ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Hexachlorophene and Bithionol, Assay of, in Solid and Liquid Soaps, Emulsions and Dusting Powders. H. G. van der Pol. (*Pharm. Weekbl.*, 1958, **20**, 881.) This paper describes a spectrophotometric method which enables hexachlorophene (2:2′-dihydroxy-3:3′:5:5′:6:6′-hexachlorodiphenylmethane) and bithionol (2:2′-dihydroxy-3:3′:5:5′-diphenyl sulphide) to be determined separately or in the presence of one another. Two equal portions of a methanolic solution or extract are separately diluted to an equal extent by a methanolic acid and alkaline buffer respectively. The two solutions, which are of equal strength and only differ in pH, are subjected to measurement as follows. The extinction of the alkaline solution is measured at 312 mμ using the acid solution as a blank, giving a measure of hexachlorophene, and at 328 mμ for bithionol using 1 cm. cuvettes in each case. Any absorption due to irrelevant ingredients is thus compensated for. Formulae are given for the calculation of the concentrations of the medicaments, and the method is specific, quick and has an accuracy of ± 2 per cent. D. B. C.

Nicotinic Acid, Quantitative Determination in Pharmaceutical Preparations. K. Howorka. (*Pharm. Zentralh.*, 1958, **97**, 521.) Whereas the cation exchanger Wofatit KPS 200 binds nicotinic acid quantitatively if used in the H-form, it cannot do so in the pyridine-form. If mineral salts are also present, an aliquot part of the solution being assayed is put through a column of the exchanger in the H-form. The difference in the amount of acid liberated can be used to find the amount of nicotinic acid present. In the case of esters and amides of nicotinic acid, saponification using 0·5 N ethanolic KOH is carried out, the solution acidified with sulphuric acid, the sulphate precipitated with excess barium hydroxide solution, and the solution made up to a definite volume. For preparations containing nicotinic acid esters and other saponifiable material, saponification and acidification is carried out as above, and the free fatty acids are allowed to rise to the surface on cooling. Hard paraffin may be used to assist the formation of a solid layer. The aqueous layer is treated as above.

D. B. C.

(+)-Pulegone, Colorimetric Estimation of, with 3:5-Dinitrobenzoic Acid. D. H. E. Tattje. (*Pharm. Weekbl.*, 1958, **93**, 1048.) In this method, 4 ml. of a solution of (+)-pulegone containing up to 0·65 mg./ml. is mixed with 5 ml. of a 4 per cent ethanolic solution of 3:5-dinitrobenzoic acid and 2 ml. of 3 N aqueous sodium hydroxide solution is added. The extinction coefficient is measured at 5375 Å against a blank containing 4 ml. of ethanol, 5 ml. of reagent and 2 ml. of 3 N sodium hydroxide about 40 minutes after the addition of the alkali. The colour remains constant for a further 8 minutes. The temperature must be controlled to within narrow limits, preferably around 20°. For (+)-pulegone, E (1 per cent, 1 cm.) = 82·3 (standard deviation, 1·599).

For (−)-piperitone and piperitenone, which may occur in pennyroyal oil, *E* (1 per cent, 1 cm.) values are respectively 128 and 235. Menthone does not react with 3 : 5-dinitrobenzoic acid. It was shown that this colorimetric method agreed with the neutral sulphite method, and was probably more specific.

D. B. C.

Piperazine, Quantitative Determination of, in Pharmaceutical Preparations. M. Hädicke. (*Pharm. Zentralh.*, 1958, **97**, 365.) Two methods are suggested involving the precipitation of piperazine with sodium tetraphenylboron or Reinecke's salt, both of which react with each nitrogen atom of the piperazine. After washing, the precipitate in each case is dissolved in acetone and then estimated titrimetrically. In the case of the tetraphenylboron complex, an argentimetric method is used with eosin as an absorption indicator, whereas with the Reineckate complex, excess standard silver nitrate solution is added followed by back-titration with standard ammonium thiocyanate solution using ferric alum as indicator. The results of both methods are in good agreement and the error in each is about ± 2 per cent. D. B. C.

