ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Digitalis Glycosides, Colorimetric Estimation of. D. H. E. Tattje. (*Pharm. Weekbl.*, 1958, **93**, 245.) The glycoside or aglycone is dissolved in 4 ml. of ethanol and the solution mixed with 5 ml. of a 0·075 per cent w/v solution of 2:4-dinitrophenylsulphone in ethanol. 1 ml. of 0·15 N aqueous sodium hydroxide is added and the colour measured at 600 mμ, against a reagent blank. When applied to digitoxin and digitoxigenin this test is much more sensitive than the picric acid, 3:5-dinitrobenzoic acid and *m*-dinitrobenzene reactions, but with gitoxigenin the difference is less marked. G. B.

Gentisic Acid, Polarographic Determination of, in Pharmaceutical Preparations. M. Jirka. (*Československ. Farm.*, 1957, **6**, 609.) For the determination of gentisic acid in tablets, a sample is ground and extracted three times with water. The combined extracts are filtered and the filtrate is made up to give a solution containing 0·33 per cent of gentisic acid. To 4·9 ml. of carbonate buffer (pH 8·7) 0·1 ml. of this solution is added and the resulting solution is polarographed in a Heyrovsky polarograph, the oxygen being removed by a stream of nitrogen. The height of the anode wave of gentisic acid is directly proportional to the concentration and the concentration in the test solution can be read from a calibration curve. E. H.

Hormones, Assay of Mixtures of, in Solution in Oil. G. Tappi, E. M. Andreoli and E. Frea. (*Pharm. Weekbl.*, 1958, **93**, 231.) The preparation under test is diluted with light petroleum, passed through a chromatographic column packed with magnesium stearate ('Florisil') and the oil washed through with a mixture of light petroleum 3, chloroform 1. Compounds containing no free hydroxyl or keto-groups (such as esters of certain steroid hormones) are eluted with a mixture of equal volumes of chloroform and light petroleum. Ketones are then removed from the column by elution with pure chloroform, and finally alcohols and phenols with chloroform-methanol. The various fractions may be assayed by colorimetric or ultra-violet absorption methods. Details are given of the analysis of a typical preparation, in which a recovery of 94–97 per cent of each hormone may be attained. G. B.

Oestrogens, Bis-phenolic, Belonging to the Stilbene Series, Potentiometric Titration of. K. Backe-Hansen and A. Wickstrøm. (*Medd. Norsk farm. Sels.*, 1957, **19**, 193.) Dienoestrol, hexoestrol and stilboestrol were titrated quantitatively with potassium methoxide in benzene-methanol solution. The end point was determined potentiometrically, and the three compounds behaved as dibasic acids under these conditions. A colorimetric determination of the end point, using azo violet as indicator was satisfactory for dienoestrol. Using 0·1 N tetrabutylammonium hydroxide in place of potassium methoxide, the titrations could be carried out in the same manner, and dienoestrol and hexoestrol could be titrated as monobasic acids in pyridine or acetone. This method was not successful for stilboestrol which behaves under these conditions as a much weaker acid, presumably owing to resonance of the symmetrical conjugated benzene-ethylene-benzene structure. G. B.

Opium Alkaloids, Identification of Natural, and Synthetic Derivatives of, by "Test-tube" Chromatography. R. Fischer and N. Otterbeck. (*Sci. Pharm.*, 1957, **25**, 242.) In "test-tube" chromatography, strips of filter paper are suspended in tubes about 25 cm. long and 1·8 cm. bore. One drop of a chloroform solution of the alkaloidal bases is placed about 1·5 cm. from the bottom edge of the paper, the chloroform allowed to dry, and the paper immersed to a depth of 1 cm. in the solvent. After the solvent has climbed to within 2 cm. of the top edge of the paper strip, the latter is dried. Temperature control is important. The advantage of the technique is that many chromatograms can be run simultaneously, and the experiment is complete in 3 to 4 hours. Using this technique it was possible to identify 19 analgesics (morphine derivatives, opium alkaloids and synthetic substances) by the differences in their R_F values by the simultaneous running of four different solvent mixtures. The only ones which could not be distinguished were codeine and eucodal, for which a suitable microchemical reaction is quoted. D. B. C.

Parathion, Spectrophotometric Determination of. H. Kita, H. Maeda, B. Hanazaki, M. Kawai and T. Takazawa. (*Bull. Tokio Med. and Dental Univ.*, 1957, **4**, 379.) A simple method is described for the determination of parathion in water. Neutralise the solution with dilute hydrochloric acid if alkaline and extract 20 ml. by shaking with an equal volume of benzene for five minutes. Weak solutions are first concentrated. The optical density is measured at 2800 Å in a spectrophotometer and the parathion content determined by reference to a standard curve prepared as follows. Weigh 0·100 g. of parathion, dissolve in 500 ml. of benzene. Take 25 ml. of this solution and make up to 250 ml. with benzene. This solution contains 20 μg./ml. of parathion. Take 0·5, 1, 2, 3, 4 and 5 ml. and dilute to 10 ml. and measure the optical density as before. G. F. S.

