ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ALKALOIDS

Lurenine, a new Alkaloid from *Lobelia Urens*. By E. Steinegger and H. Grütter. (*Pharm. Acta Helvet.*, 1950, **25**, 276.) The alkaloid was obtained from the mother liquors from lobeline hydrochloride crystallisation. The base had m.pt. 202° to 204°C. and mol.wt. 276. The reactions are similar to those of lobeline. G. M.

Morphine and Related Alkaloids, Radioactive. B. J. McIntosh, F. E. Kelsey and E. M. Geiling. (*J. Amer. pharm. Ass.*, 1950, **39**, 512.) Seeds of *Papaver somniferum* were sown in black soil and the seedlings were found to grow under suitable conditions in a sealed atmosphere for at least 36 days at temperatures below 22°C. and above 14°C. At temperatures between 14° and 18°C. the high relative humidity did not seem to be deleterious, but at higher temperatures a part of the moisture had to be removed from the sealed atmosphere. The sealed plants were placed under two daylight-type fluorescent lamps and irradiated for 16 hours a day in an apparatus from which atmospheric moisture was removed. It was found that *P. somniferum* incorporated ^{14}C into the morphine molecule after 21 days' exposure to $^{14}CO_2$. A light intensity of approximately 200 foot-candles was necessary for growing periods which were sufficiently long to allow radioactive morphine to be synthesised; thus plants grown in an atmosphere of $^{14}CO_2$ for less than 8 days produced only small amounts of radio-active morphine, or none. Morphine which contained C^{14} could be isolated from the plant by adsorbing morphine on permutit from a 50 per cent. ethyl alcoholic solution and eluting it with a compound having an ionisation constant greater than $7{\cdot}4 \times 10^{-7}$. It was found that morphine was not eluted from permutit by light petroleum, ethyl ether, carbon tetrachloride, acetone, or absolute methanol. Among related narcotic alkaloids papaverine was adsorbed by permutit from aqueous solutions and could be eluted with 50 per cent. aqueous ethanol. Narcotine was adsorbed from an ethereal solution and eluted with ethanol, while codeine and thebaine were adsorbed by permutit from aqueous solution or 50 per cent. aqueous ethyl alcohol and eluted with aqueous sodium chloride solutions. R. E. S.

ANALYTICAL

Carbon Dioxide, Determination of. J. Dallemagne. (*Bull. Soc. Chim. biol.*, 1950, **32**, 282.) A new form of apparatus consists of a conical flask of which the base is divided into two portions by means of a ring of glass fused internally to the base and concentric with the circumference. The inner ring so formed is used to contain the substance under examination, while the outer ring contains baryta solution. The ground neck of the flask is fitted with a dropping funnel, while a capillary tube with tap, sealed on at one side, allows of a connection to a burette for titration of the baryta. It is an advantage to have a magnetic stirrer in the inner ring to facilitate the disengagement of the carbon dioxide, and the whole apparatus may be oscillated continuously to break the film of barium carbonate which forms on the surface of the baryta. G. M.

Ergot, Simplified Method of Assay of. L. Fuchs and W. Himmelbauer. (*Scientia Pharm.*, 1950, **18**, 93.) 4 g. of defatted powdered ergot (sieve 0·2 mm. mesh) is treated with 80 g. of ether and 1 ml. of 10 per cent. ammonia for 4 hours, with shaking for 1 minute after each half-hour. The mixture is allowed to stand to clear, and filtered through a dry filter; 60 g. of the filtrate is evaporated to 25 ml. on the water-bath under reduced pressure and, after cooling, the ethereal solution is transferred to a separating funnel and rinsed in with a little ether. The solution is extracted by shaking 5 times with 5 ml. quantities of 1 per cent. solution of tartaric acid, 5 minutes shaking being given each time. The combined aqueous solution, freed from ether by warming, concentrated to 20 ml., and made up to 25 ml. (solution A). Of this solution, 1 ml. is treated with 2 ml. of reagent (0·20 g. of dimethylaminobenzaldehyde dissolved in a cooled mixture of 35 ml. of water and 65 ml. of sulphuric acid, with 0·3 ml. of 10 per cent. ferric chloride solution). After 20 minutes the extinction is measured in a 0·5 cm. cell, using filter S61. If the extinction is greater than 0·6, the test must be repeated, using solution A suitably diluted with 1 per cent. solution of tartaric acid. This gives the total alkaloids. For water-soluble alkaloids, 20 ml. of solution A is treated, drop by drop, with 10 per cent. ammonia solution until a slight permanent turbidity appears, and 2 drops are added in excess. The mixture is treated with 2·5 g. of ammonium sulphate and, after dissolving, the reaction is checked with litmus paper, ammonia being added, if necessary, to produce a slight alkaline reaction. The volume is then made up to 25 ml. After standing for 12 hours in the ice chest, the mixture is filtered through a small covered filter, the first 10 ml. of filtrate being rejected. The colorimetric determination is then carried out as before, using 2 ml. of solution with 4 ml. of reagent, and a 1 cm. cell. In calculating the results, and assuming that the total alkaloids are calculated as ergotamine and the water-soluble alkaloids as ergometrine, it is necessary to multiply the ergometrine figure by 1·79 before subtracting from the total alkaloids in order to obtain the water-insoluble alkaloids as ergotamine. In applying the method to galenical preparations of ergot, alcohol must first be removed. G. M.

Folic Acid in Pharmaceutical Preparations, Determination of. P. A. Ware and G. Cronheim. (*J. Amer. pharm. Ass., Sci., Ed.*, 1950, **39**, 98.) Concentrations of folic acid as low as 0·1 per cent. were accurately determined in pharmaceutical preparations coloured by the addition of liver preparations, iron salts and vitamins of the B group, by a modified Hutchings method. The method consists in diluting the sample with alkali, filtering, reducing the folic acid in the filtrate with hydrochloric acid and zinc amalgam and estimating the *p*-aminobenzoylglutamic acid so obtained colorimetrically. The liver preparations, B vitamins and iron peptonate did not interfere with the assay. In the presence of ionisable ferric salts the results were up to 10 per cent. too low. In the presence of ferrous salts the loss of folic acid ranged from 50 to 70 per cent., due to reduction of the folic acid by ferrous ions. This was overcome by adding sodium gluconate to the preparations before assay to prevent the precipitation of ferrous ions by sodium hydroxide; the results thus obtained were also up to 10 per cent. too low. The addition of gluconic acid did not produce the same effect. Interference by the intrinsic colour of the preparation was avoided by adequate dilution and the use of a sensitive colorimeter.

