ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Colchicine, Polarographic Determination of. F. Santavy. (*Pharm. Acta Helvet.*, 1948, **23**, 380.) The method, applied to the seeds, is as follows. 5 g. of the powdered seeds is macerated for 3 hours at 75°C. with 96·5 g. of water. Water is added to make the weight up to its original value, followed by 3·5 ml. of a saturated solution of lead acetate. After filtration, 60 ml. of the filtrate is treated with 0·25 g. of trisodium phosphate, and again filtered. To 2 ml. of this solution is added 2 ml. of phosphate buffer solution (*p*H 7 to 8), and, after the removal of oxygen, the polarographic curve is determined. The quantity of colchicine is obtained from a standardisation curve with pure colchicine. On account of the presence of other reducible substances, the values are about 6 per cent. high. For the same reason the method is not suitable for other parts of the plant. For tincture of colchicum, 20 g. of the tincture is evaporated on the water bath to one fourth of its volume and, after cooling, diluted with water to 17 g. The determination is then continued as before with the addition of 1 g. of lead acetate solution and 2 ml. of a saturated solution of sodium phosphate. G. M.

Digitoxin, Effect of Various Alkalis on the Sensitivity of the Baljet Reaction. F. K. Bell and J. C. Krantz, Jr. (*J. Amer. pharm. Ass., Sci. Ed.*, 1948, **37**, 297.) The Baljet test, used by the U.S.P. XIII as a colorimetric control for digitoxin, depends upon the red colour produced when a methyl alcoholic solution of trinitrophenol containing sodium hydroxide is added to a methyl alcoholic solution of digitoxin. The effect of replacing the alkali with ammonium hydroxide, lithium hydroxide, tetramethylammonium hydroxide and tetraethylammonium hydroxide was investigated. With ammonium hydroxide the colour was not produced, and lithium hydroxide made no significant difference to the test. The quaternary ammonium bases, on the other hand, gave a deeper, more intense and more stable colour, which also reached its maximum intensity more rapidly. Using these results, the following procedure was developed for preparing the reaction mixture. To 2 ml. of a 0·02 per cent. solution of digitoxin in methyl alcohol, add 0·1 ml. of a 5 per cent. solution of trinitrophenol in methyl alcohol, mix, and add 2 ml. of a 10 per cent. aqueous solution of tetraethylammonium hydroxide. The maximum colour develops in 10 minutes and remains constant, within the limits of experimental error, for about 30 minutes. The modified test is twice as sensitive as that of the U.S.P., and appreciably more sensitive than the alternative Keller-Kiliani test of the U.S.P. G. R. K.

Linoleic Acid in Edible Fats, Determination of. W. J. Stainsby. (*Analyst*, 1948, **73**, 429.) The calculation of the composition of a fat containing saturated acids, oleic, and linoleic acids involves the use of 3 simultaneous equations; the total acid equation, another involving the use of iodine values of oleic and linoleic acids, and a third involving the quantitative titration of the acidic glycerides produced by oxidation of the fat. In the third determination the fat is oxidised in anhydrous acetone with potassium permanganate followed by titration of the acidic glycerides

after the removal of the steam-volatile acid products. Results obtained with several hydrogenated cottonseed oils and with 3 samples of sesame, sunflower-seed and palm oils compared very favourably with those obtained by the thiocyanogen method, and by the spectrophotometric method involving alkali isomerisation to a conjugated acid which is subsequently estimated from its ultra-violet absorption spectrum. The method can be extended with little loss of accuracy to determine the total unsaturated acids of oils containing more than 2 unsaturated acids. In the case of fats generally with a higher acid value than that allowed by the British Pharmacopœia, errors arise and such fats should be neutralised before the determination is carried out. R. E. S.