Phenothiazine Derivatives, Separation of. A. Calò, A. Mariani and O. M. Marelli. (*Pharm. Acta Helvet.*, 1958, **33**, 126.) The properties of promazine are compared with those of its chlorine analogue chlorpromazine, with a view to finding a method of separation. This latter shows a higher mobility in iontophoresis, and is more sensitive to oxidation with iodic acid giving a more intense colour. The behaviour of promazine is similar to that of other derivatives of phenothiazine without the chlorine in the molecule. D. B. C.

Purine Derivatives, Non-aqueous Titration of. B. Salvesen. (*Medd. Norsk farm. Sels.*, 1957, **19**, 199.) Mixtures of caffeine with sodium benzoate or sodium salicylate may be titrated with perchloric acid in acetic acid solution. The most accurate results are obtained when acetic anhydride in excess of that required to remove water is added. The sample is dissolved in 2–5 ml. of glacial acetic acid, and mixed with acetic anhydride alone or with twice its volume of benzene, before titration. The first end point is detected by the use of 4 drops of a saturated solution of tropeoline OO, and corresponds to the neutralisation of the sodium benzoate or salicylate. On adding 8 drops of methyl violet and continuing the titration, the end point corresponding to neutralisation of caffeine is obtained. Mixtures of caffeine with diphenhydramine hydrochloride may be analysed in the same manner, using 5 ml. of a 5 per cent solution of mercuric acetate in glacial acetic acid, in place of the acid alone. G. B.

Reserpine, Ajmaline and Serpentine, Determination of, in Mixtures. F. Machovičová, V. Parrák, O. Lišková and J. Ružičková. (*Československ. Farm.*, 1957, **6**, 584.) Reserpine, serpentine and ajmaline are separated by chromatography on Whatman No. 1 paper impregnated with formamide-methanol (1:1). R_F values are given for the three alkaloids with chloroform and chloroform-benzene (4:1 and 1:1) as mobile phases. The spots are detected by observing the paper in ultra-violet light; the intensity of fluorescence can be increased by exposing the paper to hydrochloric acid vapour and then immersing it in 3 per cent hydrogen peroxide. Reserpine and ajmaline are quantitatively eluted from the paper with chloroform, and serpentine with methanol. The alkaloids in the eluates are estimated colorimetrically by a method based on the formation of addition compounds between the alkaloids and methyl orange. The intensity of the colour produced is measured in a Hilger absorptiometer with filters 604 and H503. E. H.

Strychnine and Brucine, Determination in the Seeds, Tincture and Extract of Strychnos. R. Fischer and S. Gharbo. (*Pharm. Zentralh.*, 1958, **97**, 101.) This determination depends upon chromatographic separation of strychnine and brucine and titrimetric estimation. It was found that when both alkaloids were adsorbed on alumina containing 5 per cent water, the strychnine could be eluted with trichlorethylene containing 0·5 per cent acetone leaving the brucine behind. It was found best to pass the strychnine eluate through another column containing dry, neutral alumina; both columns could then be eluted with methanol and the alkaloids titrated in the usual way. The extract of the powdered drug was prepared by rubbing the drug down with ammonia or caustic soda solution and dry sodium sulphate, packing in a Soxhlet extractor over a layer of alumina and extracting with chloroform for two hours. The tincture was purified by passing it through a short alumina column, eluting with methanol and evaporating, and taking up in trichlorethylene. Elution in this case was done with tetrachlorethylene containing 1 per cent acetone. The extract was diluted with ethanol and treated similarly to the tincture. The accuracy of the method was checked in each case by adding known quantities of pure alkaloids to the assayed galenical preparations and reassaying. D. B. C.

Thymol in Thyme Oil, Colorimetric Determination of. L. Fibranz, M. I. Blake and C. E. Miller. (*J. Amer. pharm. Ass., Sci. Ed.*, 1958, **47**, 133.) A colour reaction with *p*-dimethylaminobenzaldehyde was found to be suitable for the rapid determination of thymol in thyme oil. The U.S.P. reagent did not give reproducible results, but a 0·125 per cent solution in concentrated sulphuric acid was found to be satisfactory. In the suggested method the sample is diluted with chloroform and 1 ml. of the solution, corresponding to about 80 μg. of thymol, is shaken with 10 ml. of reagent for 10 seconds, allowed to stand for 5 minutes, and the colour measured in a photoelectric colorimeter with a blue filter, against a reagent blank. The result is read from a standard curve. Assays by this technique gave results in agreement with the U.S.N.F. X method, and with non-aqueous titration in dimethylformamide. It was established that the small quantities of linalol, α-pinene, *p*-cymene, geraniol and borneol likely to be present in the oil do not affect the result, but abnormally high concentrations of these compounds might interfere, since they give a colour with *p*-dimethylaminobenzaldehyde reagent. G. B.

