ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Acetyl Group, Detection of. C. J. de Wolff. (*Pharm. Weekbl.*, 1951, **86**, 273.) About 0·1 mg. is placed in a tube of 6 cm. length and 2·5 mm. diameter with 0·025 ml. of 50 per cent. sulphuric acid, and a small piece of purified asbestos is pushed down the tube to soak up the liquid. The upper end of the tube is drawn out in two places to form a lower capillary of 3 to 4 cm. length, and an upper capillary, cut off to 5 cm. length, separated from the first by a small bulb. The first capillary is drawn out to a hair-fine tube of about 5 cm., and the end of the upper one is sealed. The bottom of the tube is placed 5 cm. deep in a hole in a metal block at 150°C. for 10 minutes. After cooling, the top is opened and the tube again replaced in the block for 5 minutes, when a distillate collects in the bulb. The hair capillary is broken, and the contents of the bulb are blown out on to an object glass, made alkaline, and evaporated to dryness. The residue is dissolved in 0·001 ml. of 5 per cent. solution of lanthanum nitrate with sufficient 4N nitric acid to make the mixture clear. The drop of liquid is now held over ammonia until it becomes turbid, a drop of 0·02 N iodine is placed near the original drop, and the glass is warmed slightly. In presence of acetic acid a blue or brown-blue colour develops. A positive result is obtained with 20 μg. of diamorphine hydrochloride. G. M.

Alkaloids, Paper Chromatography of. J. B. Schute. (*Pharm. Weekbl.* 1951, **86**, 201.) Attempts to separate alkaloids, especially of the atropine series, by paper chromatography, on the assumption that the method depended on the distribution between water and another phase, led to no success, but satisfactory results were obtained by the use of water only, to which 5 per cent. of ammonia was added to prevent tailing of the spots. It is possible to use the tailed spots obtained with water alone, but there is no question of a constant R_F value in this case. Development of the alkaloid is done by allowing the paper to dry until there is no more smell of ammonia, and then exposing to iodine vapour. Different colours are given by different alkaloids. The colour generally disappears on removing the paper from the iodine vapour, but the spot may be made permanent by dipping the paper in Dragendorff's reagent. As some types of paper give a colour with iodine, it is advisable to give the paper a preliminary wash with ammonia. The kind of paper is of great importance; a good variety is Schleicher and Schull 1101. The chromatography was done from the bottom in tubes of 16 mm. diameter 1 ml. of solvent being placed at the bottom of the tube with a strip of paper of 14 cm. in length. The water content of the paper is important; the R_F is much lower if air-dry paper is used than with paper which has been saturated in the vapour phase; temperature, concentration and degree of soaking of the paper are comparatively unimportant. The method has been used for a mixture of scopolamine, atropine, apo-atropine and belladonnine; and of papaverine, thebaine, codeine, and morphine.

G. M.

Analysis, Inorganic, by Paper Ionophoresis. M. Lederer. (*Nature*, 1951, **167**, 864.) A strip of paper 1 cm. × 20 cm. was hung over a T-shaped glass rod so as to hang with its ends each in a limb of two U-tubes filled with electrolyte such as N hydrochloric acid, and the whole was covered with an invested gas jar. Carbon electrodes were placed into the other limbs and connected to a 70 to 150 volt D.C. supply. The solution to be analysed was placed at the apex of the paper strip, which was carefully moistened with electrolyte solution. After passing the current for 2 to 3 hours the paper was exposed to hydrogen sulphide or other suitable reagent. When the concentration of acid was varied it was found that 0·5 N enabled the separation of copper, cadmium, lead, bismuth and mercury to be made. The order of separation was the same as for a paper chromatogram with butanol and hydrochloric acid. Mixtures of cobalt and nickel were successfully separated by forming coloured complexes with compounds such as thiocyanates. A. D. O.

Cephæline in Emetine, Determination of. J. Schaafsma. (*Pharm. Weekbl.*, 1951, **86**, 331.) The Dutch official test for cephæline in emetine is unsatisfactory, the results being high and inconsistent, apparently owing to incomplete removal of the emetine. The following method is proposed: 0·2 mg. of emetine hydrochloride is dissolved in 6 ml. of water, treated with 2 ml. of 4N sodium hydroxide, and shaken out with 5 quantities, each of 10 ml., of ether. The aqueous layer is acidified with 3 ml. of 4N sulphuric acid, then made alkaline with 3 ml. of 10 per cent. ammonia, and the cephæline is shaken out into 4 quantities, each of 10 ml., of ether, the ethereal solutions being washed twice with 10 ml. of water. The ethereal solution is filtered, the filter being washed with 10 ml. of ether, evaporated to dryness, dried for 1 hour at 100°C., and weighed. It should not be more than 4 mg. G. M.

Colours, Artificial, Identification of. A. Fouassin. (*J. pharm. Belg.*, 1951, **6**, 3.) Colouring matter, extracted from foodstuffs, may be separated and identified by the following scheme. The colour, freed from all but traces of other substances, is shaken between light petroleum and 1 per cent. solution of ammonia. *I.* The light petroleum solution is evaporated, and the residue is dissolved in ether and shaken with 5 per cent. acetic acid. (*a*) The ether solution, containing fat-soluble colours, is chromatographed on a column of alumina, which holds back certain natural colours. The ether solution passing through is evaporated to dryness, and the residue is extracted with 5 per cent. sodium hydroxide solution, then with 1 per cent. hydrochloric acid, to extract certain colours. The residue is dissolved in light petroleum, chromatographed, and extracted by elution with light petroleum containing 5 per cent. of ether. (*b*) The acetic acid solution contains the basic colours and is passed through alumina, then made alkaline with sodium hydroxide, extracted with light petroleum, and again chromatographed. The chromatogram is separated by light petroleum containing an equal volume of ether, then with ether saturated with ammonia, with ether containing 5 per cent. of ammonia, and mixtures of ether and acetone. *II.* The ammoniacal solution is evaporated to dryness, the residue is dissolved in water and acidified with 5 per cent. acetic acid. This solution is shaken out with ether, the ether being washed with acidified water. (*a*) The ether solution is extracted with 1 per cent. ammonia and the ammoniacal solution

is chromatographed on alumina to separate alizarin. The filtrate is evaporated, taken up in 5 per cent. acetic acid and chromatographed again: eluted:—fluorescein, nitrophenols, oxy derivatives of triphenylmethane: not eluted:—halogenated derivatives of fluorescein. (*b*) The acetic acid solution is chromatographed on alumina: eluted:—amino derivatives of triphenylmethane, picric acid and a few sulphonated colours. These are separated by chromatography with 5 per cent. acetic acid, ether saturated with ammonia, and mixtures of ether and alcohol containing 5 per cent. of acetic acid or 1 per cent. of hydrochloric acid: not eluted:—most sulphonated colours of the azo, nitro, triphenylmethane, indigo, alizarin and indulin series; separated by elution with 1 per cent. hydrochloric acid, acetone with 1 per cent. of ammonia, acetone with 20 per cent. of 1 per cent. ammonia solution, acetone with 1 per cent. of hydrochloric acid, a mixture of acetone and water with 5 per cent. of acetic acid. Exact details of the position of the different colours in this scheme are not given. G. M.

