ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Acetaldehyde and Acetone, Determination of. S. D. Nogare, T. O. Norris and J. Mitchell, Jr. (*Anal. Chem.*, 1951, **23**, 1473.) The method is based on the reaction of acetaldehyde and acetone with hypoiodite solution to give iodoform which is measured spectrophotometrically at 347 mμ. Iodoform absorption is characterised by three well defined maxima occurring at 347, 307 and 274 mμ, the absorption peak at 347 mμ being the most sensitive to changes in iodoform concentration and obeying Beer's law for amounts of iodoform from 0 to 3 mg. Under controlled conditions acetaldehyde and acetone gave reproducible iodoform yields of 58 and 108 per cent. respectively, on a molecular basis. Interference was encountered from compounds which gave the iodoform reaction; a list of compounds which interfered, together with the concentration at which interference was appreciable, is given. The procedure could be used to determine 1:2-propylene glycol alone or in the presence of ethylene glycol; the glycols were first oxidised with periodate in order to convert them quantitatively to acetaldehyde and formaldehyde, acetaldehyde being then determined by the iodoform method. R. E. S.

Arsenic in Bismuth Compounds, Detection of. J. A. C. Van Pinxteren and G. Schallenberg-Heertjes. (*Pharm. Weekbl.*, 1951, **86**, 701.) The following method is recommended: 0·2 g. of the inorganic compounds (nitrate, carbonate, hydrate) is ignited and to the residue 3 ml. of stannous chloride containing hydrochloric acid, 3 ml. of water and granulated zinc is added. If 1 μg. of arsenic is present a yellow stain is produced on mercuric chloride paper. Of the organic preparations (salicylate, tannate, gallate, oxyiodetogallate) 0·2 g. is ignited with 0·2 g. of magnesium peroxide and the residue treated as described above. In all cases it was possible to detect 1 μg. of As in 0·200 g. of the bismuth compound. J. R. F.

Coumarin in the Presence of Vanillin, Test for. M. Nivoli. (*Annali Chim.*, 1951, **40**, 642.) To 1 ml. of the ethanolic solution to be tested add 1 ml. of a 1 per cent. aqueous solution of sodium hydroxide and 4 or 5 drops of a 1 in 1000 solution of colourless *p*-aminophenol in 95 per cent. ethanol. In the presence of coumarin a blue colour is obtained which reaches its maximum intensity in a few minutes. The reaction is given by 0·020 mg. of coumarin, and vanillin, even in very large excess, does not interfere. H. D.

Fluorine in Organic Compounds, Determination of. R. Belcher and J. C. Tatlow. (*Analyst*, 1951, **76**, 593.) Decomposition of the compound is effected by heating with metallic sodium in a specially designed nickel bomb, details of which are given, at a high temperature for 1 hour, and cooling. The fluoride ion is then determined gravimetrically as lead chlorofluoride. The method is suitable for the assay of the most strongly bonded organic compounds of fluorine. J. R. F.

Monosaccharides, a Colorimetric Method for the Determination of, in Organic Solvents for use in Partition Chromatography. S. Gardell. (*Acta chem. scand.*, 1951, **5**, 1011.) The determination of certain monosaccharides in solution in organic solvents, as collected during flowing chromatogram techniques, is described. The method, which is suitable for the estimation of aldopentoses, methylpentoses and aldohexoses in concentrations of 10 to 300 μg./ml. depends upon the colour reaction obtained with aniline trichloroacetate in a strong solution of trichloroacetic acid. The colour is not given by fructose and in the case of both pentoses and hexoses it shows the strongest light absorption at 370 mμ. The various factors affecting the formation of the colour are discussed in some detail. J. B. S.

Nitrates and Nitrites, Colour Reaction for. H. Barnes. (*Analyst*, 1951, **76**, 666.) It was found that a brilliant purple colour was produced by nitrates with a sulphuric acid solution of the nitrite reagent, *N*(1-naphthyl)ethylenediamine hydrochloride. For the test, 2·25 ml. of an aqueous solution was used and 2·75 ml. of nitrogen-free sulphuric acid were added, followed by 1·0 ml. of a 0·02 per cent. solution of the reagent in sulphuric acid. With 2·5 μg. of nitrate nitrogen per ml. in the test solution the liquid turns to a distinct purple in 90 seconds and an intense purple in 3 minutes. The colour is stable for some time and the limit of sensitivity is about 0·25 μg. of nitrate nitrogen per ml., although at these low concentrations the colour takes longer to develop. Nitrites gave the same reaction but potassium iodate was the only other oxidising agent tested that produced a purple colour. A table is given showing the behaviour of a number of oxidising agents under the conditions of the test. R. E. S.

Nitrites, Determination of. H. Barnes and A. R. Folkard. (*Analyst*, 1951, **76**, 599.) A number of modifications of the Griess-Ilsovay reaction for the estimation of nitrites have been examined. Of the four techniques compared, the method of Rider and Mellon showed the most sensitive results, giving an optimum absorption with an Ilford green filter (604) and a maximum colour development in a coupling time of about 25 minutes at 18° C. to 25° C. A modification of the Shinn method was also applied. The rate of colour development is extremely rapid, the maximum intensity being obtained in 10 minutes at 25° C., and the test is slightly more sensitive than the Rider-Mellon method, but the coupling reagent discolours on keeping, giving a large blank reading. J. R. F.