CHEMOTHERAPY

Antibiotic Salts of Reduced Toxicity, A New Class of. F. A. Alves M. F. C. A. N. Graça and H. L. Baptista. (*Nature, Lond.*, 1958, **181**, 182.) Amino acid salts of dihydrostreptomycin were prepared by neutralisation of a concentrated aqueous solution of the base with amino acid (3 molecules to each molecule of base), or by double decomposition between solutions of dihydrostreptomycin sulphate and the barium salt of the appropriate amino acid. The salts were isolated by freeze-drying or by concentrating solutions under reduced pressure at room temperature, dissolving the resulting syrup in methanol and precipitating with acetone. The following salts were prepared: glycinate, DL-leucinate, L-glutamate, L-methionate, *N*-acetyl-DL-methionate and *S*-ethyl-L-cysteinate. With the exception of this last compound (the anion of which has itself some tuberculostatic activity) all these amino acid salts were less toxic, as determined by intravenous injection into mice, than the sulphate or glucuronate. The leucinate and methionate are less toxic than the pantothenate and are being studied further. G. B.

Lymphotrophic Antibiotics. P. Málek, M. Herold, J. Hoffman and J. Kolc. (*Nature, Lond.*, 1958, **181**, 706.) Streptomycin, viomycin and streptothrycin have been combined with carboxylic, sulphonic or phosphorylated high molecular weight compounds to give macromolecular salts termed 'antibiolymphins', and their pharmacological properties studied. They are classified under three headings: (1) salts of antibiotic bases with polyacrylic acids (streptolymphin I, neolymphin I); (2) salts of antibiotic bases with sulphonic or phosphorylated polysaccharides (streptolymphin II, neolymphin II); (3) salts of antibiotic bases with natural polycarboxyl acids from a series of polyuronic substances and polysaccharide derivatives containing carboxyl groups (streptolymphin III, neolymphin III). The physiological behaviour of antibiolymphins lies between that of pure crystalloid and pure colloid, as shown by infusion into a peripheral lymph vessel of the hind extremity of a dog and examination of percentage of substance appearing in the thoracic drainage. Antibiolymphins are absorbed from the injection locus primarily by the lymphatic system; and high concentrations of long duration (up to 72 hours) may be produced in the lymph nodes of the drainage channels. Blood levels are generally lower than found with the normal antibiotic equivalent, but are maintained for much longer times. The acute toxicity is less than that of the parent antibiotic, the LD50 in rats and mice being raised five times with streptolymphin I and ten times with neolymphin I. J. B. S.

PHARMACY

Adrenaline, Stability of, and its Stabilization in Eye Lotions. J. Král. (*Sci. Pharm.*, 1958, **26**, 1.) The influence of the composition and the conditions of storage of some eye lotions on the stability of adrenaline contained therein was investigated. These eye lotions contained the most commonly used medicaments, e.g., zinc sulphate, boric acid, mercuric oxycyanide, silver proteinate, borax and silver proteinate diacetyl tannate, together with stabilisers such as sodium metabisulphite (0·1 to 0·8 per cent) and disodium ethylenediamine tetra-acetic acid (up to 1 per cent). Buffers were also included from pH 2 to 6. Trials were also carried out on plain solutions stored under various conditions, e.g., in the light, in the dark, exposed to air, air excluded, at room temperature

and at 32°. The most unstable eye lotions were those containing borax and silver proteinate diacetyltannate. Both required 0·2 per cent sodium metabisulphite, and the former a buffer at pH 6. D. B. C.

Antoxidant from Yeast, Isolation and Chemical Studies. M. Forbes, F. Zilliken, G. Roberts and P. György. (*J. Amer. chem. Soc.*, 1957, **80**, 385.) A new antoxidant, capable of preventing the occurrence of a haemorrhagic liver necrosis which follows dietary deficiencies in rats, has been isolated in crystalline form, $C_{16}H_{12}O_5$ from various yeasts. It was obtained by extractions with 90 per cent ethanol, removal of sterols by solution in methanol, extraction with ether and chromatography on Florisil. Yields of the order of 0·5 to 2 mg. per pound were obtained. The substance is optically inactive; the molecule contains one methoxyl group and no C-methyl groups. Of the other four oxygen functions one is phenolic and the remaining three ether links, since diazomethane gave a dimethoxy derivative. Fusion with potassium hydroxide at 200° gave an aromatic carboxylic acid without hydroxyl substituents, whilst microhydrogenation with PtO_2 as catalyst in acetic acid showed an uptake of 9 moles of hydrogen, indicating the presence of two aromatic nucleii, one being unsubstituted and the other containing the hydroxyl and methoxyl substituents. J. B. S.

