ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Ergot Alkaloids, Separation and Determination of, by Paper Chromatography. M. Pöhm. (*Arch. Pharm.*, 1958, **9**, 468.) In this process the following ergot alkaloids can be identified and determined: ergometrine, ergotamine, ergosine, ergocristine, ergocornine and ergocryptine and their respective *dextro* isomers. The chromatography is carried out on a strip 15 cm. by 45 cm. of Whatman No. 1 filter paper which has been impregnated with formamide, with the mobile phase descending. This latter consists of a mixture of solvents of low polarity —carbon tetrachloride—chloroform—benzene in a ratio 7:2:1 or carbon tetrachloride-*n*-dibutyl ether, 8:2. After the solvent front has travelled about 35 cm., the chromatography is stopped and the positions of the spots of alkaloids localised in ultra-violet light. The limit of sensitivity of this observation by means of fluorescence is about 0·2 μg. of a single alkaloid. A method is described of identifying the alkaloids (if necessary) by comparison with the movement of authentic samples. The quantitative determination is carried out by cutting out the spots and shaking with a known amount of 1 per cent tartaric acid solution and the *p*-dimethylaminobenzaldehyde-sulphuric acid reagent of the British Pharmacopoeia until the paper has disintegrated, and measuring the extinction of the blue solution at 625 mμ. In this preliminary separation certain alkaloids which are not separated require further chromatography. The water-soluble alkaloids ergometrine and ergometrinine remain at the starting point. The spot is cut out and secured in a fold in a second formamide -impregnated strip and developed with a benzene-pyridine (6:1) mixture. The water-insoluble alkaloids ergocristine and ergocornine and ergocristinine and ergocorninine require further chromatography and are treated in the same way as the water-soluble alkaloids. A process for the hydrolysis of the ergot alkaloids and the separation and quantitative determination of the resulting amino acids valine, leucine and phenylalanine is described. D. B. C.

Phenothiazine Compounds, a New Method of Determination of. G. Dusinský. (*Die Pharmazie*, 1958, **8**, 478.) A titrimetric determination of the phenothiazine compounds promethazine, diethazine, chlorpromazine and prochlorperazine is reported based on selective oxidation using either ceric sulphate or potassium bromate. A red radical is first formed by the loss of one electron, the colour of which is discharged at the end point after the loss of a second electron. The progress of the titration can thus either be followed visually or electrochemically by means of a dead-stop method. With promethazine accurate results were only obtained by the dead-stop method. The method is more specific than other methods, for example, direct neutralisation or determination with silicotungstic acid, since it is unaffected by the presence of alkaloidal bases, etc., for example, caffeine, amphetamine, codeine, barbituric acid derivatives and tablet excipients. The accuracy of the method is $\pm$ 1·5 per cent for promethazine and $\pm$ 0·5 per cent for the other compounds. D. B. C.

Thujone, Colorimetric Estimation of, with 3:5-Dinitrobenzoic Acid. D. H. E. Tattje. (*Pharm. Weekbl.*, 1958, **93**, 689.) Data are presented showing the effect of varying the concentration of each reagent involved, and also the effect of temperature, and from these data the following optimum conditions have been worked out. To 4 ml. of a solution of thujone in ethanol containing about 0·5 mg. per ml. is added 5 ml. of a 4 per cent solution of 3:5-dinitro benzoic acid in ethanol and 3 ml. of 4N sodium hydroxide and the intensity of colour measured in a 0·5 cm. cell at 5375Å against a blank identical in all respects except for the omission of thujone. There should be a fresh blank for each estimation, and the temperature should be exactly 20°. α and β-Thujones take different times to attain the maximum extinction which is also different for the two optical isomers. The method requires much less sample and is much more rapid than the hydroxylamine method. Where only the thujones are present in an oil, the two methods are in good agreement, but where other ketones and/or aldehydes are present, low results are obtained due to the specificity of the colorimetric method for thujone. Wormwood oil, however, sometimes gives anomalously high results for β-thujone. D. B. C.