G. R. K.

Fructose, A Colour Test for. R. K. Maurmeyer, E. M. Livingston and H. Zahnd. (*J. biol. Chem.*, 1950, **185**, 347.) Fructose reacts in the presence of phenol and sulphuric acid to give a green colour. Four drops of a solution of fructose (0·5 g./100 ml. of glacial acetic acid) are mixed with 10 drops of a phenol solution (0·25 g./100 ml. of glacial acetic acid) and 3 drops of concentrated sulphuric acid and heated for 5 minutes. The colour may be intensified by longer heating, but after 15 minutes it turns brown. A distinct green colour is obtained by as little as 0·1 mg. of fructose/ml. and by 1 mg. of fructose in the presence of 50 mg. of glucose. Substances which yield fructose on hydrolysis also give the colour. It is thought that the coloration is due to hydroxymethylfurfural as in the Seliwanoff reaction. Under the stated conditions arabinose and galactose give a brown colour, glucose, glycogen, inositol and lactose yellow, mannose and rhamnose red, xylose pink, whilst inulin, raffinose and sucrose, which form fructose, on hydrolysis, give the green colour. A. D. O.

Grote Reagent. J. J. M. van Sonsbeek. (*Acta pharm. internat.*, 1950, **1**, 43.) Dissolve 2 g. of sodium nitroprusside, 2 g. of hydroxylamine hydrochloride and 4 g. of sodium bicarbonate in 40 ml. of water. When effervescence has ceased, add 0·1 ml. of bromine and water to 100 ml. The reagent will keep for about a fortnight. With C : S groups it gives a green to blue colour, the optimum *p*H being 6·0 to 7·0. The Na_3 $[Fe(CN)_5H_2O]$ complex present in the reagent appears to take part in the formation of a blue compound which may appear green in the yellow colour of the reagent. CSH and CSSC radicals give a purple-red colour with Grote reagent, but the reaction is unreliable unless potassium cyanide is added. This reaction is attributed to the presence in the reagent of sodium nitroprusside which, in alkaline solution, gives the same colour with CSH groups in the absence of cyanide and with CSSH groups when cyanide is present. The reagent may be used for the identification of thiopentone (with which it gives a red colour at *p*H 4 to 8) and in place of Roux reagent for the identification of sulphonamides. G. B.

Iodine Number, Direct Titrimetric Determination of. O. Tomiček and I. Doležal. (*Acta pharm. internat.*, 1950, **1**, 31.) The following titrations may be performed with bromine in anhydrous acetic acid solution, in the presence of sodium acetate, the end-point being determined potentiometrically :—phenol, α-naphthol and resorcinol to the tribromo derivatives, thymol to dibromothymol and pyrocatechol and hydroquinone to the monobromo compounds. Under similar conditions, two atoms of bromine are added to the double bond in cholesterol, and to one of the double bonds in limonene, the results by titration being in good agreement with the theoretical value. The same method may be applied to the determination of the iodine value of oleic acid, fixed oils and volatile oils. The results by the methods of Hanŭs, Hübl, Rosemund-Kunhenn and direct titration with bromine, are compared. G. B.

Iron, Estimation by Dichromate. D. Stockdale. (*Analyst*, 1950, **75**, 150.) An investigation has been made into the relative merits of diphenylamine, diphenylbenzidine, barium diphenylamine sulphonate, ferrous phenanthroline and potassium ferricyanide as indicators in the estimation of iron by potassium dichromate. The standard electrode potential for the reduction of the dichromate ion is $-1{\cdot}36$ volts, but more usually the activity coefficients of the ions are far from unity, and the potential obtained by

adding 50 ml. of 0·1 N potassium dichromate to 25 ml. of 0·1 N ferrous solution is about $-1{\cdot}10$ volts when the final concentration of strong acid is formally normal; this potential is much influenced by the *p*H and will be increased by increasing the hydrogen ion concentration of the solution in which the reduction is taking place. Potential curves for the titration under varying conditions are given. It was concluded that all the indicators are efficient under suitable conditions, although barium diphenylamine sulphonate was considered to be the best. This indicator gives a satisfactory result when the solution is at least 0·5 N with respect to hydrochloric or sulphuric acid, while if phosphoric acid is present the colours are clear and the range of colour change is small. In the absence of phosphoric acid, titrations must be continued until the violet colour of the indicator is fully developed; the colours may be somewhat muddy, but the colour change takes place over a rather larger range of dichromate, so giving some warning of the approach of the end-point. R. E. S.

Limit Tests for Impurities. I. Investigations into the Reproducibility of Precipitation. F. Reimers and K. R. Gottlieb. (*Acta pharm. internat.*, 1950, **1**, 55.) The following limit test for sulphates is recommended. Place 1 drop of potassium sulphate solution (containing 100 µg. of sulphate ion per ml.) in a test-tube, add 1 ml. of barium chloride solution, shake during 1 minute, add 10 ml. of the solution to be examined, containing 1 ml. of 2 N hydrochloric acid and shake vigorously for 10 seconds. Compare after 5 minutes with a standard turbidity prepared from the required quantity of potassium sulphate solution, 1 ml. of barium chloride solution and 10 ml. of water. By seeding, the first, badly defined stage of precipitation (the formation of microcrystals) is avoided and the reproducibility and sensitivity of the test are improved. Nitrates reduce the sensitivity of the test, and the use of barium nitrate as a precipitating agent should be avoided. Seeding is advantageous when precipitating low concentrations of calcium as oxalate, especially in the presence of acetic acid or salts. In testing for magnesium by precipitation with ammonia, ammonium chloride and sodium phosphate the reproducibility is poor because impurities in the sodium phosphate are precipitated and act to a variable extent as seeding agents. The precision of the experiments is not improved by seeding. The effect of temperature and salts on the tests is discussed. G. B.

Menthol in Oil of Peppermint, Determination of. B. Danielsson. (*Svensk farm. Tidskr.*, 1950, **54**, 181.) In the Swedish official method for the determination of menthol in oil of peppermint, it is essential that the molecular ratio of menthol to acetic anhydride should not exceed 0·60, otherwise the results obtained are too low. It is therefore desirable to reduce the amount of oil taken for the determination to 2·5 g. The presence of water in the pyridine used reduces the amount of acetic anhydride available for acetylation and disturbs the ratio, and a more sensitive test than that given in the Pharmacopœia would be desirable. It is suggested that this may be carried out by adding to 1 ml. of pyridine, 4 ml. of light petroleum in such a way as to form a separate layer, when a white zone at the junction of the two liquids indicates water. The sensitivity is about 0·5 per cent. G. M.

Methadone, Colorimetric Determination of. J. S. Faber. (*Pharm. Weekbl.*, 1950, **85**, 719.) A quantity of the solution, corresponding to about 5 mg. of methadone, is evaporated to dryness on the water-bath, and the residue is extracted with 1 ml. of ethanol (96 per cent.). The solution

is filtered through a small filter, the residue (of sodium chloride) being re-extracted with small quantities of ethanol to give a final volume of 2 ml. To this solution is added 4 ml. of 1 per cent. w/w solution of *m*-dinitrobenzene in ethanol, followed by 4 ml. of 4N sodium hydroxide and ethanol to 10 ml. The mixture, together with a corresponding blank without methadone, is placed in a water-bath at 43° to 45°C. for exactly 10 minutes, then cooled in running water. One hour after the mixing of the solutions, the extinction is determined in a 5 cm. cell (filter S50). The degree of purity of the *m*-dinitrobenzene is important: it should have m.pt. 90° to 90·5°C., as less pure preparations give too much yellow colour in the blank.

