ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

p-Aminosalicylic Acid Solutions, Assay and Stability of. A. Ågren. (*Farm. Revy*, 1955, **54**, 225.) The violet colour given by *p*-aminosalicylic acid with ferric salts in acid solutions may be used for colorimetric determination, as the reaction is not affected by the presence of *m*-aminophenol. The solution, containing about 0·5 mg. of the compound, is treated with 1·00 ml. of ferric chloride solution (M/60 in 0·09N hydrochloric acid) and 0·50 ml. of 0·1N hydrochloric acid. The solution is made up to 100 ml., and the extinction is determined at 500 mμ. The colour does not fade rapidly, losing only 2 per cent. in intensity after 4 hours. Aqueous solutions of *p*-aminosalicylic acid are stable at ordinary temperature if the *p*H is not less than 6·0. At *p*H = 5·0 about 50 per cent. is decomposed after 10 weeks; and at *p*H 4·0 in about 10 days.

G. M.

Calcium and Magnesium, Spectrophotometric Determination of. A. Young, T. R. Sweet, and B. B. Baker. (*Analyt. Chem.*, 1955, **27**, 356.) A method for the determination of small quantities of calcium and magnesium in water has been developed, depending on the relative light absorption of the Eriochrome Black T complexes at *p*H 9·5 and 11·7. Measurement of a dye blank against a solution containing calcium and magnesium at *p*H 11·7 gives a reading which is proportional to the total calcium and magnesium present, while at *p*H 9·5 the reading is essentially a measure of the magnesium. The light absorption was measured at 630 mμ; as the blank absorbs more light at 630 mμ than the sample, the instrument was balanced with the sample in the light path the absorption of the blank then being determined. For 43 known mixtures containing 0·3 to 6·0 p.p.m. calcium (as $CaCO_3$) the average absolute error of magnesium was 0·09 p.p.m. and of calcium 0·12 p.p.m. R. E. S.

Cantharidine in Cantharides, Determination of. C. G. van Arkel and M. Meyst. (*Pharm. Weekbl.*, 1955, **90**, 38.) A comparative study was made of 5 methods for the assay of cantharides. The following procedure is recommended (based on that of the Veterinary Addendum of the Danish Pharmacopœia). 15 g. of the material (in no. 20 powder) is allowed to stand overnight with 148·5 g. of chloroform and 2 ml. of hydrochloric acid, and then shaken for a couple of hours. After filtering, 10 g. of the filtrate is concentrated to a few ml., then dried by a current of dry air at 50 to 55° C. The residue is refluxed for 5 minutes with 100 ml. of water, and the solution is filtered through a wet filter. The filter paper (9 cm. diameter) is extracted with a further 50 ml. of boiling water, which is again filtered through a wet paper, which is finally washed with 50 ml. of boiling water. The combined aqueous solutions are acidified with 2 ml. of hydrochloric acid and shaken out 3 times with 25 ml. of chloroform. The chloroform is removed as described above, and the residue is treated with 5 ml. of a mixture of 9·5 ml. of light petroleum and 0·5 ml. of absolute ethanol, with shaking for 30 minutes. The solution is decanted through a plug of cotton wool, with two washings with the above mixture, then with 5 ml. of chloroform. The chloroform is removed, the residue is dried for 30 minutes at 60° C. and weighed. A correction of 10 mg. is added to the weight obtained. G. M.

Morphine in Opium, Determination of. A. B. Svendsen and E. D. Aarnes. (*Sci. Pharm.*, 1955, **23**, 18.) The determination of morphine as dinitrophenyl-ether gives high results, as the product contains other alkaloids in addition to colouring matter. These errors may be avoided by using an absorbent in the extraction: 1 g. of the opium is rubbed down with 3 ml. of methanol and 1 ml. of 25 per cent. ammonia, and the mass is then mixed with 15 g. of alumina (Brockmann). The resulting dry mass is packed into a chromatograph tube and eluted with a mixture of 180 ml. of chloroform and 60 ml. of *iso*propanol. Morphine is extracted from the resulting solution by shaking 3 times with 0·1N sodium hydroxide (20 + 15 + 15 ml.). The solution is immediately neutralised with hydrochloric acid, and evaporated to about 25 ml. To this is added 0·25 g. of 4-fluor-1 : 3-dinitrobenzene in 30·0 ml. of acetone and 5 ml. of 25 per cent. ammonia. After standing for 4 hours the precipitated morphine ether is filtered off, washed with 2 ml. of acetone, then twice with 2 ml. of water, and dried for 1 hour at 80° C. The product is only slightly yellow and contains only traces of methoxyl. Comparative trials showed that the results obtained are appreciably lower than those by the Mannich method, and compare well with those of the lime method of the Swiss Pharmacopœia. G. M.

