PHARMACEUTICAL ABSTRACTS

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ABSTRACTORS

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ANALYTICAL

Acetone, *n*-Butanol and Ethanol—Analysis of, in Aqueous Solution. Ten cc. of distillate containing not more than 5 Gm. of alcohols is diluted to 100 cc. and 10 cc. of this dilution is added to a cold mixture of 10 cc. of 0.4*N* potassium dichromate and 10 cc. concentrated sulphuric acid in a 2.5 by 25 cm. test-tube. Two glass rods are dropped into the tube and the contents are thoroughly mixed. A stopper carrying a 1-mm. capillary tube, the lower end of which is bent at right angles, is inserted and the tube placed in a vigorously boiling water-bath. After 10 minutes it is cooled and diluted to 400 cc. in a 1-liter Erlenmeyer flask. Fifteen cc. of a 20% potassium iodide solution is then added, the flask is stoppered and allowed to stand 2 minutes, and the iodine released is titrated with 0.1*N* thiosulphate. A blank is run in the same way. The difference is designated as M_1 and has a value as shown by the equation

$$M_1 = 6.92B + 0.691A + 8.78E$$

in which M_1 is in cc. of dichromate consumed, B is equal to the weight, in grams, of butanol, A the acetone and E the ethanol. A second titration is made to obtain another equation, and one of two procedures may be used. In one, a second oxidation, exactly like the above, is applied to a sample of distillate extracted with carbon tetrachloride. Twenty cc. of the distillate is placed in a test-tube with 40 cc. of carbon tetrachloride, shaken, and allowed to stand 2 hours at 25° C. Ten cc. of the aqueous solution is removed, diluted to 100 cc. and 10 cc. of this solution oxidized as above to obtain a value, M_2, which is given by the equation

$$M_2 = 2.75B + 0.386A + 8.22E \text{ plus correction.}$$

Instead of extracting with carbon tetrachloride another equation may be obtained by carrying out the oxidation under different conditions. Ten cc. of original distillate, containing not more than 2 Gm. of alcohols per 100 cc., is diluted to 100 cc., and 5 cc. of this dilution is added to a cold mixture of 25 cc. of concentrated sulphuric acid and 10 cc. of 0.4*N* potassium dichromate and the procedure for M_1 followed. A blank is run in the same way. The difference in titration is multiplied by two to give the value, N, shown in the equation:

$$N = 24.62B + 17.68A + 8.84E$$

Then from the three equations the butanol, acetone and alcohol values may be calculated.—L. M. CHRISTENSEN and E. I. FULMER. *Ind. Eng. Chem., Anal. Edit.*, 7 (1935), 180. (E. G. V.)

Acetylsalicylates—Decomposition of. Acetylsalicylic drug mixtures kept in paper containers decompose on storing. Total salicylic acid was determined by hydrolyzing with alkali and determining the salicylic acid formed by bromometry according to Koppeschaar. The content of the preparations in free salicylic acid (*i. e.*, formed due to decomposition) was determined similarly without the previous saponification. As even pure acetylsalicylic acid decomposes under this treatment to some degree the value obtained for free salicylic acid should be diminished by 6.48%. Freshly made Kalmopyrine contained practically no free salicylic acid, a sample 6 months old contained about 12% and a sample stored for 2 years contained 44%.—V. GERVAY. *Magyar Gyógyszerésztud. Társaság Értesitője*, 11 (1935), 241; through *Chem. Abstr.*, 29 (1935), 3776.

Acid Indices of Officinal Oils and Waxes. Lime Liniment of the Belgian Pharmacopœia IV. The variations in the different methods for determining the acidity of fats and waxes recommended in the Belg. Phar. IV are pointed out and tabulated. The following changes in the paragraph relative to the technique used to determine the acid index are recommended "Dissolve 2 Gm. of the substance in 20 cc. of a mixture of equal volumes of neutral ether and chloroform; add 5 drops of phenolphthalein; titrate with a 0.1*N* solution of alcohol potassium hydroxide to the appearance of a red color persisting for 15 seconds. The acid index is equal to the number of mg. of potassium hydroxide used to neutralize the free acid of 1 Gm. of the substance analyzed (1 cc. of 0.1*N* KOH is equivalent to an acid index of 2.8056)." Acid indices for the individual fats and waxes are recommended, and since linseed oil is used in the preparation of lime liniment, the following change is urged: "The acid index of linseed oil should be less than 2.2 (equivalent to 0.8 cc. of 0.1*N* alcoholic KOH)."—GARY P. WEIL and CLAIRE ANSELME. *J. pharm. Belg.*, 17 (1935), 377–381, 399–401. (S. W. G.)

Alcohol—Determination of, in Tinctures. A comparison of different methods of determination of alcohol in tinctures showed that sufficient accuracy could be obtained by the methods of the British, Swedish or German Pharmacopœias; the two latter being the simpler and more convenient. The British method is more troublesome and requires to be checked by a determination of the refractive index of the distillate. The British method (modification II) is very suitable for the determination of alcohol in tinctures containing ether.—A. JERMSTAD and O. ØSTBY. *Norsk. Farm. Tidsskr.*, 43 (1935), 4; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 122. (S. W. G.)

Alkaloidal Salts—Estimation of, by Direct Titration of Their Acid Radicles. The author describes a method which he has used since 1927 as a control method in the preparation of compressed and hypodermic tablets. The distinguishing characteristic of his method is the use of benzyl alcohol as the solvent instead of alcohol-water solvents. A table showing some typical results would indicate that the method is quite satisfactory for the purpose intended.—FELICE A. ROTONDARO. *Am. J. Pharm.*, 107 (1935), 237. (R. R. F.)

Alkaloids—Determination of. Application of the Mercurimetric Method to New Biological Products. The mercurimetric method was successfully applied to determination of these alkaloids. They were precipitated from a 1% solution by the use of the Mayer-Valzer reagent (mercuric iodide-alkaloid-hydroiodide) and the complex destroyed by a mixture of nitric and sulphuric acids. The mercuric ion was precipitated by nitroprussiate and titrated with 0.1*N* sodium chloride. Tables of actual and theoretical equivalents are given. Apiol was detected by the following method also. To a mixture of 1 cc. of a 1% aqueous-alcohol solution of the alkaloid and 5 drops of a 2.5% aqueous-alcoholic phosphomolybdic acid solution was added 0.5 cc. concentrated sulphuric acid (d = 1.84), the mixture stoppered and shaken well. The color became an intense greenish blue, changing to red-orange on heating 2–3 minutes but returning to blue when cooled. Addition of 2–3 drops of 12% hydrogen dioxide before heating produced a yellow color which after heating changed to a persistent cerise. The reaction is sensitive to 1 mg.—A. IONESCO-MATIU and C. POPESCO. *Bull. soc. chim. biol.*, 17 (1935), 671; through *Squibb Abstr. Bull.*, 8 (1935), A-745.

Aloin—Examination of Three Samples. Solubility tests were conducted on three samples of aloin, by saturating with excess solvent and macerating for forty-eight hours with frequent shaking. These tests were done at ordinary laboratory temperatures, but under identical conditions in each case. A table is given which shows the results of these tests.—D. B. DOTT. *Pharm. J.*, 134 (1935), 648. (W. B. B.)

Alpha-Amylase—Determination of. In order to calculate the concentration of alpha-amylase in a given enzyme preparation from the amount of starch liquefied under the specified conditions, the authors have introduced a new enzyme unit, the "liquefon," defined as "that amount of starch-liquefying enzyme which will convert the standard starch paste at the rate of 25 mg. of dry starch per minute at zero time under the given experimental conditions." Since the rate at zero time is directly proportional to enzyme concentration, the number of liquefons per gram of preparation is an exact measure of the alpha-amylase content. The actual procedure follows: The 150-Gm. sample of starch paste is cooled to about 19.5° C., so that after stirring in the enzyme infusion or the sodium chloride solution, the temperature of the stirred paste is 21° ± 0.2° C. The correct time of stirring for the initial outflow is determined by running one or more blanks. Using this correct time, 15 cc. of enzyme infusion is stirred into 150 Gm. of paste and the mixture is placed in the bath at 21° C. After 59 minutes the mixture is sucked into the pipette and its outflow time is determined. The measurement of the outflow time of the mixture is begun just before the end of the hour reaction period in order to correct for the liquefaction occurring during the measurement. In order to check the stability of the paste, another blank should be run on 150 Gm. of paste which has stood for 1 or 2 hours at 21° C. The outflow time of this check blank should not deviate more than 3 or 4% from the first blank. In pipetting the 15-cc. portions it is necessary to avoid the introduction of saliva. A small cotton plug prevents contamination. From the outflow time of a given mixture the percentage decline is calculated, and from this the amount of starch liquefied is obtained from the table or equation. The enzyme content or activity of the infusion is derived from the amount of liquefied starch by means of the equation:

$$\text{Log}_{10}\, L = (S - 1078)\,(0.000565)$$

where L = liquefons per 10 cc. of infusion and S = milligrams of starch liquefied in 1 hour. From

the concentration of the infusion the number of liquefons per Gm. of preparation is calculated.—S. JOZSA and W. R. JOHNSTON. *Ind. Eng. Chem., Anal. Edit.*, 7 (1935), 143. (E. G. V.)

Aluminum—Sensitive Reagent for. Separation of Aluminum and Beryllium. The aluminum ion is precipitated in hydroalcoholic solution by ferrocyanides. The following reagent is recommended: Calcium ferrocyanide.$12H_2O$ 20 Gm., distilled water 670 cc., alcohol (96%) 400 cc. Dissolve the ferrocyanide in the water, add the alcohol, shake, allow to stand and filter if necessary. Keep the reagent in a dark place. The sensitivity is 0.02 mg. aluminum per cc. The reaction is carried out by adding the sample to the reagent and heating to boiling for several seconds; the reaction goes better if the sample contains about 0.001 Gm. aluminum per cc. The same reaction may be used for quantitative determinations by nephelometry, potentiometry, gravimetric method (drying at 85–90°) and by determination of the excess of a known quantity of the reagent used, which may be done by manganimetry using $N/10$ or $N/20$ solution, and in this case the sample should be in the form of the sulphate and the alcohol should be removed from the reagent by evaporation on a water-bath. The precipitate given by beryllium is more soluble than that given by aluminum and it may be separated by dilution and filtration, when the aluminum will remain as the precipitate.—T. GASPAR and Y. ARNAL. *Ann. chim. anal. chim. appl.* (Mar. 15, 1935); through *J. pharm. Belg.*, 17 (1935), 510. (S. W. G.)

Ammonia and Amide Nitrogen—Determination of, in Plant Tissue. The ammonia present in plant tissues as ammonium ions, that is the free or preformed ammonia, has been determined since 1850 by distillation with magnesium oxide, preferably *in vacuo*. A study of the possibilities of interference from a number of commonly found plant constituents, and of the conditions under which this determination is usually conducted, has led to the suggestion of a technique that depends upon the distillation *in vacuo* with a borax-sodium hydroxide mixture used in conjunction with a phosphate buffer solution. The ammonia is then nesslerized and determined in a Pulfrich spectrophotometer. Under these conditions, interference from other substances is minimal. The new reagent is particularly designed for determinations of ammonia in solutions to which phosphate buffers have been added, as the use of magnesium oxide is then inadmissible; its convenience, however, suggests that it may be generally applied with advantage.—G. W. PUCHER, H. B. VICKERY and C. S. LEAVENWORTH. *Ind. Eng. Chem., Anal. Edit.*, 7 (1935), 152. (E. G. V.)

Antipyrine—Contribution to the microchemistry of. Antipyrine sublimes with difficulty. If the sublimation is continued over an extended period of time crystals suggesting snow-crystals are obtained. The reaction is not definite for quantities less than 1 mg. Antipyrine may be beautifully crystallized by taking up in water and adding very fine crystals of sodium chloride. This "salting out" process results in the formation of many prismatic crystals, right angled, six-angled plates with an upper angle of 128° and side angles of 116° and oblong diamond-shaped crystals with an acute angle of 66°. If nitric acid is added to a small quantity of antipyrine a beautiful color results which, however, disappears upon evaporation of the acid. When the acid is completely evaporated white crystals result which polarize light with a brilliant play of colors. The reaction is not very sensitive, 2 mg. being required for positive reaction. If antipyrine is first salted out and then a drop of sodium nitrite solution and a drop of hydrochloric acid are added, sea-green crystals are obtained. This reaction is one of the best for antipyrine and has a sensitivity limit of 0.1 mg. and a dilution limit of 1:300. Potassium ferrocyanide followed by sulphuric acid results in star formations. In several places thin diamond-shaped crystals may be seen which have an acute angle of 82. (Limit 0.1 mg.: dilution 1:200.) Potassium ferricyanide also gives beautiful crystals especially if the antipyrine is precipitated from diluted hydrochloric acid solution with the ferricyanide and a drop of acetone added just previous to the precipitation. Needles grouped in star formations are found. (Limit $^1/_5$ mg.: dilution 1:200.) Sodium nitroprusside gives excellent crystallization in acid solution. (Sensitivity limit 0.1 mg.: dilution 1:200.) Platinum chloride gives yellowish crystals with acid solutions of antipyrine. (Limit $^1/_5$ mg.: dilution 1:200.) If sodium iodide is added to the crystals obtained with platinum chloride a black mass of fine crystals is immediately formed. This soon changes to dark red with the formation of feather crystals.—M. WAGENAAR. *Pharm. Weekblad*, 72 (1935), 642. (E. H. W.)

Arsenates—Volumetric Determination of. The conditions necessary for the volumetric determination of arsenates by means of their reduction to arsenites by potassium iodide in the presence of sulphuric acid and titration of the arsenite formed by iodine in alkaline solution were

studied. The three factors considered were the quantity of sulphuric acid and potassium iodide used and the duration of heating. Correct results are obtained when the molarity of the arsenate solution, expressed in terms of arsenic pentoxide, lies between 0.0165 and 0.00099, if 2 cc. of sulphuric acid (d = 1.8) and 0.8 Gm. of potassium iodide are used for each 10 cc. of arsenical solution and if the duration of heating on the boiling water-bath is about 10 minutes.—M. F. TABOURY and H. AUDIDIER. *Bull. soc. chim. mem.*, 1 (1934), 1570; through *Squibb Abstr. Bull.*, 8 (1935), A-748.

Arsenic—Quantitative Determination of Small Amounts of. An exhaustive investigation of the methods proposed for this determination is discussed and the following conclusions offered: (1) The methods for the quantitative determination of the arsenic content in a preparation of fairly well known composition and that in a natural product are fundamentally different. If no interferences are expected a simple oxidation-titration method is satisfactory. (2) The reduction to metallic arsenic by hypophosphite in strong hydrochloric acid solution is improved for this work. (3) The methods which depend upon the isolation of the arsenic by means of the Schneider distillation procedure are not applicable because in these microchemical technique has not been sufficiently developed. (4) For the quantitative determination of arsenic in a natural product the arsenic mirror formation or reduction by hypophosphite are methods that might be recommended. In the reduction to arsine the use of zinc powder is preferred to granular zinc. Any arsine remaining dissolved in the evolution flask is driven out simultaneously by a stream of hydrogen. The arsenic mirror is dissolved in iodine monochloride solution and the separated iodine is determined volumetrically in strong hydrochloric acid solution in the presence of cyanogen with iodate. Marsh's technique for the mirror formation is improved.—J. GANGL. *Pharm. Monatsh.*, 16 (1935), 87–92. (H. M. B.)

Arsenobenzenes—Chemical Examination of. Arsenic was determined according to Schulek and Villecz. Schulek recently proposed use of two drops of 0.5% α-naphthoflavone as indicator in micro-determinations. Samples of Revival and neoarsphenamine contained 18.32–19.63% arsenic, 9.40–10.42% sulphur and 6.64–7.65% sulphur distillable with hydrochloric acid. Solusalvarsan samples contained 1.883–1.917% arsenic. Total sulphur content was determined according to Winkler after decomposition by nitric acid and hydrogen dioxide. Sulphur distillable with hydrochloric acid was determined by method of Schulek and Dozsa.—S. LASZLO. *Magyar Gyógyszerésztud. Társaság Értesitője*, 11 (1935), 266; through *Chem. Abstr.*, 29 (1935), 3776.

Benzene—Detection of, in Alcohol. If the alcohol contains much above 0.01% benzene by volume it is diluted to approximately that value with alcohol free from benzene. A 40-cc. portion is placed in a 100-cc. glass-stoppered cylinder with 6 cc. of carbon tetrachloride. Distilled water is added to the 90-cc. mark, followed by 10 cc. of sodium sulphate solution (10 Gm. anhydrous salt to 100 cc. solution). The cylinder is stoppered, shaken and allowed to stand until the layers separate. Five cc. of the bottom layer is transferred by pipette to a test-tube. Three cc. of nitrating acid (containing 70 Gm. of 20% oleum, 45 Gm. concentrated sulphuric acid and 43 Gm. of concentrated nitric acid) is measured in a small cylinder and added to the test-tube, shaking. During 10 minutes the tube is shaken twice more, and at the end of that time, 20 cc. of distilled water is added rapidly from a cylinder. After mixing by pouring into another test-tube and back again, the bulk of the water layer is decanted and discarded. The lower layer is placed in an evaporating dish on an electric hot plate. When the carbon tetrachloride is gone, the dish is emptied into the test-tube just used, and is rinsed into this tube with 1 cc. of amyl alcohol. The dish is then rinsed into the tube using 4 cc. of caustic soda solution (140 Gm. made up to 250-cc. solution). The tube is mixed by swirling and then 1 cc. of acetone is added, the tube swirled again and placed in a rack for observation of color produced in the top layer. Pure benzene at the concentration of 1 in 10,000 by volume in rectified alcohol gives by this test a red color with a purple quality in the top layer. This color holds for some hours and then fades to a dull orange-red. As the benzene content rises above 0.01%, the color produced soon becomes too dark for identification. Pure toluene gives a slightly brownish yellow and reagent xylene produces a definite, though not intense green, which fades in 30 minutes, giving way to a dull orange. Blanks should be run.—A. C. LANSING. *Ind. Eng. Chem., Anal. Edit.*, 7 (1935), 184. (E. G. V.)

Calcium and Phosphorus Analysis—Digesting Biological Materials for. Weighed samples of suitable size are placed in 500-cc. Kjeldahl flasks, 20 to 30 cc. of concentrated nitric acid is added and the flasks are then heated gently, with frequent stirring, until the samples pass into a semi-colloidal dispersion. Heating to dryness must be avoided. The heating should require about 30

to 45 minutes. Ten cc. of 70% perchloric acid is added and the flask placed over a free flame. Very low flames are necessary during the perchloric oxidation. When fuming begins the flame is so adjusted that only a trace of perchloric acid fumes reach the upper region of the flask. The heating is continued until the solution is colorless or only a faint yellow color remains. After slight cooling 50 cc. of distilled water is added. Vigorous boiling occurs, driving out the remainder of the nitrogen dioxide fumes leaving a clear solution. The solution is filtered into a volumetric flask and the Kjeldahl is thoroughly washed. When the solution has cooled it is made to volume and aliquots are taken. Calcium and phosphorus may be determined by the usual procedures.—H. W. GERRITZ. *Ind. Eng. Chem., Anal. Edit.*, 7 (1935), 167. (E. G. V.)

Calcium Hydroxide—Solubility and Determination of. Calcium hydroxide, obtained by slaking quicklime, comes into equilibrium with water after shaking for one hour, and is much more soluble than the crystalline variety; at 15° C., the solubility of the former is 0.133%, and of the latter 0.122%, calculated as calcium oxide. The determination of calcium by weighing as oxide after precipitation as oxalate is subject to several sources of error, and should be discarded; accurate results may be obtained by the volumetric method using permanganate, provided that the precipitated calcium oxalate is washed, before decomposition with acid, with a saturated solution of calcium oxalate in water. The author recommends the use of pure precipitated calcium carbonate as a volumetric standard; a weighed quantity of the carbonate being ignited to oxide in platinum, slaked and titrated with acid using methyl orange or methyl red as indicator.—H. BASSETT. *J. Chem. Soc. Lond.* (1934), 1270; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 117. (S. W. G.)

Camphor—Titrimetric Determination of, in Drug Preparations. To substance equivalent to 0.2 Gm. camphor (or hexetone) in a 100-cc. flask add 0.15 Gm. sodium bicarbonate, a drop of 0.1% bromophenol blue and 10 cc. hydroxylamine hydrochloride (2 Gm. dissolved in 10 cc. water and 50 cc. absolute alcohol). Heat the mixture with small flame for four hours under a short reflux condenser. Cool, and add 10% hydrochloric acid until the blue color changes to yellow. Prepare a blank in the same way and to each add carbon dioxide-free 0.1*N* sodium hydroxide until a green color appears. Then add solid phenolphthalein to each solution and further titrate until a lilac color is shown by both liquids. The difference in no. of cc. required is equivalent to camphor content; each cc. of 0.1*N* sodium hydroxide is equivalent to 0.0152 Gm. camphor.—R. WOLSTADT. *Magyar Gyógyszerésztud. Társaság Értesitõje*, 11 (1935), 257; through *Chem. Abstr.*, 29 (1935), 3776.

Cellophane and Kuprophane as Dialysis Membranes. Cellophane No. 300 (Kalle and Co.) has a thickness of 20μ, and Kuprophane (Bemberg A. G.) 10μ. If the permeability of Kuprophane is 100, then cellophane is 51, and the parchment paper used for dialysis is 13. The membranes have sufficient strength when wet, and are satisfactory for rapid electrodialysis.—H. BRINTZINGER and H. OSSWALD. *Kolloid Ztschr.*, 70 (1935), 198; through *Pharm. Zentralh.*, 76 (1935), 277. (E. V. S.)