Methyl Alcohol, Quantitative Colorimetric Microdetermination of, with Chromotropic Acid Reagent. R. N. Boos. (*Anal. chem.*, 1948, **20**, 964.) The reaction of formaldehyde when heated with chromotropic acid (1:8-dihydroxynaphthalene-3:6-disulphonic acid) in the presence of sulphuric acid to give an intense violet-red colour is used as the basis for the determination of methyl alcohol. A known weight of organic material under test is mixed with water (4 ml.), distilled, and 3 ml. of the distillate collected. One ml. of this solution (diluted to contain 20 to 100 μg. of methyl alcohol per ml.) is oxidised for 10 minutes with 3 drops of dilute phosphoric acid solution (10 ml. of 50 per cent. acid diluted to 100 ml. with water) and 5 drops of potassium permanganate solution (5 per cent.); decolorisation of excess of potassium permanganate is effected by the addition drop by drop of saturated sodium bisulphite solution. Four drops of a 2 per cent. aqueous solution of chromotropic acid is added, the mixture heated at 60°C. for 15 minutes, cooled in an ice-bath, allowed to reach room temperature and then diluted to 10 ml. The intensity of colour of the solution is measured in a suitable colorimeter, the peak light absorption occurring at 5800Å. A blank determination is necessary each day as the chromotropic acid solution darkens with time. The reaction is specific and the following do not interfere: acetaldehyde, propionaldehyde, butyraldehyde, *iso*butyraldehyde, *iso*valeraldehyde, crotonaldehyde, chloral hydrate, glyoxal, benzaldehyde and phthalaldehyde. Glyceraldehyde gives a yellow colour. Good agreement was shown between the method proposed and the Zeisel method, and the method can also be used for the determination of methoxyl groups in methyl esters with a relative error of less than 2 per cent. R. E. S.

FIXED OILS, FATS AND WAXES

New Zealand Fish Oils. A. P. Oliver and F. B. Shorland. (*Biochem. J.*, 1948, **43**, 18.) The fats from 8 specimens of school or snapper shark (*Galeorhinus Australis*) selected at random were studied separately. The livers varied in oil content from 23·1 to 60·7 per cent. and contained from 66·8 to 93·0 per cent. of the total oil reserves of the fish. Tables are given which contain weights of organs and size of each specimen; proportions of tissues and distribution of fats; analytical determinations of vitamin A, unsaponifiable matter, saponification equivalent, and iodine value of liver, body, and head fats. Ester fractionation analyses of 4 of the liver oils, and of the phosphatide and glyceride fractions of the combined head and and body lipids showed that the liver fatty acids contained more palmitic acid and C_{18} unsaturated acids, but less stearic acid than the head and body lipids. The wider differences in content of C_{18}, C_{20} and C_{22}

unsaturated acids of the liver oils amounting to as much as 6·3 units per cent. were thought to be outside experimental error, although this was not conclusive in view of previous variations in accuracy. The composition of the liver fats did not appear to be influenced by the extent to which the liver was used for fat storage, in contrast to the results of Rapson obtained from a study of teleostean species. R. E. S.

Oils and Fats, Stability of. E. Sandell. (*Farm Revy.*, 1948, **47**, 699, 715.) A low peroxide content of oils and fats is not a guarantee of stability, as in the preparation of the material it is possible that natural antoxidants may have been removed without an appreciable amount of oxidation occurring. Further, traces of metals may have a great influence. Lard has a much lower stability if fish oils have been used in the animal feeding-stuffs. Finally, a strongly oxidised fat may be refined to a low peroxide content, but its stability remains poor. In order to decide on the keeping properties of a sample of oil or fat it is thus necessary to apply special stability tests. In these tests the oxidation is accelerated by raising the temperature, increasing the surface exposed to air, by light, and by traces of metals, of which copper is the most active, while manganese, iron, and chromium also have a marked action. The latter method is of little practical value, since natural antoxidants (synergists) in the oils are probably effective by reason of forming complexes with traces of metals. Accelerated stability tests do not always predict accurately the behaviour of oils and fats on storage, since the reactions may take a different course under different conditions, but they form a useful guide. When testing fatty pharmaceutical preparations, with or without antoxidants, the stability tests should be carried out under conditions approximating as closely as possible to those encountered in actual use. Results obtained by the addition of an antoxidant to a pure fat cannot be extended to a galenical preparation made with that fat. G. M.