Particle Size Analysis, Approximate. E. I. Johnson and J. King. (*Analyst*, 1951, **76**, 661.) A simple method is proposed for this determination, attempting to separate those particles that have a greater Stokes' diameter than a predetermined limit. It is believed, in conjunction with the apparatus described, to be particularly well suited for routine control use, the simplicity of the apparatus and its ease of operation compensating for the loss of some of the information obtainable by more elaborate methods. A weighed sample of powder is dispersed in water or other suitable suspending medium and placed in a fat extraction tube; two marks 12 cm. apart are made and the time t in seconds required for a particle of the size limit chosen to travel down the tube from the top mark to the lower mark is calculated from a formula derived from Stokes' law. The layer above the lower mark is blown off by the usual method, and the tube is refilled to the top mark with water, the procedure

being repeated until all fine particles are removed and the only ones left are those falling below the lower mark in time t; four such extractions are usually sufficient and the weight of coarse particles remaining in the tube is then estimated by a convenient method. Results are given for comparative determinations on two α-naphthylthiourea powders using the present method and that due to Andreason (*Ber. dtsch. keram. Ges.*, 1930, **11**, 249). R. E. S.

Phosphorus, Estimation of, by Ceric Sulphate. G. S. Deshmukh. (*Analyst*, 1951, **76**, 604.) Ceric sulphate oxidises phosphorus quantitatively to phosphoric acid. An accurately weighed sample of red phosphorus was placed in a Kjeldahl type flask fitted to a Leibig's condenser. A known volume of ceric sulphate, sufficient to give excess, was added, and the solution heated under a reflux condenser until the red phosphorus dissolved. The solution was cooled and the unchanged ceric sulphate estimated by titration against standard ferrous ammonium sulphate with *o*-phenanthroline ferrous complex as indicator. It has not been possible to apply this method to the determination of white or yellow phosphorus owing to the difficulty of weighing in the dry form. The adaptation of the procedure to determine the solubility of phosphorus in various solvents has been suggested. J. R. F.

Sodium in Serum, Rapid Determination of. P. Trinder. (*Analyst*, 1951, **76**, 596.) A magnesium uranyl acetate reagent, containing 80 per cent. v/v of ethanol is used to precipitate the sodium and protein simultaneously. The precipitate is separated by centrifuging at moderate speed. The uranium is determined in the reagent and in the supernatant liquid by a photoelectric colorimetric method and the sodium content of the serum is calculated from the loss in concentration, by the use of a calibration graph prepared with solutions of known sodium content. A single determination can be completed within 15 minutes. J. R. F.

Testosterone Propionate in Vegetable Oil Solution, Determination of. J. J. Madigan, E. E. Zenno and R. Pheasant. (*Anal. Chem.*, 1951, **23**, 1691). An attempt was made to find a method for the quantitative determination of testosterone propionate by the isolation and identification of the 2:4-dinitrophenylhydrazone, from oil solutions; experiments failed to produce quantitative recoveries and attention was given to the formation of the semicarbazone. A detailed method is given whereby the testosterone propionate is quantitatively separated as the semicarbazone, which could be weighed and identified by its m.pt. (with characteristic colour change), or by ultra-violet absorption. The ultra-violet absorption spectrum was determined in a 0·001 per cent. solution in methanol, in which maximum absorption occurred at 268 to 269 mμ (specific absorption, $E_{1\text{ cm.}}^{1\text{ per cent.}} = 725 \pm 5$ per cent.) and negligible absorption from about 320 mμ upward. The m.pt. of the recovered semicarbazone should be between 207° and 217° C. corrected, when determined in a bath heated at 3° per minute, with the capillary inserted at 200° C. R. E. S.

ESSENTIAL OILS

Orange Oil, Fermentation-inhibiting Properties of. D. A. A. Mossel (*Nature, Lond.*, 1951, **168**, 999.) As the result of an observation that non-preserved fruit drinks prepared from emulsified orange oil inhibited the fermentation of an inoculum of *Saccharomyces cerevisiæ* the author made some quantitative experiments on similar lines. It was found that 0·01 per cent. or

more of Florida orange oil (aldehydes 1·6 per cent.) increased the time required for complete fermentation of an inoculum in a semi-synthetic medium from 48 hours to at least 96 hours. The terpenes and the fraction (3·6 per cent.) containing the oxygen derivatives extracted from New Guinea orange oil were tested separately and it was found that the terpenes possessed the same order of activity as the original oil. The oxygen-containing fraction was inactive in concentrations equivalent to 0·1 per cent. of original oil, thus confirming the statement made previously by Guenther (*The Essential Oils*, 1948, **1**, 81).