Propylthiouracil in Tablets, Determination of. A. Berggren and W. Kirsten. (*Farm. Revy*, 1951, **50**, 245.) Errors in the determination of propylthiouracil due to the presence of magnesium stearate in tablets may be avoided by the following procedure. A portion of the tablet mixture, containing 0·1 g. of propylthiouracil, is boiled for 3 minutes with 50 ml. of acetone. After the addition of 2 drops of a 0·5 per cent. alcoholic solution of 1:2:5-dinitrophenol, the solution is neutralised (colourless) with 0·1 N nitric acid, 0·1 N sodium hydroxide is added to a faint yellow colour, followed by 15 drops of bromothymol blue solution and 20 ml. of 0·1 N silver nitrate. It is then titrated with 0·1 N sodium hydroxide to a permanent blue colour. If stearic acid is present in the tablet an extraction with light petroleum should precede the assay. G. M.

Sulphonamides, Titration of, with Sodium Nitrite. A. Ågren. (*Svensk farm. Tidskr.*, 1951, **55**, 229.) Diazotisation may be considered as a kind of redox process, and it has been shown that a change in potential occurs during the titration of an aromatic amine with sodium nitrite. It should therefore be possible to use a redox indicator changing colour between +0·80 and +0·95 volts. Many such indicators however are phenols or aromatic amines, which may enter into the reaction. A suitable indicator is diphenylbenzidine sulphonic acid, which may be prepared by the oxidation of diphenylamine sulphonic acid. A solution of the indicator may be prepared by mixing 0·5 ml. of 33 per cent. solution of diphenylamine sulphonic acid with 1 ml. of concentrated suphuric acid and adding gradually, with frequent shaking, 5 ml. of 0·01 M potassium dichromate. This solution must be shaken before use. For the titration, 0·5 g. of the sulphonamide is dissolved in 50 ml. of water and 50 ml. of 5 M hydrochloric acid and, after the addition of 10 drops of indicator solution, titrated with 0.1 M sodium nitrite until there is a violet colour which remains unchanged for 1 minute. Only sulphanilamide itself gives a colourless solution on diazotisation: a yellow colour is given by sulphadiazine, sulphamerazine, sulphapyridine and sulphonazol, increasing in that order. This makes it very difficult to determine the end point, which may however be observed satisfactorily by working in sodium light and increasing the amount of indicator to 50 drops. G. M.

GLYCOSIDES, FERMENTS AND CARBOHYDRATES

Sugars, Improved Spraying Reagents for, on Paper Chromatograms. J. L. Bryson and I. K. Mitchell. (*Nature*, 1951, **167**, 864.) Solutions of phenols (0·2 per cent.) in butanol, acidified immediately before use with an equal volume of 0·25 N hydrochloric acid have given good definition on chromatograms with only moderate attack on the paper. Acetic and phthalic acids proved to be too weak but good results were obtained by acidification with phosphoric acid. Upward development chromatograms, in *n*-butanol, ethanol, water (4 : 1 : 5) were prepared with rhamnose, xylose, arabinose, dextrose, galatose, mannose, lævulose, sorbose, sucrose, maltose, lactose and raffinose. These were sprayed with 0·2 per cent. ethanolic solutions of resorcinol, naphthoresorcinol, orcinol, α-naphthol and phoroglucinol, each reagent being acidfied with either an equal volume of 0·25 N hydrochloric acid or 0·1 volume of orthophosphoric acid (1·85 sp. gr.). The naphthoresorcinol-hydrochloric acid showed only lævulose, sorbose, sucrose and raffinose, but phosphoric acid revealed all the sugars listed above. It was thought that these enhanced effects might be due to the hygroscopic nature of the acid. The spot definition was good with phosphoric acid in ethanol and was not generally improved by using butanol. With α-naphthol the butanol reduced both the range of the reagent and the clarity of the spots. A reagent consisting of 2 N aniline (1 volume) and 2 N phosphoric acid (2 volume) in butanol also detected all 12 sugars. A. D. O.

Sugars, Paper Chromatography of. F. A. Isherwood and M. A. Jermyn. (*Biochem. J.*, 1951, **48**, 515.) A wide range of sugars has been examined by paper chromatography using the apparatus and procedure previously described (*Biochem. J.*, 1949, **44**, 402); the solvent used was the water-poor phase from a two phase mixture of ethyl acetate (2 vol.), pyridine (1 vol.), and water (2 vol.) freshly prepared for each run. An empirical relationship was discovered between the R_F value and the molar fraction of water (N) in the solvent. The graph of log ($[1/R_F]$-1) against − log N was a straight line for each sugar. The relationship held over a wide range of solvent mixtures, the only exceptions being those containing phenols as the organic component. The relationship was thought to be due to the strong association of the hydroxyl groups of the sugars with the water molecules in mixed solvents containing water; the sugars had the same R_F values in all solvents except phenols. If the sugars were arranged as a homomorphous series on the basis of an assumed preferential formation of a pyranose ring in solution (furanose when pyranose is impossible) it was found that members of each homomorphous series behaved similarly. The sequence of R_F values for each group of sugars e.g. aldohexose, aldomethylose, depended only on the configuration of the hydroxyl group of the ring. A detailed analysis was made of the contribution of each hydroxyl group to the observed R_F value in the case of the aldohexoses, aldopentoses and ketohexoses. It was found that if a substitute ($-CH_2OH$) was attached to carbon atom 5 of the pyranose ring then the influence of a hydroxyl group on any particular carbon atom largely depended upon whether or not the hydroxyl was on the same side of the ring as the substitute; the effect on the R_F value was different for each carbon atom. In the absence of a substitute (aldopentoses) or if the substitute was attached to carbon atom 1 of the pyranose ring (ketohexoses), it was found that the interaction between the hydroxyl groups on neighbouring carbon atoms governed the R_F value, a *cis* disposition of hydroxyls giving

a higher R_F value than a *trans* disposition. Sugars with a furanose ring had a higher R_F value than those with a pyranose ring. The R_F values of the simple pentoses and hexoses were roughly inversely proportional to their melting points. R. E. S.

GUMS AND RESINS

Arabic Acid Solutions, Effect of Cations on the Viscosity of. R. H. Schleif, T. Higuchi and L. W. Busse. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 221.) When a graph is plotted for gum arabic concentration against the specific viscosity a typical curve is obtained which shows a minimum at about 4 per cent. This curve was therefore used to study the effects of concentration and various ions on the viscosity of solutions of various salts of arabic acid. The acid itself showed the typical curve, but the viscosity was generally lower. The addition of sodium chloride or calcium chloride reduced the viscosity and altered the shape of the curve, and this was also the case with potassium, calcium, magnesium, and zinc arabates. The viscosity of potassium arabate was about equal to that of the sodium salt and was much higher than the calcium, magnesium, and zinc arabates. Ferric arabate showed a high viscosity at concentrations from 7 to 10 per cent. With the aluminium salt, concentration had only a slight effect on viscosity and neither the ferric nor the aluminium arabate was much affected by the addition of sodium chloride or calcium chloride. Butylamine arabate and trimethylbenzyl arabates had properties similar to those of the potassium and sodium salts. The hydro-arabates of ethylenediamine, diethylenetriamine and triethylenetetramine were of low viscosity which increased only slightly with concentration. The addition of sodium chloride or calcium chloride showed only a slight lowering of viscosity in the case of these three substances. A. D. O.