Rape Seed Oil, Component Acids of. M. N. Baliga and T. P. Hilditch. (*J. Soc. chem. Ind., Lond.*, 1948, **67**, 258.) The component acids of four rape seed oils—Indian (Toria, Guzerat), Polish (Danzig), and Argentine (Plate)—and of ravison and Jamba rape seed oil have been examined by crystallisation from ether at −40° C. under suitable conditions, previous to ester-fractionation. In this way it was possible to determine approximately the 3 unsaturated and 5 saturated minor component acids as well as the 4 major ones, viz., erucic, oleic, linoleic and linolenic acids. The average fatty acid composition of the 4 rape oils is: palmitic 2·5, saturated C_{16}, C_{20}, C_{22}, C_{24} (together) 5, hexadecenoic 2, oleic 15, linoleic 13·5, linolenic 8, eicosenoic 5, erucic 48, docosadienoic 1 per cent. (wt.). Ravison oil fatty acids contain less erucic (39 per cent.) and more linoleic (21 per cent.). Jamba rape oil fatty acids contain less erucic (37·5 per cent.) and apparently larger proportions of oleic (*c.* 20 per cent.) and eicosenoic (*c.* 11 per cent.) acids. The procedure for the examination of the component acids of these cruciferous seed oils, admittedly difficult to resolve, is given in detail. H. F.

PLANT ANALYSIS

Pyrethrum Flowers, Analysis of. W. Mitchell, F. H. Tresadern and S. A. Wood. (*Analyst*, 1948, **73**, 484.) A systematic study has been made of the Seil method, depending on the fact that chrysanthemum

dicarboxylic acid is not volatile in steam in contrast to the monocarboxylic acid, and of the Wilcoxon-Holaday method, depending on the fact that only the monocarboxylic acid is readily soluble in light petroleum. Pure chrysanthemum acids were used in the study and the behaviour, recovery and stability of the acids under varying conditions are reported. The Seil method was found to give low results for pyrethrin I and slightly high results for pyrethrin II, the inaccuracies being due to a temperature effect and not to mineral acid. It is suggested that the apparent loss of chrysanthemum monocarboxylic acid is due to hydration and that the resultant hydroxy-acid is partly responsible for the slightly high figures for pyrethrin II. A modified Seil method gave accurate total pyrethrum figures when compared with the Wilcoxon-Holaday method. The latter method could give accurate results for pyrethrin I and for pyrethrin II if a small modification was used. The methods were applied to pyrethrum extracts confirming the results. The presence of extraneous volatile acids was confirmed but found not to interfere with the accuracy of the results by either method. R. E. S.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Vitamin B_{12}, A Cobalt Complex. E. L. Rickes, N. G. Brink, F. R. Koniuszy, T. R. Wood and K. Folkers. (*Science*, 1948, **108**, 134.) Vitamin B_{12} appears to be a cobalt co-ordination complex which, having six groups about the cobalt atom, could involve one or more organic moieties. The presence of cobalt is significant in view of the many biological studies which have shown it to be an essential trace element in nutrition. The cobaltous ion (1 μg./ml.) was without activity for *L. lactis* as contrasted with the high potency of B_{12} (0·000013 μg./ml., half maximum growth). Spectrographic examination of B_{12} showed the presence of phosphorus; nitrogen was present but tests for sulphur were negative. Microbiological assay of an aqueous solution at B_{12} (74μg./0·5 ml.) showed that autoclaving for 15 minutes at 121°C., did not change the activity within the experimental error of $11{\cdot}4 \times 10^6 \pm 0{\cdot}6 \times 10^6$ μ/mg. Vitamin B_{12} in 0·015N sodium hydroxide solution (0·2 μg./ml.) was inactivated (microbiological assay) at room temperature as follows: 20 per cent. (0·67 hr.), 45 per cent. (6 hr.), 90 per cent. (23 hr.), 95 per cent. (95 hr.); it was inactivated in 0·01N hydrochloric acid solution (10 μg./ml.) as follows: 18 per cent. (3 hr.), 75 per cent. (23 hr.), 89 per cent. (95 hr.). R. E. S.

BIOCHEMICAL ANALYSIS

Myanesin in Body Fluids and Tissues, Determination of. E. Titus, S. Ulick and A. P. Richardson. (*J. Pharmacol.*, 1948, **93**, 129.) Two procedures are described. The more useful of these, which is generally applicable to plasma and urine, depends on the fact that under proper conditions phenolic ethers can be made to couple with the more reactive diazonium compounds. A less sensitive method for plasma determinations, involves periodate oxidation of the glycerin side chain to formaldehyde, which may then be determined colorimetrically with chromotropic acid; it gives results in agreement with the coupling procedure. Determination of

plasma levels after intravenous injections into normal dogs of doses of 50 and 100 mg./kg. shows that the compound rapidly disappears from the blood stream. The total amount of myanesin excreted in the urine was in no case more than 2 per cent. of the original dose; it would appear that the drug is distributed throughout the body water. S. L. W.