G. R. A. S.

ORGANIC CHEMISTRY

Camphor Substitutes, Water-soluble Synthetic. M. Fioretti, (*Boll. chim.-farm.*, 1951, **90**, 424.) Injections of camphor are painful and slow in action, so a water-soluble compound with the same pharmacological action is desirable. Camphoric acid is prepared by oxidising camphor with nitric acid. The m. pt. of that obtained from natural camphor is 187° C. while that from synthetic camphor is 202° C. and it is less soluble in water. This acid and its sodium salt have no action on the heart and are diuretic. Camphorsulphonic acid can be prepared by acting on camphor with concentrated sulphuric acid and acetic anhydride. The salts are soluble in water but are rapidly excreted in the urine and only a very slight camphor-like activity is shown. Another derivative is camphor-carbonic acid, prepared by the action of carbon dioxide on sodium camphor in an organic solvent. This compound, unlike the others, is not stable to heat and the solution begins to decompose at 80° C., but solutions can be heated for half-an-hour in sealed vessels in a current of steam. It is, however, without physiological action and is passed unaltered in the urine. Thus none of these bodies can be considered as a water-soluble substitute for camphor.

H. D.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Dechlorogriseofulvin—A Metabolic Product of *Penicillium griseofulvum* Dierckx and *Penicillium janczewskii* Zal. J. MacMillan. (*Chem. Ind.*, 1951, **34**, 719.) The isolation of a second "curling factor" from culture filtrates of both these organisms is recorded. Chloroform extracts of culture filtrates have been submitted to chromatography on alumina and have been shown to contain griseofulvin and also a new mould metabolite, dechlorogriseofulvin. Chromatography of similar extracts from the mycelium yielded only pure griseofulvin. Dechlorogriseofulvin, $C_{17}H_{18}O_6$, m.pt. 179° to 181° C. $[\alpha]_D^{19°\,C.}$ + 390 (*c.* 1·0 in acetone), is a neutral crystalline compound, containing three methoxyl groups. Hydrogenation with platinic oxide yielded tetrahydrodechlorogriseofulvin, identical with a compound obtained by reductive dechlorination of griseofulvin. A structure is suggested for dechlorogriseofulvin. It produces a typical griseofulvin-like response in *Botrytis allii*, although it is less active than griseofulvin itself.

J. B. S.

Hydroxytyramine (β-3 : 4-Dihydroxyphenylethylamine) in Human Urine. U. S. Von Euler, U. Hamberg and S. Hellner. (*Biochem. J.*, 1951, **49**, 655.) By partition chromatography of human urine extracts on starch columns, hydroxytyramine, adrenaline and noradrenaline have been separated and identified. The excretion of hydroxytyramine in normal urine has been confirmed and has been found quantitatively to be the most important catechol

amine present. It occurs in urine largely in the free state. The daily output of hydroxytyramine is estimated at 0·1 to 0·2 mg. and exceeds considerably that of noradrenaline and adrenaline. The fraction with *R* values corresponding with those of hydroxytyramine gives a characteristic spot in paper chromatograms and shows the same behaviour as a hydroxytyramine on colorimetric estimation and biological assay. J. R. F.

Lactose, Biological Synthesis of, from Carbon-14 Glucose. T. H. French, G. Popjak and F. H. Malpress. (*Nature, Lond.*, 1952, **169**, 71.) Carbon-14 starch, prepared by photosynthesis, was administered to lactating rabbits by stomach tube, and milk collected after 6 hours. The analytical data confirm earlier conclusions that the lactose is derived solely from the glucose intake, since the specific activities of the carbon of the lactose samples, and of the glucose and galactose fractions prepared from them by acid hydrolysis, were all the same. It is also concluded that both moieties of the lactose molecule are found in equal measure from the same source. J. B. S.

Lyxoflavin, Vitamin Activity of. G. A. Emerson and K. Folkers. (*J. Amer. chem. Soc.*, 1951, **73**, 5383.) It was considered possible that lyxoflavin might be a vitamin because of the close similarity of structure of vitamin B_2 and lyxoflavin, because vitamin B_2, vitamin B_{12} and lyxoflavin contain a 1:2-diamino-4:5-dimethylbenzene moiety linked through a nitrogen atom to a pentose, and because all three are concerned with the human body. Synthetic lyxoflavin was found to be devoid of riboflavine activity when tested in conventional assays using rats and *L. casei*. It was shown to possess growth promoting or vitamin activity in a rat assay method, the details of which are given. A. H. B.

BIOCHEMICAL ANALYSIS

Antibiotics from Streptomyces. J. Berger, A. I. Rachlin, W. E. Scott, L. H. Sternbach and M. W. Goldberg. (*J. Amer. chem. Soc.*, 1951, **73**, 5295.) Three new crystalline antibiotics were isolated from cultures of three unidentified streptomyces. The three streptomyces were isolated from soil samples and grown on a variety of media in aerated submerged culture. Although the new antibiotics were chemically different, their biological activity and certain chemical properties are so similar that they are reported here as a group. They are colourless, optically active, organic acids, and their most likely empirical formulæ are $C_{46-47}H_{80-82}O_{13}$, $C_{25}H_{40}O_7$ and $C_{34}H_{52}O_8$. Only one has a characteristic ultra-violet absorption spectrum. They are active *in vitro* against certain Gram-positive bacteria and mycobacteria but inactive against Gram-negative bacteria and fungi, rather toxic, and inactive *in vivo* against a variety of bacterial and protozoan infections. A. H. B.