Chloride and Potassium Ions—Volumetric Microdeterminations of. The chloride determination follows: Samples of the order of 1 cc. of 0.01*N* solution are titrated directly with 0.005*N* silver nitrate solution, using a 10-cc. burette calibrated in 0.02-cc. divisions. The samples are conveniently contained in the cut-off end of a test-tube. The conditions for a satisfactory endpoint with dichlorofluorescein are: approximately neutral solution, not over 2 drops of 0.01% solution of indicator, acetone added in small amounts approximating the original volume of the sample and illumination from the side or rear of the observer. For the determination of potassium, excess of chloroplatinic acid solution is added to the sample and the solution is evaporated to dryness over a water-bath. The residue is washed with successive portions of 80% alcohol and 20% ammonium chloride, both saturated with potassium chloroplatinate. The precipitate is washed into a crucible with 1 cc. hot water. The potassium chloroplatinate is reduced to chloride and platinum in neutral solution with finely divided magnesium. The chloride set free is then titrated as described above.—B. BULLOCK and P. L. KIRK. *Ind. Eng. Chem., Anal. Edit.*, 7 (1935), 178. (E. G. V.)

Chloroform and Carbon Tetrachloride—Reaction for Distinguishing between. Papaverine hydrochloride is soluble in chloroform but insoluble in carbon tetrachloride. Ten mg. of papaverine hydrochloride (or any other alkaloid having this property) is added to one cc. of the liquid ($CHCl_3$ or CCl_4) in which a small fragment of iodine has previously been dissolved. If the liquid is chloroform the violet color will change to yellow or yellowish red; if it is carbon tetrachloride the

violet color will remain unchanged and the alkaloidal salt will not go into solution. This reaction is suggested as a check to be used with other means of differentiation between these two liquids, *e. g.*, refractive index, etc.—J. ROZEBOOM. *Pharm. Weekblad*, 72 (1935), 689. (E. H. W.)

Chromatographic Adsorption and Its Applications. The method of separation by chromatographic adsorption, devised by the botanist Tswett, consists in passing a solution of the colored substances to be studied through a tower of finely powdered adsorbing material; the various pigments are adsorbed at different levels, and can be isolated and studied separately. The method is described in detail, and various applications which have been made to date are reviewed. Forty-one references.—EDGAR LEDERER. *Chimie & Industrie*, 33 (1935), 1072–1078. (A. P.-C.)

Cod Liver Oil—Vitamin Potency and Associated Characteristics of Average. In order to determine the average quality of cod liver oil purchased in the retail market, 67 samples were obtained from various sources and sections of the British Isles. The blue value, vitamin A and vitamin D values were determined. The determinations were all made by approved methods. The oils were divided into 5 groups according to localities and average blue values for each group determined. Composite oils were prepared from 64 of the samples, a composite of samples below the median, one from those above the median, and one from a mixture of the latter two. Blue values were determined directly in all cases and on the unsaponifiable portion in 36 cases. Spectrophotometric examinations of 3 of the composite samples were also made. The vitamin A and D values were determined on the composite samples. A number of tables of results are given and the possible errors introduced by the methods used and also by the "personal equation" are discussed. The following conclusions are drawn by the authors: The characteristics of average cod liver oil as obtained above are: Blue value 9.3, blue value (unsaponifiable matter) 21.8, $E\ 1\%\ 328\ m\mu$ 0.505, vitamin A (biological assay) 670.0 units per Gm., vitamin D (biological assay) 81.0 units per Gm. The vitamin assays were based upon results from 40 pairs of rats for each assay. It is calculated that the error in the vitamin A assay does not exceed -14 to $+17\%$ and that from the vitamin D assay -14 to $+16\%$ by a 22/1 chance.—RONALD S. MORGAN and HARRY PRITCHARD. *Analyst*, 60 (1935), 355–368. (A. H. C.)

Copper—Determination of, in Foods with Special Reference to Milk. A method for determining copper in foods is given in detail. The original paper should be consulted for details. Part of the authors' summary follows: 1. Diphenylthiocarbazone in chloroform is used as an extraction agent to remove copper from foods. 2. With milk containing 0.12 parts per million, reliable duplicates may be obtained using as little as 20 Gm. of milk. The error is ± 0.02 parts per million. 3. The method is applicable to foods in general and is unaffected by such metals as iron, tin, aluminum, lead, zinc, nickel and manganese. 4. After all possible precautions to avoid contamination, the copper content of sixteen samples of milk from cows of different breeds and different localities was found to range from 0.09 to 0.17 and a mean of 0.12 parts per million.—N. D. SYLVESTER and L. H. LAMPITT. *Analyst*, 60 (1935), 376–382. (A. H. C.)

Coriander (Coriandrum Sativum)—Report on Examination of Samples of Indian and Foreign. Different samples of Russian coriander contained approximately the same amounts (average 22.18%) of material soluble in petroleum ether; Moroccan, Tuticorin and local (Udamalpet) varieties were similar in their contents of ether extractives (average 20.11%). In fresh samples of all varieties the free fat acids amounted to 4.3–8.1 mg. potassium hydroxide per Gm. of oil; samples showing free fat acid values of 19.5 were definitely characterized as old stock. The free fat acid values of the ether extractives of coriander constitute a valuable index of the quality and age of the product. *New Method for Determining the Essential Oil Content of Coriander.*—Extract 50 Gm. of very finely powdered sample successively with 120 cc. and 60 cc. of 96% alcohol in two stages of 6 hours each at water-bath temperature, using a double-surface condenser. Decant the first extract and press out the second extract as thoroughly as possible with a fine muslin cloth. Dilute the combined extracts to 280 cc. with distilled water and steam-distil until the distillate is no longer cloudy. Saturate the distillate with sodium chloride and extract with small amounts of petroleum ether. Dehydrate the combined extracts with anhydrous sodium sulphate and filter into a flask containing a known amount of previously dried cocoanut oil. Wash the sodium sulphate residue and the filter paper several times with anhydrous ether to remove traces of essential oils. Remove the greater portion of the ether by means of a Soxhlet apparatus in a water-bath maintained at 45° and complete the removal of ether by drying *in vacuo* until the loss in weight is approximately 2 mg. per 0.5 hour under 660 mm. pressure. The weight which is highest

in the series after attaining this steady loss in weight represents the combined weights of the essential oil, cocoanut oil and the flask. The method gives concordant results in duplicate determinations. The cocoanut oil prevents the volatilization of the essential oil during the removal of the ether. The oven-dry samples of Russian coriander contained approximately twice as much essential oil as the others.—B. VISWANATH and C. V. RAMASWAMI. *Ayyar. Agr. Live-stock India*, 4 (1934), 583; through *Chem. Abstr.*, 29 (1935), 4130.

Creatine and Creatinine—Microchemical Identification of. The following methods for the differentiation of creatine and creatinine are given: 1. Crystallization of the sample from a drop of water on a slide and observation of the types of crystals formed. 2. Observation of crystals formed on addition of a drop of a saturated solution of picric acid or a drop of a solution containing 6 Gm. iodine and 8 Gm. potassium iodide in 150 cc. instead of the drop of water in 1. The crystals are described and those from the first two procedures are illustrated. 3. Dissolve about 1 mg. of the product in 1 drop of ammonia in a porcelain dish and add 1 drop of a saturated solution of picric acid. If the product contains creatinine, a persistent orange color develops; whereas with creatine the color of the mixture is the same as a control of ammonia and picric acid. If an orange tint which becomes stronger at first and then changes to yellow is observed, creatinine is present, the alkaline medium causing it to change to creatine. 4. Using a 1% solution of sodium nitroprusside instead of picric acid, a blood-red color is obtained with creatinine and a faint rose color with creatine.—GEORGES DENIGES. *Bull. soc. pharm. Bordeaux*, 73 (1935), 89–97. (S. W. G.)

Diiododithymol—Assay of. The tests and assay of diiododithymol are critically reviewed. The following conclusions are drawn. The Belg. Phar. IV should retain the following points: 1. Modification of the formula for diiododithymol according to Bougault (*J. pharm. chim.*, 17 (1918), 221). 2. Color: Yellowish red powder with a characteristic aromatic odor. 3. Solubility: Insoluble in water and glycerin, slightly soluble in alcohol, almost completely soluble in ether, more soluble in chloroform, very soluble in benzene; test-limit of solubility in benzene (20 p.). 4. Test of neutrality: Aqueous filtrate neutral to litmus. 5. Moisture: 1 Gm. placed in a sulphuric acid desiccator for 24 hours loses at the maximum 0.01 Gm. 6. Mineral matter: Calcination with sulphuric acid: maximum of 3.5% of ash as sulphates. 7. Determination of mineral halides: Assay limit with solution of silver nitrate, after exhaustion in the cold: maximum 1% evaluated as potassium iodide. 8. Determination of organic chlorine: Calcination with potassium hydroxide or carbonate and determination of the chlorine in the residue. 9. Free iodine: Assay limit with $N/10$ hyposulphite: maximum 0.25% iodine. 10. Iodate + free iodine: Assay limit with $N/10$ hyposulphite: maximum 0.50% iodine. 11. Determination of iodine: Technique: minimum 44% of the dried product.—LÉON LECLERCQ. *J. pharm. Belg.*, 17 (1935), 423–428, 449–453, 467–471. (S. W. G.)

Essential Oil Content of Drugs—Improved Method for Estimation of. A detailed method for the estimation of essential oil content of drugs including a description of the method of operation of the apparatus, the condition of the sample before testing and the details of the distillation is given. A table is included which shows the amount of essential oil yielded by a number of samples of drugs, herbs and spices.—T. TUSTING COCKING and G. MIDDLETON. *Perf. and Ess. Oil Rec.*, 26 (1935), 207. (A. C. DeD.)

Halides—Volumetric Determinations of. Use of Dichlorofluorescein as an Adsorption Indicator. Dichlorofluorescein has been used as an adsorption indicator in the argentometric titration of organic hydrochlorides dissolved in alcohol, and inorganic halides in alcohol or aqueous solution. The analytical results have been within experimental error of the theoretical values on pure chemicals or of values obtained by the standard Volhard procedure on chemicals of ordinary commercial purity.—K. BAMBACH and T. H. RIDER. *Ind. Eng. Chem., Anal. Edit.*, 7 (1935), 165. (E. G. V.)

Hexamethylentetramine—Determination of, and Its Decomposition in Dilute Aqueous Solutions. Reëxamination of the method previously described shows that the micromethod without distillation is practically reliable especially for rapid determinations of hexamethylentetramine in sugar-containing drug mixtures. The distillation method naturally gives more exact values. Dilute solutions of hexamethylentetramine may easily be decomposed during storage.—E. SCHULEK and V. GERVAY. *Magyar Gyógyszerésztud. Társaság Értesitője*, 11 (1935), 272; through *Chem. Abstr.*, 29 (1935), 3776.

Insulin, Commercial—Rapid Method for the Determination of Purity of, in Vitro. An acidified 0.2% solution of potassium ferrocyanide is a specific reagent for the precipitation of insulin from solutions. Several indifferent substances may then be precipitated from the insulin-free solution with picric acid. The authors have found that many chemical determinations depending on this principle may be made. These chemical determinations are useful and comparable with the physiological determinations.—I. I. NITZESCU and ST. SECAREANU. *Bull. soc. chim. biol.*, 17 (1935), 118; through *Pharm. Weekblad*, 72 (1935), 696. (E. H. W.)

Iodine—Stability of Solutions of. A study of the stability of solutions of iodine in various solvents. *Methyl Alcohol.*—A solution of iodine in pure methyl alcohol showed only a very slight change in the analytical figures after keeping 160 days in a brown corked bottle; in the commercial pure alcohol some decomposition occurred. In both cases the odor of the solution showed the formation of iodoform, due to impurities in the solvent. Methyl alcohol is not recommended as a solvent for iodine. *n-Propyl Alcohol.*—A 5% solution of iodine in *n*-propyl alcohol showed a considerable loss of iodine on keeping. When potassium iodide was also present the amount of decomposition was reduced, but was still considerable. *Glycerin.*—A solution of iodine in glycerin showed no apparent change after keeping for one year. This also applies to a similar solution containing phenol. *Benzene.*—A solution of iodine in benzene was found to have lost nearly all of its iodine after keeping for one year. Petroleum ether is to be preferred, the losses being much smaller. *Liquid Paraffin.*—With pure liquid paraffin the strength dropped to about two-thirds after a few days, and then remained constant. With a less pure oil the amount of free iodine dropped continuously. *Ether.*—A solution of iodine in ether showed no change in strength after six months. *Chloroform.*—A chloroform solution dropped, immediately after making, from 2.9% to 2.5%, and then remained constant in strength for six months. *Carbon Tetrachloride.*—This solution is stable for at least six months. *Acetone.*—In solution of acetone, iodine forms iodo-acetone, which has been used as a poison gas. The strength rapidly drops and then remains constant. *Water.*—Aqueous solutions, containing potassium iodide, are stable if kept in well-closed stoppered bottles, but not in corked bottles. *Tinctura Iodi Decolorata.*—This is a very complex product which when first prepared contains ammonium iodide and diiodoamine. It decomposes rapidly, and should be eliminated from the Pharmacopœias.—W. HÖK. *Svensk Farm. Tid.*, 38 (1934), 422, 437, 457, 477; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 125. (S. W. G.)

Lactometer—New Type, Reading Total Solids. The new lactometer herein described has a scale that reads directly in terms of percentage of total solids. The scale reading is predicated upon a butter fat content of 4% and is subject to a correction amounting to 1.2% of total solids for each variation of 1% of butter fat in the milk. Throughout its scale length the new lactometer is useful without correction for variation in the temperature of the milk provided its temperature lies between 58° F. and 62° F. Where samples are at any temperature between these limits, or can readily be brought to have temperatures within these limits, this total solids lactometer will effect great economy of time in routine milk analysis. If the readings upon it lie between 11.2% total solids and 12.7% total solids, the temperature of the milk may range within the wider limits of 56° F. to 63° F. without any necessity of correction for temperature. The use of the total solids lactometer is not intended to do away with the check by gravimetric determination of total solids in all exceptionally important cases. Its use is merely a short cut in routine work. It is an instrument deliberately made to have the sensitivity conformable to routine milk analysis of to-day, and deliberately made to give directly or after simple correction the figure (for total solids) that is otherwise arrived at indirectly by calculation through the general milk equation.—DAVID W. HORN. *Am. J. Pharm.*, 107 (1935), 212. (R. R. F.)

Methyl Salicylate—Determination of, According to D. A. B. VI. The directions for assay are clear and understandable, but the results obtained are not uniform. Due to the small amount (1 Gm.) of methyl salicylate used in the assay, slight errors in weighing or measurements of reagents cause a high percentage of error. The use of alcoholic alkali as the saponifying agent gives a slower reaction than an aqueous solution and makes exact measurements more difficult. An assay based on the determination of salicylic acid produced a low result (95%). The difficulties encountered in the assay may be eliminated to some extent by increasing the amount of methyl salicylate to 2.5 Gm.—R. ECKERT. *Pharm. Zentralh.*, 76 (1935), 237. (E. V. S.)

Micro- and Submicro-Colorimetric Determination of Iron. The author recommends the

use of hydroxyquinoline for the determination of iron in organic liquids. This method is based on the solubility of the ferric derivative of hydroxyquinoline in alcohol. The solution is strongly colored a dark green and absorbs blue radiations, and may be used for colorimetric determination. The reaction may be used for the determination of magnesium by finding the amount of hydroxyquinoline present by means of iron, and, from the hydroxyquinoline, the amount of magnesium hydroxyquinolinate.—M. J. LAVOLLAY. *Bull. soc. chim. biol.*, 17 (1935), 432; through *J. Pharm. Belg.*, 17 (1935), 533. (S. W. G.)

Micro-Copper-Pyridine Reaction—Application of, to Some Organic Acids. The author has investigated the reaction used by Zwikker for the identification of barbituric acid derivatives adapting it to some of the organic acids. The reagent consists of 4 cc. of (10%) copper sulphate solution, 1 cc. pyridine and 5 cc. of water. When a few crystals of salicylic acid are introduced into the reagent crystal clumps, prisms and sometimes irregular hexagons are immediately produced. The crystals are greenish blue and strongly birefringent. Sodium salicylate gives an amorphous precipitate which soon resolves into the above-described crystals. When acetylsalicylic acid is introduced into the reagent the drop remains clear. Upon scratching with the platinum needle, however, crystallization takes place with the formation of purplish blue prisms, rhomboids and hexagons. The crystals are dichroic. Calcium acetylsalicylate gives similar crystals after scratching. Benzoic acid or benzoates give birefringent, dichroic (colorless to blue) prisms which soon resolve into stellate groups. Cinnamic acid (dissolved in a little ammonia) gives rosettes of blue-green prisms which later form into plates. Anisic acid gives oblique dichroic prisms showing birefringence (colorless to blue). The prisms finally grow into stellate groups. Anthranilic acid gives elongated birefringent hexagons and disk-shaped crystals. Fumaric acid gives blue crystal clumps. Dr. Steenhauer states that the reaction is particularly valuable in distinguishing between salicylic and acetylsalicylic acids. Seven photomicrographs are given.—A. J. STEENHAUER. *Pharm. Weekblad*, 72 (1935), 667. (E. H. W.)

Microsublimation as a Pharmacopœial Test. The author comments upon the various microsublimation tests applied by the Swiss Phar. V. Some are practical but others are not accurate and could not be confirmed by the author. Sixteen pharmacopœial tests are considered. Microsublimation is really unnecessary for pharmacopœial purposes since chemical identification is more easily accomplished in other ways and is more convenient for the pharmacist.—ROSENTHALER. *Schweiz. Apoth.-Ztg.*, 73 (1935), 273. (M. F. W. D.)

Opium—Comparison of Proposed Methods. The authors, constituting the Group Committee on Opium Assays of the U. S. P. Committee on Revision criticize the opium assay procedure suggested by the International Committee. Although this latter committee's method yields results which check satisfactorily, the lack of sharpness in the end-point, the absence of any time-saving factors, the potential hazard attending the use of smaller quantities of samples (especially in the case of gum opium), the apparent inaccuracy of the correction factor and the inconstant variations in results obtained by different collaborators combine to establish the fact that the proposed international committee's method is inferior to the method recommended by the group committee for adoption in the U. S. P. XI.—A. RICHARD BLISS, JR., *et al.* *Am. J. Pharm.*, 107 (1935), 193. (R. R. F.)

Organic Matter in Plant Material—Destruction of, by the Use of Nitric and Perchloric Acids. Place a 4-Gm. sample of the material to be oxidized in a 400-cc. beaker and add 10 cc. of concentrated nitric acid. Cover the beaker with a watch glass and heat gently until any rapid initial reactions have subsided. Then heat to boiling and boil until the contents of the beaker are almost dry. Remove the beaker from the hot plate and add 10 cc. of dilute nitric acid (1 to 1) and 10 cc. of perchloric acid (70 to 72%). Replace the cover glass and heat very gently to a low boiling temperature, avoiding superheating. Maintain this temperature until all organic material has been removed from the sides of the beaker and from the solution, which will be indicated by a colorless or slightly colored solution. Remove the cover glass, allow the beaker to cool a few minutes and wash any adhering salts into the beaker. If the cover glass is washed with perchloric acid, the contents of the beaker need not be cooled. The above method is applicable to a wide variety of plant materials; calcium, magnesium, potassium and phosphorus are determined by standard methods.—J. E. GIESEKING, H. J. SNIDER and C. A. GETZ. *Ind. Eng. Chem., Anal. Edit.*, 7 (1935), 185. (E. G. V.)

Paraffin Wax—Tensile Strength and Density at Various Temperatures. The tensile or

breaking strength of commercial paraffin wax was investigated at temperatures between −10° and 30° C. It varies considerably with the temperature, reaching a maximum value of 32 Kg. per sq. cm. at about 3° C. The density was also measured over the same temperature interval; below 25° C. it varies in a linear manner with the temperature, having values of 0.909 and 0.922 Gm. per cc. at 25° and 5° C., respectively. There appeared to be no direct relationships between the two quantities measured.—W. F. SEYER and K. INOUYE. *Ind. Eng. Chem.*, 27 (1935), 567. (E. G. V.)

Peppermint Oils—Detection of Japanese Mint Oil in. The following test for the detection of inferior Japanese oils in oil from *Mentha Piperita* is given: The oil (0.1 cc.) measured in a 1-cc. pipette (graduated in 0.01 cc.) is mixed in a test-tube with 5.0 cc. of a 2% solution of freshly redistilled aniline in glacial acetic acid, added from a burette. The reaction mixture is examined in a 1-cm. cell of a Lovibond tintometer (B. D. H. pattern) after an interval of 10 minutes. The reaction mixture must be protected from bright light. The presence of furfuraldehyde in the Japanese oils causes a red color having a red value of 4.5 to 7.4 when determined as above. Other oils also give some red color which varies somewhat for different types of oils (French, English, Italian, American, etc.) but is very constant for each type and in all cases is much lower than the Japanese, rarely exceeding a value of 1.0. A rough quantitative estimation may be made of the extent of adulteration. Numerous tables are given showing results obtained with various types of true oils, with adulterated oils and with mixed samples of known composition. These results seem to be very satisfactory and conclusive.—D. C. GARRATT. *Analyst*, 60 (1935), 369–376. (A. H. C.)

Phenolphthalein—Irreversible Fading of. Besides the known reversible fading of phenolphthalein, an irreversible fading has been observed and investigated. It takes place on long keeping and is important when the indicator is used as a color standard. The effect is attributed to the formation of a tertiary-carbinol-carbonate ion and its subsequent reaction with hydroxyl ion, since the phenomenon is not observed with phenoltetrachlorophthalein which does not form the tertiary ion.—A. THIEL and G. COCH. *Z. anorg. allgem. Chem.*, 217 (1934), 254; through *Squibb Abstr. Bull.*, 8 (1935), A-666.