G. M.

1-Methyl-5-aminoacridine, Quantitative Estimation of. J. R. A. Anderson and M. Lederer. (*Analyst*, 1950, **75**, 318.) It was found that, by double decomposition between aqueous solutions of 1-methyl-5-aminoacridine and picric acid, a yellow insoluble precipitate, $C_{20}H_{15}N_5O_7$, was formed quantitatively. The compound was only sparingly soluble in many common organic solvents, melting at 274°C., and its formation could be used as the basis of a method for the quantitative estimation of 1-methyl-5-aminoacridine. To a boiling solution containing approximately 0·1 g. of 1-methyl-5-aminoacridine dissolved in sodium acetate-acetic acid buffer solutions, was added a saturated aqueous solution of picric acid (100 per cent. excess). After standing at 0°C. for 3 hours, the precipitated picrate was washed with a small amount of water, filtered off, and dried to constant weight at 105°C. Picrolonic acid also reacted quantitatively with 1-methyl-5-aminoacridine to give a yellow precipitate, $C_{24}H_{20}N_6O_5$, only sparingly soluble in water and in many common organic solvents and melting at 296° to 298°C., with decomposition. For the gravimetric estimation of 1-methyl-5-amino acridine, a solution containing approximately 0·1 g. was boiled and picrolonic acid solution (0·01 N, 100 per cent. excess) was added from a burette. After standing for 1 hour and cooling to 15°C. the precipitate was filtered off, washed with a limited quantity of water and dried to constant weight at 130°C. The reactions of 1-methyl-5-aminoacridine with picric and picrolonic acids were considered to be molecular.

R. E. S.

Trichloracetic Acid, a New Identification Test for. H. Hougen. (*Acta pharm internat.*, 1950, **1**, 49.) Reagent A is prepared by mixing equal volumes of 0·5 M copper sulphate solution and pyridine. Reagent B is a 10 per cent. solution of cobalt nitrate mixed with an equal volume of pyridine. On mixing 4 drops of the reagent with not more than 10 drops of the solution to be examined, the following precipitates are produced:—

Substance	Reagent A [$CuSO_4$+pyridine]	Reagent B [$Co(NO_3)_2$+pyridine]
Trichloracetic acid	Blue monoclinic crystals	Red monoclinic crystals
Perchloric acid	Violet-blue orthorhombic crystals	White orthorhombic crystals
Hydrochloric acid	Green-blue rhombic crystals	—
Oxalic acid	—	Red-violet amorphous

To confirm the presence of trichloracetic acid, both reagents should be used.

G. B.

Water in Vegetable Drugs, Karl Fischer Titration of. N. A. Hulme and A. Osol. (*J. Amer. pharm. Ass. Sci. Ed.*, 1950, **39**, 471.) The Karl Fischer reagent was prepared by dissolving 84.7 g. of sublimed iodine (U.S.P.) in 670 ml. of reagent absolute methanol. To this solution 64 g. of liquid sulphur dioxide in 270 ml. of pyridine was then added slowly, with cooling. A standard solution of water was prepared by dissolving 4 g. of distilled water in methanol to make 1000 ml. Preliminary experiments showed that the end-points with either direct or back titration were difficult to read, but that satisfactory results could be obtained by potentiometric back titrations. Two 25 ml. automatic-levelling burettes with long tips bent to allow insertion into a titration cell were set up, each attached to a reservoir. A Beckman H-2 *p*H meter fitted with a polarising adapter was used to observe the end-point. Reagent methanol and 5 ml. of Fischer reagent were placed in the cell and well mixed for several minutes. The moisture absorbed was then estimated by back titration with standard methanolic solution of water. About 250 mg. of drug in No. 60 powder was then accurately weighed and transferred to the cell together with 10 ml. of reagent as quickly as possible. After stirring for 10 minutes the excess of reagent was titrated. It was necessary to restandardise the reagent frequently because of its instability. Determinations made on samples of digitalis, ipecacuanha and American hellebore showed that the results compared favourably with those obtained by oven-drying or by toluene distillation. A. D. O.

GLYCOSIDES, FERMENTS AND CARBOHYDRATES

Cardiac Glycosides, Some New Reactions, and Paper Chromatography of. F. Jaminet. (*J. Pharm. Belg.* 1950, **50**, 297.) A mixture of k-strophanthoside, k-strophanthidin and ouabain may be separated by two-dimensional chromatography on paper. In the first stage, using a mixture of equal volumes of ethyl acetate, methanol and chloroform, ouabane is separated from the other two compounds, while in the second stage, with a mixture of 3 volumes of chloroform and 1 of ethyl acetate, the k-strophanthidin is separated. The positions of the glycosides are revealed by spraying with a solution of 0·2 g. of *m*-dinitrobenzene and 10 ml. of 10 per cent. sodium hydroxide in 40 ml. of ethanol. Three new reactions for the identification of cardiac glycosides are described. The reagents used are: a solution of antimony chloride in acetic anhydride; a saturated solution of bismuth trichloride in acetic anhydride; and phosphoric acid. G. M.

Digitalin, Paper Chromatography of. P. Mesnard and J. Devze. (*Bull. Trav. Soc. Pharm. Bordeaux.* 1950, **88**, 109, 114.) For various reasons, the usual reagents for digitalis glycosides are unsuitable for the development of paper chromatograms. The method finally adopted was a modification of the reaction of Sanchez (without vanillin), in which hydrochloric acid vapour is used to develop the colour. The concentrated acid is warmed in a porcelain dish covered with an inverted funnel, and the chromatogram is passed over the jet of vapour issuing from the funnel, at a distance of 4 to 5 cm. from it. The paper becomes brittle, but may be kept between two sheets of cellophane. By using as solvent a mixture of 20 parts of ethyl acetate with 1 part of eucalyptol, digitaline Nativelle (commercial digitoxide) gives two spots with R_F values respectively 0 and 0·88. If this chromatogram is then re-treated with acetone in a second dimension, spot No. 1 gives rise

to 2 spots. The two latter are ascribed to the presence of gitoxoside and initial heterosides. This is in agreement with the results of Ulrix, but the authors were unable to detect any gitoxigenol. G. M.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Aureotracin, A Combination of Aureomycin and Bacitracin. H. Welch, W. A. Randall and C. W. Price. (*J. Amer. pharm. Ass.*, 1950, **39**, 483.) Aqueous solutions of bacitracin and aureomycin were mixed to form a precipitate which was washed with water, frozen, and dried, resulting in a golden yellow powder which was insoluble in water and ordinary organic solvents but quite soluble in dilute alkalis and acids. The preparation was termed "aureotracin" and assay showed 300 μg./mg. activity as aureomycin and 25 μ./mg. as bacitracin. It was not lethal to white mice (20 g.) in doses of 40 mg. given by intraperitoneal injection whereas 5 to 6 mg. of the bacitracin used in the preparation was invariably lethal. Experiments on white mice showed that aureotracin was less nephrotoxic than one would expect from its bacitracin content while it possessed activity against all the organisms ordinarily affected by aureomycin and bacitracin. Results indicated that a substance different from the parent compounds had been formed; the infra-red absorption spectrum revealed many points in common with aureomycin and bacitracin, yet definite differences were apparent. R. E. S.