Blood in Urine, Chemical Tests for. H. Caplan and G. Discombe. (*Brit. med. J.*, 1951, **2**, 774.) Two tests are recommended. (1) Acidify 3 ml. of urine with a few drops of acetic acid and overlay with 1 to 2 ml. of 5 per cent. amidopyrin solution in 95 per cent. ethanol: allow 5 to 6 drops of 10 volume hydrogen peroxide to fall through the ethanolic layer. Allow to stand for a few minutes, a blue- or lilac-coloured ring is a positive reaction. This test is simple but comparatively insensitive. (2) Wash a white porcelain tile with cavities, rinse with 95 per cent. ethanol and allow to dry by evaporation. Place about 3 mg.

of *o*-tolidene hydrochloride in a cavity: add 1 drop of urine, stir with a glass rod and add 1 drop of a mixture of glacial acetic acid and 10 volume hydrogen peroxide in equal parts; a positive reaction appears as a blue colouration or spreading blue-green streaks which fade, after 5 to 30 minutes, to brown. A negative reaction is pale brown. J. R. F.

Calcium and Magnesium in Plasma, Simplified Titrimetric Techniques for the Assay of. E. S. Buckley, J. G. Gibson and T. R. Bortolotti. (*J. Lab. clin. Med.*, 1951, **38**, 751.) The techniques depend upon the fact that aqueous solutions of certain dyes at a critical *p*H have a characteristic colour which changes in the presence of a minute concentration of metal ions, and addition of sufficient ethylenediamine tetra-acetate results in a reversion to the original colour if the *p*H of the system is not altered. A description of the technique and reagents is given for the direct assay in plasma of calcium concentrations using murexide, and of the sum of calcium and magnesium concentrations using Eriochromschwarz-T. The methods were found to be reliable with concentrations in plasma of the two cations ranging from 0·10 millimolar for calcium, and 0·18 millimolar for the sum of calcium and magnesium to the clinically significant levels of 3·0 millimolar and 4·0 millimolar. Thus an indirect method for the estimation of plasma magnesium is available. A. H. B.

Indole, Colorimetric Estimation of, by the Xanthydrol Reaction. W. R. Fearon and J. A. Drum. (*Sci. Proc. R. Dublin Soc.*, 1951, **25**, 295) A sensitive method for the determination of indole, based on the production of a stable violet colour when indole and xanthydrol react in acid solution, is described. The details of the preparation of the reagents, and the method of obtaining indole from biological fluids, are given. A. H. B.

Indoxyl, Estimation of. J. A. Drum. (*Sci. Proc. R. Dublin Soc.*, 1951, **25**, 299.) The investigation of indole metabolism necessitated the estimation of urinary indican, and, therefore, the hydrolysis of indican and the condensation of isatin and indoxyl to form indirubin was examined. The replacement of hydrochloric acid, used by previous workers, by sulphuric acid was found to produce more consistent results. A colorimetric method for the estimation of urinary indoxyl, based on the above condensation, is described. The minimum quantity of indican which can be detected and estimated is of the order of 4 μg. A. H. B.

Procaine Penicillin, Determination of Total Penicillin in. A. M. Wild. (*J. appl. Chem.*, 1951, **1**, 329.) The method depends on the conversion of procaine penicillin to sodium penicillin by precipitation with sodium silicotungstate, the sodium penicillin being assayed iodimetrically. The sample of procaine penicillin is ground, weighed and stirred with water before adding the special silicotungstate reagent; the solution is filtered under specified conditions before making up to a definite volume. The assay is completed by the published Analysts Sub-Committee method (*Analyst*, 1949, **74**, 550; *J. Pharm. Pharmacol.*, 1950, **2**, 260). Using this method the total penicillin content of a sample of sodium penicillin was found to be 97·8 per cent. standard deviation 0·35; with added procaine penicillin a mean result of 97·3, standard deviation 0·32 was obtained. R. E. S.

Vitamin B_{12}, Determination of, with a Mutant Strain of *Escherichia coli*. P. R. Burkholder. (*Science*, 1951, **114**, 459.) The microbiological assay

