veratrine: Alkaloid and salts in concentration of 1%.
Veratrum Viride: Drug and preparations in concentrations of 5%. Red label.
Water, Ammonia: In concentration of 5%. Red label.
Zinc: Acetate, bromide, chloride, nitrate, sulphate, in concentrations of 5%. Red label.

Respectfully submitted,

Committee on Potent and Toxic Drugs.
A. G. DuMez
S. L. Hilton
Robt. L. Swain
A. C. Taylor
J. H. Beal, *Chairman.*

NATIONAL CONFERENCE ON PHARMACEUTICAL RESEARCH.—COMMITTEE NO. 1.

PHARMACEUTICAL DISPENSING.

REPORT FOR YEAR ENDED MAY 31, 1932.

BY WILLIAM J. HUSA, CHAIRMAN.

During the year a number of interesting and valuable contributions dealing with various phases of dispensing pharmacy have appeared in the literature.

Opthalmic Ointments.—In a recent English article (1) the preparation of opthalmic ointments containing alkaloids or alkaloidal salts was discussed. These are usually made by one of four different methods, each of which has some advantages and some disadvantages. In the first method, the free alkaloid is dissolved directly in the fatty base with aid of heat. The disadvantage of this method arises from the use of heat, which may decompose the alkaloid or form a saturated solution at a higher temperature which will crystallize on cooling. The second method involves the preparation of a neutral alkaloidal oleate, which is then mixed with the fatty base. Here again the heat used in making the oleate may cause decomposition. In the third method, a readily soluble alkaloidal salt is dissolved in a very small quantity of water and this solution is incorporated in the base. The chief disadvantage of this process is that water may evaporate from the ointment on standing, with formation of crystals of the alkaloidal salt. In the fourth method the finely powdered alkaloidal salt is mixed with the ointment base; by this method it is difficult to obtain an ointment that is really as free from gritty particles as would be desired.

The method proposed for the new British Pharmacopœia involves the use of a base composed of equal parts of yellow soft paraffin and wool fat, the mixed fats being filtered while hot and then sterilized at 150° C. for one hour. The alkaloidal salt is dissolved in the smallest possible quantity of distilled water, the melted base is added and the mixture triturated until cold.

Lascoff (2) suggested that an opthalmic prescription calling for 5% of argyrol in vaseline should be filled by dissolving the argyrol in the minimum amount of water, taking this up with a small amount of lanolin and incorporating in the vaseline.

Insolubility of Pills.—In a French journal, Henri Griffon (3) reported that a person swallowed 100 granules, each containing 1 mg. of strychnine sulphate; after 3 hours, 25 granules were recovered intact by washing the stomach, along with 15 partially disintegrated granules. Similar reports have appeared at various times, indicating that sometimes pills and tablets will not dissolve or disintegrate due to some defect in the coating or method of manufacture, or due to hardening on long storage. Griffon recommends that tests be made in artificial gastric and pancreatic juices to determine whether or not disintegration takes place.

In this connection, two Danish pharmacists have reported (4) that pills or tablets made with agar-agar disintegrate more quickly than with other excipients. In this case dilute alcohol is used as a moistening agent.

Enteric Coating of Capsules.—The enteric coating of capsules appears to have received more attention recently in this country than in others. S. L. Hilton (5) has recommended coating with shellac, using a solution of white shellac in Spirit of Ammonia, U. S. P. VIII, followed by a coating of salol.

T. J. Bowers (6) recommends that the capsules be coated by spraying with melted salol, using a straight stem medicinal atomizer. One person shakes the capsules in a glass mortar while another sprays on the salol. Bowers states that after a little practice, 100 or more capsules can be coated in less than two minutes. He also states that the salol sticks to the capsules like glue. We have tested this method at the University of Florida and have found the method very convenient and rapid, but the salol soon becomes crystalline and fails to adhere sufficiently.

For making keratin-coated capsules, Lascoff recommends (7) that the capsules first be coated with an alcoholic solution of shellac in order to harden the capsule and present a suitable surface for the keratin. The keratin, dissolved in stronger ammonia water, is then applied. The coated capsules are inserted in empty capsules of the next larger size.