Reserpine, Determination of, in Tablets by Infra-red Spectrophotometry. W. R. Maynard, Jr. (*J. Assoc. off. agric. Chem., Wash.*, 1958, **41**, 676.) This method is based on the intensity of a carbonyl band at 5·78 μ in reserpine in chloroform. Although reserpine breaks down slowly in chloroform, no other solvent could be found without encountering absorption difficulties, and the rate of decomposition is not sufficient to affect the accuracy of the assay. The concentration required is about 2 mg./ml. and a standard of this concentration is used for comparison. The most commonly occurring impurities are rescinnamine and deserpidine and these can be determined admixed with reserpine. Rescinnamine is determined by measuring the absorbance at 7·58 μ and comparing with a standard. Reserpine is found by measuring the total absorbance at 6·1 μ and subtracting that due to rescinnamine at this wavelength. Deserpidine is then determined by measuring the carbonyl absorption at 5·78 μ and subtracting the absorbance of reserpine and rescinnamine at this wavelength. Experimental results indicate an accuracy of about ± 1 per cent for reserpine. D. B. C.

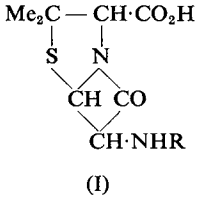
Strychnine in Nux Vomica, Determination of, by Paper Chromatography, G. P. Briner. (*Nature, Lond.*, 1958, **182**, 742.) A simplified paper chromatographic procedure is described in which a chloroform extract of the alkaloids, containing 60–20 μg. of strychnine is spotted on to Whatman No. 1 paper, and developed overnight with *n*-butanol: *n*-propanol: 0·05N hydrochloric acid (1 : 2 : 1) at 20° by an ascending technique. The paper is dried, photographed in the ultra-violet to locate the spots, which are cut out and eluted with water. The strychnine is determined spectrophotometrically in the aqueous solution at λ max 255 mμ. J. B. S.

BIOCHEMISTRY

GENERAL BIOCHEMISTY

Penicillin, Synthesis of: 6-Aminopenicillanic Acid in Penicillin Fermentations. F. R. Batchelor, F. P. Doyle, J. H. C. Nayler and G. N. Rolinson. (*Nature, Lond.*, 1959, **183**, 257.) The isolation of 6-aminopenicillanic acid

(I, R = H) from penicillin fermentations of *Penicillium chrysogenum* W.51.20 carried out in the absence of side-chain precursor, is reported. The product was detected, after removal of natural penicillins by solvent extraction at low pH, by treating with phenylacetyl chloride in the presence of sodium bicarbonate. The resulting antibiotic substance was indistinguishable from penicillin G (I, R = $CO{\cdot}CH_2C_6H_5$) on paper chromatograms; treatment similarly with phenoxyacetyl chloride gave a product indistinguishable from penicillin V (I, R = $CO{\cdot}CH_2O{\cdot}C_6H_5$).



(I)

Crystalline 6-aminopenicillanic acid has been isolated and converted into both benzyl- and phenoxymethylpenicillin, and the *N*-carbethoxy derivative (I, R = EtO) has been degraded by known methods to *N*-carbethoxyaminoacetaldehyde (isolated as the 2:4-dinitrophenylhydrazone). The antibacterial activity of 6-aminopenicillanic acid is less than that of the derived penicillins and the spectrum is different. It is destroyed by penicillinase but more slowly than benzylpenicillin, is unstable to alkali but stable to acid. The isolation of 6-aminopenicillanic acid is consistent with the view that introduction of the side chain is the last step in the biosynthetic process. J. B. S.

PHARMACY

Drug Release from Gradual Release Preparations, Determination of. D. J. Campbell and J. G. Theivagt. (*Drug Standards*, 1958, **26**, 73.) Apparatus similar to that specified in the U.S. Pharmacopoeia for tablet disintegration tests was used, the conditions being arranged to simulate *in vivo* conditions of motion, pH and temperature. The preparation was placed in the basket of the apparatus and treated with simulated gastric juice, followed by solutions containing increasing amounts of simulated intestinal fluid. The solutions were analysed, the percentage of medicament released during each hour calculated, and the general pattern of drug release determined. This procedure was applied to preparations consisting of drug embedded in inert plastic material, coated granules enclosed in capsules, and multilayered tablets, and can be used for evaluation of release patterns of most solid slow release preparations for oral use.

G. B.

Pyrogens, Investigations Concerning. G. van der Reijden. (*Pharm. Weekbl.*, 1958, **93**, 657.) In order to ascertain whether an asbestos pad could be used to make solutions pyrogen-free, a 1:50,000 solution of methylene blue was used: 10 sq. cm. of pad should decolorise not less than 300 ml. of this solution. A direct relationship existed between the area of pad and the volume of solution which could be freed from solute. When a test solution containing 4×10^6 cells of *Ps. aeruginosa* per ml. is used, 10 sq. cm. of pad should free 200 ml. of this solution from pyrogen. This contains more pyrogen than would normally occur in practice. It was found that 0·3 per cent activated charcoal was sufficient to adsorb the pyrogen from such a solution, and this was also achieved by 0·6 per cent of asbestos fibre. A rest period of a week or more between the tests was desirable for rabbits, and the test recommended which was based upon the fever reaction is described in detail. Attempts were made to design a seriological pyrogen test, but these failed because the by-products of only a few kinds of bacteria were adsorbed by erythrocytes, and even then the test was far less sensitive than the fever reaction produced in rabbits. Also haemolysis and other unwanted reactions sometimes occurred. D. B. C.