technique used employed bacteria produced by selection from ultra-violet irradiated cultures of *E. coli* W. (ATCC 9637), one strain, 113–3, showing marked responses to both methionine and vitamin B_{12}. The strain 113–3 was employed in establishing dosage-response curves for different levels of vitamin B_{12} and for methionine. It was found that the great sensitivity of the organism to relatively low concentrations of vitamin B_{12} as compared with the requirement of much higher amounts of methionine permitted the development of specific vitamin B_{12} assays of many natural materials by appropriate dilution of samples. Proof of the response of strain 113–3 to vitamin B_{12} in complex materials was obtained by making parallel determinations at different levels for vitamin B_{12} with strain 113–3 and for methionine with another strain 26–18 which was stimulated by methionine or homocystine but not by vitamin B_{12}. Details are given of the media and of the method used for the assay (of the tube type) which employed turbidity measurement for the final vitamin B_{12} estimation. It was found that adequate growth could be obtained after 15 to 18 hours of incubation on a shaking machine with the temperature at 30° C. The half-maximum level of growth occurred at about 0·12 mμ of B_{12}/ml. Under the specified conditions of assay, the organism also responded to vitamins B_{12} and B_{12a}. In duplicated assays with *Euglena* and with *E. coli*, blood serum proteins, animal tissue extracts, and various preparations of bacteria and algæ yielded satisfactory results. Whole normal blood appeared to have amounts of vitamin B_{12} too low for direct assay in the presence of free methionine. Vitamin B_{12} bound in tissues and blood serum was released by heat or enzyme treatment before assay. R. E. S.

CHEMOTHERAPY

Dimethylaminoethyl-substituted Compounds, Antispasmodic and Local Anaesthetic Activity of. J. F. Reinhard, E. T. Kimura and J. V. Scudi. (*J. Pharmacol.*, 1951, **103**, 288.) The antispasmodic and local anæsthetic activity of compounds of the type $ROCH_2CH_2N(CH_3)_2$, where R = methyl, ethyl, decyl, phenyl, β-pyridyl, etc., and of the type $\begin{matrix}R_1\\R_2\end{matrix}\!\!>\!N\text{-}CH_2CH_2N(CH_3)_2$ when R_1 and R_2 = various aliphatic groups and cyclic structures, was measured. Guinea pig ileum was used in the tests for antispasmodic activity and guinea pig cornea for the tests for local anæsthetic activity. Of the compounds tested, 17 were active against histamine, 9 against acetylcholine and 5 against barium chloride. 8 members of the series had more than 20 times the local anæsthetic potency of cocaine. The relationship between structure and activity is discussed. A. H. B.

3:3-Diphenyl-propanolamines, -allylamines and -propylamines; Pharmacological Properties of. A. C. White, A. F. Green and A. Hudson. (*Brit. J. Pharmacol.*, 1951, **6**, 560.) Atropine-like activity, shown by antagonism of carbachol *in vitro* and by mydriasis, is greater in the propanolamines than in the allylamines and propylamines. 3:3-Diphenylpropan-3-oldiethylamine is as active as atropine sulphate on a molecular basis. Antihistamine activity is greater in the allylamines and propylamines than in the propanolamines, the pyrrolidine analogues, which are both a tenth to a fifth as active as mepyramine, being the most potent antihistamines in these series. The quaternary ammonium salts are, in general, less potent antihistamines than the tertiary amines. All series showed corneal anæsthetic properties, the greatest degree of activity being in the allylamines; the most active members are a twentieth as active

as cinchocaine and cause considerable conjunctival irritation; the quaternary ammonium salts are less active than the tertiary amines. No analgesic activity was found in these series. Pharmacological action varies greatly with the nature of the basic groups in these and other related series, and in any one property in a given species the optimal groups, though commonly allied, may not necessarily be the same even in closely related series. S. L. W.

Hexamethonium and Homologues, Actions of. R. Wien and D. F. J. Mason. (*Brit. J. Pharmacol.*, 1951, **6**, 611.) A study has been made of certain actions of hexamethonium and of homologues with ethyl substituents, in which one or more methyl groups on each nitrogen atom were replaced by ethyl groups. The bis-ethyldimethylammonium homologue (hexane-1:6-bis-ethyldimethylammonium dibromide dihydrate) was one and a half times to twice as potent as hexamethonium in paralysing autonomic ganglionic transmission in both sympathetic and parasympathetic ganglia, and had a similar type of action. The bis-triethylammonium homologue was much less potent and possessed neuromuscular blocking properties absent in the other compounds. The bis-diethylmethylammonium compound was as active as hexamethonium on parasympathetic ganglia but slightly less potent on sympathetic ganglia. It is shown that the nature of the terminal groupings as well as the distance between the two quaternary nitrogen atoms is a factor determining optimal activity. Some actions of hexamethonium, such as inhibition of salivary excretion and vasodilatation are very slight and play little part in the main action of the drug, but it has an appreciable mydriatic effect. It has little effect on the heart. Gastric motility may be excited or inhibited by hexamethonium dependent on the functional innervation of the stomach in different animals. In the cat, stomach movements were increased. Gastric secretion in the dog was inhibited by both hexamethonium and its bis-ethyldimethylammonium homologue; there were reductions in volume, free and total acidity and peptic power. No inhibitory effect was exerted on gastric secretion induced with histamine. Considerably less of the compounds was excreted in the urine after oral than after intravenous administration. S. L. W.