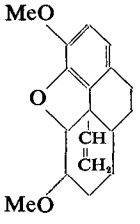
Menaphthone Sodium Bisulphite Injection, Stability of. Shu-yuan Yeh and G. A. Wiese. (*Drug Standards*, 1958, **26**, 22.) On prolonged storage, solutions of menaphthone sodium bisulphite become yellow and a precipitate forms, decomposition being accelerated by heat and light. Solutions are most stable below pH 2·5. Sodium chloride, added to the solution, improves its stability, and the addition of 0·2 per cent of sodium bisulphite is advantageous in preventing breakdown to menaphthone and sodium bisulphite. When solutions containing sodium bisulphite are stored under an inert gas the yellow colour and precipitate do not appear unless the ampoules are stored in sunlight. However, these conditions increase the rate of conversion to inactive 2-methyl-1:4-naphthaquinone-3-sulphonate. Solutions containing 0·2 per cent of sodium bisulphite and 0·7 per cent of sodium chloride, sterilised by filtration and filled into ampoules under air were shown by accelerated decomposition studies to have a shelf life of about 2½ years at 20° or 1½ years at 30°. G. B.

PHARMACOGNOSY

Digitalis Leaves, Distinction between various Types by Ring Chromatography. K. Rada. (*Pharm. Zentralh.*, 1958, **97**, 163.) The separation of glycoside complexes in purified extracts of the leaves of five species of *Digitalis* was attempted. These were *D. purpurea*, *D. ambigua*, *D. lanata*, *D. ferruginea* and *D. thapsi*. Using the same solvent mixture (xylene-methylethyl ketone 1:1) and Whatman No. 1 filter paper impregnated with formamide, zones were obtained by means of which various species of *Digitalis* could be distinguished by their R_F values and fluorescence in ultra-violet light. The method could be used for the investigation of a mixture of powdered leaves containing *D. purpurea*, *D. lanata* and *D. ferruginea*. D. B. C.

Morphine, Biogenesis of. A. R. Battersby and B. J. T. Harper. (*Chem. Ind.*, 1958, 364.) The biogenesis of morphine has been investigated by feeding

plants of *Papaver somniferum* with α-^{14}C-DL-tyrosine, and subsequent isolation of all the major alkaloids by countercurrent distribution. The morphine, diluted with inactive morphine and purified as picrate, had a constant activity of $4{\cdot}29 \times 10^5$ dis. p.m./mM. The recovered morphine was degraded via codeine methyl ether methiodide, α-codeimethine methyl ether and tetrahydrocodeimethine methyl ether. Hofmann degradation of the latter gave inactive trimethylamine (purified as picrate) and the morphenol derivative (I), which on hydroxylation with osmium tetroxide and cleavage with periodate gave formaldehyde, isolated as its dimedone derivative, which had activity $2{\cdot}02 \times 10^5$ dis. p.m./mM. It is concluded that half the activity of the original morphine is located at position 16 in accord with the biogenetic theory which incorporates one molecule of tyrosine at this point. J. B. S.



(I)

PHARMACOLOGY AND THERAPEUTICS

Chlorpheniramine Maleate in Blood Transfusions. M. Hobsley. (*Lancet*, 1958, **1**, 497.) A controlled trial in 200 blood transfusions failed to demonstrate the efficacy of chlorpheniramine maleate (10 mg. in each bottle of blood) in preventing pyrexial reactions during transfusions. No statistical evidence of such an effect was obtained and there is no argument in favour of routine antihistamine medication of the blood. The addition of any material to a bottle of blood must carry with it some danger of contamination, and this consideration must outweigh the possible avoidance of a small number of minor thermal reactions. This finding does not affect the validity of the practice of using chlorpheniramine in transfusions to patients with a history of allergy, in order to reduce the number of allergic reactions. S. L. W.

2-Hydrazine-benzazoles, Structure and Pharmacological Activity of. I. V. Panov and N. P. Bednyagina. (*Farmakologiya i Toksikologiya*, 1957, **20**, No. 6, 25.) The biological actions of 2-hydrazino-derivatives of benzothiazole (II), benzoxazole (III), benzimidazole (IV) and 1-methyl-benzimidazole (V) are compared with those of 1-hydrazinophthalazine (hydrallazine) in experiments on the isolated frog heart, on the vessels of the isolated posterior extremities of the frog, and on the blood pressure of the dog. Compounds II, III and V have no effect on blood pressure and no vasoconstricting action. In contrast to hydrallazine, compound IV, in intravenous doses of 0·5 mg./kg., produces a marked hypertensive effect in the dog. E. H.