ORGANIC CHEMISTRY

Glycerol, Purification of, by Ion Exchange. D. M. Stromquist and A. C. Reents. (*Indust. Engng. Chem.*, 1951, **43**, 1065.) Attempts were made to produce chemically pure glycerol by the use of the ion exchange process. Several requirements were necessary for the satisfactory treatment of crude glycerol solutions by ion exchange units namely:—the solution must be dilute enough and low enough in viscosity so that there is no excessive pressure drop across the exchanger beds—i.e. below 35 per cent. solids; it must be relatively free from fats and oils; turbidity must be kept to a minimum as suspended solids also hinder and retard the exchange process as well as the incidental colour removal; the temperature of the solution to be treated must be below 95°F., preferably between 70° and 80°F. As a typical example of varying arrangements of ion exchange resins, the following system was used for the purification of saponification crude glycerol: (1) Illco C-231 Primary cation exchanger, (2) Illco A-124 Primary anion exchanger, (3) Illco CA Color adsorbent, (4) Illco C-251 Secondary cation exchanger, (5) Illco A-244 Secondary anion exchanger, (6) Illco mixed bed Mixed cation and anion exchange resins. Glycerol solutions thus purified complied with the U.S.P. specification; a 95 per cent. glycerol was produced by vacuum evaporation. R. E. S.

Mercaptoimidazoles, Colour Reaction for. R. A. McAllister. (*Nature*, 1951, **167**, 863.) The three compounds used in this investigation were 2-mercaptoimidazole and its 4-methyl and 4-aminomethyl derivatives

(hydrochlorides). They were dissolved in distilled water and the solutions were adjusted to *p*H 8 with 0·1 N sodium hydroxide. These solutions were suitably diluted and an aliquot part was mixed with 2 ml. of borate buffer (*p*H 8·0) and 0·1 ml. of a 0·4 per cent. solution of 2:6-dichloroquinone-chloroimide in aldehyde-free absolute ethanol; a deep red or orange colour, soluble in chloroform, was rapidly formed. The sensitivity of the colour reaction in each case was about 10 μg. and the first two compounds named gave the most stable colours. An orange colour was given by the 4-amino-methyl compound and this tended to be unstable. Imidazole-4-5-dicarboxylic acid gave no colour. A. D. O.

Methanol-Water Solutions, Physical Properties of. C. Carr and J. A. Riddick. (*Indust. Engng. Chem.*, 1951, **43**, 692.) Many of the data on methanol and water and the methanol-water system in the literature are given at 60°F., a temperature which often is not convenient in use. This paper presents data, in tabular form, at more commonly used temperatures for density, specific gravity, shrinkage and viscosity. The density-composition and specific gravity-composition relationships were determined at about 10 per cent. composition intervals for methanol and water at 25°, 30° and 40°C. The shrinkage and viscosity-composition relationships were also determined at 25°C. The results were plotted on large-scale graph paper and the relationships tabulated for 1 per cent. intervals in composition from 0 to 100 per cent. S. L. W.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Adrenocorticotropic Hormone from Whale Pituitary Glands. F. Benz, W. Schuler and A. Wettstein. (*Nature, Lond.*, 1951, **167**, 691.) Applying Lyon's acid acetone extraction procedure to the separated anterior lobes, 4 g. of the so-called "crude prolactin" was obtained from 1 kg. of mixed glands from blue, fin and humpback whales. Preliminary purification was effected by reprecipitation from acid aqueous acetone solution, Chamberland filtration of an aqueous solution of the precipitate, and lyophilising the filtrate; the product was 0·9 g. of a powder having adrenocorticotropic activity nearly equal to that of the Armour *La-1-A* standard. By pepsin digestion of this substance and dialysis of the product in "Cellophane" tubes, a dialysate was obtained which had nearly the same activity as the starting material, while the material inside the tubes showed little loss of activity, showing that hydrolysis and dialysis were far from complete. H. T. B.

Anti-Pernicious Anæmia Factor, Crystalline. E. Lester Smith. (*Brit. med. J.*, 1949, **2**, 1367.) The work leading to the isolation of vitamin B_{12} is briefly reviewed. The fact that the isolation involved dependence upon physical properties such as solubility in salt solutions and solvent mixtures, adsorption on charcoal, alumina and silica, and partition between water and solvents is stressed, because vitamin B_{12} is devoid of characteristic chemical properties. The isolation of this vitamin results in a standardisation of dosage of anti-pernicious anæmia factors in preparations from liver since the microbiological assay method, using crystalline vitamin B_{12} as a standard, permits standardisation in terms of vitamin B_{12} activity. The further work on related factors, and the chemical work in the attempt to elucidate the structure of vitamin B_{12} are briefly mentioned. A. H. B.

Benzylpenicillin, Stability of Aqueous Solutions of. K. Pedersen-Bjergaard and M. Tønnesen. (*Svensk farm. Tidskr.*, 1951, **55**, 239.) It is known that the stability of solutions of benzylpenicillin is increased by the addition of a buffer at *p*H 6·5. Using phosphate buffer, however, it was found that there is an optimum concentration of phosphate at which the stability is a maximum, higher values resulting in a less stable solution. The optimum point varies according to the concentration of the benzylpenicillin: for a solution containing 5000 I.U./ml., the phosphate should be M/120; for 50,000 I.U. per ml., M/15; and for 100,000 I.U./ml., M/7·5. At a concentration of phosphate equal to M/1·88, the stability is no greater than in water.

G. M.

Nor-adrenaline in Calves' Suprarenals, High Concentration of. P. Holton. (*Nature*, 1951, **167**, 858.) Whole suprarenal glands were removed from decerebrate calves, 1 to 7 days old, and immediately extracted with 0·1 N hydrochloric acid. The extract was assayed against adrenaline on the rat's uterus and against both adrenaline and nor-adrenaline either on the rat's colon or on the rabbit's intestine. In 7 such extracts the nor-adrenaline content varied from 62 to 83 per cent. Glands more than 7 days old from slaughter-house animals had contents of from 48 to 74 per cent. (mean 66 per cent.); extracts from bullock's gland contained 16 to 41 per cent. (mean 31 per cent.). These differences were due to the greater absolute amount of nor-adrenaline, the amount of adrenaline being the same for all the animals. Calves' suprarenals from the slaughter-house contained more adrenaline and even greater amounts of nor-adrenaline than those taken from experimental animals.

A. D. O.

Vitamin A, Synthesis of. N. L. Wendler, H. L. Slates, N. R. Trenner and M. Tishler. (*J. Amer. chem. Soc.*, 1951, **73**, 719.) The synthesis of β-ionylideneacetaldehyde was accomplished by the following route:—a Reformatsky reaction employing β-ionone and ethyl bromoacetate to produce ethyl β-ionylideneacetate; the reduction of this produce with lithium aluminium hydride to yield β-ionylidene ethyl alcohol, followed by oxidation of this alcohol with manganese dioxide in petroleum ether to produce a mixture of the two stereoisomeric β-ionylideneacetaldehydes. Chromatographic separation gave equal amounts of pure *trans*- and *cis*- isomers, the spectra of which were measured as were those of the crystalline semicarbazones of the two isomers. Both isomeric aldehydes were oxidised by alkaline silver oxide to yield the same crystalline β-ionylideneacetic acid which was identical with the product of saponification of ethyl β-ionylidene acetate. The *trans*-aldehyde was oxidised rapidly and in fair yield, whereas the oxidation of the *cis*-aldehyde proceeded at a slower rate and gave a lower yield of acid. The two β-ionylideneacetaldehydes were independently submitted to the following series of reactions to give the same vitamin A acid, all apparent isomeric differences appearing to have vanished in the course of these reactions. The route consisted of condensation of the aldehyde with acetone in the presence of aluminium *t*-butylate to produce the C_{18}-ketone. The C_{18}-ketones obtained from the isomeric aldehydes were slightly different, and were converted independently to the C_{20}-hydroxy ester by the Reformatsky reaction using ethyl bromoacetate. Dehydration with iodine in high-boiling light petroleum gave crude vitamin A ester which was given a preliminary purification on alumina and then saponified to vitamin A acid. Reduction

of the crystalline vitamin A acid with lithium aluminium hydride yielded vitamin A. A. H. B.