PHARMACY

NOTES AND FORMULÆ

Methimazole (Tapazole). (*New and Nonofficial Remedies*; *J. Amer. med. Ass.*, 1951, **147**, 1668.) Methimazole is 1-methyl-2-mercaptoimidazole, $C_4H_6N_2S$, and occurs as an almost odourless and tasteless, white to buff, crystalline powder; m.pt. 145° to 148° C., soluble in water (1 in 4·5), ethanol (1 in 5), chloroform (1 in 4·4) and ether (1 in 125); a 2 per cent. solution has *p*H 6·7 to 6·85. An aqueous solution at first decolorises solution of iodine and then yields a brown precipitate which becomes brownish black. A 0·0003 per cent. solution in water exhibits an ultra-violet absorption maximum at about 2520 Å ($E^{1\ \text{per cent.}}_{1\ \text{cm.}}$ about 1357) and a minimum at 2200 Å. When dried *in vacuo* over phosphorus pentoxide for 24 hours, methimazole loses not more than 0·5 per cent. of its weight; it yields not more than 0·1 per cent. of sulphated ash. The amount of nitrogen present, determined by the Kjeldahl method, is 24·0 to 24·8 per cent., equivalent to 98·0 to 101·0 per cent. of methimazole. When assayed by dividing the absorption of a 0·0003 per cent. solution at 2520 Å by 135·7, it contains 96·5 to 102·5 per cent. of methimazole. Methimazole has the action and uses of propylthiouracil but is perhaps 20 times as potent. G. R. K.

PHARMACOLOGY AND THERAPEUTICS

Antimonial Compounds, Action of, on the Liver Fluke *in vitro*. T. E. Mansour. (*Brit. J. Pharmacol.*, 1951, **6**, 588.) Using both Ringer's solution and a mixture of equal volumes of bovine serum and Ringer's solution as media, *in vitro* tests of the effects of certain antimonials were carried out on preparations of the liver fluke (*Fasciola hepatica*). The tests were conducted for a maximum period of 90 minutes and kymographic records were obtained of the movements of the fluke. At least 4 flukes were used in each test. In a saline medium, in a concentration of 1:1000, tartar emetic, stibophen and neostibosan all failed to cause paralysis of rhythmical movement. On the other hand, a definite lethal action was demonstrated to tartar emetic in the presence of serum, though not to stibophen or neostibosan. The fraction of serum responsible for this action was found to be dialysable through cellophane membrane against distilled water, but not against saline solution. S. L. W.

Atropine, Action of, on the Cardiovascular System. L. A. Nalefski and C. F. G. Brown. (*Arch. intern. Med.*, 1950, **36**, 898.) The effects of atropine sulphate given by intravenous or subcutaneous injection were studied in 133 normal subjects of both sexes and various age groups, with a view to assessing its role in the treatment of coronary thrombosis. Each subject was given 0·02 mg. of atropine sulphate per kg. of body weight—this dose was considered sufficient to produce a pronounced effect on the vagi. All subjects showed an initial drop in heart rate and a subsequent rise following the administration of atropine. The effects on the heart rate were more rapid and transient with intravenous than with subcutaneous injection, and response to atropine most pronounced in persons under twenty. Blood-pressure changes varied with mode of administration but were more brisk in ages ranging from 20 to 50 years. Systolic pressures either increased or decreased but diastolic pressures invariably increased. Salivary secretion of subjects up to the age of 20 was less affected by atropine than that of subjects in older age groups. The authors conclude that if the degree of vagal tone can be measured by the changes in heart rate noted after atropine administration, then these results indicate that vagal tone is greatest in childhood and gradually decreases through the succeeding decades. Their experiments lead them to believe that atropine sulphate should play a prominent part in the treatment of coronary thrombosis. G. R. B.

Aureomycin, Topical Use of, in Skin Diseases. B. Solomons. (*Brit. med. J.*, 1951, **2**, 525.) A 3 per cent. aureomycin hydrochloride ointment in a petrolatum and wool fat base was employed in the treatment of 144 dermatological cases (sycosis barbæ, 22; folliculitis of other areas, 12; impetigo, 57; miscellaneous, 53). The ointment was applied thinly and gently to the affected areas twice a day. The most striking results were obtained in the treatment of sycosis barbæ; within a week improvement was noted in all cases, and in all except 3 cases the pustules had disappeared by the end of a fortnight. All the cases except one of folliculitis of other areas also responded to the treatment, and all except 2 of the cases of impetigo were cured within 4 to 7 days. Local sensitivity occurred in only 2 cases of the series. Aureomycin would appear to be the best available antibiotic for use in ointment form for pyogenic infections. S. L. W.

2-Carbethoxythio-1-methylglyoxaline, (C.G.1) Antithyroid Activity of. A. Lawson, C. Rimington and C. E. Searle. (*Lancet*, 1951, **261**, 619.) The antithyroid effects of this substance have been investigated in mice, rats and man.

The acute toxicity in mice is of the same order as that of thiouracil. The chronic toxicity has been examined in rats and considerable hypertrophy of the thyroid occurred; the gland concentrated only 11·5 per cent. as much radio-iodine as those of control animals. It has been compared with other anti-thyroid compounds by a new technique developed by the authors. Its activity in rats is about equal to that of 2-mercapto-1-methylglyoxaline, both being much more active than thiouracil. Its effect on the radio-iodine uptake in man was studied in a small number of subjects and the neck/thigh ratio count examined. Results showed a somewhat greater inhibition of radio-iodine take up than after 2-mercapto-1-methylglyoxaline. J. R. F.