5-Hydroxytryptamine and Reserpine, Differentiation between the Sedative Actions of. W. Kobinger. (*Acta pharm. tox. Kbh.*, 1958, **14**, 138.) The sedative actions of reserpine and 5-hydroxytryptamine (5-HT) have been compared in motility experiments using mice, in which the motility has been artificially increased by (+)-methylamphetamine or cocaine. It has been found that 5-HT counteracted the increased motility produced by (+)-methylamphetamine, the effect being linearly related to the logarithm of the dose. Reserpine had no action. Both 5-HT and reserpine antagonised the hyperactivity induced by cocaine and again both showed a relationship between sedative action and the log dose; but there was a significant difference between the regression lines. The results indicate different modes of action of 5-HT and reserpine on the central nervous system of mice. G. F. S.

Laminarin Sulphate, Physiological Activity of. W. W. Hawkins and V. G. Leonard. (*Canad. J. Biochem. Physiol.*, 1958, **36**, 161.) This paper gives a detailed account of the anticoagulant activity of laminarin sulphate. Some studies on its absorption, excretion and its activity as an antilipaemic agent are also made. In all instances its actions were compared with those of heparin. The immediate effect on the blood clotting efficiency, as measured 30 minutes after intravenous injection into dogs, indicated that laminarin sulphate is one-third as potent as heparin. The thrombin time was affected more than any other measure of the clotting efficiency of the plasma. This indicates that laminarin sulphate, like heparin, acts in an important capacity in the terminal stage of clotting as an antithrombin. It also shows anticoagulant activity when administered subcutaneously and intramuscularly. After the intravenous administration of a moderate amount of laminarin sulphate to the dog, considerable anticoagulant material passed into the urine. When large oral doses were given to the rat, absorption from the intestine was very small and much of the material passed into the faeces. When it was given intravenously, laminarin sulphate acted like heparin in clearing alimentary lipaemia in the dog and the rat. Further work on its antilipaemic properties is in progress. M. M.

Linoleic and Stearic Acids: Effect on Cholesterol-induced Lipid Deposition in Human Aortic Cells. D. D. Rutstein, E. F. Ingenito, J. M. Craig and M. Martinelli. (*Lancet*, 1958, **1**, 545.) Factors affecting the intracellular deposition of lipid were studied in human aortic cells in tissue-culture in a medium containing human blood-serum. When cholesterol in ethanol is added to the culture medium, the amount of lipid deposited in the cells is proportional to the amount of cholesterol added. Thus, at a concentration of cholesterol of 1 mg./100 ml. there is little evidence of intracellular lipid deposition; at 3 mg./100 ml. deposition regularly appears, with an increase in size of the cells: and at 5 mg./100 ml. there is considerable deposition and an enormous increase in size of cells. There is a similar proportional deposition when cholesterol bound to beta-lipoprotein is added to the culture medium. Thus, at a concentration of cholesterol of 30 mg./100 ml. there is little evidence of deposition; at 50 mg./100 ml. deposition regularly appears, with increase in size of cells; and at 70 mg./100 ml. there is considerable deposition and the cells are enormously increased in size. The deposition caused by adding cholesterol disappears in 5 days if the medium containing cholesterol is replaced by normal medium. The deposition is completely inhibited by simultaneous addition of linoleic acid (1 mg./100 ml.); it is increased by the simultaneous addition of stearic acid (1 mg./100 ml.). Thus, in tissue cultures of human aortic cells deposition of lipid can be induced by cholesterol. This is reversible and can be inhibited by an unsaturated fatty acid and potentiated by the corresponding saturated fatty acid. Details of method of preparation of the culture medium and cholesterol solution are given. S. L. W.

Methylpentynol Carbamate and Liver Function. A. A. Bartholomew, P. Chappell, E. Marley and J. S. W. Chambers. (*Lancet*, 1958, **1**, 346.) Methylpentynol carbamate was administered to 12 patients in doses of 1 to 3 g. daily by mouth for from 2 to 7 weeks. No abnormalities were discovered in tests for bile salts or pigments, urinary urobilin, serum-bilirubin, alkaline phosphatase, total plasma-proteins, serum-albumin and serum-globulin, zinc-sulphate or cephalin-cholesterol reactions, prothrombin time, haemoglobin values, blood film, and white cell count and differential. Mild disturbances of

hepatic excretory function (urinary urobilinogen) and protein metabolism (thymol turbidity and flocculation) were observed. An increase in the E.S.R. was also noted and a reducing substance found in the urine of one patient. Side-effects included anorexia, nausea, and vomiting, alterations in the mental state, and the appearance of such signs as nystagmus, pupillary anomalies, ptosis, loss of tone in the lower facial musculature, dysarthria, and ataxia. None of these abnormalities seem likely to develop on a daily oral dose of 1 g. or less.