BIOCHEMICAL ANALYSIS

Adrenaline and Nor-adrenaline in Biological Fluids and Tissue Extracts, Quantitative Separation. T. B. B. Crawford and A. S. Outschoorn. (*Brit. J. Pharmacol.*, 1951, **6**, 8.) The method described involves the separation of the amines by paper chromatography, elution from the developed chromatogram, and assay of the separated amines in the eluates by the rats' blood-pressure technique. The procedure gives consistently better and more dependable results than the method of parallel quantitative assay on the isolated uterus and colon of the rat (Gaddum and Lembeck, *Brit. J. Pharmacol.*, 1949, **4**, 401). Recovery experiments from pure solution and from plasma showed that the amines can be estimated in quantities as low as 0·25 μg./ml., with an accuracy of 75 to 100 per cent., this level of accuracy still holding when one of the amines is in twentyfold excess in a mixture. The combination of sensitivity, accuracy and objectiveness makes the procedure capable of a breadth of application not found in previously published methods. S. L. W.

Aureomycin and Terramycin, Ultraviolet Determination of. D. J. Hiscox. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 251.) The ultraviolet absorption curves of aureomycin and terramycin from 220 to 400 mμ showed multiple maxima and minima which were modified under various conditions. The following methods modify the curves suitably for the compounds to be determined. *Aureomycin :* 5 ml. of an aqueous solution (100 to 500 μg.) is heated in boiling water for 8 minutes with 5 ml. of 2 N sulphuric acid. The solution is then cooled, made up to 25 ml. and the absorption is measured at 274 and 350 mμ. The difference in absorption is proportional to the amount of aureomycin present. *Terramycin :* 3 ml. of a solution containing 25 to 250 μg. is refluxed for 30 minutes with 3 ml. of N sulphuric acid. When cool the solution is made up to 25 ml. and the absorption is determined at 249 and 312 mμ. The amount of terramycin is proportional to the difference in the absorption. Aureomycin capsules, troches and ointments were satisfactorily determined, the percentage of recoveries ranging from 100 to 115 per cent. which was equivalent to the accuracy obtainable by the biological method. The results obtained in the determination of terramycin should be in similar agreement. A. D. O.

Sodium Gentisate in Plasma and Urine, Estimation of. B. W. Meade and M. J. H. Smith. (*J. clin. Path.*, 1951, **4**, 226.) 2 ml. of plasma or 2 ml. of urine (suitably diluted to contain up to 12 mg./100 ml. of gentisic acid) is acidified with 0·5 ml. of 6N hydrochloric acid and 10 ml. of ethyl acetate is added. After shaking for 3 minutes and centrifuging for 5 minutes, 5 ml. of the ethyl acetate is removed and mixed with 5 ml. of 1 per cent. sodium bicarbonate solution. The mixture is shaken and centrifuged again for 5 minutes and then 4 ml. of the bicarbonate solution is removed, mixed with 1 ml. of Folin-Ciocalteu reagent (diluted 1 to 3 with distilled water) and 1 ml. of 1·5 N sodium hydroxide and set aside for 5 minutes. The absorption density is then measured against distilled water in a photo-electric absorptiometer in a 1 cm. cell at 660 mμ (Ilford spectrum red filter No. 608). In two cases the percentage recovery of sodium gentisate was 90·4 per cent. and 89·3

per cent. In a healthy male it was observed that the maximum plasma concentration of sodium gentisate was reached after 2 hours and that 80 per cent. of the dose taken was excreted in 8 hours. Estimations made on samples of plasma and urine from patients not receiving treatment with gentisate or salicylate gave neglible blank values. A. D. O.

Terramycin, Chemical Methods of Assay and Identification. F. Monastero, J. A. Means, T. C. Grenfell and F. Hedger. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 241.) In the first method, use is made of the orange-brown colour formed by the action of ferric chloride on terramycin. 1·0 to 2·0 ml. of a solution containing 0·5 mg. of terramycin per ml. is diluted to 10·0 ml. with 0·01 N hydrochloric acid. 10 ml. of 0·05 per cent. ferric chloride solution is added and the mixture is set aside for ten minutes. The absorption is then compared with a reagent blank in a photoelectric colorimeter fitted with a 490 mμ filter and set at 100 per cent. transmission, and is calculated by reference to a previously constructed calibration curve. The colour is stable for 2 hours. Results have been in good agreement with the microbiological method and are reproducible to within ±2 per cent. Samples which have undergone decomposition give an olive green colour 10 minutes after mixing the reagents and cannot be estimated by this method. In the second method the differential absorption of terramycin measured at 353 mμ is used, 2·0 ml. of a solution containing 0·5 mg./ml. in 0·01 N hydrochloric acid is diluted to 5 ml. with water, mixed with 0·5 ml. of 0·4 N sodium hydroxide and immersed in boiling water for 5 minutes. The solution is then cooled in ice water for 2 minutes and diluted accurately to 20 ml. 10 ml. is diluted to 25 ml. with 0·17 N hydrochloric acid and compared with 10 ml. of the untreated solution. The content of terramycin is calculated from a previously constructed calibration curve. A third method consists in heating the alkaline solution obtained in the second method for 5 to 10 minutes and then comparing it colorimetrically at 440mμ against a water blank. The two last methods give results in good agreement with one another and with those obtained microbiologically. Another possible reaction as a basis for assay is diazotisation and coupling with sulphanilic acid and measuring the colour produced at 490 mμ. When terramycin is treated with concentrated sulphuric acid a bright red colour results. This reaction is not given by other common antibiotics. The $[\alpha]_D^{25°C.}$ for terramycin in 0·1 N hydrochloric acid is −196°(c=0·5 per cent.) and in methanol it is +26°. The difference in these two figures is specific for terramycin and the former figure may be used as an estimation of purity. A. D. O.