Piperazine, Assay of, by Titration of the Monoperiodate. A. Wickström and A. Valseth (*Ann. pharm. franç.*, 1954, **12**, 777.) The rate at which piperazine reduces periodic acid depends on the hydrogen ion concentration of the solution, being a maximum between *p*H 7·5 and 8·0. In solutions containing bicarbonate, 1 molecule of piperazine reduces about 2 molecules of periodic acid in 2 hours, after which the reaction continues more slowly until a further 1 to 1½ molecules are reduced. Two reaction mechanisms seem to be involved, one producing ammonia and formaldehyde and the other ammonia and glyoxal which is further oxidised to formic acid. It is possible to assay piperazine by precipitation as the sparingly soluble monoperiodate, as follows. To 5 ml. of solution containing 15 to 40 mg. of anhydrous piperazine in ethanol (95 per cent.) add 5 ml. of ether and 1 ml. of 0·4 M hexamine in ethanol. Precipitate the salt by the addition of 0·5 M periodic acid, allow to stand for 10 minutes at 10° C., filter through sintered glass and wash the precipitate with 4 quantities of 3 ml. of a mixture of equal volumes of ethanol (95 per cent.) and ether. Dissolve the precipitate in 10 ml. of sulphuric acid (10 per cent.), dilute to 100 ml., add 10 ml. of potassium iodide solution (10 per cent.), allow to stand for 5 minutes and titrate the liberated iodine with sodium thiosulphate. Hexamine prevents the formation of diperiodate under the conditions described and counteracts the solubilising effect of any excess of periodic acid on the monoperiodate. G. B.

Protoveratrine, Methods for the Determination of. E. W. Grant and E. E. Kennedy (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 129.) The total quantity of protoveratrine in a mixture of protoveratrines may be determined by dissolving the alkaloids in 0·02 N sulphuric acid and titrating with sodium hydroxide using bromocresol green as indicator. Alternatively, titration with perchloric acid in a non-aqueous medium may be used. The intensity of the infra-red absorption band at 5·8μ due to the carbonyl linkage may also be used for the quantitative determination of protoveratrines. The proportion of protoveratrines A and B in mixtures of the alkaloids may be calculated from the ratio of the absorption coefficients at 8·52 and 8·68μ or 9·18 and 9·60μ. The accuracy of the determination is affected by the presence of other alkaloids or impurities. A method of analysis which is not affected by the presence of other veratrum alkaloids depends on the separation of protoveratrines A and B by paper

chromatography, using benzene saturated with formamide as the developing solvent. Protoveratrine A travels with the solvent, while protoveratrine B remains almost stationary. The position of the alkaloids is marked on a guide strip by the application of Dragendorf's reagent, and the appropriate portions of the other strips are extracted with ethanol, the residue after evaporation being treated with sulphuric acid. The colour is measured at 540 mμ after 18 hours, and the content of protoveratrines A and B is calculated with reference to standard solutions, similarly treated. G. B.

Quinine, Alkalimetric Determination of. W. Poethke and D. Horn. (*Pharm. Zentralh.*, 1954, **95**, 414.) Quinine affects the colour of certain indicators such as bromocresol purple and chlorophenol red, and it is therefore necessary with such indicators to titrate against an artificial comparison solution. In the case of a mixed bromocresol green-chlorphenol red indicator a suitable standard (when the end-point occurs in 20 per cent. ethanol) is an ammoniacal solution containing 2 mg. of copper and 0·1 mg. of chromium (as chromate) in 50 ml. Methyl red is unsuitable for quinine in aqueous solutions, but quite useable in ethanolic; in the latter case the end-point is sharpened by the addition of methylene blue. This mixture is especially suitable for the titration of slightly coloured solutions such as may be obtained in alkaloidal assays. G. M.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

***p*-Aminosalicylic Acid, Metabolism of, in Man.** E. L. Way, C.-T. Peng, N. Allawala and T. C. Daniels. (*J. Amer. pharm. Ass., Sci., Ed.*, 1955, **44**, 65). Studies were carried out in 5 subjects, 3 of whom received *p*-aminosalicylic acid for 1 day only and 2 over prolonged periods. Urine samples were examined for content of free and conjugated amine, and the metabolites produced from *p*-aminosalicylic acid were isolated by paper chromatography, using dioxan: water (5:1) or butanol:ethanol:3N ammonium hydroxide (4:1:5) as solvent. Ehrlich reagent was used for the detection of free amines and ferric nitrate solution (1 per cent.) for phenols. Metabolites were also isolated by the countercurrent distribution technique using 2M acetate buffer and *iso*amyl alcohol. The following were isolated: *p*-aminosalicylic acid (14–33 per cent. of the dose administered), acetyl *p*-aminosalicylic acid (28–63 per cent.), *p*-aminosalicyluric acid (0–26 per cent.) and a small proportion of *m*-aminophenol. Traces of 4 other substances were detected. G. B.