S. L. W.

Methylpentynol, Effect of, in Man. S. E. Dicker and H. Steinberg. (*Brit. J. Pharmacol.*, 1957, **12**, 479). Methylpentynol has a sedative effect and has been used to allay anxiety without affecting motor performance. Experiments in student volunteers have shown that methylpentynol in a dose of 150 mg. decreases autonomic responses caused by the anticipation or performance of a difficult test. These were shown by an increase in pulse rate and blood flow. The subjects were asked to carry out two psychological tests, a test for motor co-ordination where they had to steer a pointer over as many dots as possible on a rotating drum, and a steadiness test where they had to hold a stylus in a hole without touching the side. During the tests the subjects after methylpentynol performed worse and minded less. G. F. S.

Nalorphine and Amiphenazole, Antagonism of, to Morphine. N. A. Kruglov. (*Farmakologiya i Toksikologiya*, 1957, **20**, No. 6, 40.) Experiments on rats, in which sensitivity to pain is measured by the method of D'Amour and Smith, show that nalorphine, in doses of 2·5 to 5 mg./kg. has about the same analgesic action as morphine. With morphine an increase in the dose to 10 to 20 mg./kg. increased the depth and duration of analgesia, but with nalorphine there was no such increase. Results of comparisons of the analgesic actions of these compounds depend on the dosage levels used. Studies on rabbits show that amiphenazole effectively counters the respiratory depression produced by morphine, but at this level it evokes toxic symptoms. Its LD50 for white mice is 270 mg./kg. It enhances the analgesic action but increases the toxicity of morphine; a dose of 50 mg./kg. given 10 minutes before the test reduces the LD50 of morphine from 630 to 340 mg./kg. E. H.

Organophosphates, Protection against the Lethal Effects of, by Pyridine-2-aldoxime Methiodide. F. Hobbiger. (*Brit. J. Pharmacol.*, 1957, **12**, 438.) The interaction between cholinesterase and organophosphates leads to the formation of an inhibited enzyme. Pyridine-2-aldoxime (P-2-AM) is a powerful reactivator of phosphorylated true cholinesterase. The value of P-2-AM and the other oximes has been studied in experimental organophosphate poisoning in mice. The results have shown that in the mouse P-2-AM, the most active oxime, was less effective *in vivo* than was indicated in the *in vitro* experiments. *In vivo* the injection of 25 mg./kg. of P-2-AM, 5 minutes before ethyl pyrophosphate (TEPP), diethyl *p*-nitrophenylphosphate (E 600), 3-(diethoxyphosphinyloxy)-*N*-trimethylanilinium methylsulphate (Ro 3–0340), and 3-(diethoxyphosphinyloxy)-*N*-methylquinolinium methylsulphate (Ro 3–0422) resulted in only 10 to 24 per cent reactivation. The concentration in the blood of 1 to 4 $\times$ 10^{-4} M of the oxime, to be expected, was sufficient *in vitro* to restore within a few minutes 90 per cent of the activity of true cholinesterase. P-2-AM was more efficient when given 30 minutes after the organophosphate. The effect of 25 mg./kg. P-2-AM on the phosphorylated true cholinesterase in the brain was

negligible. The protection by 25 mg./kg. P-2-AM against lethal doses of TEPP, E 600, Ro 3–0422 and Ro 3–0340 was greater than that obtained with 30 mg./kg. atropine sulphate, but the degree of protection was determined by the organophosphate itself. Protection against lethal doses of di*iso*propyl phosphorofluoridate (dyflos), di*iso*propyl *p*-nitrophenylphosphate (D 600) and 3-(di*iso*-propoxyphosphinyloxy)-pyridine (Ro 3–0351) was negligible. The antidotal effect of P-2-AM was potentiated by atropine. Screening of new oximes for antidotal properties should include as many oximes as possible, and by doing so insecticides could be selected which are less dangerous than those widely used today. G. F. S.