GLYCOSIDES

***Digitalis purpurea*, Influence of Fermentation on the Glycosidal Content of.** D. H. E. Tattje. (*Pharm. Weekbl.*, 1958, **93**, 819.) Twenty-four batches of leaves were taken and four batches were fermented at 35° during periods each of 1, 2, 3, 4, 5 and 6 days and finally dried at 70°. Two other control batches were immediately dried at 70° after harvesting. The digitoxigenin and gitoxigenin glycosides were determined colorimetrically in all the batches, and the glycosidal content calculated on crude fibre. The gitoxigenin content of the fermented leaves was 25 per cent higher than that of the non-fermented leaves, but there was no significant difference in the content of digitoxigenin glycosides for a time of fermentation not greater than 3 days. After a longer fermentation time, however, there was a significant fall in digitoxigenin content. D. B. C.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Allicin, Inhibitory Action on Degranulation of Mast Cells Produced by Compound 48/80, Histamine Liberator from Ascaris, Lecithinase A and Antigen. B. Högberg and B. Uvnäs. (*Acta physiol. scand.*, 1958, **44**, 157.) The authors have already produced evidence that 48/80 degranulates mast cells by activating an enzyme mechanism. It was suggested that this enzyme, possibly carrying essential amino groups, was attached to the mast cell membrane. It is now shown that very low concentrations of allicin, a potent enzyme inhibitor prepared from garlic, block the *in vitro* degranulation of rat mast cells produced by compound 48/80, by a histamine liberator prepared from *Ascaris lumbricoides*, by antigen-antibody reaction using horse serum, and by lecithinase. Excess glutathione reversed the blocked degranulating processes. These observations support the theory that the degranulation of mast cells is due to the activation of a lytic enzyme attached to the mast cell membrane. This enzyme is dependent on sulphhydryl groups for its activity. Whether it is also dependent upon NH_2 groups is now being investigated. M. B.

BIOCHEMICAL ANALYSIS

Bromides, Application of Semimicro Determination of, to Physiological Fluids. D. Kaplan and I. Schnerb. (*Analyt. Chem.*, 1958, **30**, 1703.) This method is suitable for quantities of 0·01 mg. of bromide ion with an error of ± 3 per cent and depends upon the oxidation of bromide to bromate with sodium hypochlorite, and determination of the bromate iodimetrically. In the case of urine, the total halides are precipitated from protein-free urine with excess silver nitrate. The washed silver halides are treated with hydrochloric acid and zinc to displace the silver which is filtered off, and the filtrate analysed for bromide as before. For blood or serum, protein is first removed with sodium tungstate, and the protein-free fluid analysed as for urine. Bromide can also be determined in sweat, saliva and cerebrospinal fluid. D. B. C.

Catechol Amines in Urine, Simple Biological Test for. M. A. Floyer. (*Lancet*, 1958, **2**, 1154.) A rapid, although approximate, estimation of urinary catechol amines can be made by measuring the rise in blood pressure, after intravenous administration of neat, neutralised urine, in the anaesthetised rat. This method is suitable for the screening of large numbers of patients with hypertension to exclude phaeochromocytoma. Up to 15 urine samples can be tested on the same rat. The assay results are expressed as noradrenaline. Added adrenaline does not increase the pressor effect of the noradrenaline when the two are injected together so this method probably measures noradrenaline only and may therefore give a low result for total catechol amines in patients excreting a high proportion of adrenaline. In all six patients with proven phaeochromocytoma the pressor effects of the urine confirmed the diagnosis, whereas in very few instances did the urine from hypertensive patients give a measurable pressor response. There may very occasionally be some doubt in differentiating the latter cases from those of phaeochromocytoma in whom the excretion is low, but in the great majority of cases the separation is easy and reliable. M. B.

Phenylmercury Compounds, Micro-estimation of, in Animal Tissues. V. L. Miller, D. Lillis and E. Csonka. (*Analyt. Chem.*, 1958, **30**, 1705.) By this method, 5 to 20 μg. amounts of phenylmercury acetate per g. of animal tissue or 5 ml. of urine may be determined. For urine, the sample is heated with N sodium hydroxide on a water bath under a reflux condenser. The cooled mixture is treated with potassium permanganate. Excess permanganate is destroyed by adding an ammoniacal solution of hydroxylamine sulphate. Ammonium sulphamate is then added to destroy the oxidising material formed during the alkaline reduction of the excess permanganate by hydroxylamine (probably an oxide of nitrogen). The mixture is acidified with strong hydrochloric acid and extracted with chloroform into which the mercury passes as phenylmercuric chloride. The chloroform is then washed with dilute hydrochloric acid and treated with excess dithizone reagent and the transmittance at 620 mμ determined in order to determine the excess (green) dithizone present rather than the yellow phenylmercury dithizonate. The procedure is similar for kidney, liver, muscle and spleen. For brain, it is necessary to heat under reflux on a water bath with the permanganate. The method was checked by adding quantities of 2 to 20 μg. of phenylmercury acetate to urine, liver, kidney and brain and assaying. Results were within 1 μg. of the expected value.
D. B. C.