Pyrogens, their Properties and Destruction. K. D. Rudat. (*Pharmazie*, 1958, **11**, 677.) This paper includes a historical survey of work related to the initial recognition, properties and composition of pyrogens, with a discussion on their origin in solutions and their introduction via apparatus. This is followed by recommendations on the removal of pyrogens from solutions by Seitz filtration and destruction in apparatus by hot-air sterilisation at 160° to 200° for long periods. Mention is made of the preference of single-use plastic tubing over rubber tubing. B. R.

Reserpine, Oxidation of, During the Preparation as Tablets. O. Weis-Fogh. (*Arch. Pharm. Chem.*, 1958, **65**, 859.) Butylated hydroxanisole, hydroquinone, nordihydroguaiaretic acid, and propyl gallate were shown to prevent oxidation of reserpine during the preparation of tablets. The most effective antoxidant was nordihydroguaiaretic acid, a quantity of 20 μg. per 0·25 mg. tablet, dissolved in the reserpine solution before adding to the granulate, being sufficient to reduce the loss of reserpine below 1 per cent. The antoxidants did not prevent the deterioration of reserpine tablets stored in daylight. G. B.

***Salmonella abortus equi*, Chemical Analysis of Lipopolysaccharides in.** I. Fromme, O. Lüderitz, A. Nowotny and O. Westphal. (*Pharm. Acta Helvet.*, 1958, **33**, 391.) Lipopolysaccharides isolated from bacteria are extremely specific in immunisation for the particular bacteria, and the lipoid component is essential for the development of endotoxic activity. The highly purified lipopolysaccharide derived from *Salmonella abortus equi* is one of the most active of such agents for higher animals and man. This has been degraded into a phosphorylated polysaccharide and a lipid. The polysaccharide was resolved into glucosamine, galactose, heptose, glucose, mannose, rhamnose and 3-desoxy-D-fucose, and the percentage of each was determined. Stepwise hydrolysis of the lipopolysaccharide with N mineral acid for 3–5 minutes gave 45 per cent of a lipid designated A I and a phosphorylated polysaccharide fraction which was resolved into the above monosaccharides and phosphoric acid after prolonged acid hydrolysis. Lipid A I, after 30 to 60 minutes' further refluxing yielded 26 per cent of Lipid A which was soluble in chloroform and pyridine. Lipid A required 10 to 20 hours' refluxing with 6 N hydrochloric acid for complete hydrolysis into a fatty acid and water-soluble amino acids and phosphoric acid. Among the amino acids were glutamic acid, aspartic acid, α,ϵ-diaminopimelic acid, lysine, alanine and serine. Ethanolamine and other unidentified fractions were also isolated. D. B. C.

PHARMACOGNOSY

***Datura tatula*, Investigation of Mutations in.** E. Steinegger. (*Pharm. Acta Helvet.*, 1958, **33**, 357.) Mutations produced by X-rays in *Datura tatula* L. var. *inermis* Timm. are described. Small packets of seeds from one source were exposed to an equal intensity of X-rays from a copper source of known intensity. The batches were then grown for four generations with further irradiations. The following types of mutation were noticed, firstly, changes in appearance such as dwarfishness, curled leaves, small leaves, fruits and seeds and thorny fruits; secondly, plants with the tetraploid number of chromosomes and increased alkaloidal content and often correspondingly large pollen grains and seeds; thirdly, plants with pollen grains four times the normal size, but with the diploid number of chromosomes; and fourthly, diploid plants with increased alkaloidal content. D. B. C.

***Digitalis lanata* Ehrh., Changes in the Glycosidal Content of, during Development.** L. Fauconnet and D. Kutter. (*Pharm. Acta Helvet.*, 1958, 33, 369.) A method is described for the paper chromatographic separation and quantitative estimation of up to 15 active principles including some newly found glycosides in *D. lanata* Ehrh. From four to nine of these are found in the seed, three in the young plant, and twelve in the fully developed plant during the first year, and up to fifteen during the second year. Analyses on the leaves, stem and seeds showed that the distribution of glycosides was irregular, and that the concentrations varied with the time of day, the age of the plant and prevailing weather conditions. D. B. C.