Pyramidon—Microchemical Reactions for. The author gives the following microchemical reactions for pyramidon. Pyramidon is not sublimable and identification by this method is impossible. Crystallization by precipitation is best accomplished by the process of salting out. A few grains of sodium chloride are added to an aqueous solution of the substance which causes it to crystallize in prisms often exhibiting refractive coloring longitudinally. The reaction is not particularly sensitive (0.1 mg.). Mayer's reagent causes a precipitate soon resolving itself into yellowish white prisms with angles of 60° and 120°. Recrystallization from acetone improves the reaction. 0.05 mg. (1:200) may be detected. Potassium cadmium iodide and potassium zinc iodide give similar reactions. With platinum chloride beautiful crystals are obtained. These are colored violet by an oxidation product of pyramidon. The reaction works well in a 1:100 solution having a minimum sensitivity of 0.1 mg. Gold chloride gives yellow needles and rosettes which are colored black upon the addition of nitric acid. (Limit 0.05 mg. : dilution 1:200.) Picric acid gives prisms. Sensitivity 0.1 mg. : dilution 1:200. Para-nitro phenol results in beautiful needles. (Limit 0.1 mg. : dilution 1:200.) Iodine potassium iodide gives an excellent crystallization especially when acidified with hydrochloric, sulphuric or acetic acid. Upon the addition of a few drops of acetone two kinds of crystals may be seen, one woolly and yellowish and one prismatic. (Limit 0.02 mg. : dilution 1:200.) Bromine potassium bromide gives green needles with an acidified 1:100 pyramidon solution. The reaction is not very sensitive. Chinosol gives green needles in stellate formation. (Limit 0.2 mg. : dilution 1:100.) Chinosol gives no trace of crystals with antipyrine and by means of this reaction 1% of pyramidon in antipyrine may be detected. Recrystallization from acetone is not necessary in this case.—M. WAGENAAR. *Pharm. Weekblad*, 72 (1935), 612. (E. H. W.)

Red Pill (or Opium Substitute). The author gives in detail a method for the determination of heroin and morphine in a type of pill used for smoking purposes by addicts. Originally the pills were encountered in Shanghai but were later discovered in narcotic raids in the United States. They are very crude, of variable physical and chemical constitution and the work of detecting and determining narcotic alkaloids entails a great deal of tedious analysis, mainly because only traces of heroin and morphine are present, mixed with a host of other innocuous but troublesome materials.—PETER VALAER. *Am. J. Pharm.*, 107 (1935), 199. (R. R. F.)

Sterols—Behavior of, toward Digitonin. Tests showed that only those sterols with a hydroxy group on carbon atom No. 3 in the same steric position as in cholesterol, which do not have too great a variation in the side chain, give precipitates with digitonin.—E. FERNHOLZ. *Z. physiol. Chem.*, 232 (1935), 97; through *Squibb Abstr. Bull.*, 8 (1935), A-598.

Surgical Dressings. Criticism of Some of the Codex Standards. The first point which appears to merit criticism in the new Codex concerns the adopted abbreviation for gram (g). The symbol employed in the B. P. (G) should have been selected, in order to avoid the possibility of confusion between gram and grain. For the convenience and easy reference of the majority, it is suggested that the English names for surgical dressings be given predominance. The difficulties of the Dressings Sub-Committee in drawing up more stringent specifications might have been alleviated by stipulating that no consignment of any dressing should be condemned on one single examination. In the absence of research revealing tests other than visual inspection, to attempt to describe a dressing in circumspect phrases is unsatisfactory. The importance of the use of surgical dressings in the treatment of disease and the fact that most of them are invariably in contact with open wounds warrant the most exacting limits. Another omission which might be remedied in subsequent editions of the Codex is the complete absence of "Actions and Uses" in the Surgical Dressings part of the book. Throughout the whole section there is nothing to guide the apprentice. In the opening paragraph of Part II it is puzzling to find the Codex condoning a common and abused practice by the statement "substances are often added to the size (or filling) in order to increase the weight" without limiting such an offense to a definite percentage basis under the dressings concerned. In the subsequent paragraphs on tests for moisture, water-soluble extractive, foreign matter and cotton and wool, it seems advisable to augment the "dry at 100" by the addition of the words "to a constant weight." The absorbing tests might also be improved, as it is not stated how the dressing should be manipulated during compression.—J. BAIN. *Pharm. J.*, 134 (1935), 747. (W. B. B.)

TOXICOLOGICAL CHEMISTRY

Fluorine—Importance of Fluorinated Methemoglobin in the Determination of, in Industrial Hygiene. The spectral absorption curve of fluorinated methemoglobin has a very intense maximum at $\lambda = 6100$ Å. Methemoglobin cannot be detected in presence of oxyhemoglobin in proportions of less than 25%, but if the methemoglobin is converted into its fluorinated derivative, the sensitiveness is increased to 10%. Determination of the maximum optical density ($\lambda = 6100$) of the fluorinated methemoglobin affords a satisfactory method of determining fluorine that has been added to methemoglobin, within a range of 0.1 to 3 mg., and is therefore suitable for biological and toxicological analyses; for larger amounts, standard methods are satisfactory.—R. FABRE and MELLE S. BAZILLE. *14me Congrès de Chimie Industrielle, Paris*, Oct. 21–27, 1934. 5 pp. (A. P.-C.)

Humors—Chlorine Content of, after Death. The chlorine content (expressed as sodium chloride) was determined in various organic liquids (26 samples of whole blood, 18 of blood plasma, 10 of pericardial liquid, 9 of pleural serosities, 7 of peritoneal liquid, 6 of blood from the liver) of 20 corpses, the samples in all cases having been taken not later than 48 hours after death. In spite of wide variations in individual results, it is concluded that the chlorine contents of the various liquids are lower in the corpses than in the living organism, the differences indicating that after death chlorine diffuses from the richer humors toward the poorer. In diagnosing plasmatic hypochloremia by dilution of the blood of the cadaver (diagnosis of submersion in fresh water), such a conclusion must be based on a decrease in the chlorine content that is decidedly lower than the minimum that can be observed normally.—CHARLES SOUTTER. *Ann. Méd. Légale Criminol. Police Sci.*, 15 (1935), 385–405. (A. P.-C.)

Hydrocyanic Acid—Toxicology of. Hydrocyanic acid absorbed by mouth or respiration can be identified in small quantities by distillation with dichromate and sulphuric acid. The most suitable medium to receive the vapors is silver nitrate in ammonia. Hydrocyanic acid is never formed by putrefaction or decomposition of tissues.—PLUTARCO R. ORELLA. *Anales de Farm. Bioquim.*, 6 (1935), 1. (A. E. M.)

PHARMACOGNOSY

Vegetable Drugs

Cinchona—In Amani. A short historical survey of cinchona in Amani, Tanganyika Territory, is given. The alkaloid content of the various barks in different years is given, 10.55% quinine (as sulphate) in Ledger bark, and 11.21% in hybrid bark, being the highest obtained at any time. The yields of bark from the various species are given and results show that *C. ledgeriana* produces considerably less than the others. The market value of the various barks is discussed, and it is shown that the hybrid commands the best price per tree, *C. ledgeriana* having the lowest value. A description of the preparation and composition of cinchona febrifuges is given.—R. R. Leg. Worsley. *Bull. Imp. Inst.*, 33 (1935), 14–31. (A. P.-C.)

Colophony—East Indian. In Northern Sumatra, colophony and turpentine are obtained from *Pinus Merkusii*, the production in 1933 being 790 tons and 237 tons, respectively. The colophony shows an acid value of about 193, compared with a range of 145 to 185 for the American product.—*Ber. Afd. Handelsmuseum Kon. Ver. Kol. Inst.* (1934), 35; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 284. (S. W. G.)

Derris—Storage of. Derris root, kept in a dry and cool place and not unduly exposed to light, undergoes no loss of rotenone on storage. If powdered, it should be kept in well closed containers. The rotenone content of the samples examined was determined by the ether crystallization method.—I. W. Spoon. *Ber. Afd. Handelsmuseum Kon. Ver. Kol. Inst.* (1935), 90; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 284. (S. W. G.)

Diatomaceous Earth—East Indian. Deposits of diatomaceous earth in the Dutch East Indies are of four types: the Californian marine type, which occurs in a very pure form; the Hanoverian fresh-water type; two abnormal fresh-water types consisting of curved hollow tubes and of long needles, respectively. For the technical utilization of these it is necessary to decide which types are most suitable for particular purposes. In view of the cost of shipping such bulky material, it does not appear probable that export would be profitable.—E. C. J. Mohr. *Ber, Afd. Handelsmuseum Kon. Ver. Kol. Inst.* (1934), 89; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 284. (S. W. G.)

Euphorbia Prunifolia Jacq. This herbaceous plant is common as a weed in the cotton fields of lower Egypt. The morphology and anatomy of the plant are illustrated. The analysis of the plant shows the presence of resins, a caoutchouc-like substance, euphorbone and an acrid irritant vesicating principle. The plant possesses drastic purgative properties and is commonly used by the Egyptian fellaheen for that purpose.—H. Kamel and I. R. Fahmy. *Rep. Pharm. Soc. Egypt*, 6 (1934), 29; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 285. (S. W. G.)

Ispaghula—Structure and Histology of. Seeds of Plantago Ovata Forsk. A detailed report on the anatomy and histology of the seeds is given, including descriptive illustrations. The following summary is given: 1. Ripe seeds of *Plantago ovata* are collected in the Punjab and N. W. Frontier Provinces of India. One hundred seeds weigh from 0.148 Gm. to 0.195 Gm. They are "boat-shaped," about 1.4 mm. wide by 2.8 mm. long. The dorsal surface of the majority of seeds in commercial samples is pale gray-brown with an elliptical central red-brown spot; in a smaller number in each sample the red-brown spot is irregular in size and distribution or covers the whole surface. The furrow in the ventral surface represents the hilum and contains a whitish tissue of collapsed cell walls in which there are two elliptical red-brown gaps one on either side of its center, which is dark in color. 2. The single seed coat consists of: (*a*) The outer epidermis of large, colorless, mucilage cells with a cuticle; in contact with water they swell forming a mucilaginous jelly; three regions in the hemicellulosic mucilage of these cells have different staining reactions; the cells often contain starch grains; this epidermis does not extend beyond the edges of the furrow. (*b*) A layer of collapsed cellulose residues of about six rows of cells. (*c*) The inner epidermis of suberised cells with brown contents, the pigment layer, which completely invests the endosperm. 3. The cells of the endosperm have very thick cellulose walls with large simple pits. The embryo occupies almost the entire length of the seed, its cells as well as those of the endosperm, contain protein and oil. 4. When dead seeds are moistened with water, their embryos become blackened. 5. The variation in color of the seeds is due to the inclusion of a film of air in a split of varying extent in the collapsed layer of the testa; in India the splitting occurs naturally owing to changes in the humidity of the atmosphere. Seeds grown in England remain permanently brown.

The outer epidermis of the testa is easily separated from the remainder of the seed and constitutes "Ispaghula Husks." 6. The mountants which render the cellular structures most clearly evident are aniline and clove oil.—E. W. SKYRME. *Quart. J. Pharm. Pharmacol.*, 8 (1935), 161–185. (S. W. G.)

Opium—Jugoslavian. A comparison of the work of several investigators shows that opium from this country has an average of 14.5% morphine and surpasses in content that obtained from India (8%), Egypt (9.3%), Russia (9.7%), Persia (10%) and Turkey (12%). A table of comparison of this drug from 84 Turkish sources and 105 Jugoslavian sources shows that one-fourth of the Turkish samples have a morphine content of less than 10% and 86.7% of the samples had a content of 14% or less; only 15% of the Jugoslavian samples showed a content of less than 14% and 75.4% of the number had a content of 15–20%. Adulterants were found to be acacia, starch, toasted bread, apricot and quince kernels. The production in this country varies from 20,000–200,000 Kg. annually.—S. BECKER. *Pharm. Monatsh.*, 16 (1935), 85–86. (H. M. B.)

Orobanche Ramosa, L. This parasitic herbaceous plant is known in Egypt as "Haluk." The morphology and anatomy of the plant are illustrated. It contains about 3% of mannite, a small quantity of sugars and tannins, traces of the glycoside orobanchin and its decomposition products, and high proportions of proteins, carbohydrates and ash. The laxative properties for which this plant is used may be due to the mannite present.—M. A. H. MAHDI and I. R. FAHMY. *Rep. Pharm. Soc. Egypt*, 6 (1934), 35; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 286. (S. W. G.)

Pharmacognosy Syllabuses—British and American, Compared. The American pharmacognosy syllabus is considerably wider in scope than that of Great Britain, and aims "to include every crude vegetable or animal drug that the pharmacist is likely to be called upon to sell or dispense." Most of the drugs in the British Syllabuses are included in the American lists, exceptions being *Cera Flava, Creta, Coca, Mel* and *Sabina*. The American syllabus embraces 305 drugs (151 primary and 154 secondary), while the British lists only 80.—G. E. TREASE. *Pharm. J.*, 134 (1935), 680. (W. B. B.)

Withania Obtusifolia, V. Tack and W. Somnifera, Dunal. These two solanaceous species grow in Egypt. The first has been recently discovered by Tackholm. They closely resemble each other anatomically but have characteristic morphological differences. Both of them appear to contain no solanaceous alkaloid.—D. Y. HADDAD and I. R. FAHMY. *Rep. Pharm. Soc. Egypt*, 6 (1934), 41; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 286. (S. W. G.)

PHARMACY

GALENICAL

Alcohol—Concentration of, when Stored in Wooden Vessels. The author stored 60 liters of 56% alcohol in a wooden barrel, in a dry locality where the temperature was fairly high. After eight years the alcohol content had increased from 56 to 75%. He explains this by assuming that the wood of the barrel acts as a dialyzing membrane in which the water is absorbed, the alcohol behaving as a colloid. The absorbed water finally evaporates from the outer surface of the barrel. To prove his contention he placed a hydro-alcoholic mixture in two barrels, the outer surface of one being varnished. The bunghole of the varnished barrel was left open so as to allow some evaporation. After four years the alcoholic content of the mixture was somewhat less. The alcoholic content of the mixture in the unvarnished barrel however increased 4–5% in the four-year period.—P. SAUVAITRE. *Bull. soc. pharm. Bordeaux*, 73 (1935), 111; through *Pharm. Weekblad*, 72 (1935), 826. (E. H. W.)

Althea Leaves and Root—Evaluation of. Many articles have been published basing the determination of mucilaginous drugs on viscosity measurements of the extract. However, it is impossible to give a procedure which will be satisfactory for all mucilaginous drugs. In preparing an extract of the principles of althea root, a minimum of heat should be employed to prevent the solution of starch. A 1.0% extract was prepared as follows: The weighed amount of drug was lightly packed in a tall cylinder, the necessary amount of water poured on, and allowed to stand at room temperature for one hour. Every six minutes the contents were agitated by turning the cylinder through 360° on its horizontal axis. It was then poured through cotton and then filtered clear through a double filter paper. As the result of viscosity measurements run on numerous samples, it may be said that the best results are obtained by macerating a drug all of which will

pass through a 1-mm. mesh sieve for one hour at room temperature in a tall cylinder, shaking gently every ten minutes. An evaluation of althea root is suggested. In the preparation of an extract of the leaves, it was shown that the drug should be powdered as finely as possible. Moderate heat increases the viscosity, whereas heating at water-bath temperature causes a precipitate and lowers the viscosity. A determination for althea leaves is also suggested.—E. WALDSTÄTTER. *Scientia Pharm.*, 6 (1935), 61. (M. F. W. D.)

Cherry Laurel Water and Solution of Hydrocyanic Acid—Preservation of, by Paraffin Oil and Official Vaseline. The concluding article on the preservation studies reported earlier (*J. Am. Pharm. Assoc., Abstract Sect.*, 29 (1935), 71). A vaseline layer superimposed upon the solution of hydrocyanic acid, protection against light and low temperature (refrigerator) give a stable preparation.—A. GUILLAUME and G. DUVAL. *Bull. sci. pharmacol.*, 42 (1935), 211. (C. T. I.)

Chloroform—Preservation of, for Use in Anesthesia. One per cent of absolute alcohol was added to chloroform and the product was kept at 20–26° C. for 6 months in small colored flasks. On examination at the end of this period, the product was clear and had an odor of pure chloroform. Tests for chlorides, chlorine, usual organic impurities, aldehydes, carbonyl chloride, etc., were negative. However, a portion of the above liquid gave positive tests for the impurities named after being subjected to light, and the author concludes that the product should be preserved by the addition of 1% of absolute alcohol and protection from light.—ADELE LISSIEVICI-DRAGANESCI. *J. pharm. chim.*, 21 (1935), 533. (M. M. Z.)

Colloidal Silver (Protargol)—Researches on the Modification of the Physicochemical Properties of, with the Length of Time of Its Preservation. Solutions of protargol are not equally preserved on storing. The concentration of these solutions is influenced but little by the variation of the degree of dispersion of the protargol; on the other hand the quality and the color of the glass of the bottles exercises a very sensitive influence; the greatest decrease in the degree of dispersion being observed when ordinary clear glass is employed. The presence of air likewise presents a considerable effect while its absence affects the degree of dispersion very little. From the sixth day of preservation on, the solutions of collargol showed traces of coagulation. However, from the twentieth day of preservation on, a distinct diminution of the degree of dispersion was observed. The samples studied were composed of particles having diameters of 52–60 $\mu\mu$. The viscosity of the solutions varied according to the nature of the samples, the viscosity being the same when the solutions were of the same concentration. In the last case, the variation of the viscosity in the course of preservation was dependent upon the concentration; as soon as the latter was increased, the viscosity varied still more; it declined in a diluted solution, but increased in a concentrated solution (5–10%). The solutions of collargol presented clearly the properties of lyophilic colloidal solutions. The decrease in the viscosity of the solutions of collargol is in general parallel to the lowering of its degree of dispersion. Whatever may be the conditions of preservation, there is an increase in the coloration of the solutions. This variation is not parallel to the modification of the degree of dispersion. The maximum is produced when preserved in the presence of air. This fact is explained by the modification of the properties of proteins destined to stabilize the preparation.—I. A. FIALKOV and E. M. NATANSOHN. *J. Prikl. Khim.*, 7 (1934), 328–338; through *Chimie et Industrie*, 33 (1935), 674. (W. A. P.)

Drug Extraction. II. The Effect of Fineness of Powder and of Variation in Solvents on the Percolation of Belladonna Root. In connection with a general study of the fundamental principles of drug extraction, drugs of different types were used. The present report is concerned with the swelling of belladonna root in various solvents and the effect of fineness of powder in various solvents. Measurements were made (with a filar micrometer) of thin strips of cross sections before and after the addition of the solvents. A number of proportions of the following mixtures were tried: alcohol and water, glycerin and water, glycerin and alcohol. In hydroalcoholic liquids, increase in alcohol reduced swelling. Alcohol alone had practically no effect. Glycerin alone caused gradual swelling. In mixtures with water, swelling increased with increase of water. For testing fineness of powder Nos. 20, 40, 60 and 80 powders were used. For drug containing 10% of moisture, 90 cc. of menstruum seemed best to render 100 Gm. of drug "evenly and distinctly damp." U. S. P. directions for percolation were used. Various fractions were assayed for total alkaloids and total extractive. Results are tabulated. Within the limits of No. 20 and No. 80 powder, the fineness of powder was of minor importance. Several tables show the results of percolation with various alcohol and water mixtures. As the alcoholic strength in-

creases, extraction of alkaloids becomes more rapid and the yield of extractive greater. Four proportions (alcohol 5, water 1; alcohol 4, water 1; alcohol 7, water 3; alcohol 1, water 1) have approximately the same efficiency, extracting substantially all the alkaloid. Menstruum for U. S. P. fluidextract appears to be well chosen. Swelling of the belladonna is discussed in connection with the swelling of chestnut wood reported in a previous experiment.—WILLIAM J. HUSA. *J. Am. Pharm. Assoc.*, 24 (1935), 446. (Z. M. C.)

Drugs—Storage of, New Problems in. The proper storage for drugs is of growing importance as shown by: (1) The increasing skill in chemical manipulation which has led to the isolation from natural sources and the marketing of remarkably unstable substances with very definite and pronounced physiological action, whose existence was not even suspected twenty-five years ago. (2) The synthetic preparation of an increasing number of complex organic substances characterized by relative instability, in particular the metallic organic medicaments. (3) The introduction of new methods of administration, *e. g.*, parenteral methods, where the medicament is introduced outside the body's natural defenses, often in massive doses. (4) The decomposition of drugs which may be initiated by methods of sterilization. A study of the properties of insulin will indicate how easily substances of this class are inactivated. Studies on vitamin A indicate that the factors essential for stability should be the absence of oxygen, low temperature, choice of suitable vegetable oils as a solvent. Vitamin C may be kept in preserved fruit juice, which has been tyndallized in the absence of air. Evidence collected shows that solutions of irradiated ergosterol in olive oil prepared under certain defined conditions and kept at 0° C. retain their activity unchanged for two years, but are liable to lose their activity slowly at room temperature. It is important that preparation be carried out under well controlled conditions, as the stability of various makes appears to be different probably due to the difficulty of removing traces of oxygen during irradiation. A knowledge of the stability of metallic organic compounds of arsenic, gold, bismuth, antimony and mercury is essential owing to the ease with which changes may occur in their constitution. Special care must be taken to prepare fresh solutions of these metallic substances, and they should also be kept in an inert atmosphere. Sterilization, bacterial infection, chemical changes, oxidation, autoxidation and actinic reaction are other factors which influence stability.—J. E. BOWEN. *Pharm. J.*, 134 (1935), 351. (W. B. B.)