PHARMACOLOGY AND THERAPEUTICS

Chlorothiazide Derivatives, Diuretic Activity of. W. Logemann, P. N. Giraldi and M. A. Parenti. (*Nature, Lond.*, 1958, **182**, 1510.) Chlorothiazide (6-chloro-7-sulphamyl-1 : 2 : 4-benzothiadiazine-1 : 1-dioxide) is a very active diuretic drug and it can also relieve hypertension in many patients. It has an inhibitory action on carbonic anhydrase and it also causes a diuresis like that observed with the organic mercurial compounds, resulting in an increase in the excretion of sodium salts as well as water. An analysis is made of the structural conditions necessary for this diuretic activity. It was found that the activity is not largely due to the sulphamyl group. Ring closure to thiadiazin-dioxide is not necessary for diuretic activity. Chlorine cannot be omitted in these compounds and it cannot be replaced by an amino group. A free sulphonamide group is not necessary. Activity decreases rapidly with increasing molecular weight of the alkyl group. The dimethyl compound still has activity and the morpholine compound slight activity, but the *cyclo*hexyl compound is inactive.

M. B.

Chlorpropamide in the Treatment of Diabetes. I. Murray, M. J. Riddell and I. Wang. (*Lancet*, 1958, **2**, 553.) Forty-three diabetic patients were treated with the oral hypoglycaemic agent chlorpropamide (*N*-propyl-*N*-(*p*-chlorbenzenesulphonyl)urea). The patients selected were less than 10 years diabetic, over 40 years old, and had taken insulin, if at all, for not more than two years. The dose of chlorpropamide was 1 g. daily at breakfast. Urine tests (Clinitest) were made before each of the three main meals of the day. A satisfactory response was obtained in 28 of the 43 patients, and was usually evident by the second or third day, and always within 7 days. In the successful group the mean blood sugar fell from 273·5 mg./100 ml. before treatment to 161·8 mg. at the end of two weeks, while in the unsuccessful cases the comparable values were 364·9 mg. and 304·5 mg. In the successful cases the mean daily output of urinary glucose was reduced from 35·5 g. to 3·4 g. daily, whereas the mean figures in the unsuccessful cases were 58·3 g. and 59·6 g. Among the failures with chlorpropamide, 6 had been treated with the other sulphonylureas; all had failed with tolbutamide but 3 had responded to carbutamide, giving the impression that chlorpropamide is somewhat less potent than carbutamide but definitely more potent than tolbutamide. There were no serious toxic effects, but 9 patients showed side-effects (in 4 cases after the dose had been increased to 2 g.); nausea occurred in 7 cases, an erythematous rash in 1, and drowsiness in 1. In most cases which respond a single daily dose of 1 g. is sufficient and this amount should not be exceeded. If after a few days' treatment a good response is obtained the dose should be reduced. S. L. W.

5-Hydroxytryptamine, Radioprotective Action of. H. A. S. van den Brenk and K. Elliott. (*Nature, Lond.*, 1958, **182**, 1506.) The effect of pretreating rats with antagonists and specific antimetabolites, preceding the administration of 5-hydroxytryptamine (5-HT) and of tryptamine, and its effect on the acute lethality from total body X-irradiation has been investigated. Acute lethality was assessed for a 30-day period following irradiation. The loss in body weight and incidence of diarrhoea was also recorded. The antagonist used was 1-benzyl-2 : 5-dimethylserotonin (BAS phenol) and the antimetabolites used were (+)-lysergic acid diethylamide (LSD) and its brominated derivative (BOL 148).

It was found that both antagonist and antimetabolites of 5-HT alone had no significant protective action, but inhibited that of 5-HT and tryptamine. Antihistamines failed to influence the protective action of 5-HT but the radioprotective action of histamine was inhibited. Atropine and dibenzyline, which respectively block the two types of tryptamine receptors, failed to influence the protective action of 5-HT. Tranquillisation of rats with reserpine did not influence the lethality significantly. However, administration of 5-HT 5 minutes before irradiation of reserpinised rats resulted in a radioprotective effect. The results obtained suggest a close correlation between the radioprotective effect of certain amines and their pharmacological actions. M. B.