CHEMOTHERAPY

Curarising Agents Related to *d*-O.O-Dimethyltubocurarine. E. P. Taylor and H. O. J. Collier. (*Nature, Lond.*, 1951, **167**, 692.) Since laudanosine closely resembles one half of the molecule of *d*-O.O-dimethyltubocurarine, a number of polymethylenebisquaternary salts of laudanosine were examined. They were prepared either by refluxing excess of the alkaloid with a polymethylene dihalide in benzene solution or by refluxing tetrahydropapaverine with a polymethylene dihalide in benzene solution and treating the resulting bis tertiary amine with a methyl halide or sulphate. The compound decamethylene -αω-bis[1(3′:4′-dimethoxybenzyl)-6:7-dimethoxy-1:2:3:4-tetrahydro*iso*quinolinium methiodide] compound 20)

was found to be considerably more active than *d*-tubocurarine in the cat although somewhat less active than *d*-O.O-dimethyltubocurarine in curarising the tibialis muscle. It shows affinities with decamethonium salts and contrasts with curare derivatives in having a relatively low paralysing activity in the rat. However, its relationship to curare-like paralysants is shown by the fact that its action is antagonised by neostigmine. The duration of its action is of the same order as that of *d*-tubocurarine chloride. Work is proceeding on the preparation of the compound from optically active forms of laudanosine and of tetrahydropapaverine. H. T. B.

PHARMACY

GALENICAL PHARMACY

Galenical Preparations, Stability of: Oxygen Content of Water. S. A. Schou and A. Gredsted. (*Dansk Tidsskr. Farm.*, 1951, **25**, 164.) The oxygen content of water used for making solutions of oxygen-sensitive galenical preparations is important. The oxygen content of samples of distilled water, treated in various ways, was determined, with the following results. 1. Water, saturated with air at 20°C., 6·35 ml./l.: water collected directly from the still, at 20°C., 1·12 to 2·34 ml./l. (1/6 to 1/3 saturated): water, boiled and rapidly cooled to 20°C. in an open vessel, 4·0 ml./l (2/3 saturated); water, sterilised in an open autoclave at 120°C. and cooled in a flask plugged with cotton wool, 2·46 to 3·58 ml./l. (1/3 to 1/2 saturated): water, as used in the Danish Pharmacopœia for injections of ascorbic acid and ergometrine (freed from oxygen by treatment with acid and bicarbonate) 0·45 ml./l. (less than 1/10 saturated). G. M.

Galenical Preparations, Stability of, on Storage. S. A. Schou. (*Dansk Tidsskr. Farm.*, 1951, **25**, 153.) General specifications regarding the stability of galenical preparations, i.e., the permissible maximum period of storage, have been inserted in the Danish Pharmacopœia. These are often determined from experiments in which the decomposition is accelerated by storage at a high temperature. In such cases it is necessary to determine the temperature co-efficient of the reaction with some accuracy, and not to assume a general mean value of, say, an increase of 2 to 3 times for 10°C. rise of temperature. The significance of this is shown by calculating the storage periods, at 20°C., equivalent to sterilisation for 20 minutes at 120°C. Using a temperature coefficient of 2 for a rise of 10°C., the storage period is 14 days; if the coefficient is 3, the corresponding period is 800 days; and for a coefficient of 4, 42 years. G. M.

NOTES AND FORMULÆ

Electromigration in a Cation Exchange Resin. K. S. Speigler and C. D. Coryell. (*Science*, 1951, **113**, 546.) Electromigration in synthetic ion exchangers was investigated, the movement of ions in the column being followed by radiotracer technique. The experiments proved that the absorbed cations carry the current, and thus, for electrical conductivity, the wet resin acted similarly to solutions of electrolytes. An electrolytic cell with perforated electrodes was filled with a resin (in the sodium form). A thin layer of active resin containing radiosodium was embedded in the resin column 3 cm. from the anode. The activity at the beginning of the experi-

ment and after the passage of a constant current for a given time was measured by inserting the cell in a slide propelled by a screw under a Geiger-Mueller tube. The radiation emitted from each part of the tube was recorded. Within a period equal to the length of the experiment only slight spreading of radioactive material occurs unless an electric potential is applied. Both the current and the resin grain size were varied in the experiments. The following electrode reactions were shown to occur:

$$\text{Anode: } 4R' + 2H_2O = 4HR + O_2 + 4e' \quad (1)$$

$$\text{Cathode: } 4e' + 4NaR + 4H_2O = 4Na^+ + 4R' + 4OH' + 2H_2 \quad (2)$$

where R = resin radical.

As electrolysis proceeds, the hydrogen ions formed at the anode penetrate the whole sodium layer and slow down its movement. They eventually reach the cathode and then the following reaction competes with reaction (2):—

$$4e' + 4HR = 4R' + 2H_2.$$

At the beginning of the electrolysis the movement of the activity maximum is proportional to the current. The spread was found to increase with the particle size of the resin. Apart from its possible application as a separation method, resin electrolysis may find use as a method for regenerating resins without using regenerating solution, e.g., the conversion of the sodium form to the hydrogen form of the resin above. A. H. B.

PHARMACOLOGY AND THERAPEUTICS

Acute Toxicity Testing of Drugs. M. G. Allmark. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 27.) Toxicity tests on phenobarbitone sodium, pentabarbitone sodium, diphenhydramine (benadryl) and tripelennamine (pyribenzamine) were made by a prescribed procedure in 8 laboratories. For each drug, freshly prepared solutions in distilled water were injected intraperitoneally into groups of 15 healthy male mice (17 to 22 g.). Total deaths were recorded after 24 hours for benadryl and pyribenzamine, and 48 hours for the barbiturates. Doses were chosen to cause mortality rates of 20 to 80 per cent. It was found that LD50 values varied significantly between the laboratories. It was possible to determine the relative toxicities of similar pairs of drugs provided they were tested simultaneously, this procedure being more reliable than comparison of LD50 values obtained at different times or in different laboratories. G. B.

Banthine, in the Treatment of Peptic Ulcer. J. S. Berk. (*Amer. J. med., Sci.*, 1951, **221**, 567.) Banthine is β-diethylaminoethyl xanthine-9-carboxylate methobromide, a quaternary ammonium salt with an anticholinergic action. In the parasympathetic system it blocks the transmission at the ganglionic synapse and exerts an atropine-like action at the postganglionic nerve endings. In the sympathetic system it has a blocking action only at the ganglionic synapse and larger doses are required. In animals and in man, it inhibits gastrointestinal motility and reduces gastric secretion. In man, the gastric inhibition is more pronounced and lasts longer than that produced by atropine and this is probably so with the effect on gastric secretion. Banthine exerts its action within 1 minute after intravenous injection and within 20 to 30 minutes after oral dosage, and may persist for as long as 6 or 8 hours after an oral dose of 2·0 mg./kg. of body weight. The most common side effects are dryness of the mouth and blurring of vision and occasionally difficulty in micturition. No evidence of chronic toxicity has

been observed except perhaps some stimulation of the central nervous system in 6 patients with emotional instability. The recommended dosage for the treatment of peptic ulcer is up to 100 mg. every 6 hours day and night, and half this dose as a prophylactic measure after the ulcer has apparently healed.

A. D. O.

Chloramphenicol and Aureomycin, Side-Effects of. T. Tomaszewski. (*Brit. med. J.*, 1951 **1**, 388.) A survey of the side-effects encountered in 126 patients suffering from various infective conditions treated with these two antibiotics, given orally in capsules of 250 mg., has been made. Usually 2 capsules were administered every 6 hours. 70 patients (30 males and 40 females) received chloramphenicol, and 56 (32 males and 24 females) received aureomycin. The total amount of chloramphenicol given to any one patient varied from a few g. to 96 g.; the average dose was 32 g. The highest total amount of aureomycin given was 68 g., with an average dose of 28 g. The most striking changes were found in the oral cavity. Scrapings of the tongue showed a rapid disappearance of the normal bacterial flora and the establishment of a fungous flora, usually composed of *C. Albicans*, with the danger of a secondary mycotic invasion. The changes in the tongue were usually those of an atrophic glossitis; less often, a hypertrophic glossitis occurred with brown discoloration of the tongue. The side-effects are more marked in women than in men and develop more rapidly in cases previously treated with penicillin and streptomycin. The author stresses the similarity of the oral changes produced to those found in vitamin B deficiency, and reference is made to the prophylactic and therapeutic effects of treatment with vitamin B complex. S. L. W.