Urethane, Tumour-initiating Action of, and its Inhibition by Purine Precursors. F. J. C. Roe. (*Nature, Lond.*, 1955, **175**, 636.) Experiments are described which were undertaken with the object of confirming the hypothesis that urethane competes with one or more of the precursors in purine synthesis with the formation of unphysiological purine-like substances. Glycine and formate as known purine precursors were supplied in high concentration both separately and together, with urethane to groups each of 20 to 30 male mice of stock albino strain. Glycine and sodium formate were given in drinking water during the first 11 days and urethane was applied directly to the skin on the 4th and 7th days. This was followed in each case by 18 weekly applications of croton oil starting on the 22nd day. Large numbers of tumours appeared in that group in which urethane was administered without sodium formate or glycine. Tumour incidence was not significantly different in the groups in which either glycine or sodium formate were administered with urethane. Only a few tumours appeared

in the group of mice treated with both sodium formate and glycine, as well as urethane. J. B. S.

BIOCHEMICAL ANALYSIS

Azovan Blue in Plasma, Estimation of. G. A. Bedwell, J. Patterson and J. Swale. (*J. clin. Path.*, 1955, **8**, 61.) A chromatographic method is described for the estimation of azovan (Evans) blue in plasma, which is not invalidated by the presence of opalescence or hæmolysis. A 10 ml. venous sample of blood is obtained exactly 10 minutes after the intravenous injection of 20 ml. of a 0·1 per cent. solution of the dye. The packed cell volume is determined by Wintrobe's method and the remainder of the dyed sample is centrifuged for 15 minutes. To 4 ml. of the dye-plasma 2 ml. of a dilute teepol solution is added, the mixture is warmed to 50° C. for 10 minutes and transferred to a column of degraded amorphous cellulose. The dye separates as a narrow band on the surface of the column and is eluted with aqueous acetone. The eluate is collected and the intensity of colour determined in a Spekker absorptiometer against a blank of aqueous acetone. The concentration of the dye is estimated from a standard calibration curve. Consistent recoveries of 97 per cent. were obtained and the analyses were not affected by the presence opalescence or hæmolysis. G. F. S.

Cobalt in Biological Materials, Microdetermination of. B. E. Saltzman. (*Analyt. Chem.*, 1955, **27**, 284.) A method is given in which the cobalt compound of 1-nitroso-2-naphthol is formed at *p*H 3 to 4 in aqueous solution and is extracted by shaking with chloroform. Poor recovery was obtained at lower *p*H values; the chloroform extract was purified by shaking with dilute hydrochloric acid to decompose any copper complex and to remove entrained salts. After evaporation of the chloroform extract the residue is ashed by heating with nitric acid and sodium sulphate. The final determination is made by a nitroso R salt method which has been improved to give reliable results and very close adherence to Beer's law. Analyses using the method given showed a 95 per cent. recovery on microgram quantities of cobalt added to 25 g. samples of bone. The cobalt content of normal tissues ranged from 0·03 μg. per g. (rabbit bone) to 0·11 μg. per g. (rabbit kidney). R. E. S.

Hypertensin, Preparation and Assay of. W. S. Peart. (*Biochem*, J., 1955, **59**, 300.) The rapid concentration of hypertensin was achieved by adsorption on to charcoal from serum and subsequent elution by glacial acetic acid; the hypertensinase activity of the serum did not affect the yield. The method involved a preliminary treatment of the serum with charcoal, followed by incubation with renin in the presence of more charcoal, the hypertensin then being eluted from the charcoal with acetic acid. Large quantities of the hypertensin could be prepared by this method, the yield in terms of (—)-noradrenaline being 0·5 to 1·0 mg./l. of serum and the dry weight of material in the acetic acid eluate 100 to 200 mg./l. The yield was assayed by the pressor response produced in the anæsthetised rat (urethane 100 mg./kg. intraperitoneally); the blood pressure was lowed by pentapyrollidinium tartrate in polyvidone solution (2·5 mg./100 g. subcutaneously). Comparisons were made with stock solutions of hypertensin and with (—)-noradrenaline; details of the assay method are given. R. E. S.

Pepsin in Gastric Juice, Estimation of. A. W. Williams. (*J. clin. Path.*, 1955, **8**, 85.) A simple method is described enabling the determination of low concentrations of pepsin in gastric juice to be made, and through dilution the

removal of pepsin inhibitors. The method is based on the conversion by pepsin of edestin to edeston which does not become opalescent when mixed with a saturated solution of sodium chloride. To 1·0 ml. of stock edestin solution add 1·8 ml. of 0·1 N hydrochloric acid and 0·2 ml. of gastric juice. Incubate at 37° C. and at intervals of 2 minutes remove a few drops of the mixture into a saturated solution of sodium chloride. Digestion is complete when there is no further opalescence (usually 10 to 15 minutes). The time taken is compared with that for a standard solution of pepsin treated in the same way. G. F. S.