Stilbœstrol, Hexœstrol and their Glucuronides in Urine, Colorimetric Estimation of. F. H. Malpress. (*Biochem. J.*, 1948, **43,** 132.) Methods of preliminary extraction are described which enable estimations of these œstrogens and their glucuronides in urine to be made, using the nitration method of Malpress. Detailed methods of extraction are given for free stilbœstrol and hexœstrol and for their monoglucuronides in cow's urine; modifications necessary for similar extractions from human urine are also described. It was found that hydrolysis of the urine resulted in destruction of added glucuronide and it was therefore essential to prepare extracts of urines before hydrolysing; traces of peroxide if present in ether used for extraction also reduced the recoveries of the œstrogens. Using the processes described, recoveries ranging from 66 to 79 (mean 70) per cent. were obtained for known amounts of stilbœstrol added to cow's urine, and from 52 to 64 (mean 60) per cent. for known amounts of stilbœstrol glucuronide; recoveries from human urine gave mean values of 80 and 63 per cent. for the free and conjugated forms respectively. The comparatively low recoveries of the glucuronide were due to the decomposition during hydrolysis. With hexœstrol recoveries of 70 per cent. of free œstrogen and 74 per cent. of hexœstrol glucuronide were obtained from cow's urine; for human urine the recovery was 85 per cent. for both free and combined forms. Volumes of urine used for estimation should contain from 0·5 to 2·0 mg. of œstrogen. Blank values for the free œstrogen process using cow's urine fell normally within the range 0·05 to 0·2 mg. of œstrogen/100 ml. of urine, although occasionally these values were greatly exceeded, blanks of 2 mg. being obtained. Blank measurements for the corresponding conjugated-œstrogen method were invariably low and of the order of 0·05 to 0·2 mg. of œstrogen/100 ml. of urine. The values given by the simplified modification applicable to human urine were less than 0·05 mg. of œstrogen for the free process, and less than 0·15 mg. of œstrogen for the conjugated form, from 100 ml. of urine. R. E. S.

Streptomycin in Tissues and Urine, Chemical Determination of. V. C. Jelinek and G. E. Boxer. (*J. biol. Chem.*, 1948, **175,** 367.) The previously reported method of estimation of streptomycin by determining the fluorescence of its acridyl hydrazone has been extended to permit the estimation of streptomycin in body tissues and in urine. The various methods of determining streptomycin are compared and analytical details of the isolation and estimation of streptomycin in lung, brain, heart, liver and spleen tissue and in urine are given. The recoveries of known amounts of streptomycin added to urine and tissues are recorded; they varied considerably. Human urine containing from 2 to 50 μg./ml. gave results of 95± 6 per cent.; dog liver gave recoveries of 103 ± 14 per cent.; rabbit brain gave recoveries of 99 ± 6 per cent. The lower limit of sensitivity was 2 μg./ml. of urine and 2 μg./ml. of tissue. The method was found to be of value in the determination of streptomycin in urine and tissues following parenteral administration. R. E. S.

Suramin in Plasma, Estimation of. J. C. Gage, F. L. Rose and M. Scott. (*Biochem. J.*, 1948, **42,** 574.) A method for estimating suramin

in aqueous solution or in serum and plasma is described. The procedure depends on the colour change (deep red to pale yellow) observed when suramin is added to 2-*p*-dimethylaminostyryl-6-acetamidoquinoline methochloride. The corresponding change in absorption is from λ_{max} 495 mμ to λ_{max} 450 mμ for the two colour bands, with the greatest difference between the two curves at 505 mμ. Plasma proteins do not interfere with the suramin reaction and the concentration of the drug in plasma may be determined by comparing the optical density of the dye solution (at 505 mμ), to which has been added diluted plasma (in sufficient 0·9 per cent. sodium chloride solution to prevent globulin precipitation), with that of the dye solution without suramin. Satisfactory results were also obtained using an absorptiometer with an Ilford 603 blue-green filter. The procedure yields similar results to those obtained using the hydrolysis method followed by diazotisation and coupling with methyl-α-naphthylamine. The hydrolysis products of suramin have been investigated and the specificity of the method is discussed.