Tyrothricin, Stability of Solution of. I. Schaldemore. (*Svensk Farm. Tidskr.* 1950, **54**, 701.) Tyrothricin is practically insoluble in water, but is soluble to some extent in the presence of cetyltrimethylammonium bromide. A solution containing 0·05 per cent. of the latter with 0·025 per cent. of tyrothricin is stable for at least 6 months, and is only slightly altered on heating in an autoclave. The solution of the two components has a somewhat greater bactericidal action than the two compounds separately. G. M.

Vitamin A, Hydrolysis and Esterification during Absorption. E. Eden and K. C. Sellers. (*Biochem. J.*, 1950, **46**, 261.) The fate of free and esterfied vitamin A during absorption by bovines and sheep has been studied. The procedure adopted was to determine the relative concentration of vitamin A alcohol and ester in the intestinal contents, mucosa, lymph and blood after dosing the animals (sheep and calves) with one or other form of the vitamin. The interval between dosing and slaughter was chosen as 4 hours, that being the time at which maximum concentration is mostly reached. Vitamin A alcohol or ester (5,000 I.U./kg. of body weight) was given to calves and sheep which were slaughtered after 4 hours, the concentrations of vitamin A alcohol and of ester being determined in the blood before and after dosing and, on slaughter, in the intestinal contents and wall and in the lymph. After 4 hours almost complete hydrolysis of vitamin A esters had occurred in the intestinal lumen of some animals, whereas in others hydrolysis was only partial. Determinations made on the mucosa after dosing with vitamin A ester showed that the ester fraction contained 73 and 56 per cent. of the total vitamin A in calves and sheep respectively. The values obtained after dosing with vitamin A alcohol were 82 and 77 per cent. respectively, showing that esterification had occurred. After passing across the intestinal wall the absorbed vitamin A apparently remained esterified, as the rise in the vitamin content of the intestinal lymph following administration of either form was

nearly all in the ester fraction. Details are given of the methods used for the preparation of plasma and lymph extracts for chromatographic separation on alumina columns. R. E. S.

BIOCHEMICAL ANALYSIS

Antibiotics, Turbidimetric Assay of. D. A Joslyn and M. Galbraith. (*J. Bact.*, 1950, **59**, 710.) A method has been developed which can be used for determining the antibiotic strength of fermentation liquors and similar preparations, or of purified antibiotics for which no standard has been developed. The procedure employs a heavy inoculum of a culture which has been incubated for only a short period, since study of the inhibitory effect of antibiotics on growth, as indicated by turbidity, showed that the lag phase of cultures would thereby be almost entirely eliminated and, further, the sensitivity is greatest when the inoculum is taken at the period of most active growth. 1 ml. quantities of a series of dilutions of the sample are mixed with 8·8 ml. of brain-heart infusion broth and inoculated with 0·2 ml. of a culture which has been kept in an ice-bath after reaching an optical density of 0·456, corresponding to 35 per cent. light transmission as measured in a photoelectric colorimeter. A variety of organisms can be used; if the culture is of *Escherichia coli*, the inoculum used is a 1:8 dilution of the culture of optical density 0·456. The tubes are incubated until the light transmission of similarly treated control tubes containing distilled water is reduced to 38 per cent. of its original value (optical density, 0·420). The optical density of each sample is then determined from the percentage light transmission, and the percentage growth in each tube is calculated by dividing the optical density by the optical density of the control and multiplying by 100. The percentage inhibition is the difference between 100 and the percentage growth; 50 per cent. inhibition is taken on the end point. Replicate assays on successive days agree within 5 per cent. If a standard preparation is available the same procedure is followed, duplicate rows of the standard being treated in the same way as the unknown. H. T. B.

Blood and Plasma, Measurement of Specific Gravities of, by Standard Copper Sulphate Solution. R. A. Phillips, D. D. van Slyke, P. B. Hamilton, V. P. Dole, K. Emerson, Jr., and R. M. Archibald. (*J. biol. Chem.*, 1950, **183**, 305.) Drops of plasma or whole blood are allowed to fall into a graded series of copper sulphate solutions of known specific gravities. On entering the solution each drop becomes encased in a sac of copper proteinate and remains whole for 10 to 15 seconds during which time it rises or falls according to the specific gravity of the solution. No adjustment is needed of temperature within the range 4° to 40°C. The stock solution of copper sulphate contains 159·0 g. of copper sulphate ($5H_2O$) per l. at 25°C. and the standards are prepared by dilution. The blood is pipetted into test tubes containing either 1 mg. of oxalate or 0·2 mg. of heparin per ml. of blood used. Plasma is obtained by centrifuging the sample after the determination on the whole blood has been made. For reliable results it is necessary to keep the surfaces of the standard solutions clean and bubbles must be avoided when taking blood sample from a finger. The standard deviation for whole blood was $\pm$ 0·0004 and $\pm$ 0·0003 g./ml. for plasma. The method may not be used for blood which has been stored for short periods and for transudates or exudates. Drops of whole blood balanced in solutions of

equal specific gravity, whilst plasma balanced in solutions 0·0007 g./ml. lighter than the plasma itself. A. D. O.

Penicillin Types, Paper Partition Chromatography of. G. A. Glister and A. Grainger. (*Analyst,* 1950, **75,** 310.) A modified rapid development technique for microchromatographic assay of the different penicillins using developed standards is given. It was concluded that the inclusion of penicillin K with G as developed standard would greatly improve the accuracy of the quantitative procedure, G, F and dihydro F being calculated as usual with the G standards, and K being calculated separately with a standard of similar type. Mixtures containing appreciable amounts of penicillin X should be accompanied by standards which include X. In the determination 9 buffered strips of filter paper are used, 3 for each standard and 3 for the test, and identical volumes of the standards and the test sample are spotted on to their respective strips. When the spots are dry the strips are developed for 3½ to 4 hours using diethyl ether saturated with distilled water at room temperature. When development is complete the strips are removed and placed on the surface of *B. subtilis*-seeded agar. Diffusion is allowed to proceed for half-an-hour and the plates are then incubated at 27°C. overnight, following which the maximum zone widths are measured and the averages are calculated. The results were obtained from the expression: Mean max. zone width high G standard − Mean max. zone width low G standard ≡ G slope log conc. ratio (e.g., 100/1). A similar procedure is followed for penicillin K. The mean maximum zone widths of G, F and dihydro F of the test divided by the G slope, give values the antilogs of which are proportional to the activities (in *B. subtilis* units) of these types; similarly, the mean maximum width of the K zone of the test divided by the K slope gives a value whose antilog is proportional to its activity. The individual proportionate activities can be expressed as a percentage of the sum of the activities to obtain the percentage activity (*B. subtilis* units) for each type. The percentage activity (*S. aureus* units) may be obtained by using this organism in place of *B. subtilis* in the technique. R. E. S.