Pepsinogen (Uropepsin) in Urine, Determination of. M. B. Jørgensen. (*Scand. J. clin. Lab. Invest.*, 1954, **6**, 303.) A method for the quantitative determination of urinary pepsinogen is described, in which hæmoglobin is used as a substrate. 15 ml. of urine is dialysed against distilled water in cellophane tubes for 4 hours. The sample is then quantitatively transferred to a 20 ml. flask and the volume made up to 20 ml. with water. 1 ml. of this dilution is incubated for 30 minutes at 37° C. with 2 ml. of a hæmoglobin substrate and the reaction is then stopped by the addition of 10 ml. of 0·3 N trichloroacetic acid. The amount of aromatic amino-acids is determined in the filtrate, after filtration through Whatman No. 50 filter paper, by reading the extinction coefficient against 0·3 N trichloroacetic acid at 2750 Å. The results are read from a standard calibration curve for known dilutions of L-tyrosine in 0·1 N hydrochloric acid. Blank determinations are run alongside. The pepsinogen activity is expressed as mg. tyrosine liberated (1 mg. tyrosine is equal to approximately 10 μg. of Armour crystalline pepsin). In 70 routine determinations (in duplicate) the mean pepsinogen was equivalent to 0·354 mg. of tyrosine, with a standard deviation of 0·023. G. F. S.

CHEMOTHERAPY

***N*-Bis(β-chloroethyl)amino-acids and Related Compounds as Tumour Growth-retarding Agents.** M. Ishidate, Y. Sakurai and M. Izumi (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 132.) The nitrogen mustard derivatives *N*-bis(β-chloroethyl)glycine and -alanine were prepared by acid hydrolysis of the corresponding *N*-bis(β-chloroethyl)alkyl cyanides, obtained by the simultaneous condensation of bis(β-chloroethyl)amine with the hydroxyalkyl sulphonate and sodium cyanide. *N*-Bis(β-chloroethyl)taurine was made by the alkylation of taurine with ethylene oxide and chlorination with thionyl chloride. The compounds were more hydrophilic and less toxic than the aliphatic nitrogen mustards, and had no vesicant action on the skin. When the free carboxyl group was converted into an ester or an amide, toxic compounds were produced. The minimum effective dose against ascite sarcoma cells was about the same as for nitrogen mustard. The activity of the *N*-oxide derivatives of these compounds was lower than that of the parent substance. In neutral aqueous solution the *N*-oxides were found to undergo gradual transformation into hydroxylamine derivatives. G. B.

Cycloserine, Antibacterial Activity and Blood and Urine Concentrations of. H. Welch, L. E. Putnam and W. A. Randall. (*Antibiotic Med.*, 1955, **1**, 72.) Cycloserine is the generic name for a new antibiotic produced by *Streptomyces orchidaceus*. It is a water-soluble product of relatively low molecular weight and appears to differ in its mode of action from other known antibiotics. It has a wide but relatively low antibacterial activity. *In vitro* studies on 117 strains of

organisms representing 15 genera (gram-positive and gram-negative) showed this activity to be not significantly different among the genera tested. This lack of selective activity may indicate that the antibiotic exerts its inhibitory effect by interfering with a component of an enzyme system or essential metabolite common to all the bacteria tested. Its acute or chronic toxicity in mice, rats, dogs and monkeys is low and not unlike that observed with penicillin. With doses of from 1 to 4 g. daily by mouth, blood and urine concentrations are higher than those obtained with other antibiotics. The percentage of drug excreted in urine with a given dose is apparently higher than that seen with the broad spectrum antibiotics. The drug has been found effective in certain difficult urinary infections caused by organisms whose *in vitro* resistances are considerably higher than the concentration of the antibiotic obtained in the blood. Its effectiveness in these infections and in preliminary trials in pulmonary tuberculosis, in spite of its ineffectiveness in mouse tuberculosis, warrants further laboratory and clinical studies. S. L. W.

PHARMACY

NOTES AND FORMULÆ

Methacholine Iodide and Succinylcholine Iodide in Solution, Stability of. L.-E. Tammelin and L. Larsson. (*Svensk farm. Tidskr.*, 1955, **9**, 229.) A theoretical treatment is made of the previous work of Larsson (*Acta chem. scand.*, 1954, **8**, 1017) and Tammelin (*Acta chem. scand.*, 1953, **7**, 185) on the hydrolysis of choline esters. The *p*H values at which the lowest rate of hydrolysis occurs were 4·2 for acetyl-β-methylcholine iodide and 3·6 for succinylcholine iodide; at these minimum hydrolysis *p*H values the times for 10 per cent. hydrolysis at 25° C. for both esters was 2 years. A stabilised solution could be prepared by dissolving the appropriate ester in 5 per cent. glucose solution and adjusting the *p*H to the minimum hydrolysis value. R. E. S.