PHARMACOLOGY AND THERAPEUTICS

Aspirin: Occult Blood in Faeces following Administration. L. Th. F. L. Stubbé. (*Brit. med. J.*, 1958, **2**, 1062.) Occult blood in the faeces occurred in about 70 per cent of 180 persons (mostly between 40 and 60 years of age) to whom aspirin in the form of tablets was given in doses of from 750 to 3000 mg. daily for periods of 14 days or more. Results obtained with 140 patients in the rheumatology wards were entirely comparable to those found in a control group of 40 healthy volunteers. The quantity of aspirin administered did not greatly influence the occurrence or seriousness of the result. Identical results were obtained whether the aspirin was given in powder form suspended in water or whether it was given as tablets. The value of coated tablets is doubtful, as 15 out of 20 patients gave a positive benzidine reaction following administration of such tablets. On the basis of the strength of the benzidine reaction in a number of cases it was shown that the quantity of blood lost following aspirin administration may not always be ignored, especially if the patient is already anaemic. Sodium salicylate tablets, whether coated or uncoated, did not give rise to a positive benzidine reaction. S. L. W.

Batyl Alcohol, Erythropoietic Stimulatory Activity of. J. W. Linman, F. H. Bethell and M. J. Long. (*J. Lab. clin. Med.*, 1958, **52**, 596.) In controlled experiments, racemic batyl alcohol, the monoglycerol ether of *n*-octadecyl alcohol, was administered subcutaneously to normal rats in doses of 12·5 and 25 mg. daily for 4 weeks. Batyl alcohol stimulated erythropoiesis apparently through accelerating erythroblastic cellular division but without associated augmentation in haemoglobin synthesis. This response was manifested by erythrocytosis due to microcytes with decreased osmotic resistance, reticulocytosis and myeloid erythrocytic hyperplasia. The substance also stimulated thrombopoiesis and probably granulopoiesis. The chemical, physical and physiological characteristics of batyl alcohol are similar to those of the thermostable, ether-soluble plasma erythropoietic factor, indicating that they may be the same or related compounds. The authors suggest that all aspects of myelopoiesis may be under the influence of humoral regulatory mechanisms and that batyl alcohol, produced in yellow bone marrow, may be of primary importance in such a system. W. C. B.

Chloroquine in the Treatment of Rheumatoid Arthritis. H. Fuld and L. Horwich. (*Brit. med. J.*, 1958, **2**, 1199.) Thirty-nine patients with rheumatoid arthritis largely resistant to other forms of treatment were treated with chloroquine and the results followed up for periods of up to 4 years. Complete remission was obtained in 12 patients, a major improvement in 19, and minor or no improvement in 8. The regimen adopted was as follows: (1) chloroquine,

600 mg. daily initially, reduced only when gastric irritation made it necessary (maintenance dose, 200 to 400 mg. daily); as no benefit from the chloroquine can be expected for some 3 weeks from the start of treatment, calcium aspirin was given during this period for symptomatic relief: (2) bed rest for several weeks or until the E.S.R. had returned to normal: (3) induced pyrexia (T.A.B. vaccine intravenously): (4) weekly transfusions of 1 pint of fresh blood for 3 or 4 weeks (in 11 patients): (5) injection of hydrocortisone acetate into single joints: (6) physiotherapy after acute stage. The drug was well tolerated by the majority of patients. Relapses while on chloroquine were not observed in this series. S. L. W.

Cyanocobalamin: Oral Administration in Pernicious Anaemia. J. N. M. Chalmers and N. K. Shinton. (*Lancet*, 1958, **2**, 1298.) From a study of 22 cases of pernicious anaemia in relapse further evidence is presented that oral cyanocobalamin can be absorbed and utilised by these patients. Daily oral doses of from 20 to 500 μg. of cyanocobalamin were given for periods varying from 15 days to 50 months. The drug was taken in a single dose, usually first thing in the morning. It was given as a syrup containing the cyanocobalamin in a 2-drachm dose. The syrup contained 20 per cent w/v sucrose and a small amount of sodium carboxymethylcellulose, with colouring and flavouring substances. The larger the daily oral dose, the more prompt is the response and the return of the serum-vitamin-B_{12} level to the normal range. Long-term studies show that daily oral doses of 100 μg. or more of cyanocobalamin can be effective in maintenance therapy, but there can be haematological and clinical remission without a return of serum-vitamin-B_{12} level to normal. Parenteral therapy with cyanocobalamin is still the most reliable method of ensuring freedom from relapse in pernicious anaemia but oral treatment taken daily may be effective. S. L. W.