Steroids in Urine, Determination of. F. Jayle, O. Crépy and O. Judas. (*Bull. Soc. Chim. biol.,* 1949, **31,** 1592.) When the concentration of steroids is high (i.e. in the last 3 weeks of pregnancy) from 100 to 200 ml. of the urine is treated with 15 per cent. of its volume of concentrated hydrochloric acid, and refluxed for 1 hour. In other cases 500 ml. is mixed with 15 per cent. of concentrated hydrochloric acid and 2 per cent. of 10 per cent. solution of phosphotungstic acid. After refluxing for 1 hour, and cooling, the mixture is placed in the ice chest for 3 hours and filtered. The residue is taken up in 5 per cent. ammonia, acidified, and filtered again, the residue being washed with a little water. For clinical work it is sufficient to wash the first precipitate with 60 ml. of water. The hydrolysed solution is then extracted 4 times with 20 per cent, of its volume of ether, the extracts being washed twice with 9 per cent. solution of sodium carbonate, corresponding in all to 20 per cent. of the volume of the urine, and finally 3 times with water, in all 10 per cent. of the volume of the urine. The ethereal solution is concentrated to 50 or 100 ml. and extracted 3 times with, in all, one-third of its volume of N sodium hydroxide. The mixed alkaline solutions are acidified to *p*H 3 and extracted in 3 operations with, in all, half the volume of ether, the mixed ethereal extracts being washed twice with one quarter of their volume of sodium carbonate solution, and 4 times with one-third of

their volume of water. After evaporating to dryness, the residue is taken up in 5 to 10 ml. of alcohol. For the colorimetric determination, the reagent used is prepared by adding 3·6 parts of melted phenol to 5·6 parts of concentrated sulphuric acid at a low temperature. The mixture is then diluted with an equal volume of sulphuric acid and kept in an ice chest. Aliquots of the alcoholic solution of 0·6 to 1 ml. (0·1 to 0·5 ml. in the case of advanced pregnancy) are evaporated to dryness in hæmolysis tubes, and the residue is treated with 0·4 ml. of reagent. The tubes are closed with corks covered with tin or lead foil, and heated for 10 minutes in the water-bath, each tube being shaken after 1 minute and at 2 or 3 minute intervals. After cooling in crushed ice, each tube is then treated separately by adding 0·35 ml. of water, heating 1 minute in the water bath, cooling for 30 seconds in ice water, and adding 1·25 ml. of a mixture of equal volumes of acetone and water. After exactly 1 minute the colour is measured, preferably at 520 mμ. The tubes are then kept in the dark for 18 to 24 hours until the pink colour disappears, and the colour is again determined in order to give a blank value due to impurities. The colorimetric determination is standardised with œstrone. G. M.

PHARMACY

DISPENSING

Blood, Tears and Tissue, Preparation of Solutions Iso-osmotic with. C. G. Lund, K. Pedersen-Bjergaard and E. Becker Rasmussen. (*Acta pharm. int.*, 1950, **1**, 3.) Curves are given for the freezing point depression of the following aqueous solutions:—calcium lævulinate, cetrimide, histidine chloride, hydroxyquinoline sulphate, maphenide, morphine sulphate, neostigmine bromide, pethidine hydrochloride, pilocarpine nitrate, sodium acetate, sodium metabisulphite, strychnine hydrochloride, sulphadiazine sodium, sulphamerazine sodium, sulphathiazole sodium and tubocurarine chloride. The quantity of sodium chloride to be added to produce an iso-osmotic solution can be calculated graphically, and for this purpose a mirror image of the standard freezing-point curve for sodium chloride, corrected for the separation of ice, is included. The curves are based on vapour pressures determined by comparison with standard sodium chloride solutions using a pair of thermocouples in a Dewar vessel. Where possible the solutions have been compared with sodium chloride solutions for hæmolysis of red cells, and results in accord with the vapour pressure data have been obtained. G.B.

Sodium *p*-Aminosalicylate, Isotonic Solution of. H. A. M. Steenbergen. (*Pharm. Weekbl.*, 1950, **85**, 473.) Commercial sodium *p*-aminosalicylate occurs either anhydrous or with 2 molecules of water. An isotonic solution should contain 2·80 per cent. of the anhydrous salt, equivalent to 2·45 per cent. of the acid. The solution may be made by dissolving 2·45 g. of the acid and 1·34 g. of sodium bicarbonate in 30 ml. of water. After completion of the reaction, the *p*H is adjusted to 7·5, and the solution is diluted to 100 ml. Sterilisation is by heating for 30 minutes at 100°C.

G. M.

GALENICAL PHARMACY

Aneurine Mononitrate in Pharmaceutical Preparations, Stability of. J. C. Bird and R. S. Shelton. (*J. Amer. pharm. Ass.*, 1950, **39**, 500.) Six pharmaceutical laboratories co-operated in studying the stability over 12

months of aneurine mononitrate in the following pharmaceutical products: (a) plain uncoated tablets containing 25 mg. of aneurine mononitrate; (b) soft gelatin capsules, plain, 10 mg. of aneurine mononitrate each; (c) soft gelatin capsules containing tartaric acid to give *p*H 3·8 in water, and 10 mg. of aneurine mononitrate each; (d) elixir, using aromatic elixir U.S.P. adjusted to *p*H 4 (aneurine mononitrate 5 mg./ml.); (e) sterile solution adjusted to *p*H 3·8, 5-ml. ampoules containing 50 mg./ml. Tablets proved to be the most stable preparation with negligible loss. The soft gelatin capsules in both cases lost about the same amount (6 to 8 per cent.) at room temperature, but at 40°C. the capsules containing tartaric acid lost considerably more (about 2½ times) than the others. The elixir was the least stable preparation, losing almost 15 per cent. at room temperature and nearly 42 per cent. at 40°C.; in addition, samples turned a darker yellow although generally maintaining clarity. The ampoules lost potency in manufacture to the extent of 7 per cent. at room temperature and 12 per cent. at 40°C.; the solutions had a yellow colour, which, in the case of the samples stored at 40°C., turned deeper as time progressed, showing a turbidity and a yellowish precipitate after 12 months at 40°C. R. E. S.