Galenical Tinctures of D. A. B. VI. Intimate Knowledge of the Tincture. The eight various menstruums used in the preparation of the 41 tinctures are listed with examples. The official definition as given in the D. A. B. is discussed literally. Vinegars are also included. *Types and reasons for the Spontaneous Changes in Tinctures.*—For a complete understanding, the knowledge of the causes of turbidity and of the deposits in the tinctures is necessary. Likewise a knowledge of the solubilities of the constituents of the drug in the menstruum used and the temperature of manufacture is required. Variation in temperature of the tincture stored may be different from that of the manufacturer but sufficient to cause a sedimentation. Changes by oxidation and reduction may be due either to external factors such as sunlight, or internal factors, by certain constituents such as ferments, enzymes, hormones or vitamins. *Old and New Possibilities of Examinations.*—The author cites physico-physiological properties grouped to distinguish tinctures such as color, color and odor, and color and taste. Some tinctures possess all three attributes. The comparison of the color tone to a color scale, *e. g.*, Ostwald color scale, is preferred. The residue remaining after evaporation of the tincture may be used as a test. The alcohol number, *i e.*, the cc. of alcohol in 10 Gm. of tincture determined after saturation with potassium carbonate, is a newly introduced test. The author reviews certain documents on the history of the introduction of capillary analysis as a means of detection in pharmacy and cites Friedrich Goppelsroeder as the Father of Capillary Analysis.—HERMANN KUNZ-KRAUSE. *Pharm. Zentralh.*, 76 (1935), 174, 205. (E. V. S.)

Iodine—Antiseptic Power of Certain Solutions of. This is a confirmation of the work of LaWall and Tice and of Karns. The tinctures of iodine usually employed are much too concentrated; the formula containing iodine, 2 Gm.; potassium iodide, 2.4 Gm.; and diluted alcohol (about 50%) a sufficient quantity to make 100 cc., possesses a raised germicidal power, does not irritate the skin and penetrates easily, has a saline concentration near that of the serum, mixes perfectly with water and answers all needs.—T. SATRIANO. *Ann. Farm. Bioquim.*, 5 (1934), 37–50; through *Chimie et Industrie*, 33 (1935), 674. (W. A. P.)

Iodine Ointment—Non-Staining. During the course of the examination of a number of

samples of non-staining iodine ointment a large variation in iodine content was noted. Investigations were carried out regarding the absorption of iodine by different bases under varying conditions. Iodine is only slowly absorbed by a base of melted vaseline (B. P. 1923) and prolonged heating is necessary to effect combination. This results in the loss of a large proportion of iodine, especially if an open vessel be used. The National Formulary (Great Britain) directs the iodine to be rubbed down with arachis oil in a warm mortar until solution is effected. Melted soft paraffin is then added and the whole thoroughly mixed. A sample made strictly according to these directions does not result in a non-staining preparation. On heating there is a further gradual absorption of iodine by the base, but at the same time loss of free iodine occurs. The directions given by the B. P. C. 1934 are to mix the iodine with the arachis oil, add the yellow soft paraffin and heat gently with occasional stirring at a temperature not exceeding 60° until complete combination is effected, as indicated by the disappearance of the brown color. However, complete combination is not a practical proposition nor is it necessary in order to produce a non-staining preparation. Further, contrary to the B. P. C. statement, the disappearance of the brown color is not an indication of complete combination—the brown color disappears when the free iodine falls below about 0.7%. During the manufacture of the N. F. and B. P. C. 1934 ointments a dark brown resinous substance is produced which sticks to the sides and bottom of the vessel. The formation of this substance results in a serious loss of iodine, since 17.26% iodine was found in the alcohol-soluble portion of the substance, and 4.46% iodine in the alcohol-insoluble portion.—R. W. RICHARDSON. *Pharm. J.*, 134 (1935), 589. (W. B. B.)

Kaolin—Emulsifying and Suspending Power of an Extracolloidal, "Kaolin Blanc Extra-Colloidal Suspensiv" (Gignoux & Co., Lyon, France). This product consists of particles 250 times smaller than the finest baryte and 20 times smaller than the regular colloidal kaolin, possesses unusual water-absorptive power, remains suspended in water, stabilizes emulsions of both types inactive, tasteless and odorless. For liquid emulsions 1–5% is necessary; for pastes or thick emulsions at least 7% and it must always be added to the water. For concentrations to 7% an egg beater may be used to bring about dispersion; if mechanical stirrers are used concentration to 17% may be obtained. It is used as an absorbing, wetting and gelatinizing agent in various pharmaceutical and cosmetic preparations such as toothpastes, skin salves, antiseptics, disinfectants, for emulsification, suspension and dispersion of pigments, oils, waxes and resins, as an adhesive, thickening and emulsifying agent for creams, face milks and liniments, as an extraction medium for pomades and drugs and in a dry condition for shampoos and face powders.—*Riechstoff-Ind. Kosmetik*, 10 (1935), 112. (H. M. B.)

Ointment Making. Bases include the two forms of wool fat, petrolatum, absorption bases from lanolin, benzoinated lard, cold cream and greaseless bases from glyceryl monostearate or vanishing cream. Anhydrous is seldom used alone and petrolatum is added to it to make it spread easily. Ointments for the face, sunburns, etc., are often made with cold creams or greaseless cream bases. Lanolin and its bases are employed when quick penetration is desired; petrolatum when slow action is wished. Lanolin has supplanted benzoinated lard which is not so easily absorbed and tends to become rancid. Hydrogenated oils as cottonseed are being used for tin ointments to which they impart good body, spreading qualities and sufficient absorptiveness for ordinary purposes. Waxes are added only to give body; beeswax is preferred since it makes the ointment less granular; cocoa butter is often added for emollient effect. Other bases used which are not so desirable are glycerite of starch and casein cream. The function of an ointment is to (1) promote healing, (2) allay pain and (3) protect the affected area from infection and the air. Effective antiseptics are mercury salts and phenols. The details of commercial manufacture are given.—ANON. *Drug and Cosmetic Ind.*, 36 (1935), 687–688. (H. M. B.)

p_H—Pharmaceutical Study of. This concludes a report begun in the previous JOURNAL, taking up first p_H and stability of galenical preparations. A considerable number of the various findings are reported. With ergot preparations there are also contradictory statements. Confusion in literature is increased by the undependable results of various assay methods. Six investigators have concluded that p_H of the fluidextract and alkaloid solutions should be adjusted to about 3.0 but they do not agree about which acid is best. Others think this figure questionable. Adjusting hydrogen-ion concentration has been quite successful with aconite preparations. Swanson did the original work recommending that p_H values of tinctures and fluidextracts be adjusted between 2.5 and 3.00. Among miscellaneous vegetable preparations which can be im-

proved by adjusting p_H are Compound Tincture of Gentian, preparations of veratrum, gelsemium, nux vomica and B. P. Compound Tincture of Cardamom. Scoville has studied a large number of tinctures of lesser importance, precipitation being increased in some, retarded in others. Miscellaneous chemical preparations have had considerable study. Some of these are Syrup of Ferrous Iodide and Syrup of Hydriodic Acid, solutions of arsenous iodide, solutions of potassium arsenite, Donovan's Solution, Solution of Iron and Ammonium Acetate, Iron and Ammonium Citrate, Solution of Magnesium Citrate. Fungous growths in Acid Solution of Phosphates can be prevented by addition of acid and precipitation in Compound Elixir of Glycerophsophates was reduced by addition of lactic acid. P_H affects color of Elixir of Ferric Pyrophosphate. P_H of Spirit of Ethyl Nitrite changed greatly during deterioration. Various hypochlorite solutions show much variation in p_H. There is evidence that hypochlorous acid ionizes in an amphoteric manner. P_H is an important factor in the stability of alkaloids during sterilization; p_H of solutions for injection must be stabilized to a value comparable to p_H of blood. Buffering to the physiological p_H, solutions of morphine, cocaine, tutocaine and larocaine for injection is important. Decomposition of morphine at high temperatures and at different p_H values has had considerable investigation. Cocaine requires an acid medium for stability. Various investigations are reported. Dissociation constants for cocaine and its hydrolysis products have been determined. The results are given. Other alkaloids discussed are procaine, atropine, homatropine, cinchona alkaloids, hydrastine, physostigmine and pilocarpine. Miscellaneous organic compounds studied were sodium luminal, thiosulphates, benzyl alcohol solutions, urotropin solutions, strophanthin solutions, iodoform in solution, hydrogen peroxide solutions, phenol neoarsphenamine. Fundamental principles, not yet of practical value, have been established. Ions which are in an adsorbed state have reaction qualities different from free ions. Hydrogen-ion concentration measurements on synthetic solutions in connection with pyrophosphates have been of value. The presence of a transition point at p_H 4.3 between the two types of oxidation, addition of oxygen and evolution of hydrogen has been demonstrated. A number of p_H values for the maximum stabilty against hydrolysis of esters have been determined and some of these are given. Olivier has claimed that the influence of the hydrogen-ion concentration upon hydrolysis is conditioned by the nature of the compound. A bibliography of more than 300 references is appended.—FREDERICK F. JOHNSON. *J. Am. Pharm. Assoc.*, 24 (1935), 498. (Z. M. C.)

Pills—Adsorptive Properties of Substances Used in the Preparation of. The author summarizes his work as follows: 1. Of the vegetable constituents employed in the preparation of pills the greatest adsorbing power in relation to strychnine is found in althaea and licorice roots. 2. The adsorbing properties of a dandelion powder are insignificant; they are lower than those of yeast extract. In the preparation of pills with strychnine it is most rational to use dandelion root as the inert constituent. 3. The vegetable constituents employed in the preparation of pills cannot be looked upon as indifferent, because adsorbing the therapeutic substance from the pillular mass they influence the pharmacodynamic effect of the therapeutic agent. 4. Considering the change in conditions of the pharmacological activity of therapeutic substances it is necessary to work out exactly the nature of constituents employed in the preparation of pills, so as to know what vegetable constituents must be used for a given substance. 5. Pills containing alkaloids must not be kept for a long period of time.—T. TSCHERIKOESKYA. *Sovets. Pharm.* (1935), 1–7. (A. S. S.)

Plants—Ultrafiltration and Its Application to the Extraction of the Active Principles of. A description of the preparation of ultra-filters. The active principles of belladonna, henbane and strophanthus pass through an acetate-collodion filter, of porosity calculated to let pass only crystalloids as Graham understood that term, and can thus be obtained in a very pure state.—L. I. BRACCIO. *Boll. chim. farm.*, 74 (1935), 185; through *Chem. Abstr.*, 29 (1935), 4517.

Propylene Glycol—Use of, As a Solvent. Experiments were carried out to ascertain the value of propylene glycol as a solvent for pharmaceutical use. From the results of these experiments, it appears that propylene glycol is not as good a solvent as ethylene glycol of defatted cochineal, but in the case of cudbear it is superior. Propylene glycol is a solvent of the constituents of aloes which react with ammonia, and of the tannins in catechu. It is suggested that further work should be done to test the non-toxic properties accredited to propylene glycol.—J. RAE. *Pharm. J.*, 134 (1935), 590. (W. B. B.)

Pyrethrum—Deterioration of. The loss of insecticidal activity of pyrethrum is due to

oxidation and is activated by light. It can be partially inhibited by hydroquinone or tannic acid. Some slow loss of potency occurs during storage, the cause of which is unknown. Extracts dissolved in kerosene and other inert solvents are fairly stable. Strong soaps and alkalis may be deleterious because they hydrolyze the esters.—F. TATTERSFELD. *Chem. Trade J.*, 96 (1935), 273; through *Squibb Abstr. Bull.*, 8 (1935), A-937.

Raspberry and Strawberry Flavors. Raspberry extract may be prepared by pulping the fruit, allowing it to ferment with sugar at 25–30° and concentrating by distillation; sugar and acid should be in ratio of 100 : 47. Addition of vanillin or vanilla extract is desirable. Cheaper extracts may be fortified with synthetics such as: iso-butyl formate, or acetate, iso-butyl acetate, iso-amyl butyrate and iso-butyrate. Other substances used in large proportions are ethyl formate butyrate, iso-butyrate, oenanthate, iso-amyl acetate and acetaldehyde. Small quantities of clove oil and alpha-ionone and traces of ethyl benzoate, neroli oil, terpeneless lemon oil, cinnamon oil, orris oil and methyl salicylate have also been recommended. In the case of strawberries, the fermentation process is omitted and the alcohol recovered by distillation *in vacuo*. It should be fortified by the addition of ethyl methyl phenyl glycidate ("Aldehyde C16"). Traces of methyl salicylate and pimento oil, coumarin with or without vanillin and the following esters may be employed: iso-amyl butyrate, and iso-butyrate, ethyl formate, acetate, butyrate, iso-butyrate, pelargonate, benzoate and cinnamate, iso-amyl formate and valerate, benzyl acetate and valerate. Other constituents are benzaldehyde, eugenol, clove oil, cinnamon oil, neroli oil, terpeneless orange oil, orris oil and cognac. The sugar to acid ratio should be 100 : 16.—H. STANLEY REDGROVE. *Am. Perfumer*, 30 (1935), 193–194, 222. (G. W. F.)

Solution of Adrenaline (1–1000)—Practically Neutral, with Good Keeping Qualities. The following formula is recommended: Adrenaline 1 Gm., *N* hydrochloric acid 5.45 cc., solution of sodium bisulphite (d. 1.33) 5 cc., sodium chloride 7 Gm., water enough to make 1000 cc. The amount of hydrochloric acid used is the quantity theoretically required to form the hydrochloride of the adrenaline, and the p_H of the solution is 3.8.—LOUIS JULIEN. *J. pharm. chim.*, 22 (1935), 53–59. (S. W. G.)

Solution of Bismuth and Ammonium Citrate, B. P. C. 1934. It is suggested that 20 cc. of distilled water be used in preparing Liquor Bismuthi et Ammonii Citratis B. P. C. for mixing the citric acid and the bismuth subnitrate, instead of 2 cc. as stated by the B. P. C. Also, more detailed instructions regarding the washing of the bismuth citrate should have been given in the B. P. C. regarding this solution.—R. D. KOTWAL. *Pharm. J.*, 134 (1935), 564. (W. B. B.)

Solutions—Sterilization of, for Injection. Many drugs intended for parenteral administration are of a heat-labile nature, the heat stability varying with the drug under consideration. The degree of thermostability and the loss in activity of the solutions during periods of storage at ordinary temperatures are closely related problems. All apparatus used in the preparation of Solution of Adrenaline Hydrochloride B. P. must be sterile, and, together with the ingredients, should be free from alkali, iron and ammonium salts. A routine method for preparing this solution is to dissolve the chlorbutol and sodium chloride in 90% of the finished volume of hot sterile distilled water, stopper the vessel with a sterile rubber bung and allow to cool. Place the adrenaline in a small bottle, displace all the air by an inert gas such as nitrogen and add a few cc. of sterile distilled water followed by the hydrochloric acid measured from a sterile pipette. Pour this solution into the solution of chlorbutol and salt, rinse the smaller vessel with several quantities of sterile distilled water, add to the main solution, make up to volume, displace all air from above the solution, stopper and mix well. In regard to solutions of morphine salts, the p_H value, often a good guide to the extent of decomposition, gives little assistance, a highly decomposed sample having a p_H showing little variation from a normal solution. It seems, however, that the change is one of oxidation, and a more stable solution may be made by preparing it under aseptic conditions, with the total exclusion of atmospheric oxygen. A satisfactory 50% solution of dextrose has been prepared by the routine method of dissolving the requisite amount of dextrose B. P. in an equal quantity of boiling, distilled water contained in alkali-free resistance glass apparatus. The solution so obtained is filtered through a bed of fine kieselguhr on a Büchner funnel and corrected to volume when cold by a further suitable addition of water. It is then ready for sterilization at 10 pounds for half an hour.—H. GARTSIDE. *Pharm. J.*, 134 (1935), 507. (W. B. B.)

Sterile Solutions—Preparation of Some. Detailed directions are given for preparing sterile solutions of the following for intravenous therapy: camphoric acid and salts, camphorcarboxylic

acid and salts, camphorthiocarboxylic acid and salts, (p-$CH_3C_6H_4S$-)$_2$, naphthoresorcinol, ninhydrin, sodium polythionates, quinine, copper and urotropine salts, tetraglycolyl orthosilicate, dyes, diphenyl derivatives, erythritol tetranitrate and nitroglycerin.—E. CHIERICI. *Boll. chim. farm.*, 74 (1935), 145; through *Chem. Abstr.*, 29 (1935), 4516.

Sterilization Notes. The article contains a summary of the conclusions from discussions on papers on sterilization. In brief, the conclusions are: (1) Ampuls must be previously cleansed, and sterilized by hot air at 160° for two hours; (2) distilled water should be used; (3) neutralized and sterilized oil must be used for oily liquid injections; (4) greatest of aseptic conditions should be observed; (5) autoclaving at temperatures between 110° and 120° for fifteen to twenty minutes is the perfect method of sterilization; (6) bacteriological control should be maintained over preparations if filters are used; (7) neutral glass should be used for ampuls; (8) stocks should be renewed frequently.—ANON. *Pharm. J.*, 134 (1935), 384. (W. B. B.)

Sterilization Notes. Samples of olive oil and almond oil, submitted to sterilization by heating to temperatures of 150° C. to 155° C. for one hour, were examined at intervals in order to detect any effects due to heating. Sterilized olive oil showed considerable loss of color and had developed a greenish shade. Almond oil was slightly less colored than an untreated sample. The acid value of the two oils, after treatment, was the same as before treatment. No increase in the acidity was noticeable at weekly intervals for a month. The conclusion is that the treatment causes no subsequent deterioration. R. A. O'Brien and H. J. Parish state that the accumulated experience of some years convinces them that heating contaminated oil to 150° C. for an hour ensures sterility, whatever the contamination. They also state that "the prescribed method of Tyndallization may fail to sterilize contaminated oils." Novocaine dissolved in 0.001N hydrochloric acid is stable when sterilized in a current of steam, and hydrolysis on autoclaving is not more than 2%. Hydrogen-ion concentration is not affected by sterilization. The p_H value of novocaine solutions should not be more than 5. Ampuls for novocaine solutions should be made of Jena glass, since the action of a minute quantity of alkali on an unbuffered solution can alter the p_H value and cause strong hydrolysis.—ANON. *Pharm. J.*, 134 (1935), 647. (W. B. B.)

Suppository Mold—Apparatus, Small Scale, for Pharmaceutical Manufacturing. The mold, made of a nickled brass alloy, prepares 100 suppositories and weighs about 6 Kg. The form is divided horizontally into two halves at a point where the suppository has the greatest diameter. The two halves fit together by four guide grooves with springs at the corners, and are tightened by

two wing nuts. The method of assembling and using the mold, as well as the proper preparation of the suppository mass, is described in detail.—GÄRTNER and SCHENKER. *Schweiz. Apoth.-Ztg.* 73 (1935), 357. (M. F. W. D.)

Tincture of Ginger, Strong. The last British Pharm. reinstates Tinct. Zingib. Fort. after its having been omitted from the two intermediate issues. The changes after an interval of nearly fifty years are practically negligible; "moderately coarse powder" replaces "fine powder," directions for the process of percolation have been deleted and metric weights and measures are used.—C. E. DODSLEY. *Pharm. J.*, 134 (1935), 602. (W. B. B.)

Water-Sterilization of, by a New Quartz Lamp. An apparatus is described for the sterilization of water and such oils as cod liver, soya bean, rape, etc.—*Riechstoff-Ind. Kosmetik*, 10 (1935), 111. (H. M. B.)

Pharmacopœias and Formularies

Pharmaceutical Formularies and the Belgian National Formulary. A historical review of the formularies and dispensatories of many countries with special emphasis on the Belgian publications.—O. Van Schoor. *J. pharm. Belg.*, 17 (1935), 383–388, 405–410, 430–434. (S. W. G.)

Pharmacopœial Questions from Practitioners. Two preparations of the Swiss Pharm. V—Tablets of Ipecac and Opium and Pastilles of Sodium Bicarbonate—are considered. The formula of the first differs considerably from that in the fourth edition and should no longer bear the synonym Vignier Tablets. The title of the second preparation should be Compound Pastilles of Sodium Bicarbonate.—J. B. L. *Schweiz. Apoth.-Ztg.*, 73 (1935), 321. (M. F. W. D.)

Pharmacopœias—The Oldest of Switzerland. A brief history of some of the outstanding pharmacopœias is given. The earliest ones were private enterprises, the first appearing in Basle in 1561. Before this the mention of drugs was made in price lists, the first of these being dated 1404. Pharmacopœias as such are of comparatively recent origin. The first Swiss Phar. appeared in Latin in 1865, the second in 1872, the third in 1893 and the fourth in 1907. The earliest record of an apothecary shop is found in Basle in 1250.—Anon. *Schweiz. Apoth.-Ztg.*, 73 (1935), 269 (M. F. W. D.)

U. S. P. Revision. The Committee of Revision of the Pharmacopœia of the United States 1930–1940 has issued the U. S. P. X Interim Revision Announcement No. 4, which includes revised or new texts for Magnesia Magma, Oil of Lemon, Non-destearinated Cod Liver Oil, Large Poison Tablets of Mercury Bichloride and Small Poison Tablets of Mercury Bichloride. The tests become official on October 1, 1935. The revised text omits the manufacturing details for milk of magnesia, but adds more exacting requirements for uniformity and purity than were in the old text, these being capable of enforcement through appropriate tests. For purposes of minimizing the action of magnesia magma on glass containers, 0.1% of citric acid may be added. The modification of the standards for oil of lemon brings them into conformity with new developments in manufacture, and authorizes the official use of a domestic oil of lemon. Increasingly large importations of so-called "undestearinated cod liver oil," for subsequent destearination, made desirable appropriate standards and tests of this non-destearinated cod liver oil. The poison tablets of mercury bichloride must be of a distinctive color (not white) and shall be of an angular or irregular shape (not discoid). When sold in quantities for household use they should be dispensed in glass containers of a distinctive angular shape, having irregular or roughened sides or edges. On the exterior of each container must be placed a red printed label bearing the word "Poison" and a statement indicating the amount of corrosive mercuric chloride per tablet.—Anon. *Pharm. J.*, 134 (1935), 748. (W. B. B.)