Chloramphenicol in Whooping-Cough. H. C. A. Lassen and L. C. Grandjean. (*Lancet*, 1950, **260**, 763.) Chloramphenicol was given for 3 to 5 days to 100 patients, most of whom were in the first 2 or 3 weeks of the disease. Of the 80 cases with positive cultures before treatment 73 became negative within 9 days of chloramphenicol being started. The frequency of the paroxysms fell sharply and the general condition rapidly improved. In 93 cases the chloramphenicol was administered rectally in suppositories, the 7 older children and adults took it in capsules by mouth. The rectal dosage was as follows: up to 6 months, 0·5 g. plus 0·25 g. 4 times on the first day and 5 times on the next 4 days; from ½ to 1 year, 0·75 g., plus 0·5 g. 4 times on the first day and 5 times on the next 3 days; from 1 to 6 years, 1 g., plus 0·5 g. 4 times on the first day and 5 times on the next 4 days. From 6 to 12 the dosage, by mouth, was 1·5 g., plus 0·75 g. 4 times on the first day and 5 times on the next 5 days; and over 12, 3 g., plus 1·5 g. 4 times on the first day and 5 times on the next 5 days. Seven children had perianal dermatitis which disappeared one or two days after withdrawal of chloramphenicol and 4 had slight diarrhœa for a few days. Chloramphenicol seems to be the most effective remedy so far tried in whooping-cough and should be used in every case in infancy. S. L. W.

Cinchoninic Acid Derivatives, Antipyretic Activity of. T. H. Maren. (*J. Pharmacol.*, 1951, **101**, 313.) In clinical trials of 3-hydroxy-2-phenylcinchoninic acid in acute rheumatic fever there was observed a rapid diminution of fever, malaise and polyarthritis. The present study was undertaken in order to find if derivatives of cinchoninic acid, particularly those with a 3-OH group, have antipyretic activity in the experimental animal. In preliminary work 3-hydroxy-2-phenylcinchoninic acid (HPC) was found to be

a potent antipyretic in the rabbit, dog and cat. 7 derivatives of cinchoninic acid (those with a 3-OH or 2-Ph substituent) were found to have antipyretic activity in the yeast fevered rat. Of these, the most active was 3-hydroxy-2-phenyl-quinoline-4:8-dicarboxylic acid. Several compounds, including HPC, were considerably more active than salicylic acid or cinchophen. S. L. W.

Digitalis: Experiences with the Guinea-pig Assay. E. Jacobsen and V. Larsen. (*Acta Pharmacol. Toxicol.*, 1951, **7**, 35.) This is an appraisal of the efficiency of the Knaffl-Lenz technique for bio-assay and standardisation of digitalis preparations based on the results obtained by the authors over a period of 15 years, the method having been employed on 807 guinea-pigs in 107 groups. According to their observations the lethal dose of digitalis is not proportional to body-weight, but to body-weight $^{0.686}$. The lethal dose decreases with increasing infusion time, i.e., the more of the drug that is infused per minute the higher the lethal dose, the reason being, presumably, that it takes some time before the glycosides are fixed in the tissues. The average infusion timed use in these experiments was 29 minutes. The estimated standard deviation of a group of 7 to 8 animals tested with the same is found to be $\pm$ 9·5 per cent. The lethal dose of a digitalis preparation is independent of the concentration of the glycosides in the injected solution. The percentage standard deviation within a group of animals is found to be independent of the amount of liquid injected. The standard deviation calculated from the whole of the authors' material was found to be $\pm$14 per cent. S. L. W.

3-Hydroxy-2-Phenylcinchoninic Acid (H.P.C.) in Collagen Diseases. J. B. Rennie, J. A. Milne and J. Sommerville. (*Brit. med. J.*, 1951, **1**, 383.) This clinical trial on a small series of cases was prompted by the discovery that when the pituitary was intact H.P.C., like A.C.T.H., reduced the ascorbic acid content of the rat adrenal. The cases treated were 4 patients with acute rheumatic fever, 2 with polyarteritis nodosa, 3 with scleroderma, and 3 with lupus erythematosus. The dosage used was 20 mg./kg. of bodyweight by mouth daily, increased in some cases to 40 mg./kg. In 7 of the 12 cases administration was continued for 1 week, in the rest for 2 or 3 weeks. The drug was administered in coated tablets because of its bitter flavour The fever and acute arthritis were speedily relieved in rheumatic fever. The results in polyarteritis nodosa were equivocal. The most striking effects were obtained in scleroderma; improvement occurred in all 3 cases. The results have so far been maintained in 1 case, but were only temporary in 2. Very slight and inconsistent improvement followed administration in chronic lupus erythematosus. Toxic effects were infrequent and were less severe than those which may follow the use of sodium salicylate; they consisted in slight nausea, diarrhœa, and, more rarely, vomiting. S. L. W.

Insulin, Clinical Comparison of Modifications of. J. L. Izzo and S. L. Crump. (*J. clin. Invest.*, 1950, **29**, 1514.) A clinical comparison was made of the effects of various modifications of insulin on 19 women diabetics selected because of variations in insulin requirements, age and duration of disease. The modifications used were a 2:1 mixture of unmodified insulin and standard protamine zinc insulin, two specially modified forms of protamine zinc insulin described respectively as N.P.C-40 and N.P.H-50, globin insulin with zinc, and standard protamine zinc insulin. Blood sugar determinations on each patient were made 4 times daily. 24-hour urines were collected in 4 periods and the sugar content determined. The

results were examined statistically to obtain figures for inter- and intra-daily variations of blood sugar and of urinary sugar. The patients fell broadly into two groups on the basis of variability in response; the stable group were relatively insensitive to insulin while the unstable were relatively sensitive, but individuals varied in sensitivity from time to time. The different insulins showed no differential ability to control the variability of the response although the pattern of the variability in the unstable group varied with the kind of insulin. The 3 modifications of standard protamine zinc insulin produced no conspicuously high or low responses. Globin insulin with zinc gave consistently high points in the morning and low points in the afternoon and evening, while standard protamine zinc insulin produced consistently low points in the morning and high points in the afternoon or evening.

H. T. B.

Khellin in the Treatment of Angina Pectoris. C. A. Armbrust, Jr., and S. A. Levine. (*Amer. J. med. Sci.*, 1950, **220**, 127.) Khellin, one of the three active substances isolated from the fruit of *Ammi visnaga*, was given to 53 patients with angina pectoris in the form of Eskel tablets, containing 75 per cent. of khellin and 25 per cent. of visnagin (assayed as khellin equivalent). The dose was 40 mg. thrice daily. An optimal response is likely to occur after 2 weeks' treatment and all patients were observed for at least this period. About 60 per cent. of the cases showed improvement manifested by a decrease in the number of trinitrin tablets required, a smaller number of attacks and decreased severity of those that occurred, and an increase in the distance the patient could walk. About the same percentage of patients experienced unpleasant side effects, consisting of nausea, anorexia and dizziness, which in some patients were sufficiently severe to cause refusal to take the treatment. Khellin is thought to be of definite value in the treatment of angina pectoris but its usefulness would be enhanced if the undesirable side effects could be eliminated.