Chorionic Gonadotrophin, Prolongation of Action. K. Didcock, J. M. Robson and A. A. Sharaf. (*Brit. J. Pharmacol.*, 1951, **6**, 445.) The period of action of chorionic gonadotrophin is considerably extended when the hormone is administered as a compressed implant made with magnesium monostearate. The duration of such implants was investigated by determining their effect in immature mice, implants weighing 1 mg. and containing one part of active material with 3 parts of excipient being inserted subcutaneously in the upper dorsal region. The active material was absorbed from the implant and produced an effect lasting for about 20 days. Other experiments suggest that the period of absorption depends on the relative proportion of active material and excipient, and that periods of action suitable for the clinical use of the material could be obtained by varying the relative proportions of the gonadotrophin and the magnesium monostearate. Macroscopic examination revealed no reaction round the implanation sites. S. L. W.

Cinchona Alkaloids, Oxytocic Action of. D. K. de Jongh, E. G. van Proosdij-Hartzema and A. Th. Knoppers. (*Arch. int. Pharmacodyn.*, 1951, **88**, 84.) The oxytocic action of quinine, hydroquinine, quinidine, cinchonine and cinchonidine, either alone or in combination with pituitary or ergometrine, was investigated *in vitro* (using uteri of rats and guinea pigs) and *in vivo* (using rabbits, cats, guinea pigs and rats). Oxytocic effects *in vitro* were regularly observed with quinine in concentrations of $1:5 \times 10^4$ and upwards; for the other alkaloids the minimum active concentration was $1:10^6$. The paralysing concentration amounted to $1:10^5$ for all the alkaloids. No potentiation by quinine of the pituitary or ergometrine effect was observed *in vitro*. Oxytocic effects were usually obtained *in vivo* with all the alkaloids in doses of 0·5 to 10 mg./kg. intravenously. Higher doses (20 mg./kg.) sometimes paralysed the uterus. There were no important differences between the 5 alkaloids. Quinine *in vivo* did not enhance the pituitary effect, though in rare instances it enhanced the ergometrine effect. S. L. W.

Cortisone, Antitoxic Action of. F. Boyer and L. Chedid. (*C.R. Acad. Sci., Paris*, 1951, **233**, 1232.) Cortisone protects mice against infection with *Salmonella typhi*, but is not as effective as chloramphenicol. Injections of 2 to 5 mg. of cortisone allowed 40 per cent. of mice infected with a culture to survive 8 days, while 10 mg. of chloramphenicol allowed 100 per cent. to survive from the same dose of culture, which killed 100 per cent. of the controls. With *Salmonella* toxin however 77 per cent. of those treated with 1 to 5 mg. of cortisone survived 48 hours, while only 37 per cent. of those receiving 10 mg. of chloramphenicol and 20 per cent. of the controls which received no treatment survived. With antigen O (Ty II) (1 mg. given by injection), 2 and 4 mg. of

cortisone gave 100 per cent. survival for 48 hours and 90 per cent. for 6 days; chloramphenicol 10 mg. *per os* gave 80 per cent. and 60 per cent. survival respectively, only 20 per cent. of the controls surviving. With antigen Vi, 2 mg. of cortisone caused 90 per cent. to survive 48 hours and 70 per cent. 6 days, with 0·25 mg. 1 hour before and 0·25 mg. 16 hours after there were no survivors, with chloramphenicol (10 mg. *per os*) 50 per cent. survived 48 hours and 40 per cent. 6 days. Against diphtheria toxin cortisone had no effect. H. D.

β-Naphthyl-di-2-chloroethylamine (R48); Oral Treatment of Polycythæmia Vera. K. Iversen and E. Meulengracht. (*Brit. med. J.*, 1951, **2**, 510.) 6 patients with polycythæmia vera of several years standing, most of whom had already received other treatment such as X-rays, intravenous nitrogen mustards, or repeated venesection, were treated orally with β-naphthyl-di-2-chloroethylamine in a dosage of 300 to 600 mg. daily. Treatments were given in series, alternating with free intervals, the course of the disease being followed with weekly blood counts; in only 2 patients was it possible to give the drug continuously (200 mg. daily). In 5 out of the 6 cases a marked fall in the percentage of hæmoglobin and red-cell counts occurred, and, parallel with this, a decrease in the redness and a subjective improvement. In one of the patients the remission has lasted for 15 months. The substance is a potential bone-marrow poison and a fall of leucocytes was observed in most cases, and it is essential that patients should be carefully and constantly controlled by blood counts during treatment. Gastro-intestinal symptoms were not observed during these trials. S. L. W.