Non-Official Formulæ

Cellulose Varnish. A varnish containing, *e. g.*, benzylcellulose 5–18, benzine 18–40, toluene or xylene 25–45 and butyl acetate 20–35% or benzylcellulose 2–12, benzine 50–80 and ether 25–80%, used for pharmaceutical or toilet purposes, is contained in a collapsible tube and used as required.—J. Wald and G. Legrand. French Pat., 777,999. (Mar. 6, 1935); through *Chem. Abstr.*, 29 (1935), 4526.

Cleansing Cream Containing Magnesium Hydroxide. A cleansing cream which is solid at room temperature contains beeswax 1–6, petrolatum 30–60, mineral oil 30–60, free magnesium hydroxide 0.5–6.0 and water 10–30%. U. S. Pat. 1,999,161 relates to a skin cream comprising petrolatum, a cholesterol alcohol, ceresin wax, magnesium hydroxide and water.—Bruce Walton (to Chas. H. Philips Chemical Co.). U. S. Pat. 1,999,160 (April 23); through *Chem. Abstr.*, 29 (1935), 4136.

Cosmetic Pomade. A pomade contains paraffin 40, camphorated oil 24, camphorated alcohol 130, sulphur extract 1 Gm. and tincture of iodine 40 drops.—F. Balzarelli and C. Baldini. French Pat., 778,236 (Mar. 12, 1935); through *Chem. Abstr.*, 29 (1935), 4526.

Cosmetics—Progress in, in 1934. A discussion of the progress made in 1934 in producing new shaving, hair and skin creams, face lotions and packs, sunburn and suntan preparations; depilatories, eye and lip cosmetics, bath, tooth and mouth products is offered.—Karl Pfaff. *Riechstoff-Ind. Kosmetik*, 10 (1935), 88–92. (H. M. B.)

Dentifrices. Oils, fats or waxes are used as means for giving to the preparations the desired consistency. Examples contain (1) liquid paraffin 200, gum tragacanth 20, soap 30, sodium

perborate 30, saccharin 0.5, essential oils 2 and calcium carbonate 250 Gm., and (2) olive oil 200, potassium acid phosphate 20, gum tragacanth 20, saponite 20, saccharin 0.5, essential oils 2 and calcium carbonate 250 Gm.—G. BEHR. French Pat., 778,232 (Mar. 12, 1935); through *Chem. Abstr.*, 29 (1935), 4525.

Derris Root—Uses of. Derris is effective against the following parasites: many caterpillars, probably all larvæ of leaf-eating wasps, many beetles and their larvæ, turnip fleas, flower wasps, plant lice and red spiders. It is of no value against wasps, adult flies and moths, certain kinds of caterpillars, many beetles and scale insects. The powdered root, mixed with 40 parts of talc, makes a very good insect powder for dogs and cats.—*Ber. Afd. Handelsmuseum Kon. Ver. Kol. Inst.* (1934), 90; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 300. (S. W. G.)

Face Powders—Trends in. A sample of face powder taken from an early Roman tomb analyzed by the British Museum was found to be much like modern powders and to contain talc, lead carbonate, chalk and clay. In the intervening period little has been done but to eliminate the poisonous ingredients and to better balance the properties. Recent discoveries take two forms: (1) face powder bases and (2) the substitutes. The former are really ingredients intended to improve slip and because of their adhesiveness to supplant stearates; others are intended to provide better covering power and adhesiveness, the slip being provided by talc. The substitutes are intended to provide all of the necessary properties of a face powder, *i. e.*, covering power to a correct degree, slip, adhesiveness and sufficient absorbing power to hold perfume and color. The outstanding property to be concerned with is covering or hiding power. There is a real demand for a powder which does not become translucent and some new bases have been developed to utilize the principle of diffusion of light through the use of uniform infinitely fine (10 microns or less) particles of a particular shape rather than depend upon the reflection of light from varying percentages of opaque pigments.—F. CHILSON. *Drug and Cosmetic Ind.*, 36 (1935), 685–686. (H. M. B.)

Grease Paints. Grease paints are made up of two main constituents, namely, a dry base and a fat base. The dry base is selected from raw materials such as zinc oxide, kaolin, precipitated chalk. The more expensive dry bases are titanium oxide and subnitrate of bismuth which are used in high-class grease paints. The fats used for the fat base have to be so selected that the product will only melt at a temperature higher than that of the blood. The fat base should be made up of selected material such as hard paraffin, soft paraffin, liquid paraffin, beeswax, lanolin and oils such as kernel and almond oil. The adhesion of the grease paint to the skin of the face is one of its main features. The perfume is added to the fat base, and the coloring matter to the dry base. Thorough incorporation of the one base with the other is absolutely essential, and any failure in this respect would ruin the entire composition.—A. G. AREND. *Perf. Ess. Oil Rec.*, 26 (1935), 254. (A. C. DeD.)

Hair Dyes—Manufacture of. A discussion of the manufacture of hair dyes including the system of preparation and the examining of the dyed hair is given.—A. G. AREND. *Perf. Ess. Oil Rec.*, 26 (1935), 211. (A. C. DeD.)

Hair Lotion. The lotion contains alcohol 420, camphor 15, ammonia 22, turpentine oil 40 and camomilla decoction 415 Gm.—HENRI FAGNY. French Pat., 776,966 (Feb. 8, 1935). (T. G. W.)

Hormonöl Supra (Chemische Laboratorium Dr. Kurt Richter, Berlin) is the pure oil of *Chelonian Athecæ* Sp. *Sphargidæ* (giant turtle oil?) from Mexico. The oil penetrates the epidermis of the human skin extending through the corium to the subcutaneous tissues. It represents the most natural and strongest astringent known being completely absorbed by the human skin. It closes large pores and removes wrinkles. Since the oil is drying it may be used as such for oily skins; for dry skins, however, it should be used with about 10% vegetable oil (almond oil). The following formula for a skin cream is offered: Hormonöl Supra 20%, white American petrolatum 15%, lanolin 10%, Hydrocerin 10%, spermaceti 5%, water 45%. To obtain the maximum astringent action a cream should contain at least 20% of the oil. In preparing the cream do not stir any more than is necessary for emulsification; no more air than is necessary should be introduced. Since the oil begins to decompose at 35° C. it should not be heated over a direct flame and in a cream the oil should be added when the mass has cooled to this temperature. The value of the oil depends upon its high vitamin content and the presence of certain hormones which have a specific action on slackened cellular tissue. It may be substituted in part for oils used in fatty or

night creams and also enter the composition of nourishing, wrinkle and other creams.—*Riechstoff-Ind. Kosmetik*, 10 (1935), 111–112. (H. M. B.)

Lanolin and Its Uses. The following formulas are suggested: *adeps lanæ cum aqua:* adeps lanæ 75%, distilled water 25%; *pharmaceutical lanolin ointment:* adeps lanæ anhydr. 65, distilled water 20, mineral oil 15; *lanolin cream:* petrolatum 100 Gm., lanolin anhydrous 300 Gm., water 600 Gm; *lanolin cold cream:* fatty almond oil 4200 Gm., white beeswax 600 Gm., spermaceti 600 Gm., lanolin 1800 Gm., stearin alcohol 200 Gm. (may be omitted), water 2800 Gm., borax 50 Gm., *boroglycerin-lanolin prescription:* A. Dissolve 10 Gm. boric acid with heat in 40 Gm. glycerin and add 200 Gm. water. B. Paraffin 200 Gm., liquid paraffin 500 Gm., anhydrous lanolin 50 Gm., stearin alcohol 20 Gm., cholesterin 10 Gm. Fuse one with another until solution results. In perfuming lanolin creams too delicate odors do not permeate while stout strong odors are too rough. The following are suggested: chypre, violet, honeysuckle, benzyl acetate, certain hyacinth compounds and aldehydes. Lanolin powders may be prepared by dissolving lanolin in acetone and incorporating with the powder, or by fusing lanolin 10, stearin alcohol 1 and mineral oil 5, slowly adding 20 Gm. water containing 1 Gm. potassium stearate, cooling, adding 50 Gm. of water to form an emulsion. Add this to 300 Gm. powder, dry, pulverize and sift. In superfatting soaps, 5% of lanolin is easily absorbed by soaps. It causes reduction in lathering power which may be corrected by addition of coconut oil, triethanolamine (2–5%) or stearin alcohol (2–5%). Lanolin promotes water in oil emulsions.—Josef Augustin. *Am. Perfumer*, 30 (1925), 187, 188, 192. (G. W. F.)

Mouth Wash Powders. The powders comprise a stabilized oxygen-yielding compound mixed with a silver-containing compound and preferably also with an acid substance. The oxygen-yielding compound, *e. g.*, urea-hydrogen dioxide, alkali peroxide-pyrophosphate, alkali perborate or percarbonate, is preferably free from water of crystallization and is stabilized in known manner, *e. g.*, with magnesium silicate. The silver compound may be an inorganic salt, *e. g.*, silver nitrate, silver sulphate or the silver chloride-ammonium compound, or an organic salt, *e. g.*, silver acetate, or the benzoate, salicylate, or *p*-hydroxy-benzoate. Citric, tartaric, boric or phosphoric acid, etc., or acid compounds, *e. g.*, acid phosphates are used preferably in such proportion as to neutralize only 40 to 60% of the alkalinity of the oxygen-yielding compound. Flavorings and perfumes may be added. In an example, dehydrated sodium borate 30 is mixed with the silver salt of *p*-hydroxy-benzoic acid 1.6 and tartaric acid 11.25 Gm.—*Deutsche Gold- und Silber-Scheideanstalt vorm. Roessler.* Brit. Pat., 421,692 (Dec. 28, 1934); through *Chem. Astr.*, 29 (1935), 3785.

Dispensing

Apomorphine Hydrochloride—Preparation of, for Injection. The Spanish Phar. method gives the most stable solutions. Although present methods do not yield solutions which are permanently colorless, there is no loss of activity associated with the appearance of the green color.—D. Ponte. *Giorn. farm. chim.*, 84 (1935), 53; through *Chem. Abstr.*, 29 (9135), 4517.

Arsenical Fowler Solution. The author discusses the change in formulas for Fowler Solution involved in the third and fourth editions of the Belg. Phar. In the B. P. III the formula was, Arsenic trioxide 1 part, Potassium carbonate 1 part, Water 2 parts. This was changed in the B. P. IV to, Arsenic trioxide 1 part, Potassium bicarbonate 1 part, Water 2 parts. The chemical reactions involved in the preparation of Fowler Solution are discussed with several references to the literature.—G. Verschuere. *Pharm. Tijdschr. Nederland.-Indie*, 13 (1935), 41. (E. H. W.)

Bakelite Containers. In order to utilize bakelite ointment jars, it is not sufficient to see that they are not attacked. Attention should be given to the ointment itself which may undergo alterations, especially modifications of coloration. This is noticeable in phenolic preparations. It is necessary to direct the attention of the manufacturers of bakelite to these facts.—Bucchi and Schenke. *J. suisse pharm.*, No. 20 (1935), 242; through *J. pharm. Belg.*, 17 (1935), 511. (S. W. G.)

Calcium Gluconate for Injection. Various methods of manufacturing calcium gluconate are mentioned. The method of preparing solutions for injection as used by the firm of Merck, Darmstadt, is as follows: calcium gluconate, pure, for injection "Merck" is dissolved in the proper amount of water by warming and then heated under a reflux condenser for two to three hours. The warm filtered solution is then run into carefully rinsed and sterilized ampuls, being sure that

none of the liquid remains in the neck of the ampul. The ampuls are then sterilized for one hour at 100° on at least three successive days.—C. A. ROTHENHEIM. *Pharm. Acta Helv.*, 10 (1935), 114. (M. F. W. D.)

Capsules—Accuracy and Speed Factors in. Methods employed in determining contents of capsules are: (1) dissolving contents of capsule and subsequent evaporation of solvent; (2) assay of ingredients; (3) emptying contents and weighing; (4) using empty capsule as counterpoise; (5) weighing a number of filled capsules at the same time using an equal number of empty shells as a counterpoise, changing empty shells for others after one or two operations. Objections are enumerated. One manufacturer said that the weight of empty shells of the same lot rarely varied more than 3% of the average weight. Empty shells made by different manufacturers may show a difference in wall thickness and hence in weight. One said that a 10% error would be the maximum. A table shows results obtained by weighing different batches taken at random from stock. Another table shows two methods. Two prescriptions of 12 capsules each were used. With one, each capsule was weighed on an analytical balance and the average weight of the same size empty capsule subtracted; with the other, the contents of the capsule were emptied on a tared watch glass and then weighed on an analytical balance. In both instances results were near theoretical. Of the three general methods for filling capsules, weighing each capsule is most accurate but is impractical for ordinary dispensing. The other two, "the punching method" and "the blocking method" are considered. Factors to be taken into consideration in any comparison are quantity of material per capsule, nature of material, use of the same prescription. Five prescriptions were filled, each by the two methods by the same operator. Tables show the results obtained. A 10% variance was arbitrarily selected, either plus or minus, from the theoretical average weight. The tables show a striking uniformity in the degree of accuracy obtained by average operators working under ordinary conditions by either punching or blocking methods. The punching method required about one-third less time. Of the 100 prescriptions filled only nine were within the 10% limit of variance, five of them filled by punching, four by blocking. The author concludes that comparative accuracy between blocking and punching is in direct ratio to the skill of the operator. Less time is required in punching than in blocking and with a comparable deree of accuracy. Results of the study indicate that a tolerance of more than 10% should be established. Average weight of an empty capsule obtained by the method described may be used as a tare in determining weight of filled capsules.—JOHN W. LEE. *J. Am. Pharm. Assoc.*, 24 (1935), 469. (Z. M. C.)

Chloral Hydrate Suppositories—Preparation of. For preparing suppositories containing from 0.1 to 1.0 Gm. chloral hydrate in each, the author suggests the following: the powdered chloral hydrate is mixed in a mortar with one-third of the "Astrafat" the other two-thirds of the mass melted and added, the whole mixed, and when of proper consistence, poured into chilled molds. A series of suppositories containing up to 1.0 Gm. of chloral hydrate in each was prepared and the solidification and melting points tabulated. After two days the suppositories showed no crystals of chloral hydrate under the microscope. An investigation of chloral suppositories made with hydrogenated peanut oil of the Swiss Pharm. V, showed them to be too soft and not easily removed from the mold.—H. LEHMANN. *Schweiz. Apoth.-Ztg.*, 73 (1935), 297. (M. F. W. D.)

Error in Dispensing—Margin of. Determination of the Reasonable or Permissible. V. Liquids. Though liquid prescriptions are usually measured, possibilities for error are greater than commonly held. Most of them are too small to be of practical significance. The three considered in this study in the order of importance are (1) the nature of the liquid to be measured (2) shape and size of graduate used, (3) the personal equation. The first test aimed to determine relationship between size and shape of graduate and magnitude of error. The second test aimed to determine how magnitude of error was affected by physical properties such as color, viscosity. Liquids were measured in both cylindrical and conical graduates by 100 senior students. The liquid was poured from a quart bottle into the graduate, then to prescription bottle, then to a tared container and accurately weighed. Quantities were 10 cc., 25 cc., 50 cc. and 100 cc. The magnitude of error is greater with conical graduates. The larger the graduates and the larger the volume the smaller the percentage of error. Error due to personal equation is indefinite and impractical to measure. It is revealed by a definite trend in a series of measurements by an individual. It might be due to defective vision, to natural carelessness or to some other trait. In the second series of tests, concerned with physical properties, the magnitude of error was in the following order: Distilled Water, Elixir of Iron, Quinine and Strychnine (color), Syrup (viscous, clear)

Milk of Magnesia (opaque), Castor Oil (oily). Color has a tendency to increase error and so does viscosity. The large error for Castor Oil, 4.49%, is doubtless due to the fact that the refractive index is so near that of glass that adherence of the oil is not detected and insufficient time is allowed for drainage. The large error with Milk of Magnesia is due to the impossibility of draining. Results of the 100 workers are summarized in a table and another table shows per cent deviation from average weight. "From the data obtained it appears that twice the standard deviation is a reasonable margin of error for the measurement of the volume of liquids." This would permit acceptance of the following:

Shape of Graduate	Distilled Water 10 Cc.	25 Cc.	50 Cc.	100 Cc.	Elixir I. Q. & S. 100 Cc.	Syrup 100 Cc.	Milk of Magnesia 100 Cc.	Castor Oil 100 Cc.
Cyl.	97%	94%	96%	95%	93%	94%	93%	93%
Con.	95%	98%	95%	95%	95%	96%	95%	94%

MARVIN J. ANDREWS. *J. Am. Pharm. Assoc.*, 24 (1935), 477. (Z. M. C.)

Histamine Injection. The preparation containing histamine acid phosphate 1 mg., isotonic salt solution 1 cc. and phenol 0.005, is used as an antirheumatic. The recommended dosage is two to three subcutaneous injections a week for four weeks.—*Bull. Ch. Synd. Pharm. Seine* (Feb. 1935); through *J. pharm. Belg.*, 17 (1935), 404. (S. W. G.)

Hospital Dispensary Methods. A brief survey of hospital dispensary conditions, more specifically pertaining to the average time taken per patient at the dispensary stage.—*Pharm. J.*, 134 (1935), 353. (W. B. B.)

Mercury Pill B. P. 1932—Note on. The undernoted modification is suggested for the official formula for Mercury Pill:

B. P.		Modification	
Mercury	33 Gm.	Mercury	33 Gm.
Syrup	14 Gm.	Syrup	12 Gm.
Liquid glucose	15 Gm.	Liquid glucose	12 Gm.
Glycerin	5 Gm.	Glycerin	1 Gm.
Licorice	33 Gm.	Licorice	40 Gm.
		Tragacanth	2 Gm.

The tragacanth should be mixed with the second portion of the licorice and incorporated in the mass. The quantity of glycerin has been reduced because there is enough hygroscopic material even without any glycerin at all.—P. BOA. *Pharm. J.*, 134 (1935), 356. (W. B. B.)

Methylene Blue Injection. The following formula of De Raymond is given: Methylene blue 10 Gm., sodium thiosulphate 50 Gm., saccharose 97 Gm., distilled water enough to make 1000 cc. Put up in 2-, 5- and 10-cc. ampuls for intravenous injections.—*Bull. Ch. Synd. Pharm. Seine* (Feb. 1935); through *J. pharm. Belg.*, 17 (1935), 404. (S. W. G.)

Pill Masses. A brief survey is given of the various pill excipients prescribed by the British, Belgian, Dutch, French, Italian, Jugoslavian, German and Swiss Pharmacopœias. The author claims to have satisfactorily prepared a large number of pills using as the liquid excipient a mixture of anhydrous glycerin and glucose. The author includes a compilation of the formulæ of the above pharmacopœias for Blaud's pills.—C. A. ROTHENHEIM. *Schweiz. Apoth.-Ztg.*, 73 (1935), 285. (M. F. W. D.)

Vehicles—Compositions for Use as, for Other Substances. A silica gel suitable as a vehicle for other substances, *e. g.*, in therapeutic or cosmetic preparations, is obtained by introducing SiF_4 into an aqueous solution of H_2SiF_6 of Sp. Gr. at least 1.14, separating the gel formed and washing the gel with water until it ceases to have a H_2SiF_6 reaction. The gel contains hydrofluoric acid in adsorptive combination and has disinfectant properties. A high hydrofluoric acid content is obtained by using H_2SiF_6 of high concentration and operating at a high temperature. Temperatures of 0–50° may be used. Water or steam may be added during the reaction to keep the H_2SiF_6 concentration constant.—J. BLOCH and E. BLOCH. Brit. Pat., 424,015 (Feb. 13, 1935); through *Chem. Abstr.*, 29 (1935), 4524.

PHARMACEUTICAL HISTORY

Apothecaries of the Hague. This historical review cites the mention of certain early apothecaries of the Hague in the records of the city. Among them are Pieter Willems de Vryes 1561,

Gregorius van Moersele 1562 and Gregorius de Apothecker 1563. The establishment of an apothecary in the time of Albrecht van Beyeren Colaert van Burustre (or Barastre) in 1397 is also mentioned.—A. J. VAN HUFFEL. *Pharm. Weekblad*, 72 (1935), 751. (E. H. W.)

Cosmetics in Recent Times—History of. The second of a series of articles. ALBERT HAUENSTEIN. *Riechstoff-Ind. Kosmetik*, 10 (1935), 95–96. (H. M. B.)

Homeopathy—History of. An address reviewing the history of homeopathy.—J. KATZ. *Pharm. Zentralh.*, 76 (1935), 269, 286. (E. V. S.)

Pharmacy at the Beginning of the 19th Century. This article, one of a series on historical pharmacy, describes Dutch pharmacy at the beginning of the nineteenth century. Rather of interest is the fact that in 1812 the population of Amsterdam was nearly 200,000 and the number of pharmacists 150. To-day the population is four times as large but the number of pharmacists remains nearly the same.—A. J. VAN HUFFEL. *Pharm. Weekblad*, 72 (1935), 822. (E. H. W.)