Incompatibilities.—The incompatibilities of silver protein compounds were discussed in an article published in England (8). It was stated that silver protein compounds are liable to precipitate alkaloids from solutions of their salts on account of the alkalinity, which is variable even in different samples of the same product. A 10% solution of argyrol gave a precipitate with very small quantities of cocaine hydrochloride, but was compatible with comparatively high proportions of cocaine nitrate. No incompatibility was observed in solutions containing 2% of cocaine hydrochloride and 10% of protargol, silver nucleinate or a non-proprietary brand of silver-vitellin. It was concluded that owing to the variations in the silver protein compounds it is inadvisable to mix them with cocaine salts, but if the alkaloid is necessary it should be used in the form of the nitrate.

In a Swiss journal, J. B. Lang reported (9) that an ointment consisting of cold cream with 2% of mercuric chloride becomes red, due to precipitation of basic mercuric chloride due to alkalinity of the borax present in the cold cream. This was prevented by addition of an amount of boric acid equal to the borax used.

Rupp and Poggendorf reported (10) that chloral hydrate reacts with both medinal and luminal in water solution, the chloral hydrate being hydrolyzed to chloroform and the barbituric acids being precipitated.

According to Ritsema (11) a precipitate occurs in the following solution on standing over night:

℞	Zinc sozoiodolic.	0.02
	Novocain	0.02
	Sol. Adrenaline (1/1000)	20.00
	Aq. borat.	15.00

The precipitate is novocain sozoiodolate. If one uses cocaine instead of novocain there is no precipitate at this concentration.

Fraase states (13) that there is no incompatibility between sodium bicarbonate and acetylsalicylic acid in capsules containing $2^1/_2$ grains of each substance, unless moisture is present far in excess of normal.

Some reports have also appeared on the stability of solutions of acetylsalicylic acid. As is well known, this substance is only slightly soluble in water, but is more soluble in solutions of sodium or potassium citrate. According to Stroud (14), in such solutions about 40% of the acetylsalicylic acid hydrolyzes into acetic and salicylic acids in three days at room temperature. If the fresh solution is boiled a few minutes, complete hydrolysis takes place, hence Stroud warns against the use of heat in preparing these solutions. Germuth (15) studied the rate of hydrolysis of acetylsalicylic acid in ethanol, glycerin, water and various mixtures of these solvents. Hydrolysis increased with time and with increasing percentage of water. A mixture of equal parts of ethanol and glycerin, in presence of water, caused slightly less hydrolysis than was brought about by either solvent alone with water. A. H. Clark (16) also worked on this problem. According to his results, the best proportions for keeping hydrolysis at a minimum are as follows: 3 parts of potassium citrate are dissolved in 15 or 20 parts of water, 1 part of acetylsalicylic acid is added, and the solution is saturated with sugar.

The precipitation of strychnine from solutions of its salts sometimes observed on addition of alkali iodides has been variously ascribed to alkalinity of the iodide, salting out of the strychnine salt, formation of the hydriodide and formation of a complex iodide. Hargreaves (17) reported that when strychnine sulphate solutions are treated with alkali iodide or HI, strychnine hydriodide is formed, having a solubility of 1 Gm. in about 345 cc. of H_2O at 25°, but much less soluble in presence of excess of soluble iodide. Strychnine periodide, of low solubility, is formed when a very dilute solution of iodine reacts on strychnine hydriodide.

Lanwermeyer reported (18) on the incompatibilities of a number of drugs including amidopyrine, acriflavine (base), acriflavine hydrochloride, anesthesin, barbital, barbital sodium, butesin, butyn, neonal, phenobarbital sodium and ephedrine salts.

Emulsions.—An interesting emulsion was described in an English article (19). The prescription was for a cod liver oil emulsion containing, among other ingredients, lime water and mucilage of acacia. The difficulty arose from the fact that emulsions made with lime water are of the water-in-oil type, while acacia emulsions are of the oil-in-water type, and two such emulsions are as immiscible as oil and water alone.