Dequalinium in the Treatment of Skin Infections. R. B. Coles, C. Grubb, D. Mathuranayagam and D. S. Wilkinson. (*Brit. med. J.*, 1958, **2**, 1014.) Dequalinium chloride (Dequadin), in the form both of paint and cream, was used in 241 patients suffering from various skin conditions. Cure, or considerable improvement, resulted in 43 out of 51 staphylococcal skin infections, usually within a week; good results were also obtained (27 improved out of 35) in conditions of mixed aetiology in which staphylococcal or monilial infections played an important part. The results were especially gratifying in cases of secondarily infected eczema and infective eczematoid dermatitis round the ears and in the body folds. On the hairy areas, the beard and scalp, the paint was particularly useful. Eight out of 13 cases of ringworm were cleared or improved. Non-infective conditions did not respond. It appeared to be as effective as antibiotic preparations and dyes, and is colourless and pleasant to use. Apart from 3 cases of sensitisation, no irritant or toxic effects were observed, and it can be used on the mucous membranes and on the skin of infants. In 37 cases of pruritic skin conditions a dequalinium cream containing 0·5 per cent prednisolone showed a superior effect to the plain dequalinium cream and was successful in all cases. S. L. W.

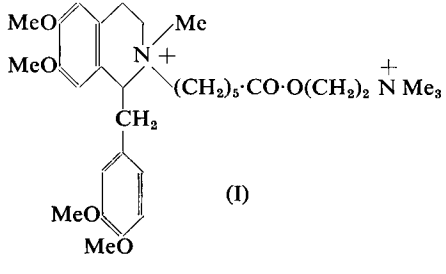
Methyprylone and Quinalbarbitone Compared as Hypnotics. T. J. Thomson. (*Brit. med. J.*, 1958, **2**, 1140.) The hypnotic effect of methyprylone (Noludar) was compared with that of quinalbarbitone, using the double-blind technique, in 128 patients ranging from 24 to 74 years of age, all of whom required hypnotic drugs. Powders of ascorbic acid were used as a control. The results were assessed by sequential analysis. No important difference could be detected

between the apparent hypnotic action of 200 mg. of methyprylone and the control powder, and no important differences were discovered between the hypnotic effects of 400 mg. of methyprylone and 100 mg. of quinalbarbitone.

S. L. W.

Morphine Derivatives, New, Acute Pharmacological Studies of Some. R. Okun and H. W. Elliott. (*J. Pharmacol.*, 1958, **124**, 255.) The analgesic properties, acute toxicity and effects on gastrointestinal motility of morphinone, 6-methylmorphine, 6-methyldihydrodesoxymorphine, 6-methylenedihydrodesoxymorphine and 6-methyl-7-hydroxydihydrodesoxymorphine were studied in mice. Morphinone was less potent in its analgesic effect and had a lower therapeutic index than morphine itself, but the remaining compounds, although their effects were briefer, were considerably more potent than morphine and their therapeutic indices were higher. All five compounds had weaker inhibitory effects than morphine on gastrointestinal motility. 6-methylenedihydrodesoxymorphine appeared to be the most promising compound, being, on a weight basis, 82 times as powerful as morphine in its analgesic action and only twice as toxic. Further tests on this compound were carried out on dogs in which it was again shown to be many times more potent than morphine in its analgesic effect although shorter in its duration of action. The respiratory depression produced by large doses of the compound was antagonised by nalorphine. Side effects were minimal suggesting that the compound may be clinically useful as a short-acting analgesic. W. C. B.

Neuromuscular Blocking Agents, Some New. H. O. J. Collier, J. M. Z. Gladych, B. Macauley and E. P. Taylor. (*Nature, Lond.*, 1958, **182**, 1424.) The advantage of suxamethonium in producing muscular relaxation during anaesthesia is its brevity of action but its disadvantage is that it has no satisfactory antagonist and that it sometimes causes post-operative muscle pains and stiffness. Laudexium (laudolissin) is antagonised by neostigmine and does not cause muscle pain but it is of longer duration of action than suxamethonium. Compounds have therefore been made, incorporating some of the chemical features of each into one molecule, in an attempt to obtain a substance which has the valuable properties of both suxamethonium and laudexium. Three series of compounds were investigated; the symmetrical bis-esters, the unsymmetrical mono-esters, and the symmetrical bis-amides. All the compounds were examined by intravenous administration to cats, recording blood pressure and tibialis muscle twitch. The potencies and durations of the neuromuscular blocking actions of the new compounds were compared with those of suxamethonium chloride or sometimes with those of tubocurarine chloride or laudexium methosulphate. Neostigmine methosulphate was used in antagonism tests. It was found that the only compound more active than suxamethonium was the unsymmetrical mono-ester, No. 43 (I), which was about