Penicillin, Environmental. J. C. Gould. (*Lancet*, 1958, **1**, 489.) Penicillin was detected in the environment in a general hospital. The amount recovered was greatest nearest those rooms where penicillin was being handled or administered. Air may be contaminated in two ways, either directly, by droplet nuclei (the dried residue of droplets atomised from syringes and sprays), or indirectly by the raising of dried spilt penicillin as dust. The concentration of penicillin is sufficient when inhaled in air, dust and fomites to inhibit penicillin-sensitive *Staphylococcus aureus* and to leave the nares free for colonisation with penicillin-resistant strains. Environmental penicillin is an important factor in the colonisation of hospital nasal carriers with penicillin-resistant *Staph. aureus*, and in the cross-infection of persons receiving or not receiving therapeutic antibiotic. The environment of a penicillin factory was shown to be similar to that of the hospital, and all the carrier strains of *Staph. aureus* were penicillin-resistant. S. L. W.

Phenethyldiguanide; Hypoglycaemic Action. R. I. Nielsen, H. E. Swanson, D. C. Tanner, R. H. Williams and M. O'Connell. (*Arch. int. Med.*, 1958, **101**, 211.) This is a study of the effect of phenethyldiguanide (PEDG) on blood sugar in intact and eviscerated animals, on the hepatic glucose output and on the degradation of insulin ^{131}I. Ten guinea pigs received 10 mg./kg. of PEDG subcutaneously twice daily, and a further 10 received an equal volume of saline by the same route. At the end of six weeks there was no difference in the weights of the animals in the two groups; the ratio of organ weight to body weight was the same in both groups and no histological changes were seen in the liver, kidney, spleen or pancreas. The compound was found to be effective orally, intramuscularly, intraperitoneally and subcutaneously, but the latter route gave the most consistent response. The response threshold was abrupt; 15 mg./kg. produced little or no hypoglycaemia, whereas 20 mg./kg. produced a marked response in 2 hours, killing approximately 50 per cent of the animals within 4 to 12 hours. Although the hypoglycaemia was accompanied by a marked fall in hepatic glucose output, it was found that hypoglycaemia was also produced in the absence of a functioning liver and was still present in the absence of the intestine and pancreas, so that the effect cannot be due to a decreased absorption from the intestine nor to the stimulation of insulin secretion. It was found that the degradation of insulin ^{131}I was inhibited by prior administration of the compound, but it was not felt that this action is of significance in the production of hypoglycaemia. S. L. W.

***N*-Phthalyl Glutamic Acid Imide (K 17), Antithyroid Activity of.** J. McC. Murdoch and G. D. Campbell. (*Brit. med. J.*, 1958, **1**, 84.) This tasteless, white, crystalline substance is an imide of glutamic acid and a derivative of

piperidine. It has been reported to have a "calming psychological effect," and has been used extensively on the Continent, in doses of 25 to 40 mg. two to four times daily, as a daytime sedative, and in doses of 50 to 100 mg. as a night-time hypnotic. It would appear to be non-toxic. On the basis of observations that it causes a marked reduction of the raised metabolic rate in hyperthyroidism, the effects of the drug on the thyroid uptake of radioactive iodine were assessed in 9 euthyroid patients. The results showed that it has a mild but definite antithyroid activity when given in doses of 200 mg. or more. The mode of action is at present unknown and it would seem unjustifiable to use it for long-term sedation or hypnotic therapy pending a study of its long-term effects in a larger number of patients. S. L. W.

17α-Propyl-4:5β-dihydro-19-nortestosterone, a New Hypotensive Steroid, Pharmacology of. F. M. Sturtevant. (*J. Pharmacol.*, 1957, **121**, 369.) This is a new antihypertensive steroid with no endocrinological, anti-inflammatory or anaesthetic properties. The compound significantly lowered the blood pressure of metacorticoid, metarenal and adrenal-regeneration hypertensive rats in acute and chronic states. Metacorticoid and metarenal hypertensive rats were prepared from month old male rats implanted with deoxycortone in wax or subjected to a two-stage uninephrectomy and contralateral kidney-wrap with latex. Adrenal-regeneration hypertensive rats were prepared by a one-stage right nephrectomy-right adrenalectomy-left adrenal enucleation. They were prepared three months before the tests began. In the 4:5-dihydro series, the only 17α-alkyl derivatives that were significantly active were the propyl, *iso*propyl and methyl compounds, while the ethyl and hydrogen compounds were inactive. In the 4-dihydro series the 17α-ethyl and α-propyl compounds were active. The former compound is the anabolic agent norethandrolone. G. F. S.

Secergan, a Quaternary Phenothiazine Compound having Anticholinergic and Ganglionic-blocking Actions. S. Wiedling. (*Acta pharm. tox. Kbh.*, 1958, **14**, 112). Secergan, 10-(α-dimethylaminopropionyl)-phenothiazine methobromide, has a powerful antagonistic action to spasms of smooth muscle induced by acetylcholine, nicotine, 5-hydroxytryptamine and histamine, but only a weak action against barium, adrenaline or noradrenaline. It has a hypotensive action in the anaesthetised rabbit due to a ganglionic-blocking action and the peripheral actions of adrenaline and noradrenaline are potentiated. G. F. S.