Suppositories.—Schroff (20) has contributed to our knowledge of suppositories by extending the work of Rapp, who showed that the presence of water is of greatest importance for the absorption of drugs from the intestine. Schroff indicates that suppositories with a base of cacao butter and a small amount of water may be made either as water-in-oil emulsions or oil-in-water emulsions. When quick action of a drug is desired Schroff recommends that a suppository be used in which the solution or paste of the drug is the continuous or external phase. Drugs which have a local action should be suspended or dissolved in water as the dispersed or internal phase of the suppository. Typical formulas for suppositories used by Schroff are:

Oil-in-Water Emulsion.			Water-in-Oil Emulsion.		
Natr. iod.		0.10	Natr. iod.		0.10
Aq. dest.		0.15	Aq. dest.		0.15
Lecithin		0.02	Cholesterol		0.04
Ol. cacao	*ad*	2.00	Ol. cacao	*ad*	2.00

As indicated, the nature of the emulsion depends upon whether lecithin or cholesterol is used as the emulsifying agent.

Sterilization of Solutions.—It is well known that certain solutions for injection cannot be sterilized by use of heat on account of the instability of the drug toward heat. Such solutions may be sterilized by filtration through a germ-proof filter. In an English journal, Hunwicke describes (21) the three main types of bacteria filters in use: (*a*) kieselguhr, represented by the Berkefeld filter, (*b*) porcelain (Chamberland and Doulton), (*c*) asbestos (Seitz). With the Berkefeld filter the entire apparatus must be sterilized in an autoclave. Porcelain filters are slower than the Berkefeld and the only really satisfactory cleaning process is to heat to redness in a muffle furnace. The Seitz filters are essentially discs of compressed asbestos and here again the whole apparatus must be autoclaved before use. It is stated that such solutions should not be made and dispensed by the pharmacist unless they are tested bacteriologically for sterility, because filtration is a less certain method of sterilization than heat, and contamination may occur during filling. The author states that this work requires apparatus which is hardly likely to be available in the small pharmacy, and that the difficulties cannot be overcome by makeshifts, but that the work appeals to many who are particularly interested in the professional side of their work.

There has been some demand for an autoclave that would be practical for the retail pharmacist. Greenish and Holder (22) of England have devised such an autoclave which is made similar to household pressure cookers.

For sterilization of novocain solutions, Rae suggests (23) filtration through a Chamberland filter, since heat caused decomposition, even when the solution was heated to 55–60° for one-hour periods on three successive days. However, J. Abildgaard (24) states that 2% solutions of novocain in *N*/1000 HCl suffer no appreciable decomposition when autoclaved for 20 minutes at 120° C. Eschenbrenner and Rosenberg (25) recommend that sterile solutions be prepared by combining filtration through a Seitz filter with the addition of 0.2% of Nipasol-Sodium.

Accuracy of Dispensing.—The subject of accuracy in dispensing has become a live one in the United States, following reports that of 100 prescriptions filled by 100 different drug stores in the District of Columbia, 67 were found to have been filled unsatisfactorily. The federal food and drug administration which conducted this test has jurisdiction only over drugs moving in interstate commerce and in the District of Columbia and the territories, but it was pointed out that state and city officials have authority to make similar checks elsewhere. As pointed out in the *N. A. R. D. Journal* (26) such publicity is damaging to pharmacy and every owner of a drug store should check and double check the accuracy of himself and all his clerks.

According to Butler (27) there has been considerable discussion from time to time in England as to the percentage error that should be allowed as unavoidable in the dispensing of medicines and the general opinion seems to be that an error of 10% should be allowed.

The accuracy of various methods of dividing powders was determined by J. Büchi, whose results appeared in a Swiss journal (28). Some of these methods are not used in the United States but the relative accuracy is of interest. Büchi reported that the dividing of powders with a spatula by the eye was very uncertain, the maximum error amounting to 24.5%; he recommends that this method should not be used. The use of "powder shears" is more accurate, especially in dividing crystalline powders, the maximum error being 8.7%. Another method used is to plug a cylinder with powder and divide by means of a device. In this process the error is 5.8%. Büchi states that the best method of dispensing powders is to weigh each powder. With the ordinary hand balance the error was 4.1% while with the Barnhart dispensing scales the error was not more than 1%.