(I)

seven times as active as the reference compound, and appears to be one of the most potent synthetic neuromuscular blocking agents known. It was of long duration of action and did not show antagonism by neostigmine. Cats maintained by artificial respiration tolerated very large doses. The only compound briefer in action than suxamethonium was the symmetrical bis-ester No. 41 (structure given), which was of relatively low potency, and antagonised by neostigmine. M. B.

Nicotinamide, Tranquillising and Antiserotonin Activity of. D. W. Woolley. (*Science*, 1958, **128**, 1277.) Nicotinamide in a concentration of 0·01M completely inhibited the response of the isolated uterus from oestrogenised rats to 5-hydroxytryptamine (5-HT). The concentration of 5-HT used was just sufficient to elicit a maximal contraction of the untreated muscle. The antagonism did not appear to be strictly competitive. The same concentration of nicotinamide was only slightly effective in reducing acetylcholine-induced contractions of the uterus. Sodium nicotinate in a concentration of 0·01M was without antagonistic action to 5-HT in this tissue. In mice, large doses of nicotinamide protected the animals against the effects of hydroxytryptophan. The large doses of nicotinamide used also caused marked tranquillisation of the animals which was more severe than that produced in mice by reserpine.

W. C. B.

Normorphine, Analgesic Properties of, in Patients with Postoperative Pain. L. Lasagna and T. J. De Kornfeld. (*J. Pharmacol.*, 1958, **124**, 260.) The analgesic effects of subcutaneously administered morphine and normorphine were compared in controlled tests on 60 patients suffering from post operative pain. Normorphine in doses of 40 mg. was found to have approximately the same analgesic effect as 10 mg. of morphine. These results supply evidence against the theory that *N*-demethylation of morphine is necessary before its analgesic effects are produced in man. The authors conclude that it is unlikely that normorphine will offer any advantage over morphine in the treatment of acute pain. W. C. B.

Podophyllotoxin, Pharmacology of. G. Valette, M.-L. Hureau and J. Cariou. (*Ann. pharm. franç.*, 1958, **16**, 169.) Podophyllotoxin was shown to stimulate peristalsis in the small intestine and colon of the cat and rat (*in situ*). In experiments on the isolated organs, podophyllotoxin was found to have a depressant action on the rat duodenum, but it stimulated contraction of the rat colon and guinea pig ileum. Podophyllotoxin antagonised the action of acetylcholine on the rat duodenum, and potentiated the effect of histamine on the guinea pig ileum. Podophyllotoxin dissolves in blood serum in which it combines with serum albumin. A similar effect has been observed with anthraquinones and anthranols and may be the basis of their action on the intestine.

G. B.

Pyridine-2-aldoxime Methiodide and Diacetyl Monoxime against Organophosphate Poisoning. H. Edery and G. Schatzberg-Porath. (*Science*, 1958, **128**, 1137.) The protective actions of pyridine-2-aldoxime methiodide (PAM) and diacetyl monoxime (DAM), separately and in combination, were studied in white male mice against poisoning by tetraethylpyrophosphate, dyflos, bis(dimethyl amido) fluorophosphate and diethyl-*p*-nitrophenyl phosphate. Statistical analysis of the results showed that DAM potentiated the protective action of PAM against tetraethylpyrophosphate and bis(dimethylamido)

fluorophosphate but not against dyflos or diethyl-*p*-nitrophenyl phosphate. DAM administered alone showed a weak protective action against tetraethyl-pyrophosphate but was ineffective against bis(dimethylamido) fluorophosphate and diethyl-*p*-nitrophenyl phosphate. Residual cholinesterase in the brain and blood of animals which had either died from, or had survived, the poisoning was determined and practically no difference was observed in the two cases. The authors conclude that the results do not support the assumption that the protective action of the antidotes can be attributed mainly to their ability to reactivate cholinesterase. W. C. B.