Noradrenaline and the Suprarenal Medulla. D. M. Shepherd and G. B. West. (*Brit. J. Pharmacol.*, 1951, **6**, 665.) The sympathomimetic amine present in embryonic adrenal glands of cat, rabbit, guinea pig, dog and man is noradrenaline; very small amounts of adrenaline may also be present. Although no evidence has been obtained of the presence of hydroxytyramine and dihydroxyphenylalanine, large amounts of noradrenaline show that this amine must be a precursor of adrenaline in these mammals. Indeed, noradrenaline may itself be the hormone of the gland in the early days of life. It is suggested that in the adult glands the degree of methylation of noradrenaline is related to the relative cortical size. In animals where the cortex is large relative to the medulla, methylation of noradrenaline is almost complete and often only adrenaline is found in gland extracts. When there is little change with age in the ratio of cortical size to medullary size (as in the fowl) there is also little change in the relative amount of noradrenaline in the gland. Animal experiments show that exhausted adrenal glands have only about one-fourth the activity of healthy glands. As the total activity in exhausted adrenal glands of man is about 0·24 mg./g. (31 estimations) this would indicate that a total activity of about 1 mg./g. might be found in healthy individuals. S. L. W.

Procaine Amide for Cardiac Arrhythmias. J. M. Kinsman, W. R. Hansen and R. L. McClendon. (*Amer. J. med. Sci.*, 1951, **222**, 365.) Procaine has a digitalis-like action on the heart but the hydrochloride is rapidly hydrolysed in the blood and is acetylated in the liver so that its effects are of relatively short duration. Procaine amide (pronestyl) is hydrolysed only slowly in the body; it is excreted in the urine, and is not acetylated in the liver. It is readily absorbed from the gastro-intestinal tract and is therefore active when given orally but to secure rapid action intravenous administration is desirable and the authors studied its action in 41 patients with various cardiac arrhythmias when

given by this route. The compound was administered as a 10 per cent. solution at a rate of not more than 200 mg. per minute and usually at half this rate. Doses ranged from 0·5 to 2 g. Arrhythmias of supraventricular origin except auricular ectopic contractions and paroxysmal auricular fibrillation were not affected. Ventricular ectopic contractions were abolished in 12 out of 14 patients and ventricular tachycardia was abruptly stopped in 2 out of 4. Subjective toxic effects were rare but objective toxic effects were frequent; they included a fall in peripheral blood pressure and in pulmonary arterial pressure, a decrease in cardiac output and an increase in circulation time and in intraventricular conduction time. The authors conclude that the intravenous route should be reserved chiefly for patients with paroxysmal rapid heart action who are in immediate danger of death, and for patients under anæsthesia.

H. T. B.

Quinidine, Effects of Parenteral Administration of. H. Blinder, J. Burstein, W. Horowitz, E. Gersh, and R. Smelin. (*Arch. intern. Med.*, 1950, **36**, 917.) The authors studied the effects of a stable injection solution of quinidine lactate administered parenterally to 59 subjects divided into three groups. 22 had normal hearts, 15 abnormal (with regular sinus rhythm) and 22 with cardiac arrhythmias. The effects of the quinidine lactate were assessed by electrocardiogram. Special note was made of toxic effects. It was first given intravenously in a dosage of 0·65 g. The toxic effects encountered when given by this route make its therapeutic use dangerous, and after a limited trial its use was discontinued. Toxicity is directly related to speed of injection when quinidine is given intravenously. Intramuscularly, quinidine lactate (0·65 g.) is relatively painless and no more toxic than quinidine orally in similar dosage. This route of administration has the added advantages of providing more rapid and uniform absorption and of obviating possible gastric intolerance to the drug. In subjects with a normal sinus rhythm maximal cardiac effect is attained in about 30 minutes. The duration of peak effect is between 2 and 4 hours in subjects with normal hearts and at least 6 hours in those with abnormal hearts. A small but significant quinidine effect persists for at least 24 hours. The following dosage schedule is recommended for intramuscular injection: when rapid therapeutic effect is important, hourly administration; when a speedy response is not required, 3 to 4 hourly injections. G. R. B.

Streptomycin, Interference of Aureomycin, Chloramphenicol and Terramycin with the Action of. E. Jawetz, J. B. Gunnison and R. S. Speck. (*Amer. J. med. Sci.*, 1951, **222**, 404.) The authors find that each of the antibiotics aureomycin, chloramphenicol and terramycin reduces the bactericidal action of streptomycin *in vitro*, the effect being most marked during the first 12 hours of incubation. The antagonism is most pronounced with bacteriostatic concentrations; with concentrations which are themselves bactericidal the effect is much less. Chloramphenicol exhibits greater antagonism than an equal weight of either of the other two antibiotics. Chloramphenicol did not affect the activity of streptomycin on a suspension of *Klebsiella pneumoniæ* in Ringer's solution, in which no multiplication of the organism was taking place. The same effects were demonstrable in experimental infections in mice. The interference was observed only with organisms sensitive to streptomycin; with a strain of bacterium resistant to streptomycin, terramycin may have a synergistic action. With aureomycin and terramycin the antagonism is relatively slight and therefore may not be significant clinically but this may not be true of chloramphenicol. H. T. B.