Folic Acid in Liquid Pharmaceutical Preparations, Stabilization of. R. P. Tansey and G. H. Schneller. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 34.) Solutions of folic acid with riboflavine, *p*H 4·5 to 5·5 were investigated. The solutions contained propylene glycol as a solubiliser for folic acid, and methyl and propyl *p*-hydroxybenzoate to prevent the growth of moulds. Stabilisers were added and the content of *p*-aminobenzoylglutamic acid (the decomposition product of folic acid) determined at intervals by diazotisation and coupling with Bratton and Marshall reagent. The total folic acid (free and decomposed) was determined similarly after treatment with zinc amalgam. When solutions were stored in diffused daylight in bottles of amber glass, 0·02 per cent. of nordihydroguaiaretic acid or 0·05 per cent. of butylated hydroxyanisole or ethyl hydrocaffeate effectively retarded the decomposition of the folic acid. Propyl gallate and dihydrobenzopyrone were less effective, while sodium formaldehyde sulphoxylate, sodium bisulphite thioglycerol, thiourea, glycine and ascorbyl palmitate had no significant effect. Decomposition was more rapid in solutions kept in direct daylight in flint glass bottles, but the same substances were effective in retarding the decomposition. At higher *p*H levels the protective effect of these substances was less marked. G. B.

Procaine Solutions, Aniline as a Decomposition Product of. E. Zöllner and G. Vastagh. (*Pharm. Zentralh.*, 1955, **94**, 3.) The normal course of decomposition of procaine solutions leads to *p*-aminobenzoic acid. In view

of the possibility of decarboxylation of the latter compound, and of the reported presence of butylaniline in amethocaine solutions, this question was investigated. After 1 hour's heating at 100° C. at *p*H 4·5, no appreciable amount of aniline could be detected, but at *p*H 2 appreciable quantities were formed. Of 60 preparations for injection, 14 were found to contain aniline in quantities of 10 to 120 μg./ml. These were mostly the ones which were the subject of complaints of undesirable side reactions. G. M.

Sorbic Acid as a Fungistatic Agent. D. D. Puls, L. F. Lindgren and F. P. Cosgrove. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 85.) Solutions containing 0·05 to 0·4 per cent. of sorbic and benzoic acids were tested for fungistatic activity against *Aspergillus niger* and an unidentified species of penicillium. Paper discs soaked in the solutions under test were placed on plates of inoculated medium and the zones of inhibition measured after incubation at 30° C. Sorbic was superior to benzoic acid in these tests and appeared to be a satisfactory preservative for mucilages of acacia and tragacanth and for solutions of guar gum and sucrose when stored at 5, 25 and 37° C. for 30 days. G. B.

PHARMACOGNOSY

***Datura stramonium*, Effect of Removing the Flowering Tops on the Alkaloidal Content.** F. H. L. van Os, E. Drijfhout and F. K. Klompsma. (*Pharm. Weekblad*, 1955, **90**, 209.) A significant increase in the alkaloidal content of *D. stramonium* var. *inermis* plants was found as a result of removing the flowering tops during growth. Removal when the plants were about two thirds developed produced better results than when they were mature. The chlorophyll content was also increased by this earlier treatment. The yield of fresh weight was, however, diminished, since the development of many side shoots was prevented. Removal of the flowers also produced an increase in alkaloidal content. This increase was maintained by repeated removal but the ultimate increase was less than that obtained by removing the tops. None of the treatments described had any effect on the ratio of hyoscyamine to hyoscine. J. W. F.

***Mentha* Species, Composition of Essential Oils of.** A. G. Rooth and R. Hegnauer. (*Pharm. Weekbl.*, 1955, **90**, 33.) The composition of a number of oils of *Mentha* species is given in the table below.

Species	Acid value	Ester per cent. as menthyl acetate	Acetylation value	Alcohols per cent. as menthol	Carbonyl compounds percent. as menthone	
					by hydroxyl-amine	by dinitro-phenylhydrazine
M. aquatica ..	7·9	10·2	26·5	7·4	4·9	—
M. verticillata ..	2·6	21·6	24·9	7·0	4·5	5·2
M. longifolia ..	10·2	31·9	73·4	20·5	18·7	21·5
M. niliaca	5·3	4·3	35·1	9·8	72·4	67·0
M. velutina ..	3·2	—	28·6	8·0	—	66·4
M. rotundifolia ..	11·0	22·3	84·1	23·5	20·5	32·6
M. spicata	6·0	25·5	41·7	11·7	62·5	63·7
M. dalmatica ..	18·1	—	49·2	13·7	64·9	66·3
M. gentilis	4·7	22·9	40·4	11·3	36·8	39·0

It may be noted that none of the wild and non-hybrid forms give a pharmaceutical oil. It appears that an intensive synthesis of menthol or of carvone results only from the combination of the genes of 2 or 3 species. The interpretation of the course of the biosynthesis of the different terpenes is made very difficult by the great number of different chromosome races which appear to exist. It is known that in practically all *Mentha* species there are both morphological and biochemical varieties. G. M.