United States Patents Granted for Medicines during the Pioneer Years of the Patent Office. "Patent" means open, not secret. A patent cannot be granted for a medicine of secret composition and the term, "Patent Medicine," applied to medicine of secret composition is a misnomer. Patenting a medicine does not preclude telling fairy tales about it; therapeutic claims in the description of some of the patents for medicines are false and fraudulent. In this paper some interesting phases in the patenting of medicines are related and the history from its beginning in England is discussed, a number of well-known remedies being mentioned. Our Constitution gives the power to "Promote the progress of Science and useful arts by securing, for a limited time, to authors and inventors the exclusive right to their respective writings and discoveries." The first law under this provision was enacted in 1790 and provided for a board consisting of the Secretaries of State and War, the Attorney-General and the President. Thomas Jefferson, Henry Knox and Edmund Randolph made the first board. The first patent was issued to Samuel Hopkins to cover a process for manufacturing "Pot and Pearlash." No grant for any medicine was issued under this law. A new law was issued in 1893. The first patent dealing with therapeutic matters was issued in 1796 to a physician for a device for removing pain, the acme of fraud. In 1836, a fire destroyed records, patents, drawings and designs but Congress had published Indexes which were filed elsewhere and titles of the patents were preserved in this way. In 1836, a new law was passed and numbering of patents was begun. Between 1790 and 1836 about 75 patents covering pills, medicines, ointments and salves were issued. These are listed with name of medicine, date and patentee. The John Cullen process patent for "Liquid Magnesia" in 1818 was probably the first for a medicine; the product resembles our present solution of magnesium citrate, and even then magnesium compounds were recognized as having aperient properties. A photostatic copy of a "Diaphoretic or Sweating Powder" patent is given and also a summary of other Howard Patents: Bitter Tonic, Tincture of Myrrh Compound, Antispasmodic tincture, Astringent tincture. Others mentioned are Chlorine Cosmetic, in 1833; Ointment for Curing Many External Diseases, 1835; Ointment for Cure of Cancer, in 1836; Thomson's Improved System of Botanic Practice of Medicine, in 1836. Photostatic copy of a page of the latter is given.—LYMAN F. KEBLER. *J. Am. Pharm. Assoc.*, 24 (1935), 485. (Z. M. C.)

PHARMACEUTICAL LEGISLATION

Food and Drug Legislation—National. The text of a radio address. Reference is made to the first step in food and drug legislation in 1850, the passage of the present law in 1906 and the growing recognition of need for its revision. S5, popularly called the Copeland Bill, contains valuable features of the present law. It eliminates provisions that have caused courts to make interpretations that afford avenues of escape for unscrupulous, it extends provisions to cosmetics and advertising, it amplifies and reinforces some provisions that safeguard public health, it strengthens procedural provisions. The Bill contains definitions of foods, drugs and cosmetics. The definition of standards are broad. If it becomes law, the motive of fear upon which much advertising is based should be disposed of because statements of fact are required. If there is not sufficient consumer interest it is in danger of not becoming a law.—RALPH W. CLARK. *J. Am. Pharm. Assoc.*, 24 (1935), 490. (Z. M. C.)

Laws and Orders Regarding Pharmacy in 1934. A review of laws and orders which include general matters, sickness compensation, management of pharmacies, legislature, pharmaceutical concessions, improvements, help, the commerce of new remedies, spirits, serums, narcotics, and

statements introducing new remedies, patented medicines, etc.—WALTER SCHMIDT. *Pharm. Zentralh.*, 76 (1935), 240, 253. (E. V. S.)

PHARMACOLOGY, TOXICOLOGY AND THERAPEUTICS

PHARMACOLOGY

Carotene and Vitamin A—Absorption of. A study has been made of the absorption of vitamin A and carotene administered to a patient suffering from a condition which led to part of the contents of the thoracic duct being diverted into the pleural cavities. Analysis of the fluid removed at intervals from the chest cavities enabled approximate estimations to be made of the amount of vitamin A and carotene absorbed by the way of the chyle. It was found that a relatively small proportion of the carotene administered orally could be accounted for by the pigment found in the chylous fluid, whereas in the case of vitamin A, the amount recovered was such as to indicate an almost complete absorption. The vitamin, administered as the free alcohol, was found present in the lymph mainly in the esterified condition, and it is thought probable that the linkage with the fatty acids during passage through the intestinal walls accounts for the much higher coefficient of absorption as compared with that found when carotene was given. Observations on the chylous fluid show that over a range of reaction, much wider than that encountered in body fluids, no trace either of carotene or of vitamin A passed a dialyzing membrane. Both compounds appeared to be present in colloidal form and closely associated with the highly dispersed fat.—J. C. DRUMMOND, M. E. BELL and E. T. PALMER. *Brit. Med. J.*, 1 (1935), 1208. (W. H. H.)

Castor Oil—Purgative Action of, and Alimentary Disequilibrium. Experimental evidence is presented showing that the purgative action of castor oil is due to an alimentary disequilibrium. If the castor oil be introduced into a diet properly balanced, no nutritive disturbances or laxative actions become manifest; the oil is assimilated by the animal. The authors deduce that the truly active principle and very probable cause of purgation is the ricinoleide. The pigeon was used as the test animal.—R. LECOQ and J. SAVARE. *Bull. sci. pharmacol.*, 42 (1935), 161. (C. T. I.)

Chemical Constitution and Taste—Relations between. In previous studies of the variations in taste, attention was directed principally to modifications of the carbonyl and imide groups. The research reported in this paper followed the observation that the better known synthetic sweet compounds, such as saccharin and dulcin, are derivatives of ammonia in which one or more hydrogen atoms are substituted by negative radicals. The author studied the products derived from ammonia by substitution of an acyl radical for a hydrogen, *i. e.*, the acetyl radical and halogenated acyl radicals. The following compounds were prepared from aqueous or alcoholic ammonia and the ester: acetamide, monobromoacetamide, monochloroacetamide, dibromoacetamide, dichloroacetamide, tribromoacetamide, trichloroacetamide, monoiodoacetamide. With the chlorides and the bromides the taste became more sweet with increase in number of halogen atoms introduced into the acyl radical, or as the radical becomes more negative. The p_H values for 1% solutions of the dihalogen substituted compounds are higher than for the mono- or trihalogenated compounds. The p_H values are lower for those compounds of bitter or pungent taste.—ANTONIO GIACOLONE. *Gaz. Chim. Ital.*, 65 (1935), 129–131. (ANNE E. WHITE)

Cocaine Salts—Study of the Activity of Different. A series of solutions of salts of cocaine containing in 100 cc. the same quantity (0.892 Gm.) of cocaine base or 1 Gm. of cocaine-HCl was prepared, and the reactions were regulated by means of the corresponding acids to p_H 4. The solutions were assayed on the rabbit's cornea according to J. Régnier (*Bull. sci. pharmacol.*, 30 (1923), 580, 646). The following values represent the percentage concentrations of cocaine-HCl which are the anesthetic equivalents of the solutions studied: Citrate 0.2, lactate 0.4, tartrate 0.6, sulphate 0.8, phosphate 1.0, hydrochloride 1.0, hydriodide 1.2, sulphocyanate 1.5, formiate 2.5, acetate 2.9, salicylate 4, benzoate 5, phenylacetate 12. These results do not follow the theory that only the liberated base is responsible for anesthetic action. The following conclusions are drawn: 1. The activities of the salts do not arrange themselves according to the degree of hydrolysis. 2. Certain acids (particularly citric) exhibit actions entirely unfavorable to the utilization of the alkaloid; the solution of cocaine citrate being almost totally unabsorbed by the rabbit cornea. 3. The solubility in cellular lipoids is not the only factor as claimed by the Meyer and Overton theory, since the salts arrange themselves according to an order determined by Hofmeister on albuminoid substances.—J. RÉGNIER and R. DAVID. *J. pharm. chim.*, 22 (1935), 16–22. (S. W. G.)

Coffee and Decaffeinated Coffee—Effect of, upon Tremor in Normal Men and Women.

Seven young men and an equal number of women received coffee on one day of each week for several weeks and decaffeinated coffee or no special beverages on the intervening days. With the hand in a static position and the forearm supported to the wrist, the vertical movements of the index finger were magnified by an optical lever and recorded photographically. The rate of the tremor remained approximately constant throughout the experimental period even when the different beverages were administered. The amplitude of the tremor was increased for several hours after a single dose of coffee, but was not changed by decaffeinated coffee. In the women coffee containing caffeine equivalent to 2 mg. per Kg. of body weight produced an increase in the amplitude of the tremor, but in the majority of the men the effective dose was double this size.—KATHRYN HORST and J. R. WILLSON. *J. Pharmacol.*, 54 (1935), 147. (H. B. H.)

Corydaline Hydrochloride—Action of, on the Isolated Small Intestine. Corydaline is the alkaloid from *Violeta Bulbosa* (*Corydalis cava*) and corresponds to the formula $C_{22}H_{27}O_4N$. It suppresses the peristalsis of the small intestine.—PEDRO N. SIVORI. *Rev. Centro Estud. Farm. Bioquím.*, 25 (1935), 209. (A. E. M.)

Curare and Its Constituents—Pharmacology and Therapeutics of. A full historical and geographical survey of what is known about curare. The author found one sample of curare which had what he termed a "lissive" action, that is, the power to remove pathological rigidities without interfering with voluntary movement; thus he was able to relieve tetany in dogs after removing the parathyroids, and to relieve chronic spastic disease in man. He has examined many specimens of different varieties of Strychnos in further search for the lissive action. The lissive action is not shown by the crystalline curarine chloride prepared by King.—R. WEST. *Proc. Roy. Soc. Med.*, 28 (1935), 565; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 305. (S. W. G.)

Acetanilid—Ratio of Toxicity of, to Its Antipyretic Activity in Rats. In rats fevered by yeast injections, a dose of 12.5 mg. per Kg. of acetanilid produces an average fall in temperature of 0.6° C., while smaller doses are without significant effect and larger doses produced greater effects. Twelve and one-half mg. per Kg. has been taken to be the minimal therapeutic dose for rats. In normal animals, 50 mg. per Kg. of acetanilid produces a significant decrease in temperature, similar to the fall produced in fevered animals by 12.5 mg. per Kg. The lowering of the temperature of the normal animal may be considered an early undesirable effect. The dose fatal to 50% of the rats is 800 mg. per Kg. A therapeutic ratio of 64 : 1 for the antipyretic effect of acetanilid in rats has been obtained.—PAUL K. SMITH and W. E. HAMBOURGER. *J. Pharmacol.* 54 (1935), 346. (H. B. H.)

Adhesive Plaster—Irritants in. Patch tests with 8 varieties of adhesive plaster manufactured by six companies were made on 120 subjects, the patches left on for 48 hours and the reactions read. Fifty patients showed a reaction to one or more of the adhesives, with the least number of reactions for one adhesive 16% and the greatest number 25%. In addition there were 13 late reactions. Six, out of the group which showed marked reactions at the first removal of the adhesive tape with continued intensification at the second inspection, were tested with South American Para rubber (I), starch (II), lanolin (III), orris root (IV), iodine-rosin (V), olibanum (VI), gutta siac (VII), beeswax (VIII), Burgundy pitch (IX), zinc oxide (X) and wood rosin (XI). In this group there was sensitization to at least two of the ingredients of adhesive plaster. Six were sensitive to IX, 5 to I, 3 to XI, 2 to VI, 2 to VIII, and one each to III, IV and VII. In the group showing only a slight erythrema at the first inspection but who developed delayed reactions, tests were made on 12 persons: at the first inspection there were two reactions to V and 3 reactions to XI. Three patients who showed nothing more than erythrema at the site of the patch were patched with the 11 ingredients but no positive reactions were obtained and none of the reactions lasted 72 hours. The authors conclude that skin reactions are due to traumatic phenomena or to hypersensitivity to one or more of the ingredients of the plaster. They suggest that non-irritating types of resins and rubber should be substituted for the present types used.—L. SCHWARTZ and S. M. PECK. *Pub. Health Repts.*, 50 (1935), 811; through *Squibb Abstr. Bull.*, 8 (1935), A-915.

Alcoholism—Experimental Studies in. IV. Attempts to Modify the Concentration of Alcohol in the Blood after Intravenous Administration of Alcohol. The influence of various substances and procedures (diathermy, epinephrine, insulin, caffeine, carbon dioxide, oxygen, olive oil, physiological salt solution and magnesium sulphate) upon the concentration of alcohol in the human blood stream after intravenous administration of alcohol was tested. The maintenance of an elevated body temperature by diathermy apparently caused an increased rate of disappearance

of alcohol from the blood; none of the other procedures tried had any effect that could be considered significant.—ROBERT FLEMING and DOROTHY REYNOLDS. *J. Pharmacol.*, 54 (1935), 236. (H. B. H.)

Alkaloids—Distribution of, in Different Parts of Central Nervous System and their Quantitative Microdetermination in Tissues. II. Quinine and Mescaline. Quinine (I) appeared and disappeared more rapidly in the portions of the nervous system rich in cells. The concentration of I in the blood was at first a little more and then somewhat less than in the brain; the concentration in the liver and kidneys was much the highest. I was extracted from the tissues and determined by the fluorescence in sulphuric acid solution. Mescaline (II) determined by sublimation, showed a similar distribution to I although a greater concentration of II in the spinal fluid was observed. Dogs and monkeys were used in the experiment.—M. VOGT. *Arch. exptl. Path. Pharmakol.*, 178 (1935), 560; through *Squibb Abstr. Bull.*, 8 (1935), A-969.

Alkaloids—Distribution of, in Different Parts of Central Nervous System and Their Quantitative Microdetermination in Tissues. I. Scopolamine and Atropine. A study of the distribution of scopolamine and atropine in various parts of the central nervous system, at various intervals following the administration to dogs and cats and in the presence of ether and morphine. The greatest amount of alkaloid was found in the portions rich in cells, particularly the cerebral cortex, and the lowest amounts in the nerve fibers and spinal fluid. The liver and particularly the kidney contained more alkaloid than the cortex. The blood contained approximately the same amount of alkaloid as the brain. The alkaloids were determined by their mydriatic effect in mice. Data are given for the absorption on animal charcoal of the hydrochlorides of apomorphine, bulbocapnine, quinine, strychnine, atropine, scopolamine and mescaline, from $M/100$ and $M/1000$ solutions thereof.—F. VEIT and M. VOGT. *Arch. exptl. Path. Pharmakol.*, 178 (1935), 534; through *Squibb Abstr. Bull.*, 8 (1935), A-969.

Allium—Contribution to the Determination of Preparations of. Daily oral administration of 0.5 cc. of garlic juice decreased or prevented calcification (sclerosis) and prolonged life from 12.9 to 30- > 50 days in mice fed high protein diets and 0.2–0.3 cc. per day of irradiated ergosterol (Vigantol). Similar results were obtained with *Allium ursinum* L. (I). This property of the allium preparations may be used for their bioassay. The allium preparations had no oral toxicity. The press juice of fresh I had such low toxicity by intravenous injection that it was practically not detectable in the mouse.—U. HINTZELMANN. *Arch. exptl. Path. Pharmakol.*, 178 (1935), 480; through *Squibb Abstr. Bull.*, 8 (1935), A-948.

Ascorbic Acid (Vitamin C)—Comparison of Oral and Subcutaneous Administration of Protective Doses of. The minimal protective dose by mouth is twice as large as that by subcutaneous injection.—H. C. HOU. *Proc. Soc. Exptl. Biol. and Med*, 32 (1935), 1391. (A. E. M.)

Bismuth-Lecibis—An Injectable Preparation of. Lecibis, a lecithin-containing oily solution of bismuth tri-camphocarbonate, has been investigated. Dogs and guinea pigs have been used in this work and results show it to be relatively rapidly absorbed. After one intramuscular injection in a dog, the elimination begins quickly and continues for weeks.—GEORGE KINGISEPP and JUTA OLESK. *Deut. Med. Wochschr.*, 61 (1935), 997–1000. (H. R.)

Blood Alcohol. Its Relation to Intoxication in Man. In general, intoxication is not noticeable in the human until the blood alcohol concentration is greater than 0.2%; from 0.31 to 0.4% there is a marked intoxication; alcoholic stupor is definite between 0.41 and 0.5%; above 0.5% coma and death may result.—R. G. TURNER. *Proc. Soc. Exptl. Biol. Med.*, 32 (1935), 1548. (A. E. M.)

Bone Phosphatase—Activity of, in Chronic Fluorine Poisoning. The effect of chronic fluorine poisoning upon bone phosphatase was studied by comparing the phosphatase activity of control rats at various ages prior to weaning with that of rats of the same age whose only source of fluorine was the milk of the mother rat on a diet containing fluorine. The number of rats in each litter was the same. The rats used for comparison were killed at the same age, and an extract of bone phosphatase from the hind legs prepared under identical conditions. Bone phosphatase activity for the control rats showed an increase with age from the time of birth to the age of thirty days, whereas that of the poisoned group showed a decrease from the time of birth, reaching a minimum at about fifteen days of age and returning to the normal for the control rats at thirty days of age. This decrease in bone phosphatase activity harmonizes with the obvious retardation of calci-

fication in the bones of young fluorine poisoned rats.—JOHN O. THOMAS, R. H. WILSON and FLOYD DE EDS. *J. Pharmacol.*, 54 (1935), 160. (H. B. H.)

Bulbocapnine—Ratio between Effective and Lethal Doses of, in the Cat. The minimal effective and minimal lethal doses of bulbocapnine vary markedly in the cat; in this series the former ranged from 2 to more than 4 mg. per Kg., the latter from 70 (and less) to 130 mg. per Kg. Body weight does not appear to be a factor responsible for this variation. The ratio between M. E. D. and M. L. D. ranged from an estimated low of 1:15 to 1:57 in this series While most animals under lethal and sub-lethal dosage showed strychnine-like convulsions predominately, several manifested these effects only transiently, and one not at all.—R. S. AMADON and A. H. CRAIGE. *J. Pharmacol.*, 54 (1935), 334. (H. B. H.)

Digitalis—Relationship of Potency of, as Determined by Different Methods. Among the group of samples of digitalis leaf, two (D and F) were found to be equally effective by the usual Hatcher-method of slow intravenous infusion into the mammal (cat and dog). To cause the same mortality in groups of frogs after injection into the lymph-sac, however, there was required 45% more of leaf F than of leaf D; in the frog therefore leaf F was significantly weaker than leaf D. On the other hand, by clinical assay and by determinations of toxicity in experimental cumulative poisoning (dog), tinctures of leaf F were, if anything, slightly more potent than tinctures of leaf D. In preliminary experiments the clinical assay-method was shown to be capable of distinguishing among tinctures of the relative strengths 75 : 100 : 125. In the cases of these two samples of digitalis leaf, therefore, assay in the mammal indicated potency more accurately than assay in the frog.—R. C. LI and H. B. VAN DYKE. *J. Pharmacol.*, 54 (1935), 151. (H. B. H.)

Digitalis Lanata Ehrh.—Pharmacological Investigation on. The toxicity of the leaves of *Digitalis lanata* is distinctly greater (25%) than that of *Digitalis purpurea*. The toxicity of the powdered *Digitalis lanata* does not vary, even after a year of storage in an atmosphere of carbon dioxide. The leaves treated with chloroform and dried in a current of warm air are less active than those dried at ordinary temperature and without special treatment.—A. RABBENO and C. MARINII. *Boll. Soc. Ital. Biol. Sper.*, 9 (1934), 748–750; through *Chimie et Industrie*, 33 (1935), 677. (W. A. P.)

Dinitrophenol—Action of, on Rate of Oxidation of Ethyl Alcohol in Vitro. At a p_H of 7.4 concentrations of dinitrophenol from 1–5,000,000 to 1–20,000,000 slightly increased the rate of oxidation of alcohol by rat liver *in vitro*, while higher concentrations slightly diminished it. This indicated that under some conditions an increase of tissue metabolism produced by dinitrophenol is accompanied by an increased rate of oxidation of alcohol.—H. W. NEWMAN, W. C. CUTTING and M. L. TAINTER. *Proc. Soc. Exptl. Biol. Med.*, 32 (1935), 1479. (A. E. M.)

Drugs—Absorption of, Through the Oral Mucosa. II. The ratio of sublingual to similarly effective subcutaneous doses was determined as follows: Cocaine 2, diacetylmorphine 3, thebaine greater than 4, emetine greater than 6.—ROBERT P. WALTON. *Proc. Soc. Exptl. Biol. Med.*, 32 (1935), 1486. (A. E. M.)

Drugs—Absorption of, Through the Oral Mucosa. III. Fat-Water Solubility Coefficient of Alkaloids. The oil-water solubility coefficient is an important factor in the selective oral absorption of alkaloids. Other factors which are significant are relative potency, degree of local vasoconstriction, irritation and alkalinity or acidity.—ROBERT P. WALTON. *Proc. Soc. Expt. Biol. Med.*, 32 (1935), 1488. (A. E. M.)

Drugs—Distribution of, in Different Parts of Central Nervous System and Their Quantitative Microdetermination in Tissues. VI. Chloral Hydrate. Data are given on the distribution of chloral hydrate (I) in various parts of the nervous systems of cats and dogs, at various intervals after administration. I was extracted from the tissues with ether, and the ether residue taken up in dilute sulphuric acid. I was determined by reduction with zinc dust in acetic acid solution and titration of the chlorine according to the Volhard method. I appeared and disappeared more rapidly from the portions rich in cells. Maximum concentration was reached in a few minutes in all parts.—M. VOGT. *Arch. exptl. Path. Pharmakol.*, 178 (1935), 628; through *Squibb Abstr. Bull.*, 8 (1935), A-969.

Ephedrine—Observations on Dogs under Continued Influence of. Remarkable constancy is found in the systolic blood pressure of dogs in standard conditions. Ephedrine produces a disturbance of nitrogen metabolism, probably by diminishing the assimilation of protein. A transient diuresis is always observed. Glycosuria usually persists after withdrawal. Tolerance to the

pressor action of ephedrine is manifested. Ephedrine administration in doses that maintain a continuous hypertension may be continued for 2 weeks without other effects; the blood pressure and protein absorption return to normal within a few days of withdrawal.—ERIC OGDEN and A. R. TEATHER. *J. Pharmacol.*, 54 (1935), 320. (H. B. H.)