***Viscum album* L., Phytochemical and Pharmacological Studies.** G. Samuelson. (*Svensk Farm. Tidskr.*, 1958, **62**, 169.) *Viscum album* L., the mistletoe, is reported to contain both hypotensive principles and a cardiotoxic substance known as viscotoxin. By using suitable solvents, ion exchange resins and paper electrophoresis, the author isolated a small quantity of viscotoxin in a very pure form. Preliminary studies showed that it is a polypeptide which, contrary to previous reports, contains only eleven amino acids (not seventeen) and no sugar group. Tryptophan was also absent. The toxicity on mice was 1·14 ±0·77 mg./kg. intraperitoneally and 2·61 ± 0·18 mg./kg. subcutaneously. Two hypotensive fractions and one hypertensive fraction were also isolated and shown to contain ninhydrin-reacting substances. No choline or arginine could be found in the plant. J. W. F.

APPLIED BACTERIOLOGY

β-Glycyrrhetic Acid and Some of its Derivatives, Bacteriostatic Action of. R. Benigni and E. Franco. (*Pharm. Weekbl.*, 1958, **93**, 114.) 18α-Glycyrrhetic and glycyrrhizic acids and the related triterpenoid compounds ursolic, asiatic and oleanolic acids were shown to be inactive against all the organisms used in the tests, and monoammonium glycyrrhizinate showed only slight activity against *Escherichia coli*. Under the same conditions β-glycyrrhetic acid was shown to be active against *Staphylococcus aureus*, *Corynebacterium diphtheriae*, *Bacillus anthracis*, *Pseudomonas aeruginosa* and *Mycobacterium paratuberculosis*; it was slightly less effective against *Streptococcus faecalis*, *Strep. haemolyticus*, *Shigella flexneri* and *E. coli*. The maximum activity, determined by measurement of the zones of inhibition, was observed with a concentration of 0·1 per cent. The potassium derivative of β-glycyrrhetic acid was less active than the free acid against *Staph. aureus*, *Strep. faecalis*, *Corynebact. diphtheriae* and *B. anthracis*. γ-Glycyrrhetic acid was active against a few species including *Staph. aureus*, *B. anthracis* and *Myco. paratuberculosis*. The variable results which have been reported from the use of glycyrrhetic (glycyrrhetinic) acid in dermatology may have been due to variations in the sensitivity of the infecting organisms to β-glycyrrhetic acid, the identity and purity of the preparations used, and the use of alkaline materials in the ointment bases, causing the formation of the less active salt. G. B.

Phenolic Compounds, Interaction of, with Bacteria. A. H. Beckett, S. J. Patki and A. E. Robinson. (*Nature, Lond.*, 1958, **181**, 712.) Addition of hexylresorcinol to washed suspensions of *E. coli* caused the release of 'cell exudate', which shows absorption in the ultra-violet (max. 260 mμ). Rapid release (10 min.) of cell exudate was proportional to hexylresorcinol concentrations when these were low, but a limiting value was reached when the drug concentration was increased to a bactericidal level. On the other hand, hexylresorcinol taken up by the bacteria was proportional to the concentration of the drug, no limiting value being reached, so that at a bactericidal concentration the amount of hexylresorcinol found per bacterium is greater than that required to form a close packed monomolecular layer surrounding the organism. These results support the accepted view that phenolic compounds act at the cytoplasmic membrane. Addition of cetomacrogol reduced the uptake of hexylresorcinol from solutions by *E. coli* at all concentration levels of drug, and the antibacterial activity of the latter was completely abolished. It is suggested that the non-ionic agent (cetomacrogol) prevents interaction of the drug with the cytoplasmic membrane. J. B. S.

***Plantago lanceolata*, Antibacterial Properties of Extracts of.** M. Felková. (*Pharm. Zentralh.*, 1958, **97**, 61.) The antibacterial activity of alcoholic extracts of fresh leaves of *Plantago lanceolata*, collected throughout the vegetative season, is compared using as test organisms *Staphylococcus areus*, *Streptococcus β-haemolyticus*, *Bacillus subtilis*, and *Escherichia coli*. The zones of inhibition on agar cultures were compared under controlled conditions, a blank being performed with the solvent. Activity was significant and varied considerably throughout the year although there was a peak in all cases just before the flowering season. This peak represented greatest activity except for *Staph. areus* against which activity became greatest later in the season. The least affected organism was *E. coli*. The results with extracts made with physiological saline were negative except against *Staph. areus*. D. B. C.