H. T. B

Methonium Compounds, Excretion of. G. E. Milne and S. Oleesky. (*Lancet*, 1950, **260**, 889.) From a study of the excretion of hexamethonium compounds in man the authors draw the following conclusions: (1) any of the drug absorbed from an intramuscular depot, and probably from the bowel, is excreted quantitatively in the urine; (2) in renal failure the drug sometimes accumulates in the body; thus, the use of the drug in patients with poor renal function is dangerous; (3) because of poor absorption from the bowel, large oral doses must be given to have any effect, but the variability of absorption makes this method of administration difficult to control. The actual amount absorbed per day can be estimated from the amount present in a 24-hour specimen of urine. Destruction in the bowel may actually take place but gastric juice and trypsin do not affect the compounds.

S. L. W.

Pervitin Treatment of Hypnotic Poisoning. C. Verth. (*Dtsch. med. Wschr.* 1951, **76**, 806.) A report is given on 46 cases of hypnotic poisoning treated with pervitin: 22 serious cases were given up to 60 ml. per day, in all up to 160 ml. In 10 cases the patients awoke up to 5 days after the first injection; 12 died. Milder cases had 0·5 to 27 ml. and awoke during the injection or up to 38 hours afterwards. It does not appear that pervitin is of any value when more than the fatal dose has been taken and absorbed. The enormous doses given produced no permanent ill-effects, though there

might be a transient restlessness and occasionally hallucinations. There was no tendency to habit formation. Owing to the rapid recovery with pervitin, the danger of complications such as pneumonia is reduced. G. M.

Pyrogenic Action, Quantitative Definition of. R. Charonnat and P. Lechat. (*Ann pharm. franc.*, 1951, **9**, 22.) The authors challenge the linear relation between temperature response and dose of a pyrogenic substance reported by Molitor and others, and show that the experimental results reported by these authors are insufficient to justify such a law: a more complicated law is required. In some cases an empirical expression of the type $\Delta = (\log p)^n$ reproduces the experimental results with considerable accuracy. Actually, the curve for rise of temperature rises steeply at first but becomes presently almost a straight line. If this straight portion is continued back to the axis the point where it cuts (Δ_o) is the rise of temperature which would result if the phenomenon showed this linear course throughout. This ordinate corresponds, on the actual curve, to a point of which the abscissa is B, i.e. B is the dose necessary to obtain a mean hyperthermy equal to Δ_o with 3 rabbits. To characterise a pyrogen there is given a pyrogenic index, i.e. $\Delta_o B$, where Δ_o is in °C and B in g./kg. of body weight. For a diluted pyrogen the index is thus a corresponding sub-multiple of that of the pure substances. Comparative values of some constants are given in the table below:

	Δo(°C)	B	I_P
Eberthella pyrogen	1·85	$1{\cdot}22 \times 10^{-5}$	152000
Adenosine triphosphoric acid ...	0·8	$9{\cdot}5 \times 10^{-4}$	840
Adenosine	1·66	0·03	55
Thymonucleic acid	1·4	0·05	28

G. M.

Pyrogens, Nature of. R. Charonnat and P. Lechat. (*Ann. pharm. franc.*, 1951, **9**, 17.) The authors have examined the pyrogenic activity of several compounds with a view to seeing whether such experiments could give an indication of the nature of pyrogens. Positive reactions were obtained with yeast nucleic acid, thymus nucleic acid, adenosine, and adenosine triphosphoric acid and negative reactions with adenylic acid, adenine and guanosine, also with specially purified phenol and *p*-cresol. In the case of adenosine, however, it was shown that the effect was due to an impurity. By treatment of an active sample of adenosine with charcoal, the pyrogen, and all the phosphorus, were retained on the charcoal. The authors conclude that such materials should be purified before being used for injection: that the presence of phosphorus is not a certain indication of pyrogenic activity; and that the biological products mentioned might possibly serve as a source for the isolation of pyrogens. G. M.

Streptomycin and *p*-Aminosalicylic Acid: Combined Therapy in Experimental Tuberculosis. A. G. Karlson and W. H. Feldman. (*Proc. Mayo Clin.*, 1949, **24**, 510.) Guinea-pigs inoculated 25 days previously with virulent tubercle bacilli were divided into 4 groups and treated for 133 days as follows: group 1, 6 mg. of streptomycin daily; group 2, 2 mg. of streptomycin daily; group 3, *p*-aminosalicylic acid 4 per cent. in the diet; group 4, 2 mg. of streptomycin daily, plus *p*-aminosalicylic acid 4 per cent. in the diet. Necropsy and histopathologic examination revealed that the combined use of the two drugs produced a therapeutic effect better than that

produced by either drug alone in the same doses, and that the results of the combined treatment were comparable to those obtained with the larger dose of streptomycin. S. L. W.

Surital Sodium: A New Thiobarbiturate for Intravenous Anæsthesia. E. A. Gain, M. Yates, Z. Hoar, E. H. Watts. (*Canad. med. Ass. J.*, 1951, **64**, 32.) Surital sodium is the sodium salt of 5-allyl-5-(1-methylbutyl)-2-thiobarbituric acid. A 5 per cent. solution is clear light yellow and has *p*H 10 to 10·5; reduction of *p*H results in precipitation. It is prepared for use by the addition of neutral distilled water. Surital sodium was used in 490 cases, for induction, induction and intubation, as a hypnotic with regional anæsthesia, for total anæsthesia supplemented with nitrous oxide and oxygen, and for basal anæsthesia by the rectal route in children. Surital was used in every case in which thiopentone would otherwise have been chosen. The intermittent injection technique was the most frequently used method of administration; the continuous intravenous drip of 0·2 or 0·1 per cent. solution was occasionally used for hypnosis during regional analgesia. The patients varied in age from 3 weeks to 82 years and included all risks and all types of surgical procedures. The duration of anæsthesia varied from 3 minutes to 255 minutes and the amounts of surital used ranged from 0·13 to 2·5 g. Decreased respiratory depression, laryngospasm and circulatory depression, increased potency and more rapid recovery, are its apparent advantages over the intravenous barbiturates in current use. The complications and contraindications are the same as for thiopentone. S. L. W.

Terramycin, Pharmacological and Clinical Studies. R. J. Sayer, J. C. Michel, F. C. Moll, W. M. M. Kirby. (*Amer. J. med. Sci.*, 1951, **221**, 257.) Terramycin administered orally is absorbed rapidly with the appearance of antibacterial activity in the serum within 1 hour of administration. Most individuals attain a maximum concentration of 2·5 to 10 μg/ml. after 2 to 3 hours; this level is maintained for about 4 hours and thereafter the concentrations steadily decline so that 0·1 to 0·5 μg./ml. is present at the end of 24 hours. No cumulative effect was noted after repeated daily doses of 1 g. or after administration of 1 g. every 6 hours. Individuals receiving 1 g. every 6 hours maintained blood levels of 5 to 10 μg./ml. throughout the 24-hour period. With a dose of 250 mg. intravenously a serum level of 5 to 10 μg./ml. is attained at the end of 1 hour, and 1 to 5 μg./ml. is present at the end of 12 hours. Clinical improvement was noted in 24 of 28 patients with urinary tract infections, with urinary sterilisation in 20. Clinical improvement was also observed in 18 of 21 children with whooping-cough, and in 22 out of 25 children, and all of 13 adults, with bacterial pneumonia. Adults were given 1 g. of terramycin orally every 6 hours and children smaller doses according to weight. 10 adults with pneumonia received 250 mg. intravenously twice daily. Toxic reactions (nausea, vomiting and diarrhœa) were uncommon and in only one case did they necessitate discontinuing the drug. S. L. W.