Ergoclavine—Action of, on Diuresis. Ergoclavine is a new alkaloid obtained from ergot of rye and has pharmacological action similar to that of ergotoxine and ergotamine. With respect to its action on diuresis, ergoclavine in doses of 0.0075–0.04 mg. per Kg. intramuscularly diminished considerably the amount of fasting urine in dogs, and also inhibited the diuresis following the ingestion of water or sodium chloride solution, but to a smaller extent than did the injection of 0.15–0.2 mg. of ergotamine. Unlike the latter compound, ergoclavine did not decrease diuresis caused by a urea solution, but rather increased it.—E. ZUNZ and O. VESSELOVSKY. *Compt. rend. soc. biol.*, 119 (1935), 534; through *Squibb Abstr. Bull.*, 8 (1935), A-925.

Ergoclavine and Sensibamine—Action of. The author concludes that the new ergot alkaloids, ergoclavine and sensibamine, produce pharmacological effects identical in character and intensity with those of ergotoxine, and therefore with those of ergotamine also. These comparative studies were made upon the isolated guinea pig and rabbit uterus as well as upon the "vasomotor reversal" preparation of the cat.—A. VARTIAINEN. *J. Pharmacol.*, 54 (1935), 259. (H. B. H.)

Ethyl Alcohol—Effect of Certain Drugs on the Metabolism of. Alcohol was administered to dogs by stomach tube in doses of 1.5 or 3.0 Gm. per Kg. and determinations of blood alcohol made over a period of twelve hours. The normal blood alcohol curve was not changed by the administration of one unit of insulin per Kg., either when the insulin was given alone or with sufficient glucose to prevent a drop of blood sugar. Large doses of thyroxine or desiccated thyroid administered some days prior to the alcohol experiment caused very little change, if any, from the normal curve. On the other hand the disappearance of body alcohol was greatly accelerated by the administration of dinitrophenol in a dose of 7.5 or 15 mg. per Kg., the rate of alcohol consumption by the tissues being about doubled in some cases. Dinitrocresol in a dose of 7.5 mg. per Kg. produced about the same results as did twice this dose of dinitrophenol. Determinations of the loss of alcohol by breath showed that only a small part of the effect produced by the dinitro compounds was due to increased excretion by the lungs. The doses of the dinitro compounds necessary to cause much acceleration in body oxidation of alcohol are probably too toxic for them to be of any practical use in the treatment of acute alcoholism and the results are presented solely for their scientific value.—R. N. HARGER and H. R. HULPIEU. *J. Pharmacol.*, 54 (1935), 145. (H. B. H.)

Lanadigin, Digitoxin and Ouabain—Cumulative Poisoning by. Lanadigin (or digilanid C) has been considered, by clinical test, to be a relatively non-cumulative glucoside. It was compared with U. S. P. ouabain and digitoxin by assay in the frog and dog and found to be of the same toxicity as digitoxin in the dog but about twice as toxic as digitoxin in the frog. In cumulation experiments in dogs, lanadigin proved clearly to be a more powerful cumulative poison than either ouabain or digitoxin.—H. B. VAN DYKE and R. C. LI. *J. Pharmacol.*, 54 (1935), 161. (H. B. H.)

Local Anesthetics—Relation of p_H and Surface Tension to Activity of. The authors report observations upon the relation between surface tension and physiological activity for ten local anesthetics at varying known hydrogen-ion concentrations. The following substances were studied: B-4-Morpholine-ethyl benzoate hydrochloride, B-4-morpholine-ethyl cinnamate hydrochloride, B-4-morpholine-ethyl phenylurethan hydrochloride, B-4-morpholine-ethyl α-naphthylurethane hydrochloride, G-4-morpholinepropyl benzoate hydrochloride, G-4-morpholine-propyl cinnamate hydrochloride, G-4-morpholine-propyl phenylurethane hydrochloride, G-4-morpholine-propyl α-naphthylurethane hydrochloride, cocaine and procaine. Both surface tension lowering and anesthetic activity vary with the p_H in a manner paralleling the titration curves, indicating that both effects can be attributed only to the base. No correlation between surface tension lowering by the individual compounds and their physiological activity could be detected.—JOHN H. GARDNER and JOSEPH SEMB. *J. Pharmacol.*, 54 (1935), 309. (H. B. H.)

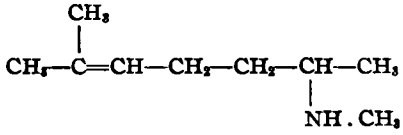
Luteal Hormone—Biological Study and Testing of. The horns of the rabbit uterus at time of puberty appear small, very slightly vascular and slightly muscular. Only a very small amount of blood vessels are visible, and the epithelium is simple. Injection of luteal hormone alone pro-

duces no change. If some follicular substance is included, there is an increase in diameter in the horns of the uterus, the muscular appearance changes and the secretion is altered. Further injection causes intense reactions, the horns become extremely large, moist and congested, the muscular layer disappears and blood vessels appear in the form of a network. These vessels are dilated. The determination is carried out as follows: Inject subcutaneously into a 600–800 Gm. Parisienne rabbit, at time of puberty, during 6 consecutive days, 4 mg. per day of crystalline follicular substance contained in an oil solution. Also inject subcutaneously during the next 6 days the substance to be studied, in an oil solution. At the end of the twelfth day the animal is killed, the uterus removed and placed in formaldehyde solution. An examination in an Ultrapak is immediately carried out. Standard unit setup is the amount of luteal substance which corresponds to the physiological activity obtained by injection into an 800-Gm. rabbit at age of puberty, after subcutaneous administration of follicular substance, of 0.2 mg. of crystalline luteal hormone prepared in oil solution and injected during 6 consecutive days.—H. PENAU and H. SIMONNET. *J. pharm. chim.*, 21 (1935), 485. (M. M. Z.)

Male Hormone—Biological Estimation of, upon the Hardhead. A critique of the two currently used methods of standardization supplemented with a report of an improvement in the castration technique of Glaser and Haempel. B.'s technique consists in anesthetizing the fish with urethane or soneryl and then making as short a ventral incision as is possible with the aid of fine scissors at the area of the genital buds. The gonads are exposed carefully with the aid of surgical forceps, and then removed. The operative area is dried with absorbent cotton or surgical gauze; "painted" with ether and sealed with collodion. The per cent recoveries by this technique, on two lots, were 89 and 100, respectively, as compared with the approximate 50% recoveries obtained with the straight G. and H. technique. B. finds the intramuscular route the best method of giving the orchic extracts to the test objects. In no instance, did a non-active extract, as determined on castrated test objects, prove to be active when intact fish were used. Careful temperature control and utilization of as large a number of fish as is practical are of paramount importance for accurate work.—A. BEAUNE. *Bull. sci. pharmacol.*, 42 (1935), 193. (C. T. I.)

Mannide and Isomannide—Fate of, in the Animal Body. The chemistry of mannitol, isomannide and mannide is reviewed briefly and the structural formulæ are given. The results are summarized as follows: 1. The removal of 2 molecules of water from 1 molecule of mannitol with the formation of isomannide or mannide destroys the capacity of mannitol to be stored as glycogen in the liver of the white rat. 2. Mannide significantly increases the respiratory quotients of white rats, while isomannide does not. 3. Isomannide and mannide are ineffective in relieving insulin shock in mice and are also incapable of raising the fasting blood sugar level of rabbits.—J. C. KRANTZ, JR., W. E. EVANS, JR., and C. J. CARR. *Quart. J. Pharm. Pharmacol.*, 8 (1935), 213–217. (S. W. G.)

Methylamino-methyl Heptene—Pharmacological Action of. This compound has the formula



It is a sympathetico-mimetic-amine which stimulates the respiratory center and to a lesser degree other parts of the central nervous system. It relaxes those smooth muscles which have an inhibitory innervation from the true sympathetic the stomach, intestine, etc., but it dilates the pupil, stimulates the heart and will sometimes restore a heart with fibrillating auricles to a normal beat. With correct dosage and under suitable conditions the drug is capable of producing a great rise of arterial pressure which may not come down to normal for two or three hours. On intravenous injection of the drug the volume of the kidney, spleen, etc., shrinks, the stomach relaxes, the mucosa of the nose and pharynx shrinks greatly, and the bronchioles dilate. The drug has a trade name "octin," is markedly slower in action than epinephrine, and will have a very considerable clinical use.—D. E. JACKSON. *J. Pharmacol.*, 54 (1935), 152. (H. B. H.)

Morphine—Action of, as a Metabolic Stimulant. Fifty-one successful experiments were made upon four dogs studied systematically at the fourth, eighth, sixteenth and twenty-fourth hour after the daily injection. The average metabolic increases for the entire twenty-four hours were

found very significant, being respectively: 11.2, 7.3, 4.8 and 14.8%. The authors emphasize the importance of maintaining the adult animals at constant body weight and upon a practically perfect state of rest during the tests which were made in a copper chamber with closed Benedict Universal Apparatus.—H. G. BARBOUR and JANET ANDREWS. *J. Pharmacol.*, 54 (1935), 137. (H. B. H.)

Morphine, Codeine, Heroine and Dilaudid—Comparative Study of Analgesia Produced in Normal Subjects by. The table gives the average results from five subjects, selected for their analgesic response, to whom various doses of the four drugs were administered subcutaneously at weekly intervals. Five sensitive face spots as determined with von Frey hairs were employed to measure the degree of analgesia. Neither the subject nor the observer had knowledge of the drug or dosage used.

	Dose Required to Give Equal Peaks of Analgesia. Mg.	Peak of Analgesia Reached. Minutes.	Duration of Analgesia. Minutes.	Subjective Dgree of Depression.	Subjective Degree of Euphoria.
Morphine sulphate	8	90	200	5	1
Codeine phosphate	64	30	150	1	0
Heroine hydrochloride	1–1.5	30	130	2	4
Dilaudid hydrochloride	0.8	90	165	3	1

No definite correlation can be made between the subjective sensation of depression and the actual analgesia obtained. In confirmation of Mullin and Luckhardt it is noted that hyperalgesia often follows the period of analgesia even though the individual is still subjectively depressed at the time. A most constant and striking finding is the difference in time required after administration for the various drugs to produce their maximum analgesic action. Although solubility is not the only factor involved, rapid onset of analgesia does occur with the most soluble salts.—C. C. PFEIFFER and M. H. SEEVERS. *J. Pharmacol.*, 54 (1935), 156. (H. B. H.)

Nicotine—Contribution to Pharmacology of. This study was made to determine the nature of the nicotine action causing failure of respiration in cats. Application of fairly large doses of nicotine to the floor of the fourth ventricle failed to paralyze respiration. The minimal lethal dose by intravenous injection was found to be consistently smaller than by intracarotid injection. Following the administration of the minimal lethal dose stimulation of the phrenic nerve and of the diaphram directly showed that the myoneural conjunctions had been completely, or almost completely, paralyzed. A record of phrenic nerve potentials showed that when the muscles of respiration had ceased to function as a result of nicotine, the intermittent discharges from the respiratory center continued as in the normal. From the above evidence the authors conclude that nicotine causes respiratory failure as a result of a curare-like peripheral paralysis.—HARRY GOLD and FREDERICK BROWN. *J. Pharmacol.*, 54 (1935), 143. (H. B. H.)

Parathyroid Hormone—Use of Rabbits in the Standardization of. The blood serum of rabbits has been found to respond to injections of parathyroid extract given together with oral administrations of calcium chloride. The variations in the calcium concentrations in the serum of rabbits was found to be of a qualitative rather than a quantitative nature. The method of Hamilton and Schwartz (*J. Pharmacol.*, 46 (1932), 285) or its modification by the author may be used to detect, but not to measure small quantities of parathyroid hormone. The results of the experiments are given in tables and plotted curves.—F. J. DYER. *Quart. J. Pharm. Pharmacol.*, 8 (1935), 197–212. (S. W. G.)

Phenobarbital—Effects of Phenacetin and Aspirin, Respectively, upon Action of. Whereas acetylsalicylic acid antagonizes the hypnotic action of phenobarbital, phenacetin in no way diminishes its activity. Phenacetin may exert a protective influence by antagonizing the toxic effects of phenobarbital.—ALFRED GILMAN and HENRY G. BARBOUR. *Proc. Soc. Exptl. Biol. Med.*, 32 (1935), 1634. (A. E. M.)

Pituitary Extract—Hypersensitiveness to. A case report in which a 28-year-old housewife, without personal or family history of allergic diseases, exhibited a severe hypersensitivity to a dose of pituitary extract at the birth of her seventh child. Massive swelling of the lips and face was noted, and the patient complained of a swollen tongue. She began to have difficulty in breathing, which was evidently due to obstruction in the upper respiratory tract. The edema of the larynx

increased rapidly and she had more respiratory difficulty. The administration of epinephrine relieved the situation and she recovered completely. Subsequent skin tests showed positive reactions to cattle, hog and human pituitary extracts, but negative reactions to cerebral cortex and skeletal muscle extracts of cattle, hogs or humans.—F. A. SIMON. *J. Am. Med. Assoc.*, 104 (1935), 996. (M. R. THOMPSON)

Potassium Salts—Diuretic Action of. Doses of from 0.1 to 0.2 Gm. per Kg. daily for several days of potassium chloride, nitrate, bicarbonate, acetate and citrate were given by mouth to normal individuals and patients having edema; in some of the latter, kidney disease was present. These salts lead to the increase of excretion of water and potassium in the urine; the most regular and sustained diuresis occurred with the nitrate. The kidney was able to concentrate the potassium of the serum approximately fifty times. When this concentrating function is preserved in renal disease, potassium salts seem to be well tolerated.—NORMAN M. KEITH and MELVIN W. BINGER. *J. Pharmacol.*, 54 (1935), 148. (H. B. H.)

Pukateine—Pharmacological Action of. The alkaloid, pukateine, can be extracted from the bark of the Pukatea tree (*Laurelia Novæ-Zealandiæ*, Monimiaceæ). It has the formula, $C_{18}H_{17}O_3N$, and the constitution has been established by Barger and Girardet. In the form of the hydrochloride pukateine has the following minimal lethal doses in terms of grams per kilogram body weight: frog, 0.25 (anterior lymph sac); mouse, 0.18 (subcutaneously); rabbit, 0.12 (intravenously) and 0.2 (subcutaneously). It tends to depress all muscle tissue with the possible exception of the uterus. It depresses conductivity of the nerves. The action upon the central nervous system is similar to that of morphine, the depressive effect being most marked upon the respiratory center. It produces a peripheral vaso-dilatation and this in conjunction of the diminished cardiac output produces a fallen blood pressure. The effect on the refractory period and the ability to prevent cardiac fibrillation is also described.—WILLIAM S. FOGG. *J. Pharmacol.*, 54 (1935), 167. (H. B. H.)

Pyrethrins—Action of, on Marine Animals. A pharmacodynamic study of the neuromuscular toxic activity of pyrethrins. The tests were carried out (1) by placing the test object in dilute emulsions of the pyrethrins; thereby allowing the animal to absorb the toxic agents by the respiratory tract, and (2) by administering the pyrethrins hypodermically. In each instance control tests were carried out to ascertain the effect of the dilutions of alcohol present in the emulsions. The pyrethrins are more active upon fish, crustacea and cephalopod molluscs when the toxic agents are taken up by the respiratory tract. Fish are also very sensitive to hypodermic doses. The echinoderms are practically unaffected by pyrethrins when administered by either of the above routes.—O. GAUDIN. *Bull. sci. pharmacol.*, 42 (1935), 145, 222. (C. T. I.)

Retrorsine—Action and Toxicity of. Retrorsine, an alkaloid of *Senecio retrorsus*, in the form of a hydrochloride induces weakness and paralysis of the extremities of frogs in the dosage of 1 mg. per Gm. In white mice it causes acute death within two and one-half hours, with clonic convulsions, in the dosage of 290 or more mg. per Kg., injected intravenously. Doses of 70 to 145 mg. per Kg., produce no convulsions but hepatic necrosis and renal degeneration in the majority of animals, and finally death in one to eight days. In guinea pigs, the minimal lethal dose of retrorsine hydrochloride by intravenous injection is approximately 320 mg. per Kg. An amount equivalent to 50% of the minimal lethal dose, repeated every other day for four doses, failed to bring about any visceral changes in ten days. The guinea pig is apparently less susceptible than the mouse to this alkaloid. Retrorsine has a depressor and a hyperglycemic action. It inhibits isolated rabbits' intestines, but contracts isolated guinea pigs' virgin uteri.—K. K. CHEN, A. LING CHEN and CHARLES L. ROSE. *J. Pharmacol.*, 54 (1935), 299. (H. B. H.)

Sedatives and Hypnotics. The author discusses the physiology of the nervous system briefly and mentions some of the desirable qualities in medicaments. He describes the pharmacological action of the various classes of sedatives and hypnotics such as chloral, paraldehyde, the barbital derivatives, bromides, cocaine, organic bromine compounds, scopolamine and others.—ALFRED FRÖHLICH. *Scientia Pharm.*, 6 (1935), 57. (M. F. W. D.)

Sodium Propyl-Methyl-Carbinyl-Allyl Barbiturate. A Short-Acting Hypnotic. The drug was compared with pentobarbital sodium and amytal. Oral administration causes earlier appearance of ataxia. The duration of anesthesia was longer than with pentobarbital and about the same as with amytal. However, the time of recovery was only half that of sodium amytal.—EDWARD E. SWANSON. *Proc. Soc. Exptl. Biol. Med.*, 32 (1935), 1563. (A. E. M.)

Sodium Thioethanesulphonate—Metallic Derivatives of, in Therapeutics. Organometallic compounds containing the —SH group in which H is replaced by gold, bismuth, antimony, mercury and other heavy metals, were prepared by the following series of reactions: $CH_2BrCH_2Br + Na_2SO_3 = CH_2BrCH_2SO_3Na + NaBr$; $CH_2BrCH_2SO_3Na + NaHS = HSCH_2CH_2SO_3Na + NaBr$; treatment of the mercaptan with gold chloride gives $AuSCH_2CH_2SO_3Na$, amorphous, very light yellow, containing 53% gold (theoretical 54.7%), remains unchanged when heated to 170°, above 170° gradually turns yellow and becomes light brown at 280°, easily soluble in water to a barely perceptible yellow, insoluble in oil and in all organic solvents, unaffected by the usual reagents for gold (except hydrogen sulphide which produces first a brown coloration and finally a precipitate of sulphide; stannous chloride in hydrochloric acid solution and nitric acid destroy the complex with precipitation of gold. A 5% solution, when injected subcutaneously or intramuscularly, is easily absorbed; it produces no shock phenomenon when injected intravenously. In spite of its high gold content, it is a little less toxic than most of the other gold thioderivatives (about 0.05 Gm. per kilo body weight), with the exception of the metallic thioderivatives of sugars; but the lower toxicity of the latter is accompanied by a correspondingly low activity.—AUGUST LUMIÈRE and FÉLIX PERRIN. *14me Congrès de Chimie Industrielle, Paris,* Oct. 21–27, 1934. 3 pp. (A. P.-C.)

Spinal Anesthesia in the Rabbit. Therapeutic Coefficients. The minimal lethal dose as well as the minimal anesthetic dose by subarachnoidal injection was established for several anesthetics upon rabbits. From these two threshold concentrations the therapeutic coefficients for these anesthetics can be calculated as follows: metycaine, 4.0; procaine, 6.6; panthesine, 8.0; nupercaine, 11.4; tutocaine, 12.0; and pantocaine, 30.0.—R. N. BIETER, R. W. CUNNINGHAM, O. LENZ and J. W. MCNEARNEY. *J. Pharmacol.*, 54 (1935), 137. (H. B. H.)

Syntropan—Contribution to the Pharmacology of. The results of the various tests carried out, together with reproductions of kymograph tracings, are presented. The following conclusions have been drawn: 1. Syntropan has m. l. d. 1.1 Gm. per Kg. of body weight of toad intralymphatically in 18 hours and 316 mg. per Kg. of body weight of rabbit hypodermically in 40 minutes. Post-mortem examination revealed no organic lesions. The heart was arrested in diastole with venous congestion. 2. In the toad and rabbit, syntropan in small doses stimulates the cerebrum and, if the dose is high, convulsions occur, which are central in origin. In fatal doses the drug paralyses the cerebrum and the respiratory center. 3. In stronger solutions, syntropan acts like atropine in antagonizing the effect of arecoline hydrochloride on heart, intestine and ureter. 4. In the dog, syntropan in moderate doses lowers the blood-pressure in spite of the acceleration of heart beat and vasoconstriction. The drug depresses the cardiac muscle directly. Syntropan stimulates the respiratory center in small doses. 5. There is no evidence that syntropan is a valuable drug for the relaxation of plain muscle tissue. In fact the uterus and mesenteric vein respond to the drug by a rise of tone. 6. The drug has practically no action on the gastrocnemius muscle of the toad in a 1:1000 solution. 7. The dilatation of the pupil of the rabbit produced by strong solutions of syntropan is inferior to that produced by atropine in more dilute solutions.—KARAM SAMAAN and MOHAMED I. EL ASREEGY. *Quart. J. Pharm. Pharmacol.*, 8 (1935), 186–196. (S. W. G.)