PHARMACOLOGY AND THERAPEUTICS

Aldosterone, Anticortisol Action of. H. Selye. (*Science*, 1955, **121**, 368.) The question whether aldosterone is an antagonist of glucocorticoids has been investigated. 96 female rats averaging 160 g. were bilaterally adrenalectomised and then subdivided into 4 groups. Hormone treatment was commenced on the day of adrenalectomy. Cortisol as hydrocortone acetate microcrystals (400 μg. daily in 0·2 ml. of aqueous suspension) was given subcutaneously in the chest region, and aldosterone (20 μg. daily in 0·2 ml. of sesame oil) was injected into the inguinal region. The inflammation produced was quantitatively assessed by preparing granuloma-pouches 48 hours later by injecting 25 ml. of air under the dorsal skin, following this immediately by introducing 0·5 ml. of 1 per cent. croton oil into the air space. 14 days after adrenalectomy the animals were killed. The results showed that aldosterone slightly but significantly diminished the bodyweight loss and also the inhibition of inflammatory-exudate formation, but did not suppress the thymus and spleen. In a second experiment, 36 female rats averaging 160 g. were treated by preparing the pouch on the first day, adrenalectomising and giving the steroids 48 hours later and increasing the dose of aldosterone to 25 μg. twice daily. Cholesterol and deoxycorticosterone were given to controls. All the animals were killed on the 12th day. The dose level of aldosterone was found to inhibit a variety of characteristic cortisol actions, being approximately equally as active as deoxycorticosterone. Thus the concept according to which the balance between two opposing naturally secreted corticoids can regulate the course of various biologic phenomena has been demonstrated. J. R. F.

α-Amino-acids, Mercurated Amides of. W. O. Foye and R. A. Mode. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 76.) A series of *N*-(3-acetoxymercuri-2-methoxypropyl) hippuramides of the general formula shown below were prepared from benzoylated glycine, methionine and phenylalanine.

$$C_6H_5{\cdot}CO{\cdot}NH{\cdot}CHR{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CH(OCH_3){\cdot}CH_2{\cdot}HgOOC{\cdot}CH_3$$

N-Allylhippuramides were prepared by refluxing with allyl *iso*thiocyanate. The mercury derivatives were obtained by reaction between the *N*-allylhippuramides and mercuric acetate in methanol. The compounds were found to exhibit good diuretic activity when administered intravenously to dogs although the leucine and phenylalanine derivatives had only a weak effect. The glycine derivative was effective when administered orally. G. B.

Butylamine, Substituted, Hypotensive Properties of. R. Charlier, M. J. Dallemagne and E. Philippot. (*Arch. int. Pharmacodyn.*, 1954, **100**, 127). The meriquinone of 4-(4′-oxyphenyl)-4-(3″-methyl-4″-oxyphenyl)-butylamine-2 and 4′: 4-dehydro-4 (4′-oxyphenyl)-4 (3″-methyl-4″oxyphenyl) butylamine-2 (designated L 1935), when injected intravenously into dogs caused a sharp, prolonged fall in blood pressure, which was in the main due to histamine release. That other factors were also concerned in the vasodepressor action was demonstrated by the drug's being effective after oral administration; also the fall was never entirely blocked by antihistamines. In addition, L 1935 had a direct vasodilator action, blocked transmission through the superior cervical and vagal ganglia, and blocked the vasopressor effects of bilateral carotid occlusion and of injections of lobeline and of acetylcholine after atropine. Sometimes the ganglia were stimulated before being blocked. Like other hypotensive

agents, L 1935 decreased the cardiac output. The drug also decreased the neuromuscular blocking activity of decamethonium, while being itself almost without blocking activity. On the isolated frog rectus abdominis muscle L 1935 caused a slow contracture and antagonised the action of acetylcholine, but not that of potassium chloride. G. P.

Carbimazole in Thyrotoxicosis. K. Kirkeby and O. Rømcke. (*Lancet*, 1955, **268**, 374.) Carbimazole differs from methimazole in the replacement of the hydrogen of the sulphydryl group by a carbethoxy group and it was hoped that, in addition to being tasteless, the drug would give a more constant supply of active methimazole to the thyroid gland. The drug has been given to 56 patients with thyrotoxicosis, in 29 of whom the diagnosis was recent; the remainder had relapsed after operation or treatment with other substances. Initial dosage was 30 to 50 mg. daily; 40 mg. is probably the optimal dosage in most cases, producing an average fall of 0·9 per cent. per day in the basal metabolic rate. In most cases a normal B.M.R. was produced in 3 to 12 weeks; 4 cases needed 3 to 5 months, the delay probably being due to low initial dosage. In nearly all patients a rapid subjective improvement occurred, with disappearance of nervousness and palpitations, gain in weight and a rise in serum cholesterol. The only side effect was the appearance of a rash in 1 patient necessitating discontinuance of treatment. Goitrogenic reactions occurred in 4 patients but disappeared during continued treatment. Although the dosage by weight is about the same as that of methimazole, the difference in molecular weight due to the carbethoxy group results in the amount of active substance in a given dose being much less than in the same weight of methimazole and this probably accounts for the lowered incidence of side effects. H. T. B.