Iodine-Propylene Glycol Solutions. L. Gershenfeld and B. Witlin. (*J. Amer. pharm. Ass.*, 1950, **39**, 489.) Iodine was found to dissolve in propylene glycol to an extent of 1·36 per cent. at 50°C. immediately after trituration, and to an extent of 3·5 per cent. after 48 hours. On mixing with water clear solutions were obtained which on standing yielded crystals of free iodine. Solutions of iodine and a soluble iodide in aqueous propylene glycol had freezing-points below −24°C. if a minimum of 25 per cent. of propylene glycol was present; the bactericidal efficiencies of such solutions (with the exception of preparations containing 0·25 per cent. of iodide) were identical with the bactericidal efficiencies of tincture of iodine (U.S.P. XIII) and iodine solution (N.F. VIII). For a satisfactory aqueous preparation of free iodine possessing an effective bactericidal efficiency, non-stinging and non-irritating, and where it is desired that it possess a low freezing-point, the following formula was suggested: iodine (2 per cent.) and sodium iodide (2·4 per cent.) in distilled water containing 25 to 50 per cent. of propylene glycol. In toxicity studies in rabbits intravenous injections of 1·5 ml. of such a preparation (30 mg. of free iodine) per kg. of bodyweight did not prove fatal although 35 mg./kg. of bodyweight killed the animals; hæmatological studies on surviving animals did not reveal marked abnormal changes. R. E. S.

Vitamin A, Stability of Preparations of. H. Lindholm and P. Terp. (*Arch. Pharm. Chem.*, 1950, **57**, 480.) A preparation of vitamin A ("Adetamin") in oil shows a very satisfactory stability under favourable conditions, i.e., if the oil used has a low peroxide content and the preparation is kept in well-filled bottles. Under these conditions there is little advantage in keeping in an ice chest. A corresponding preparation made with vitamin A ester is much more stable, this difference becoming very marked under unfavourable conditions of storage. The official period of validity for adetamin drops (made with vitamin A alcohol) is 3 months. This could be increased considerably if the ester was used for the preparation. G. M.

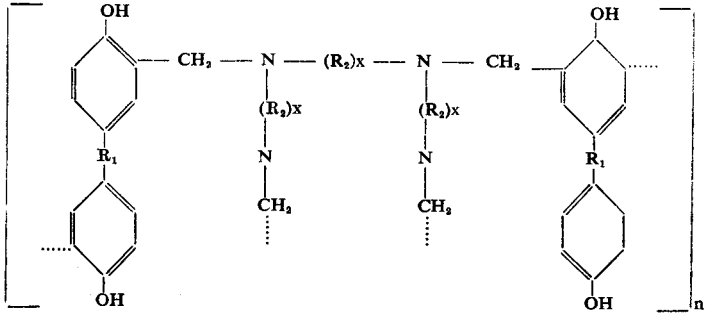
Vitamins A and D, in Capsules, Stability of. K. Nilou, H. Lindholm and P. Terp. (*Arch. Pharm. Chem.*, 1950, **57**, 332.) Cleanliness is an important factor in the preparation of vitamin capsules. The presence, in the filling apparatus, of a residue from a previous filling may result in complete destruction of the vitamin after 6 months storage, whereas when made

with clean apparatus the loss in strength was below 10 to 15 per cent. Two factors which were found to have no influence on the stability of the vitamin were the presence of air bubbles in the capsules, and bubbling carbon dioxide through the concentrate. Temperature of storage does not appear to be very significant. Capsules made with crude liver oil are better than those made from the refined oil, apparently owing to destruction of natural anti-oxidants in the refining; in fact, the natural anti-oxidants appear to have a stronger action than hydroquinone. Maximum stability is obtained by using vitamin A in the form of ester. Moisture, whether in the atmosphere or in the gelatin coating, has an unfavourable influence on stability. The stability of vitamin D is so much greater than that of vitamin A that it does not need to be taken into consideration. G. M.

NOTES AND FORMULÆ

Paramethadione (Paradione). (*New and Nonofficial Remedies; J. Amer. med. Ass.*, 1950, **143,** 970.) Paramethadione, 3 : 5-dimethyl-5-ethyloxazolidine-2 : 4-dione, is a clear, colourless liquid with an ester-like odour; specific gravity 1·1180 to 1·1240; refractive index 1·449. It is slightly soluble in water, the *p*H of a saturated solution being about 6·4, and freely soluble in ethanol, benzene, chloroform and ether. When treated with barium hydroxide, it yields a bulky white precipitate. Paramethadione is distinguished from trimethadione in the following way. Heat about 2 g. with 10 ml. of a 25 per cent. solution of sodium hydroxide on a water-bath for 30 minutes, and evaporate to about 2 ml., when a heavy precipitate separates; cool, acidify to Congo red with hydrochloric acid, extract with ether and remove the ether; the needles of the *N*-methylamide of α-hydroxy-α-methylbutyric acid thus obtained melt at 83° to 85°C. after recrystallisation from benzene; when the needles are heated with sodamide a strong odour of methylamine is produced and the vapours turn litmus paper blue. Paramethadione yields not more than 0·05 per cent. of ash. It contains 98 to 102 per cent. of paramethadione and is assayed by shaking with alcoholic sodium hydroxide and titrating the excess of alkali with hydrochloric acid, using cresol purple as indicator. Paramethadione is used for the same purposes as trimethadione; it is given in an initial daily dose of 0·9 g., adjusted thereafter to suit the needs of the patient. G. R. K.

Polyamine-methylene Resin (Resinat). (*New and Nonofficial Remedies; J. Amer. med. Ass.*, 1950, **143,** 1068.) Polyamine-methylene resin is a polyethylene polyamine methylene substituted resin of diphenylol dimethylmethane and formaldehyde in basic form. The structural formula may be represented as follows :—



It occurs as a light amber, granular, freely flowing powder with no appreciable odour, insoluble in water, alcohol, ether and dilute acids and alkalis; water extracts a small amount of coloured material. Polyamine-methylene resin loses not more than 15 per cent. of its weight when dried at 105°C. for 4 hours; ash, not more than 1·0 per cent.; arsenic limit, 0·8 p.p.m.; heavy metals limit, 10 p.p.m. When an aqueous extract is mixed with resorcinol solution and carefully poured onto sulphuric acid, no discolouration occurs at the interface (absence of formaldehyde); addition of the aqueous extract to a solution containing sodium carbonate monohydrate, mercuric chloride and sodium chloride gives not more than a slight white precipitate (absence of free ammonia). The acid-consuming capacity of the resin is estimated by shaking with an excess of 0·1N hydrochloric acid, filtering and titrating the unabsorbed acid; 1 g. should consume not less than 50 ml. of 0·1N hydrochloric acid. Polyamine-methylene resin contains 14 to 16 per cent. of nitrogen, determined by the Kjeldahl method. It is administered as capsules, powder or tablets in the treatment of hyperacidity and peptic ulcer, in a dose of 0·5 to 1 g. every 2 hours. G. R.K.

PHARMACOGNOSY

Alkaloids in Solanaceous plants, Distribution of. O. Ollsson. (*Farm. Revy*, 1950, **49**, 617.) Stems of *Atropa belladonna*, free from leaves, were divided into five portions of equal length (10 to 12 cm.) and analysed for alkaloidal content. This was found to range from 0.47 per cent. for the uppermost length to 0.13 per cent. for the lowest one, the change being uniform throughout the length. The leaves contained 0.33 per cent., and the green shoots (10 to 12 cm. long) with leaves 0.51 per cent. The distribution of alkaloid in air-dried drug was as follows.