5-Hydroxytryptamine, The Action of, on the Human Uterus. W. J. Garrett. (*Arch. int. Pharmacodyn.*, 1958, **117**, 435.) Strips of myometrium cut from the anterior wall of non-pregnant human uteri removed at hysterectomy were suspended in oxygenated Ringer-Locke solution and their movements recorded on a smoked paper by conventional methods. Spontaneous rhythm occurred after a latent period of 2–3 hours. 5-Hydroxytryptamine (5-HT) in concentrations up to 100 μg./ml. usually decreased the background tone of the muscle and the frequency of the spontaneous contractions. The amplitude of the spontaneous contractions was, however, increased. Larger concentrations of 5-HT (100–500 μg./ml.) caused a sustained contraction of the muscle upon which the spontaneous contractions were superimposed. Kymograph records of uterine activity in volunteer patients were taken in pregnancy and labour by means of a small hydrostatic balloon passed into the lumen of the uterus through the cervical canal. Intravenous infusions of 5-HT from 2·2 to 300 μg./min. had little effect on uterine contractility and no marked side effects were observed. In one case, 200μg. of 5-HT was given by rapid intravenous injection and in this case mild stimulation of the uterus was observed. The author concludes that 5-HT has little significance in the physiology of human myometrial contraction since the observed effects were produced only by concentrations considerably higher than those which exist under physiological conditions. W. C. B.

Iron Preparation, Oral, Gastrointestinal Tolerance to. D. N. S. Kerr and S. Davidson. (*Lancet*, 1958, **2**, 489.) Ferrous sulphate, ferrous gluconate, ferrous succinate, ferrous calcium citrate, and "known" and "unknown" control pills containing lactose, were administered to 93 healthy young women in a double-blind trial. The ferrous sulphate, gluconate, and succinate pills each contained 35 mg. of iron; of these, and of the control pills, the dose was one three times daily. The ferrous calcium citrate was prepared in pills containing 17·5 mg. of iron, and these were given in a dose of two pills three times daily. All the pills were identical in size, shape, colour and coating. The pills were taken from Mondays to Fridays during 6 successive weeks, and at the end of each week a questionnaire was completed giving details of any symptoms experienced during the preceding week. Virtually no toxic effects were reported from the "known" control pills, but the exactly similar "unknown" control pills, which were thought by the subjects to contain iron, produced as many side-effects as the pills which did contain iron. None of the four iron pills was found significantly more toxic than the inert pills. It was therefore concluded that intolerance to these iron preparations, in the dosage given, was mainly psychological in origin. S. L. W.

Reserpine, Researches on the Mechanism of Sedative Action. S. Garattini and L. Valzelli. (*Science*, 1958, **128**, 1278.) A series of experiments were carried out on female rats kept in constant temperature rooms at 0°, 22°, 29° or 37° to determine whether a relationship exists between the sedative action of reserpine, 5-hydroxytryptamine (5-HT) release and hypothermia. The sedative action of reserpine was evaluated by the potentiation of sleeping time after the intraperitoneal administration of pentobarbitone. Brain 5-HT was extracted and measured spectrophotometrically and rectal temperature was determined with a resistance thermometer. The rats were injected with 2·5 mg./kg. of reserpine 4 hours before the determinations were made. The results showed that increasing room temperature from 22° to 37° did not change body temperature, nor did it affect the sleeping time after pentobarbitone. It did, however, cause a small increase in the content of brain 5-HT. After reserpine was injected, barbiturate sleeping time was prolonged only when 5-HT was released. This occurred, together with a fall in body temperature, with the rats kept at 22° and 29°. With those kept at 37°, body temperature was unchanged and brain 5-HT increased after the administration of reserpine; under these conditions reserpine showed no evidence of sedative activity. Reserpine significantly decreased the body temperature of rats kept at 0° but there was no change in brain 5-HT and no sedation. The results supply further evidence in support of the hypothesis that the sedative action of reserpine takes place only when there is 5-HT release. The onset of hypothermia was not always associated with sedation and it was not correlated with 5-HT release. W. C. B.