Salicylate Anaemia. W. H. J. Summerskill and A. H. Alvarez. (*Lancet*, 1958, **2**, 925.) Severe 'iron deficiency' anaemia of uncertain cause had required continuous treatment with iron for 5 and 10 years respectively in a man of 47 and a woman of 40; total hysterectomy had failed to influence the anaemia in the woman. Habitually heavy consumption of salicylate compounds for headaches had coincided with the onset and subsequent course of the anaemia in both patients. Occult bleeding from the gastrointestinal tract was demonstrated during controlled periods of salicylate medication (10 grains of soluble aspirin twice or four times daily). After salicylate consumption had been greatly reduced anaemia did not recur during follow-up periods of 10 and 7 months without iron therapy. Salicylate consumption is put forward as a possible cause of anaemia, and where this is suspected as a causal factor the effect of withdrawing the salicylate should be tried before treatment with iron or alternative procedures such as total hysterectomy or laparotomy (which was contemplated in both these patients). S. L. W.

Triamcinolone: Comparison with Prednisolone in Rheumatoid Arthritis. F. D. Hart, J. R. Golding and D. Burley. (*Lancet*, 1958, **2**, 495.) The treatment of 24 patients with rheumatoid arthritis and of 1 with psoriatic arthopathy was changed from prednisolone to triamcinolone and, after periods varying from 5 to 70 days, back to prednisolone. The dose ratio of triamcinolone to prednisolone was 4/5. Of the 25 patients, 11 preferred triamcinolone, 3 preferred prednisolone, and 11 were indifferent. Measurement of sedimentation rate and digital tenderness remained unchanged; finger swelling and grip strength altered in only 5 patients, each of whom improved on triamcinolone. There were no acute rebound symptoms on changing to either drug. In only 5 cases was subjective improvement more than slight, in each case in favour of triamcinolone. Of 7 patients who complained of dyspepsia on prednisolone, 3 improved on triamcinolone and 3 deteriorated. In 3 patients abdominal striae appeared within 3 weeks of changing to triamcinolone, and 3 patients noticed post-prandial flushing on triamcinolone but not on prednisolone. Although triamcinolone does not differ greatly in its therapeutic action or side-effects from prednisolone it is a useful alternative steroid. S. L. W.

Triamcinolone in Lupus Erythematosus. E. L. Dubois. (*J. Amer. med. Ass.*, 1958, **167**, 1590.) Twenty-nine patients with systemic lupus erythematosus were treated with triamcinolone for periods of up to 14 months. The average initial dosage in mild cases was 20·6 mg. daily, and the average maintenance dose used to control mild exacerbations was 26 mg. daily. The pattern of clinical improvement closely paralleled that obtained by previous treatment with the older steroids. The fever abated in 24 hours, joint pains disappeared in several days, and pleural effusions and cutaneous lesions subsided in one to two weeks. Retinal changes, anaemia, adenopathy, and cachexia, gradually improved, and

renal abnormalities often returned to normal during steroid-induced remissions, though long-standing renal lesions were unaffected. The cutaneous side-effects, particularly Cushingoid appearance, hirsutism and striae were more marked than with the older steroids. The most serious side-effect was muscle weakness, most marked in the quadriceps groups, which appeared in 6 patients; the weakness gradually cleared on changing to another steroid. No cases occurred among 7 males in the series, and no male patients showed Cushingoid features. A major difference between triamcinolone and other steroids was a tendency, in 18 patients, towards progressive gradual weight loss, some of which was fluid loss. There was no evidence of sodium retention or potassium loss. There was evidence of peptic ulceration in only one patient, who received 96 mg. daily. Fourteen of the patients had received previous steroid therapy, and 7 of them were better controlled and felt better with triamcinolone than with other steroids. S. L. W.

Trimeglamide, A New Sedative and Soporific Drug. G. Cronheim, J. T. Gourzis and I. M. Toekes. (*Science*, 1958, **128**, 1570.) Trimeglamide (trimethoxybenzoyl-glycine diethylamide) has in animals a somnifacient action which is not preceded or followed by excitement or ataxia. In dogs the oral soporific dose was 50 mg./kg. and sleep lasted 2 to 6 hours. Sleeping animals could be easily aroused; when they responded normally to external stimuli. There were no effects on blood pressure, heart rate and respiration. Larger doses (100 mg./kg.) prolonged the sleep in cats. In dogs side effects appeared, emesis, muscle twitching and slight ataxia. Raising the dose to 500 mg./kg. had a stimulant effect, superimposed upon the soporific action, characterised by restlessness, purposeful locomotion, slight ataxia and some disorientation. There was an absence of hypnosis or anaesthesia. In man single or repeated oral doses of 500 to 1500 mg. caused sedation and drowsiness. There were no changes in electroencephalographic records and there was no hypnosis or anaesthesia. The acute toxicity was very low. Dogs, cats and mice have tolerated single oral doses of 500, 770 and 2000 mg./kg. respectively. In mice and dogs trimeglamide significantly prolonged the sleeping time and some tolerance developed to this effect following repeated doses of trimeglamide. Trimeglamide had an anticonvulsant effect in mice against electro-shocks.