Sources of Dispensing Information.—A great deal of information as to methods of filling various prescriptions appears in the questions and answers columns of pharmaceutical journals. The answers prepared by J. Leon Lascoff published in the *Practical Druggist, New York Pharmacist* and *New York Journal of Pharmacy*, and the prescriptions discussed by S. L. Hilton in the *American Druggist* are worthy of study by every prescriptionist. Owing to the large number of such prescriptions, it is beyond the scope of this report to consider them in detail here. The pharmacist may also find it advantageous to follow the new items published in the *Journal of the American Medical Association;* for example, the issues for May 1932 include such items as tincture of metaphen, and ampuls of sodium iodobismuthite and sodium iodide in ethylene glycol.

Related Investigations.—In addition to the scientific and professional studies, a great deal of information relating to various other phases of prescription work has been published during the year. Thus a number of articles have appeared dealing with methods of promoting the use of U. S. P. and N. F. items in prescriptions. C. B. Jordan published (29) a survey of the nature of the prescriptions filled and analytical work conducted in professional stores. L. A. Seltzer contributed an article (30) on prescription pricing. Monell and Brown (31) studied the average prices of prescriptions in Buffalo, N. Y., and Columbus, O. A report on the Maryland prescription count was presented (32) by R. L. Swain. E. N. Gathercoal supplied information (33) on the use of fluidextracts during the past 50 years. The preliminary report of the U. S. P.-N. F. prescription ingredient survey for 1931 appeared (34). The work of the St. Louis Drug Survey was carried on. These projects indicate that almost all phases of pharmaceutical dispensing have been actively studied during the year.

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IMPORTANT ANNOUNCEMENT!

Beginning in the July issue of the JOURNAL, the second report on the professional phase of the National Drug Store Survey of the United States Department of Commerce will be printed in several instalments. This publication, written by Frank A. Delgado and Arthur A. Kimball, is entitled: *"THE PROFESSIONAL PHARMACY."* ("An Analysis of Prescription Department Activities.")

This report is believed to be one of the most complete studies of pharmaceutical economics ever made. The information contained therein should be of practical value to all branches of the profession and industry—proprietors of professional and commercial type pharmacies, educators and students of pharmacy, wholesalers and manufacturers of pharmaceuticals. Suggestions for improved practice are made on the basis of the findings of this detailed investigation. If these suggestions are applied, it is believed that increased prescription business and volume will be realized.

Four professional pharmacies located in St. Louis, Missouri, provided the test laboratories about which the study was centered, a detailed analysis of their complete operations being made. In addition, 35 proprietors of professional pharmacies located throughout the country answered a questionnaire containing 66 questions. These questionnaire replies make it possible to present an even more complete picture of professional pharmacy operation than was at first contemplated. Wherever such information is of value, the findings in the professional pharmacies are compared with those of 13 commercial type drug stores, reported in the Survey's first publication on prescription department activities, entitled: "Prescription Department Sales Analysis in Selected Drug Stores." A large number of prescriptions, 10,000 filled by the professional pharmacies and 10,000 filled by the commercial type stores, were analyzed from every practical point of view, the results of this analysis forming one of the most important sections of the report.

Some questions which have caused much conjecture in the profession for years are authoritatively answered in "The Professional Pharmacy." For example—What are the minimum requirements to be met in opening a professional pharmacy? How can simplification of the pre-

scription department inventory be effected? What are the leading prescription ingredients—those prescribed most frequently? Does the new school of physicians, those who have graduated since the World War, lean more toward manufacturers' trade-named specialties than toward official U. S. P. and N. F. products? What changes have prescriptions undergone since 1910? What is the average cost of materials and selling price of different types of prescriptions? These and many other questions of a similar type will be answered in this publication.

After the report has been published in the JOURNAL, it will be reprinted in pamphlet form and will be available at the office of the Secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION, at a minimum price consistent with cost, to be announced later.

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