Carbonic Anhydrase Inhibitors and Antacids, Effect of, on the Development of Gastrointestinal Ulcers during Treatment with Depot-Histamine. J. W. E. Harrisson, E. W. Packman, P. S. Guth, N. Back and W. S. Chernick. (*J. Amer. pharm. Ass., Sci. Ed.*, 1955, **44**, 123.) Guinea-pigs were treated with diphenhydramine and injection of histamine diphosphate in a mixture of oil and beeswax. This treatment generally produced gastro-intestinal ulceration within 24 hours. A series of antacids was administered orally, twice daily, to the animals in the form of aqueous suspensions. Dihydroxyaluminium sodium carbonate was the most effective in the prevention of ulceration, followed by dihydroxyaluminium aminoacetate, calcium carbonate and sodium carbonate. The carbonic anhydrase inhibitors Diamox (2-acetylamino-1 : 3 : 4-thiadiazole-5-sulphonamide and Dirnate (*p*-carboxybenzenesulphonamide), administered by subcutaneous injection did not inhibit ulceration. G. B.

Chlorpromazine as a Therapeutic Agent. J. H. Moyer, V. Kinross-Wright and R. M. Finney. (*Arch. intern. Med.*, 1955, **95**, 202.) Chlorpromazine was employed in the treatment of 412 unselected patients suffering from neuro-psychiatric disorders; 217 were out-patients with neuroses and other minor emotional disorders, and 195 were psychotic patients. The ambulatory patients were given 5 to 50 mg. of chlorpromazine 3 or 4 times daily by mouth (after meals). Treatment in the psychotic patients was initiated with 50 mg. intramuscularly every 4 to 6 hours, the dose being doubled after 24 hours; by the 3rd or 4th day the route of administration was gradually changed from intramuscular to oral, and the dose increased daily by 200 mg. until improvement in the basic illness was observed. The usual maximum dose in these patients ranged between 1000 and 1600 mg. per day; the maximum dose was continued for a week or ten days and gradually reduced to a maintenance level. In the group of ambulatory patients excellent results (total remission or relief of

symptoms) were obtained in 135; good results in 61, and poor in 21. In the psychotic patients remission was obtained in 96, improvement occurred in 92, and 17 remained unchanged. A further series of 338 patients suffering from nausea and vomiting due to various causes (including a wide range of drugs) were treated with chlorpromazine in doses of 10, 25 or 50 mg., orally or intramuscularly, at varying intervals as needed to control symptoms. Excellent results (complete cessation of vomiting and relief of nausea) were obtained in 243 of the patients, good or fair results in 81, and poor results in 28. The nausea and vomiting of pregnancy responded very well. 55 out of 78 patients obtained complete relief and only 4 were complete failures. During the course of these studies 10 patients with persistent and intractable hiccoughs were given chlorpromazine. In 6 of the patients hiccoughs were arrested within 20 minutes of an intramuscular injection of 25 mg. of chlorpromazine; two required a second dose, and two did not respond. Among the side-effects noted was dermatitis (27 cases), confusion, with disorientation (4 cases), and Parkinsonian syndrome (14 cases). S. L. W.

Codeine and Morphine, the Action of, on Cardiac Arrhythmias. A. Leimdorfer. (*Arch. int. Pharmacodyn.*, 1955, **100**, 333.) Experiments in dogs, under light pentobarbitone or thiopentone anæsthesia, have shown that codeine and morphine can prevent the appearance of cardiac arrhythmias provoked by adrenaline or (—)-noradrenaline. Ventricular extrasystoles were induced by intravenous injections of 0·005 to 0·014 mg./kg. of adrenaline or 0·002 to 0·007 mg./kg. of noradrenaline. The dose of codeine phosphate was 1–2 mg./kg. and of morphine sulphate 2·5 to 4 mg./kg., both being given in four equally divided doses. The results obtained were in agreement with the clinical reports of the disappearance of ventricular extrasystoles after oral administration of codeine and the successful treatment of paroxysmal ventricular tachycardia with small intravenous injections of morphine. G. F. S.