G. F. S.

Vitamin B_{12} Absorption in Pernicious Anaemia. M. Schwartz, P. Lous and E. Meulengracht. (*Lancet*, 1958, **2**, 1200.) A study of the absorption of radioactive vitamin B_{12}, by the Schilling's technique, has shown that a blockage of absorption is common with patients with pernicious anaemia who have been treated orally for long periods with vitamin B_{12} and a purified preparation of hog pyloric mucosa. This blockage rarely occurs with unpurified preparations of whole pylorus. The blockage appears to be related to the hog intrinsic factor, a resistance having developed preventing absorption of B_{12}. Such patients absorb B_{12} bound to human intrinsic factor obtained from fundus mucous membrane. Absorption also occurs when vitamin B_{12} is given with rat gastric juice. It is suggested that blockage is due to an antibody being present directed against the activity of the intrinsic factor in hog pyloric mucosa.

G. F. S.

Yeast Extract and Ribonucleic Acid, Radiation Protective Effects of. K. D. Detre and S. C. Finch. (*Science*, 1958, **128**, 656.) In controlled experiments, the intravenous or intraperitoneal injection of a crude autolised extract of yeast was shown to provide a moderate degree of radiation protection in rats and mice

subsequently irradiated with a lethal dose of X-rays. In a further series of similar experiments, the protective effect of a commercial yeast ribonucleic acid preparation was studied and found to be considerably more effective than the yeast extract. These results indicate that ribonucleic acid, or a substance associated with it in the yeast autolysate, may be the principal radiation protective factor. W. C. B.

APPLIED BACTERIOLOGY

Mercurials, Microbiological Assay of in Pharmaceutical Products. D. V. Carter and G. Sykes. (*Analyst*, 1958, **83**, 536.) In order to compensate for the effects of other ingredients, a control preparation is made containing all the basic ingredients of the test preparation but no mercurial. A known amount of the mercurial under test is then incorporated in the control preparation in the same concentration as is assumed to be present in the test preparation, or in graded amounts if desired. Both test and control preparations are then treated in one of three ways. Firstly, serial dilutions are made in a broth of recommended composition and innoculated with a recommended strain of *E. coli* using a diluted culture and incubated at 37° for 48 to 72 hours. The end point is the greatest dilution at which no growth occurs. Secondly, one standard drop of undiluted culture is added to each tube and the result is read after 4 hours at 37°. The broth is weakly buffered to balance any acidity or alkalinity in the test material and contains bromocresol purple. The acid produced by the growth of the organism is sufficient to cause a colour change, which greatly assists with preparations such as creams which give turbid dilutions. Thirdly, a plate-diffusion method may be used following the same procedure as in the assay of penicillin in the B.P. using a recommended formula for nutrient agar and a culture of *Staph. aureus*. This method is more precise but is sensitive only to one part per million, whereas the first method is sensitive to 0·2 and the second to 0·05 parts per million. A table of comparative results is given. D. B. C.

Ristocetin and Framycetin: *In Vitro* Activity. R. W. Fairbrother and B. L. Williams. (*Lancet*, 1958, **2**, 1353.) Sensitivity tests by the serial dilution technique were carried out to assess the *in vitro* activity of ristocetin and framycetin. Ristocetin was shown to be particularly effective against Gram-positive but has little effect against Gram-negative organisms. The pneumococcus was the most sensitive organism; *Str. pyogenes* and *Str. faecalis* were also sensitive. *Staph. aureus* was relatively resistant. Three strains developed a two-fold increase in resistance after 12 passages. Framycetin was shown to have a wide range of activity against both Gram-positive and Gram-negative organisms. The pneumococcus was the most sensitive organism. Strains of *Staph. aureus* showed wide difference in sensitivity and 25 out of 50 were relatively resistant. *Str. pyogens* and *Str. faecalis* show a similar pattern and are both moderately resistant. Activity against Gram-negative organisms was very variable; only 5 out of 23 strains of *Ps. pyocyanea* could be classified as sensitive. Resistant strains of *Staph. aureus* develop rapidly—2 strains showed an eight-fold increase in resistance by the twelfth passage; *Ps. pyocyanea* showed an even more rapid development of resistance. The clinical application of ristocetin is likely to be limited but it may prove useful in infections due to antibiotic-resistant *Staph. aureus* and of enterococcal endocarditis. S. L. W.