Thyroxine, Active Principle of. O. Thibault and A. Laxhaze. (*C.R.Acad. Sci., Paris*, 1951, **232**, 1318.) The action of thyroxine in catalysing oxidations and sensitising to the action of adrenaline is only observed after a period of latency corresponding to the time of transformation into an active substance. This transformation may be effected *in vitro* by the action of intestinal mucous tissue. Since it is probable that the thyroxine is

decarboxylated to thyroxamine, the biological action of the latter compound was tested. The results showed that synthetic thyroxamine has an action on the isolated intestine similar to that of preparations of activated thyroxine obtained by the action of intestinal mucous tissue on thyroxine. G. M.

Trivalent Sodium Antimony Gluconate in Schistosomiasis. M. Eofan and S. Talaat. (*Trans. R. Soc. trop. Med. Hyg.*, 1950, **44**, 123.) This is a preliminary note on the treatment of schistosomiasis with this compound. Trivalent sodium antimony gluconate (T.S.A.G.) is an amorphous solid very readily soluble in cold water. Aqueous solutions are very liable to become cloudy and to show a deposit on standing; this deposit invariably forms if solutions are heated. The following general instructions should be observed in its use. Ice-cold sterile distilled water must be used to dissolve it, resistance-glass vessels should be used, and the strength of solutions must not be less than 5 per cent.; the solutions must be prepared aseptically, further sterilisation is unnecessary and in no circumstances should the solutions be heated; solutions must be administered as soon as prepared. 30 cases of urinary schistosomiasis were treated with a 6 per cent. solution intravenously, a dose of 3 ml. being given daily for 6 successive days to an adult weighing 60 kg. Children received dosage according to weight. Of the 30 patients, 8 were passing living ova in the urine after a period of observation of 1 to 2½ months. The results in a further 6 patients who were given a 12-day course appeared to be better, but the number was too small for comparison. There were few reactions and a striking absence of coughing. Vomiting occurred in two cases and an urticarial rash in one. The authors conclude that sodium antimony gluconate is effective in schistomomiasis and is better tolerated than tartar emetic and sodium antimony tartrate.
S. L. W.

Tuberculous Infection of Cornea of Mouse for Testing Antituberculous Substances. R. J. W. Rees and J. M. Robson. (*Brit. J. Pharmacol.*, 1950, **5**, 77.) This is an extension of the corneal method originally employed in the rabbit. Female albino mice were employed and the same bovine strain of *Mycobacterium tuberculosis* was employed as in the rabbit tests. The mouse requires a larger inoculum than the rabbit (1,000 as against 300 organisms) to produce an active tuberculous corneal infection in 100 per cent. of animals. Deep anæsthesia is essential for the injection, but as a sufficiently deep anæsthesia with ether resulted in a high mortality, the mice were given a preliminary dose of α-bromoisovalerylurea 15 minutes before inoculation; the drug was given by stomach tube as an aqueous suspension in 6 per cent. gum acacia in a dose of 0·4 g./kg. of body weight. The injection immediately produced a readily visible opaque bleb. The volume of the inoculum was about 0·01 ml.; one eye only in each animal was inoculated. In the untreated mouse cornea the lesions reach a maximum by about the 30th day, then slowly decrease in size, and finally become stabilised at about the 50th day. Tests with streptomycin, *p*-aminosalicylic acid and sulphetrone showed that (1) streptomycin markedly prolongs the incubation period, (2) *p*-aminosalicylic acid always prolongs the incubation period but the effect is less striking than with streptomycin, (3) sulphetrone does not prolong the incubation period beyond the normal in half the animals. A combination of streptomycin and *p*-aminosalicylic acid is more effective than either drug alone. All the drugs were given either by the mouth or by subcutaneous

(*Continued on page 606*)

rarely, if ever, in human medicine, is not indicated as being a veterinary preparation but is provided with a range of adult human doses.

Doses are no longer stated at the foot of each monograph, but are given in posological tables at the end of the book, showing maximum and usual doses for adults and children.

It is clear that the monographs carried forward from the previous edition have been carefully studied and revised in many particulars in order to provide useful information and reasonable standards of purity.

Congratulations are due to those responsible for the detailed work of preparation and to l'Ordre National des Pharmaciens for discharging its duties as publisher in so successful a manner.

T. C. DENSTON.

ABSTRACTS (*Continued from page 602*)

injection. Compounds for assay should be given either at the time of, or 24 hours before, the inoculation of the eyes. S. L. W.

Vitamin D, Criterion for Dosage of. P. Fournier. (*C.R.Acad. Sci., Paris*, 1951, **252**, 1019.) In rats on a suitable diet, the fæcal excretion of calcium is increased 3 times when they are deprived of vitamin D, although the elimination in the urine is unaffected. Actually, in place of the determination of total calcium, it is more convenient to determine the ratio of calcium to an inert substance (titanium dioxide) added to the diet. The curve of variation of calcium excreted with doses of vitamin administered is logarithmic. Response to treatment may be seen earlier than with the other criteria generally employed, and it is not necessary to sacrifice the animals. A statistical study, using a large number of animals, is desirable to determine the relative accuracy of this process. G. M.

BACTERIOLOGY AND CLINICAL TESTS

***Pseudomonas pyocyanea* Contamination of Disinfectant Solutions.** E. J. L. Lowbury. (*Brit. J. industr. Med.*, 1951, **8**, 22.) The occurrence of *Pseudomonas pyocyanea* infections in wounds adequately covered using a "no-touch" dressing technique led to the testing for sterility of a number of solutions, including 2 per cent. soap, 1 per cent. cetrimide and 10 per cent. Dettol, actually in use in hospital dressing stations and operating theatres. All of 18 samples of soap solution, 6/23 of cetrimide solution and 3/9 of Dettol solution were contaminated by *Ps. pyocyanea*. The infected samples were all taken from corked bottles and a higher proportion of positive tests was obtained from the cork than from the solutions. After replacing all the corked bottles by screw-capped bottles, no contamination of the contents by *Ps. pyocyanea* was found. Of 541 swabs examined in the year preceding the change of container, 18·5 per cent. contained *Ps. pyocyanea*. Of 104 examined in the succeeding three months, only 3 (2·8 per cent.) contained the organism, 2 being from old cases. The survival of the organisms in concentrations which would be lethal to them in ordinary *in vitro* tests is considered to be due to the presence of growth-promoting substances in the cork, possibly aided by a protective envelope of dried exudate from the wound in which the contaminating organism had previously grown. It is recommended that liquids for application to wounds be dispensed in small screw-capped bottles and sterilised after filling, either by autoclaving or, if this is impossible, by boiling. H. T. B.