Cycloserine in the Treatment of Pulmonary Tuberculosis. I. G. Epstein, K. G. S. Nair and L. J. Boyd. (*Antibiotic Med.*, 1955, **1**, 80.) This is a preliminary report on the treatment with cycloserine of two groups of patients suffering with pulmonary tuberculosis. In one group of 8 patients, only recent infection was present and the patients had not received any prior antimicrobial therapy. A second group of 29 patients presented active, far-advanced pulmonary tuberculosis of long duration; all had been in hospital for at least a year and had been under intensive treatment with streptomycin, isoniazid and *p*-aminosalicylic acid, to all of which they were clinically and bacteriologically resistant. The cycloserine was administered orally, in capsules containing 250 mg., in doses of from 1 to 1·5 g. daily, for from 6 weeks to 4 months. In all of the acute cases there was a rapid and marked clinical response, with a temperature return to normal and disappearance of cough and expectoration; within 8 weeks sputum and gastric washings became negative and there was marked roentgenographic improvement. In the 29 chronic patients, clinical improvement occurred in all but one, and roentgenographic improvement in 20. Up to the present, sputum concentrate determinations show conversion in 76 per cent. of the patients, and, in cases with a negative sputum, gastric washings showed 85 per cent. free from tubercle bacilli. Cycloserine was well tolerated and there was a low incidence of side-reactions. On the basis of neurologic symptoms it was necessary to discontinue treatment in 4 of the patients; no other toxic manifestations were observed. The authors conclude that although the study has not progressed sufficiently to allow judgment as to the relative efficacy of cycloserine as compared with streptomycin and isoniazid, the data

available are sufficient to indicate that cycloserine is a potent antituberculosis antibiotic. S. L. W.

Pentolinium Tartrate Combined with Rauwolfia in Hypertension. C. W. C. Bain, F. Ashton and B. P. Jones. (*Brit. med. J.*, 1955, **1**, 817.) This is a report on a series of 17 cases in which stabilisation had been achieved on pentolinium tartrate (Ansolysen) alone and which were later restabilised on that drug with the addition of rauwolfia alkaloids (Rauwiloid), 4 mg. daily, taken in a single dose each evening. All the patients had essential hypertension. Their blood pressure before treatment varied from 300/160 to 240/130. None had evidence of renal involvement. The average dose of pentolinium tartrate when given alone was 840 mg. a day. The average daily dose of that drug when combined with rauwolfia alkaloids was 240 mg.; one patient who required 440 mg. a day was restabilised on the combination at 60 mg. a day. The corresponding decrease in the undesirable effects following the use of pentolinium tartrate, e.g., constipation, dry mouth and visual disturbances, was very great, and some patients who had found it impossible to continue with pentolinium tartrate alone are now well stabilised and able to lead active lives. Where formerly postural hypotension was a problem, this has been less evident on the combination. The authors conclude that the combined use of these two drugs seems to offer a promising treatment of hypertension. S. L. W.

Piperazine Derivatives, Effect of, on Intestinal Helminths. T. L. Dunn. (*Lancet*, 1955, **268**, 592.) The drugs diethylcarbazine, piperazine hydrate and piperazine adipate were tested against roundworm and hookworm infestation of children of 1 to 14 years in New South Wales. Tests for ova were made by the salt flotation method. The highest egg counts before treatment were 153,000/g. of fæces for ascaris, 54,000 for necator and 13,000 for tricocephalus. Piperazine adipate (75 mg./kg.) proved the most effective against *A. lumbricoides* and *T. dispar* in 45/47 and 28/31 cases the children being ova-free 2½ weeks after treatment. (Ova in the cases not cured were very scanty). The hydrate (85 mg./kg.) was effective in 20/26 cases and 4/22 cases respectively under the same conditions. Diethylcarbazine (13 mg./kg.) was successful in 12/54 against *A. lumbricoides*. 41 children with *Necator americanus* treated with diethylcarbazine, 28 with piperazine hydrate and 7 with the adipate showed no change in egg counts, and 4 children with *Hymenolepsis nana* treated with the adipate were also unaffected. The hydrate caused most worms to be passed on the second day of treatment, whereas with the adipate evacuation extended to the 3rd and 4th day. No toxic or unpleasant side reactions occurred with either the hydrate or the adipate. Contrary to manufacturers' directions a single daily dose was given and no aperient. It is suggested that factors such as food intake may have affected the results. J. R. F.

Reserpine in Hypertension. I. Singh. (*Brit. med. J.*, 1955, **1**, 813.) Twenty-three cases of hypertension were treated with reserpine; 24 had benign hypertension, 2 had malignant hypertension, 1 was associated with chronic nephritis, 2 with arteriosterosis, and 3 with anxiety state. All had been under care for periods varying from 2 months to 7 years. Fifteen patients whose basal systolic blood pressure at the time of treatment was above 200 mm. Hg. were treated with reserpine 1·5 mg. daily; 18 patients whose pressure was below 200 were treated with 0·75 mg. daily. In the former group 2 patients were reduced to below 145/90, 5 below 160/100, 7 below 170/110, and 10 below 185/115. In the latter group 12 patients were reduced to below 145/90 and 18 below 160/100. Lack of adequate response was associated with chronicity of hypertension and myocardial and/or renal failure. Periodic fluctuations up to plus 45/20 mm.

(ABSTRACTS *continued on p. 560.*)