Part of Plant	Alkaloids
Datura stramonium :—	per cent.
Leaf	0·38
Petioles	0·61
Leaf blades	0·34
Green shoots without leaves	0·60
Green shoots with leaves	0·35
Fruit	0·66
Fruit cortex	0·05
Seeds (half-ripe)	0·40
Tap root with branches	0·23
Root branches alone	0·36
Hyoscyamus niger :—	
Veins of leaves	0·15
Leaf blades with large veins removed	less than 0·005
Green shoots with leaves	0·13
Green shoots without leaves	0·11
Thinned-out plants, a few cm. high, June 21st	0·09

G. M.

Belladonna, Alkaloidal Content of Mature and Immature Leaves. W. R. Brewer and L. D. Hiner. (*J. Amer. pharm. Ass. Sci. Ed.*, 1950, **39**, 638.) At harvest time (i.e., early flowering time), belladonna plants were cut off 6 to 8 inches above the ground, leaving several large leaves on the remaining part of the stem. 3½ to 4 weeks later, the young leaves (less than 2 inches long and bright green in colour) were collected, and also the old leaves (5 inches or longer and less bright in colour). The young

leaves of *Atropa belladonna* contained a higher percentage of alkaloid (mean, 0·458 per cent.) than the old leaves from the same plants (mean, 0·282 per cent.). G. B.

Cocoa Shell, Anatomy of. W. Bondeson. (*Farm. Revy*, 1950, **49**, 693.) The author gives a new interpretation of the microscopical appearance of the schlerenchymatous layer of cocoa shell. Characteristic forms observed are: parenchyma gaps, that is, one- or few-celled surfaces of residual thin-walled cells; crack lines, regarded as initial stages of rhexigenic intercellular spaces; and gaps, representing rhexigenic intercellular spaces, which are in general irregularly band-shaped, parallel with one another, and run at right angles to the longitudinal axis of the seed. G. M.

Solanaceous Drugs. Time and Space in Culture. W. R. Brewer and L. D. Hiner. (*J. Amer. pharm. Ass. Sci. Ed.*, 1950, **39**, 639.) Ammonium sulphate, applied as a fertiliser to belladonna to increase the alkaloidal yield of the aerial parts of the plant, is best used at an early stage, the third week, when the plants are 6 to 8 inches high. The greatest alkaloidal yield is obtained by harvesting the aerial parts at the time of flowering. The highest yield per plant is obtained by growing in an 18 × 18 in. spacing, but the greatest yield of belladonna per acre is achieved in a 12 × 12 in. spacing. For first year hyoscyamus (biennial variety) the greatest yield per plant, and per acre, is obtained by using an 18 × 18 in. spacing. G. B.

***Strophanthus sarmentosus* and Some Related Species, Seeds of.** H. W. Youngken and V. H. Simonion. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 615.) The samples examined had the following macroscopical characters:—

	S. sarmentosus P.DC.	*S. Nicholsoni*	*S. Courmonti*	*S. gratus*
Colour	Reddish-brown to brownish - grey with a greenish or yellowish tinge.	White when viewed from the base; yellowish - brown when viewed from the apex.	Mostly brown but sometimes brownish-grey or greenish-grey.	Dull brown of uneven intensity.
Shape	Ovate-lanceolate.	Broadly ovate.	Lanceolate to broadly ovate.	More or less fusiform, irregularly flattened and irregularly twisted with sharp angles along the margin.
Size	10×4×2 mm. ...	15×5×3 mm.	9×3×1 to 1·5 mm.	15 to 19×2·5 to 3×1 to 1·5 mm.
Hairs	Thin-walled, unicellular of variable length, apices not very sharp-pointed.	Densely covered with long white to pale yellow glistening hairs.	Light yellow; not so densely covered as *S. Nicholsoni*.	Glabrous.
Raphe	—	—	Less marked than in *S. Kombé*.	Prominent.

The microscopical characters are described and illustrated. Calcium oxalate occurs in the cotyledons of *S. sarmentosus* in the form of monoclinic prisms in clusters or conglomerates, rarely as single crystals, and in rhombohedral crystals or aggregate clusters in the hypodermis. In *S. Courmonti* there are numerous cubical crystals of calcium oxalate (in single prisms, twin prisms, clusters and conglomerates) in the sub-epidermal region of the seed coat. Calcium oxalate is absent from the seed coat, endosperm and cotyledons of *S. gratus*. The following colours are obtained by treating

sections of the seeds with 80 per cent. sulphuric acid:—*S. sarmentosus*, pale rose-red, which develops first in the endosperm and then in the cotyledons; *S. Nicholsoni*, light yellow through yellowish, pale rose and red to violet; *S. Courmonti*, yellow, orange-red, and then after ten minutes, violet, and *S. gratus*, orange to pink. G. B.

PHARMACOLOGY AND THERAPEUTICS

Atropine and Allied Alkaloids, Excretion in Urine. M. Tønnesen. (*Acta Pharmacol. Toxicol.*, 1950, **6**, 147.) Investigations have been made into the excretion of atropine, hyoscyamine and scopolamine in the urine of rabbits and rats after oral, subcutaneous and intravenous administration. The average percentage excretions are tabulated below:—

	Rats			Rabbits		
	Atropine	Hyoscyamine	Scopolamine	Atropine	Hyoscyamine	Scopolamine
Oral	0·55	1·0	1·2	1·0	1·9	2·0
Subcutaneous ...	10·0	43·0	13·0	28·0	23·0	8·5
Intravenous ...	33·0	19·0	18·0	23·0	23·0	30·0

The average percentage excretions of the three alkaloids in the urine of human subjects after oral and subcutaneous administration are as follows:—

	Atropine	Hyoscyamine	Scopolamine
Oral	12·7	14·8	0·96
Subcutaneous	19·8	17·7	3·4

Hyoscyamine was shown not to be racemised to atropine but excreted as hyoscyamine in the urine. In rabbits, excretion took place within 5 hours of intravenous injection and in human subjects within 14 hours of oral administration. The alkaloids were not excreted in conjugated form.

S. L. W.

Chloroform-Adrenaline Ventricular Fibrillation; Protective Action of Parpanit, Diparcol and Other Drugs. G. C. Meirsman-Roobroeck. (*Arch. int. Pharmacod.*, 1950, **83**, 353.) Both parpanit and diparcol were found by the author to be very efficient in preventing chloroform-adrenaline ventricular fibrillation in dogs. This protection is thought to be due to a direct action on the myocardium and to paralysis of the vagal synapses. No curative effect was noted. Acetyl-β-methylcholine was also found to have a long-lasting protective effect, probably due to depression of excitability of the myocardium. Dibenamine, dihydroergotamine and other adrenergic blocking agents offered similar protection, though given in doses generally believed to be too small to produce their adrenergic blocking effect. The author concludes that the main causal factor in this type of ventricular fibrillation is a direct stimulation of the myocardium, that an adrenaline hypertension may sometimes be an important though not an essential factor, and that the role played by the vagus is not a preponderant

one. The protecting agents act by depressing the myocardium or by blocking the stimulating effect of adrenaline on the myocardium. The effect on the adrenaline hypertension and on the vagal function seems to be much less important. S. L. W.