Tessalon in Pulmonary Insufficiency and Irritative Cough. R. L. Wilson, S. M. Farber and W. Mandel. (*Antibiotic Med.*, 1958, **5**, 567.) The drug, ω-methoxypoly(ethyleneoxy)ethyl *p*-butylaminobenzoate (Tessalon), is a cough suppressant that appears to act by suppressing the afferent arm of the Hering-Breuer reflex. It is chemically related to the local anaesthetic, amethocaine, with the addition of a long chain glycol. The respiratory effects of intramuscular and oral preparations of the drug were studied subjectively and by tests of physical effort in 30 patients with pulmonary fibrosis or emphysema. The drug was given intramuscularly in a dose of 5 mg. in 17 of the patients, the standard physical tolerance test being evaluated one hour after injection. Some of the tests were repeated following a week on the oral preparation in a dose of 150–200 mg. daily. The most constant finding was an increase in the amount of physical effort that could be tolerated, which occurred in 12 out of the 17 patients. This was associated in those patients with an increase in the tidal volume as the exercise progressed, and a less rapid augmentation of the respiratory rate than occurred before the drug was administered. In some patients the recovery from maximal hyperventilation to normal respiration appeared accelerated. The recovery to normal respiration after a standard exercise was markedly improved in almost every case. In 20 patients who were given the drug orally a subjective evaluation only showed that 18 were improved or much improved, with less cough and less shortness of breath and increased effort tolerance. In a further group of 37 patients with pulmonary tuberculosis the daily administration of 150 mg. orally had a beneficial effect on the cough in a significant number. There is evidence that the effects of the drug may persist beyond the period of administration. The only toxic reactions noted were one case of mild erythema and one of transient skin itching.

S. L. W.

Triamcinolone Arthritis. R. Wells. (*Lancet*, 1958, **2**, 498.) Fourteen patients, all of whom had previously been receiving optimal doses of prednisolone for various conditions without any incidence of important side-effects, were transferred to triamcinolone. Of 9 with no previous history of joint symptoms, 3 developed arthritis; in 2 of these the condition resembled acute rheumatoid arthritis. It is suggested that arthritis may be a side-effect of triamcinolone therapy. S. L. W.

APPLIED BACTERIOLOGY

Blankets and Hospital Infection. H. Schwabacher, A. J. Salsbury and W. J. Fincham. (*Lancet*, 1958, **2**, 709.) Two experiments were made to assess the effect of blankets on bacterial infections in hospital. The first experiment showed that the use of freshly washed blankets, disinfected with quaternary ammonium compounds, for each patient admitted to a test ward, reduced the total bacterial count (and especially the *Staphylococcus aureus* phage-type 80, which was previously endemic), and also decreased cross-infection. The second experiment showed a moderate reduction of the bacterial count when terylene blankets were used instead of woollen blankets. But the total bacterial count was reduced more, and there was no cross-infection, when cotton blankets were used. After the first washing, cotton blankets did not produce the fluff which seems to a major factor in the spread of infection. It is suggested that the following measures would probably result in a great diminution in bacterial counts in hospitals: (1) woollen blankets should be replaced by cotton ones washed at 100° before use; (2) on admission, every patient should be given a bed covered with freshly washed sheets and cotton blankets; (3) all blankets should remain on the beds—ambulant patients may have separate blankets, which should be regularly washed, for use when not in bed. S. L. W.

Blankets and Hospital Infection: Fibre Composition of Hospital Dust. T. A. Pressley. (*Lancet*, 1958, **2**, 712.) All samples of airborne dust in three hospitals (in Melbourne) consisted essentially of cellulose fibres; very few wool fibres could be found. The cellulose fibres presumably came from sheets, towels, clothes, ward dressings, and bandages. Since dust from one hospital using all-wool blankets showed a fibre distribution similar to that from two other hospitals using wool-cotton union blankets it is unlikely that the cotton warp of the union blankets contributed materially to the air-borne cellulose. Most samples subjected to bacterial examination contained coagulase-positive *Staphylococcus aureus*. This suggests that the cross-infection with the *Staph. aureus* is primarily due to transfer of the bacteria by some agency other than the fluff from blankets, and therefore the replacement of woollen blankets with those made from other textile fibres, or the application of an oiling technique to blankets only, is unlikely to reduce cross-infection. S. L. W.

***Salmonella typhimurium* Infection, Dust-borne.** J. G. Bate and U. James. (*Lancet*, 1958, **2**, 713.) In the infants' ward of a children's hospital seven outbreaks of gastro-enteritis over 11 months were caused by *Salmonella typhimurium*, phage-type 2. The infection was not being spread by human carriers nor from the central milk-kitchen. The source of infection was finally found in the dust-bag of a vacuum floor-polisher. Since suction-cleaning and polishing of the floors by machines fitted with disposable paper dust-bags has been substituted, there has been no case of *S. typhimurium* infections. S. L. W.