Thyroid—Pharmacology of, in Man. A review, with discussion, of the effects produced by thyroid, thyroxin and certain compounds structurally related to thyroxin upon clinical patients. The iodine content of desiccated thyroid, with its relationship to calorigenic activity receives interesting consideration. It has been calculated that in a normal man the thyroid forms thyroxine or its equivalent at the rate of about 0.3 mg. a day and that there are about from 10 to 14 mg. in the body outside of the thyroid gland. Following the intravenous administration of a single dose of 10 mg. of thyroxine to a patient with myxedema, there is a marked lag in the clinical improvement behind changes in the metabolic rate, the period of highest metabolism being characterized by intoxication and the period of falling metabolism by improvement. Observations on the calorigenic action of diiodotyrosine, thyronine, diiodothyronine and N-acetyl thyroxine show that the amino group, the diphenyl ether group and all four iodine atoms are essential for the maximum effect of thyroxine. Of special interest is the rather rapid return of the metabolism to the level before treatment following a single dose of diiodothyronine (from seven to eight days, respectively, in two patients with rates of minus 35% and minus 40%) compared with the slow return following a single dose of thyroxine (from seventy to eighty days at a level of minus 40%). The increase

in metabolism produced by dinitrophenol in myxedema, with little or no clinical improvement, suggests that there may be different types of altered metabolism that cannot be differentiated by changes in the rate of oxidation alone. As the complexity of the molecule of various thyroxine compounds increases, the greater will be their absorption from the gastro-intestinal tract and hence the less the effect of alkali in augmenting the absorption. As a result of digestion with pepsin, data have been obtained which suggest that nearly all the calorigenic activity of the whole gland is possessed by less than half of the total iodine (acid-insoluble precipitate). The acid-soluble portion does possess slight calorigenic activity and after a single large dose the metabolism appears to return to its level before treatment more rapidly than after an equal change produced by the acid-insoluble precipitate. This finding has an important bearing on the U. S. Phar. method of standardizing desiccated thyroid by a determination of the total organic iodine. After heating with approximately normal sodium hydroxide for four hours, desiccated thyroid loses more than two-thirds of its calorigenic activity, whereas thyroxine is unaffected by the same treatment. This finding has an important bearing on the proposed standardization of desiccated thyroid by a determination of its thyroxine content. The subcutaneous administration of extracts of the anterior lobe of the pituitary produced an increase in basal metabolism in eighteen of twenty-eight patients of various types, including two with hypopituitarism, ten with low basal metabolism of unknown cause, several with nontoxic goiters, including three patients with mild myxedema, and one case of exophthalmic goiter. During the injections in the patient with exophthalmic goiter, a mild case of the disease became a moderately severe one.—W. O. THOMPSON, *et al. J. Am. Med. Assoc.*, 104 (1935), 972. (M. R. THOMPSON)

Trichlorethylene—Contribution to Pharmacology of. Trichlorethylene in amounts of 0.12 cc. per 100 Gm. of rat subcutaneously did not influence oxygen consumption. In perfused amphibian heart it had solely a depressant effect. When administered by inhalation to etherized dogs, it produced a fall in blood pressure and tended to diminish the rate and increase the depth of respiration. The influence of the drug on the coronary flow (Moravitz preparation) was irregular, in some cases it produced a decrease and in others an increase in the rate of flow. The authors are of the opinion that the drug exerts no specific influence on the coronary circulation. The relief afforded by trichlorethylene in certain cases of angina pectoris might be accounted for on the basis of its sedative action.—J. C. KRANTZ, JR., C. J. CARR, RUTH MUSSER and W. G. HARNE. *J. Pharmacol.*, 54 (1935), 327. (H. B. H.)

Ureas—Relative Anesthetic Effects of Various. Hypnosis has been found to be a property quite common to the ureas. With respect to hypnotic effectiveness, in the alkyl ureas molecular weight is a determining factor, as with the aliphatic alcohols. In general, in the aliphatic ureas, the hypnotic potency decreases in the following order; monoalkyl ureas, symmetrical dialkyl ureas (methyl series), unsymmetrical dialkyl ureas, symmetrical dialkyl ureas (ethyl series) and trialkyl ureas. The toxicity values are not consistent, thus making generalization concerning this property difficult. In the aryl and alkylaryl ureas, molecular weight is not an important factor in determining hypnotic effectiveness. In these series, the position of a substituent group in position isomers is more important.—J. S. BUCK, A. M. HJORT and E J. DE BEER. *J. Pharmacol.*, 54 (1935), 188. (H. B. H.)

Vitamin B—Studies of Crystalline. IV. Injection Method of Assay. A modification of the Smith injection technique for vitamin B assay is described which is quick, convenient and reasonably accurate. The material to be tested is injected from a tuberculin syringe through a 26-gage needle into the fleshy part of the rat's hind leg. As much as 0.75 cc. of the liquid (p_H 4.0–6.0) containing as high as 10% solids can be introduced into each leg subcutaneously with satisfactory results. The effect can be noted within 12–48 hours. With an adequate dose, the symptoms of paralysis disappear entirely with an accompanying gain in weight. If the dose is very inadequate, the symptoms are not alleviated and may become definitely worse and there is generally a loss in weight. If the injected dose is barely adequate, a partial cure may result. With minimum curative doses paralysis recurs in 5–10 days after successful treatment. As a result of an extremely large dose, animals have remained cured for as long as 32 days. Surviving animals that are not cured by the first injection are used again after the lapse of one day. Those that are cured or definitely improved are kept on the depletion diet until paralysis recurs and are then reinjected. In this way, the same rat can be used several times. The curative dose according to the response standard established is 5γ. The minimum dose which completely cures practically every animal

is 7.5γ.—M. AMMERMAN and R. E. WATERMAN. *J. Nutrition*, 10 (1935), 25; through *Squibb Abstr. Bull.*, 8 (1935), A-1019.

TOXICOLOGY

Amidopyrine—Toxic Reactions of. Therapeutic doses of amidopyrine, *e. g.*, 0.2–0.648 Gm., can exert a harmful effect on the general condition of sensitive persons (fever, chill, nausea, headache, etc.) and on the activity of blood-forming organs. The effect on the granulocytopoietic apparatus is stimulating as well as inhibitive; decrease in the total granulocyte value and increase in the immature and young elements. In individual cases, there is a subsequent leukocytosis. The amidopyrine effect extends to the monocyte- and lymphocyte-producing organs and also to erythropoiesis. These changes recede spontaneously when the drug is discontinued, otherwise it is to be expected that the initial symptoms advance to a marked granulocytopenia with typical clinical manifestations. Three cases described by Bonsdorff, of which two were fatal, illustrate this. It is of utmost significance whether other antipyretics are capable of producing granulocytopenia. Antipyrine, the parent substance of amidopyrine and its derivatives, fall in this group. Several cases of granulocytopenia have already been reported with antipyrine. Salicylic acid has not yet been found to be an offending substance in humans, but it has been observed to cause granulocytopenia in animals. Barbituric acid preparations are dangerous because they are often combined with amidopyrine. Indeed, one of the acids, 5-ethyl-5-phenyl-barbituric acid (Luminal) has been reported as causing a decrease in the granulocytic value in animals.—B. v. BONSDORFF. *Klin. Wochschr.*, 14 (1935), 465; through *Squibb Abstr. Bull.*, 8 (1935), A-563.

Arsine—Poisoning by. A detailed description of a case in which an accidental fatal poisoning was traced to arsine from the circumstances accompanying the accident and the clinical symptoms, in spite of the fact that no arsenic was found in the analysis of the viscera. Death occurred 8 days after the victim had cleaned out the sludge from a tank 1 m. high by 2 m. in diameter, used for the purification of pyrites burner gases, the work having required only about 10 min. The sludge consisted of 13% iron sulphate, 84% lead sulphate and 2.6% arsenious oxide; instead of wooden tools, as usual, the victim had used an iron scraper which showed distinct signs of attack by acid. It was concluded that, in spite of the preliminary washing with water, there remained sufficient acid in the sludge to react with the scraper, with evolution of hydrogen which reacted with the arsenious oxide to form arsine.—J. LECLERCQ and H. SPRIET. *Ann. Méd. Légale Criminol. Police Sci.*, 15 (1935), 362–366. (A. P.-C.)

Arsphenamine—Ocular Reactions Due to. In twenty cases of primary and secondary syphilis (19 had early syphilis) treatment with arsphenamine produced toxic ocular reactions of varying degree. The initial signs were usually subjective and unilateral and frequently so slight as to produce no detectable eye changes; usually, however, there was slight haziness of the vitreous or blurring of the nerve head. Continuation of arsphenamine aggravated the condition producing considerable optic neuritis and possibly secondary optic atrophy. Vision improved fairly rapidly and returned to normal if the arsphenamine was discontinued when the first symptoms were observed. Further antisyphilitic treatment with iodides, bismuth or mercury caused no ocular symptoms and did not prevent the return of the eye condition to normal. Subsequent treatment with arsphenamine was possible in most cases if given cautiously with cessation at the first signs of ocular symptoms, but some cases showed hypersensitivity to the drug. Of the twenty cases with ocular symptoms, nine showed other arsphenamine reactions including nitrotoic reactions, dermatitis and postarsphenamine hepatitis with jaundice. None of the cases showed any signs of neurosyphilis.—J. J. SKIRBALL and F. M. THURMON. *Am. J. Syphilis & Neurol.*, 19 (1935), 197; through *Squibb Abstr. Bull.*, 8 (1935), A-644.

Atropine—Action of, on Reanimation of Heart in Secondary Chloroform Syncopes. The author points out that reported differences in the action of atropine in the heart in chloroform poisoning have been due to differences in the mode of injection. The author has injected atropine directly into the heart successfully, in contrast to results reported following injections into the jugular vein.—L. GARRELON. *Compt. rend. soc. biol.*, 118 (1935), 854; through *Squibb Abstr. Bull.*, 8 (1935), A-646.

Aurotherapy—Dangers in. Therapeutic use of gold may cause modifications in the blood (eosinophilia and agranulocytosis). The symptoms which are associated with true saturation (coated tongue, nausea, diarrhea) resemble the picture obtained in the case of uremia; in fact, in

these cases, amounts of urea as high as 50–60 cg. have been found. It is well to detect these slight azotemias, since they are forerunners of polynucleosis and therefore of saturation. Regular examination of the constituents of the blood should be carried out during gold therapy.—R. DUVAL. *Bruxelles-Méd.*, No. 23 (1935); through *J. pharm. Belg.*, 17 (1935), 472. (S. W. G.)

Benzene—Experimental Research on the Toxicity of the Vapors of. Concentration of Benzene in the Blood and Speed of Removal. A study of guinea pigs, weighing 800–850 Gm. and subjected to benzene vapors, showed that the benzene content of the animal, especially with higher concentrations (20–50 mg./liter) is a linear function of the duration of inhalation, up to 20 minutes. The most severe symptoms are noticeable when the benzene content of the blood is 2.6–2.8 mg. per 100 Gm. of animal. Benzene vapors introduced into the animal by inhalation disappear quickly from the blood, when air is free from vapors, and the symptoms vanish. The vapors are eliminated chiefly by the lungs and partly by the kidney.—MARCEL PERONNET. *J. pharm. chim.*, 21 (1935), 503. (M. M. Z.)

Bichloride of Mercury—Quantitative Study of Renal Injury in a Case of Acute Poisoning by. A quantitative study of a case of acute mercuric chloride poisoning showed that extensive renal damage occurred almost immediately, lasted for several weeks and then improved slowly with return to normal function three and one-half months after poisoning.—R. H. FREYBERG and F. H. LASHMET. *Am. J. Med. Sci.*, 189 (1935), 392; through *Squibb Abstr. Bull.*, 8 (1935), A-589.

Bromides—Toxic Reactions of. A report of five cases of bromide intoxication observed in general medical practice. The recommended treatment is sodium chloride orally (6–8 Gm. daily), by hypodermoclysis or intranvenously.—E. H. HASHINGER and C. C. UNDERWOOD. *J. Kansas Med. Soc.*, 36 (1935), 183; through *Squibb Abstr. Bull.*, 8 (1935), A-752.

Carbon Monoxide Poisoning—Chronic. Effects on persons exposed to carbon monoxide for many years show that occurrence of chronic carbon monoxide poisoning cannot be doubted. Carbon monoxide-hæmoglobin is dissociated through abundant ventilation but this does not take place completely. A residue of carbon monoxide-hæmoglobin always remains.—HERMAN GERBIS. *Deut. Med. Wochschr.*, 61 (1935), 991–994. (H. R.)

Datura Stramonium—Food Poisoning from. The authors describe an epidemic of food poisoning in Amsterdam involving at least 34 cases. The epidemic was caused by a grocery firm supplying a preserving factory leaves of *Datura Stramonium* in error, for savory.—H. PEETERS and J. C. DE JONG. *Pharm. Weekblad*, 72 (1935), 715. (E. H. W.)

α-Dinitrophenol—Chronic Lesions Produced by. When administered to guinea pigs in amounts approximating the human therapeutic dose, α-dinitrophenol produced hepatic lesions giving no external symptoms and shown to be due to the nitro groups.—R. JONNARD. *Ann. Méd. Légale Criminol. Police Sci.*, 15 (1935), 181–183. (A. P.-C.)

Mercurial Diuretics—Reaction at Site of Injection of, as Influenced by Theophylline. It has been demonstrated in animals and in man that the presence of theophylline in combination with a mercurial diuretic definitely decreases the local toxic reaction.—ARTHUR C. DEGRAFF and ROBERT C. BATTERMAN. *Proc. Soc. Exptl. Biol. Med.*, 32 (1935), 1546. (A. E. M.)

Methylene Blue, Methemoglobin and Cyanide Poisoning. Methemoglobin does not accumulate in significant quantities in the blood of dogs after intravenous injection of clinically recommended quantities of methylene blue. This fact, however, should not bring into question the proposed methemoglobin explanation of the dye's action in cyanide poisoning. The failure of methemoglobin to accumulate is explicable on the basis of the known behavior of the reactions involved, namely, the reduction of the formed methemoglobin by leuco-methylene blue and the enzyme systems present in the erythrocytes, and the rapid disappearance of the injected dye from the blood. *In vivo* formation of methemoglobin is readily demonstrable after administration of both cyanide and methylene blue because of the stability of the cyanmethemoglobin which is formed. Considerably more than half of 2 M. L. D. of subcutaneously administered cyanide is demonstrably bound in the circulating erythrocytes of dogs injected with methylene blue immediately before administration of the cyanide. When the dye is injected continuously throughout the period of cyanide absorption a still greater fraction of the cyanide is bound in the blood. The principal action of methylene blue in counteracting the toxic effects of cyanide appears to depend,

therefore, upon methemoglobin formation. In the absence of experimental demonstration that methylene blue can replace the cyanide sensitive catalysts which are concerned with vital processes, the methemoglobin explanation appears to be all that is required.—WILLIAM B. WENDEL. *J, Pharmacol.*, 54 (1935), 283. (H. B. H.)

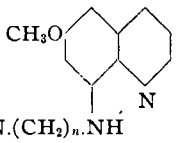
Phenolphthalein—Reactions Caused by. A survey of the literature on reactions caused by phenolphthalein shows that the reports deal mainly with the general constitutional effects, *e. g.*, syndromes in which circulatory, renal or nervous disturbances predominate, and with cutaneous eruptions. The total number of reactions observed is small considering the extensive use of the drug. Most of the reactions were noted after a single or occasional average dose. Nine cases of systemic disturbances resulting from an overdose and 6 cases of possible cumulative action are somewhat offset by 11 reported instances of no apparent ill effects from overdosage. The laxative dose of the white phenolphthalein is 3 times that of the yellow which contains more of a residue known as the "dark bodies." Compounds from which phenolphthalein is prepared and related derivatives were not responsible for the cutaneous lesions, nor was the vehicle responsible for the eruptions. Chemical and microscopical examination of the blood and urine in normal persons showed no noticeable difference before and after use of the drug. Eruptions may appear after the first dose suggesting previous contact, or the occasional use of an average dose may bring on a sudden development of hypersensitivity. Phenolphthalein, but none of the other commoner drugs, reproduced the cutaneous lesions. The reactions suggest an allergic response in persons sensitized to the drugs. In most cases skin tests are negative. Abramowitz assumes that there is a form of specific hypersensitiveness, allergic in nature, in patients who have eruptions due to phenolphthalein. He also suggests that other tissues besides the skin may become sensitized accounting for the general reactions that develop.—E. W. ABRAMOWITZ. *Arch. Dermatol. Syphilol.* 31 (1935), 777; through *Squibb Abstr. Bull.*, 8 (1935), A-974.

Refrigerating Agents—Toxicity of the Newer. Air-conditioning apparatus is generally of the water-injection type, and as the water comes into direct contact with the air that it cools, it is important that it be not contaminated through leaks by the cooling gases. The new cooling agents (ethyl chloride, dichloroethylene, dichloromethane) are less toxic than carbon dioxide, ammonia or sulphur dioxide; but all cooling agents are injurious to the human organism when they modify the composition of the atmosphere. Fluorine compounds (CF_2Cl_2, $CFCl_3$, CF_3Cl, etc.) recently proposed in America are not without drawbacks. Efforts should therefore be directed along the lines of improvement of the apparatus to render practically impossible contamination of the cooling water or of the cooled atmosphere.—R. LANDSBERG. *Rev. Gén. Froid*, 15 (1934), 239–241; through *Chimie & Industrie*, 33 (1935), 1111. (A. P.-C.)

Toxicity—Relation of, to Mode of Administration. After the injection of 15.5 cc. procaine (scurocaine) (I) solution containing 0.00012 Gm. epinephrine (adrenaline) per 3 cc. or a total of 750 mg. I, into the exposed femoral artery of a 13-Kg. dog, the dog showed an intense excitation for 10 minutes. The injected foot was used awkwardly, but was not paralyzed, and the animal was completely normal on the following day. A month afterwards, the same dog, though considerably weakened from other experiments, was given 700 mg. I intravenously in the same leg as previously injected. Respiration became slow and deep and after 5–6 movements ceased entirely and the heart stopped beating. With the intravenous injection 0.25–0.5 cc. "soluprotin" the phenomenon of intense shock was obtained regularly, but the injection of 1 cc. into the artery was followed by some local reactions but no indication of a general reaction. Similarly the injection into the artery of 20 cc. acetylcholine, 1 mg. epinephrine (adrenaline), 1 ampul of cobra toxin, amounts which could not be injected intravenously, gave only varied local reactions. Up to 5 cc. of the compound (somnifen) of 5-allyl-5-isopropyl barbituric acid with 5,5-diethyl barbituric acid diethylamine had to be injected into the femoral artery to obtain a simple quieting effect although general anesthesia was obtained with 3 cc. intravenously. On the other hand the injection into the femoral artery of the sodium salt of 5-cyclohexenyl-1,5-dimethylbarbituric acid (sodium evipal) produced almost the same anesthesia as the intravenous injection. The author suggests that the injection of some of these substances into the arteries may be characterized by a loss of toxicity without a loss of the desirable effects.—P. GOINARD. *Compt. rend. soc. biol.*, 118 (1935), 689; through *Squibb Abstr. Bull.*, 8 (1935), A-631.

THERAPEUTICS

8-Aminoquinoline—Derivatives of, as Antimalarials. IV. Compounds referable to the formula



were prepared, where N is represented by 6, 7, 9 and 11, respectively. The therapeutic indices of the compounds were, in the order given, 13.3, 33.3, 40 and 5. Homologs containing an uneven number of methylene groups in the side-chain were more active and had a higher index than those possessing an even number of such groups. The relatively high index of 40 in the case of the nine-carbon side-chain was occasioned chiefly by the low toxicity of the compound. The preparation of the greater number of compounds was based upon the use of α-ω-glycols. By use of the dibromide and the bromido-acetate, the corresponding ω-diethylaminoalkyl acetates were obtained. Heating the latter with hydrobromic or hydrochloric acid gave the diethylaminoalkyl bromide or chloride, which was then condensed with 8-amino-6-methoxyquinoline. The stabilities of the compounds increased with the length of the side-chain. Diethylaminopentyl chloride undergoes cyclization upon distillation; the higher homologs, with less ease, after three to four months' standing.—O. J. MAJIDSON, O. S. MADAJEWA and M. W. RUBZOW. *Arch. Pharm.*, 273 (1935), 320. (L. L. M.)

Amyl Nitrite—Use of, in Cases of Contraction Ring. A paper describing the use of amyl nitrite during labor in the rare condition in which a ring of persistently contracted muscle occurs in the body of the uterus, and prevents the delivery of the child. Amyl nitrite when administered causes relaxation of this ring. The author has tested the effect of amyl nitrite upon isolated strips of human uterus suspended in a bath, but he did not observe much effect.—C. R. CROTF. *Proc. Roy. Soc. Med.*, 28 (1935), 481; through *Quart. J. Pharm. Pharmacol.*, 8 (1935), 303. (S. W. G.)

Antipyretics. Antipyretics should only be sold on a physician's order and recognized as palliatives until the irritating cause is removed. Acetylsalicylic acid (I), the least dangerous of the drugs, might be excepted from such restriction. Acetanilide (II) so loudly declaimed as a cause of cardiac weakness and excluded from the B. P. and Canadian Formulary, is undoubtedly efficient and perhaps not more dangerous than 1,5-dimethyl-4-dimethylamino-2-phenyl-3-pyrazalone (III, amidopyrine) which has replaced it as the official drug. *p*-Aceto-phenetide (IV, phenacetin) is not so dangerous and 1,5-dimethyl-2-phenyl-3-pyrazalone (V, antipyrine, phenazone) is credited as being even less harmful. I is much less dangerous but also much less efficient. 2-Phenyl-4-quinolinecarboxylic acid (VI, cinchophen) decreases fever and pain of acute articular rheumatism and like the others, may relieve pain of chronic lesions in muscles and joints, but its use should be carefully controlled. The evidence of the use of combinations of antipyretics with sodium bicarbonate or other alkali or caffeine is drawn largely from the use of relatively acute toxic doses. Sodium bicarbonate does, however, protect I in the stomach and its use is a little more credible than caffeine. The synergistic effects of combinations of III and barbiturates or IV and diethyl-barbituric acid (VII) have been reported. Many cases of agranulocytic leucopenia have resulted from the use of III-barbiturate combinations; the IV–VII combination might be more extensively tested. Codeine (VIII) has, compared with morphine, little value in relieving pain, yet appears to be effective in certain headaches. Clinical experience seems to justify the combination of VIII with antipyretics. The combination IV–VII–VIII may frequently replace morphine.—V. E. HENDERSON. *Can. Med. Assoc. J.*, 33 (1935); through *Squibb Abstr. Bull.*, 8 (1935), A-989.