Opium Alkaloids, Toxicity of. F G. Drommond, C. G. Johnson and C. F. Poe. (*Acta pharmacol., toxicol.*, 1950, **6**, 235.) The toxicity of papaverine, narcotine and codeine when injected intraperitoneally into white rats has been investigated, and their effect on the fermentative action of bacteria has been studied. Narcotine had LD50 750 to 825 mg./kg. and papaverine 62 to 64 mg./kg. Codeine was about as toxic as papaverine. Because of its low solubility, papaverine was first injected as a suspension, but this caused irregular results, especially with high doses. Both narcotine and papaverine caused a short period of depression followed by excitation, the depression lasted longer with narcotine. Sex had little effect on toxicity, but with narcotine the older rats seemed more susceptible. For the antibacterial tests, the alkaloids were dissolved in lactose-phenol red broth and incubated at 37°C. Narceine, narcotine, papaverine and codeine were about equally toxic for species of *Escherichia* and *Aerobacter*. Gas formation was prevented by narcotine only at concentrations above 1 in 15 and by codeine, which was the most toxic compound, at 1 in 60. At the lower concentrations narceine and narcotine, and sometimes papaverine, caused increased gas formation. Tests against *Eberthella typhi* and *Staphylococcus aureus* showed that neither organism was inhibited by codeine at 1 in 20, narcotine at 1 in 10 or papaverine at 1 in 30, after 15 minutes contact, but a saturated solution of narceine inhibited *Eberthella typhi* after 10 minutes. None of the compounds showed much activity when tested by the wet filter paper method against *Staphylococcus aureus*. A. D. O.

Phenylindanedione, Prothrombopenic Action of. L. B. Jaques, E. Gordon and E. Lepp. (*Canad. med. Ass. J.*, 1950, **62**, 465.) The authors investigated the effect of 2-phenylindanedione-1:3, given orally, on the prothrombin times of dogs and rabbits. The drug was found to possess properties similar to those of dicoumarol in its ability to lengthen the prothrombin time, cessation of the drug resulting in a return of prothrombin time to normal levels in from 24 to 30 hours. It is only a weak prothrombopenic agent compared with dicoumarol, having only about one-tenth the potency, and a single dose has only a slight effect; if, however, repeated doses at frequent intervals are administered, the prothrombin time can be increased to very high values. 1 mg./kg./8 hours, which compares closely with the clinical dose of 300 mg./24 hours for dicoumarol, increases the prothrombin time to approximately twice the normal value. While, as with dicoumarol, overdosage results in a hæmorrhagic condition, this is completely reversed on withdrawal of the drug and the resultant return of the prothrombin time to normal. Although the drug appears to be excreted by the kidneys, renal damage was only observed with extremely large overdosages of the drug in terms of its ability to maintain a prolonged prothrombin time. No gross toxic effects were observed with 8·3 mg./kg./8 hours administered for 48 days to dogs. S. L. W.

Radioactive Iodine in the Diagnosis of Hyper- and Hypothyroidism. W. F. Perry and J. P. Gemmell. (*Canad. med. Ass. J.*, 1950, **62**, 484.) This is a report of an investigation to decide which radioactive method for the determination of thyroid functioning is best suited for clinical use. Three groups of patients were studied, namely, euthyroid (persons whose tissues

receive the normal amount of thyroid hormone daily irrespective of the anatomical state of the thyroid gland), hyperthyroid and hypothyroid. The radioactive iodine was given orally in 50 to 100 ml. of water; in most cases the dose was 100 microcuries, but where thyroid uptake and urinary excretion only were considered 50 microcuries was sufficient, and if urine excretion only was to be measured 10 microcuries was adequate. It was found that the measurements combining the sharpest differentiation with the greatest simplicity were the determination of the 24-hour thyroid uptake of radioactive iodine and the estimation of the amount of the isotope excreted in the urine between 15 to 24 hours after administration. The concentration of radioactive protein-bound plasma iodine was found to be greater in hyperthyroid subjects at all times examined, while those with hypothyroidism had concentrations comparable to the euthyroid subjects. The procedures for estimating the radioactive protein-bound plasma iodine in plasma, the radioactivity of the urine, and the thyroid uptake of radioactive iodine are described.

S. L. W.

Thyroidal Activity, Measurement of. G. F. Somers. (*Analyst*, 1950, **75**, 537.) Chemical assays are suitable for gland extracts, because almost all the acid-insoluble iodine is in the form of L-thyroxine. The method of the British Pharmacopœia, 1948, based on acid-insoluble organic iodine, is preferable to that of the United States Pharmacopœia, 1947, based on total organic iodine. Chemical methods are not satisfactory for preparations containing DL-thyroxine, or iodinated protein. There is no very simple and precise biological method. There is great variation in response between individual animals, and the assays on animals do not give a true index of the activity in man. Methods which have been described depend upon:— rate of carbon dioxide evolution and oxygen uptake in guinea-pigs or mice, antagonism by anti-thyroid drugs in chicks or rats, increase in rate of amphibian metamorphosis, increase in resistance of mice to acetonitrile poisoning, loss of body-weight in guinea-pigs and increase in susceptibility of mice to anoxia. G. B

BACTERIOLOGY AND CLINICAL TESTS

Triglycollic Ether of Acetoxy-mercuri-phenol, Antibacterial Properties of. M. Welsch and M. Urbain. (*Arch. int. Pharmacod.*, 1950, **83**, 431.) The authors have made a comparative study of the bacteriostatic and bactericidal properties of this new antiseptic, to which they have given the name of 670 Labaz. Its bacteriostatic activity against *Staphylococcus aureus* was found to be of the same order as that of merthiolate and mercurochrome; it has a less marked bacteriostatic action against *Bacterium coli*, though its action is still evident even in dilutions of 1 in 20,000. The selectivity of the action of 670 Labaz is perhaps comparable with that of penicillin. It is also comparable with penicillin in that it exerts its bacteriostatic action irrespective of the richness or poorness of the bacterial growth. Its bactericidal activity, both against *Staph. aureus* and *Bact. coli* is greater than that of merthiolate or mercurochrome and it has a phenol coefficient of 36. Thick aqueous suspensions of a number of Gram-positive bacteria were found to be sterilised in 10 minutes by 670 Labaz 1 in 5000, and of Gram-negative bacteria by 1 in 1000. Bacterial suspensions contaminated with organic matter were sterilised in 3 to 4 hours by 670 Labaz 1 in 1000. The authors recommend the use of this antiseptic as a skin disinfectant and for the prophylactic treatment of wounds. S. L. W.