R. E. S.

CHEMOTHERAPY

Dienœstrol and Hexœstrol, Tetra-alkyl Substituted Analogues of. J. B. Niederl and P. Weiss. (*J. Amer. chem. Soc.*, 1948, **70**, 2894.) By conversion of the phenols, *p*-xylenol, thymol and carvacrol into the corresponding 2:5-dialkyl-4-hydroxypropiophenone, tetra-alkyl analogues of dienœstrol and hexœstrol were prepared. The tetra-alkylated hexœstrols derived from thymol and carvacrol showed only feeble œstrogenic activity when injected subcutaneously in oily solution into ovariectomized rats. The compound derived from *p*-xylenol, 3:4-*bis*(2′:5′-dimethyl-4′-hydroxyphenyl)-hexane, in contrast, gave positive œstrus response in all the rats at 50 and at 5 μg. dose levels and in most of the rats at 2 and 1 μg. dose levels thus comparing favourably with its dimethyl analogue, 3:4-*bis*-(5′-methyl-4′-hydroxy-phenyl)-hexane prepared from *o*-cresol. F. H.

Sulphones: Studies in the Chemotherapy of Tuberculosis. E. Hoggarth and A. Martin. (*Brit. J. Pharmacol.*, 1948, **3**, 146.) The testing of a large number of sulphones and related sulphonates and sulphonamides against *M. tuberculosis in vitro* is recorded. On the basis of high *in vitro* activity ten new compounds were selected for therapeutic tests on mice. Therapeutic activity was found with 4:4 diaminodiphenylsulphone and with 2:4′ diamino-5-thiazylphenylsulphone, but no activity was observed with any of the others. Therapeutic tests in mice show that high *in vitro* activity does not necessarily lead to activity *in vivo*. S. L. W.

Thiohydantoins and Thioimidazoles. M. Jackman, M. Klenk, B. Fishburn, B. F. Tullar and S. Archer. (*J. Amer. chem. Soc.*, 1948, **70**, 2884.) As it had previously been shown that 2-thiohydantoin possessed half and 2-thioimidazole one and a half times the anti-thyroid activity of 2-thiouracil, and that enhancement of activity occurs on substitution of 2-thiouracil, a series of 5-alkyl-2-thiohydantoins and 4-alkyl-2-thioimidazoles has been prepared and examined. It was found that substitution in the 5-position did not result in any significant increase in the anti-thyroid activity of 2-thiohydantoin. In the 2-thioimidazole series, substitution in the 4-position increased the activity, 4-*n*-propyl-2-thioimidazole, the most active compound prepared, being about three times as active as 2-thioimidazole and about five times as active as 2-thiouracil. F. H.

PHARMACY

DISPENSING

Oils and Fats, Sterilisation of. J. Kessler. (*Pharm. Acta Helvet.*, 1948, **23**, 387.) Oils and fats cannot be sterilised either in free steam or in the autoclave. Dry heating (90 minutes at 160°C.) is satisfactory.

G. M.

Sterilisation Technique, Efficiency of. O. Bang and A. T. Dalsgaard. (*Arch. Pharm. Chemi.*, 1948, **55**, 699.) For testing the efficacy of various methods of sterilisation, the authors used garden soil. This material required at least 20 minutes at 120°C. to produce complete sterility. The results of the tests showed that in 61 per cent. w/w alcohol, heating at 100°C. for at least 1 hour in a sealed container was necessary for complete sterilisation. When suspended in oil, the dry heating required was at least 10 hours at 140°C., 3 hours at 160°C., or 1 hour at 180°C. The alcohol method may be applied to the sterilisation of procaine hydrochloride and of boric acid in powder, also to laminaria. In the latter case the material is kept under 61 per cent. alcohol for 24 hours to extract soluble salts, then transferred to tubes, covered with the diluted alcohol, and closed with cotton wool and a loosely screwed-on lid. After 1 hour in flowing steam, the alcohol is removed and the tubes are dried at 105°C.

G. M.

PHARMACOLOGY AND THERAPEUTICS

Conessine, *iso*Conessine and *neo*Conessine, Pharmacological Properties of. R. P. Stephenson. (*Brit. J. Pharmacol.*, 1948, **3**, 237.) Conessine, an alkaloid obtained from the bark and seeds of *Holarrhena antidysenterica*, and its isomers, *iso*conessine and *neo*conessine (prepared by treating conessine with sulphuric acid) possess properties very similar to those of quinine and quinidine; in doses, however, in which quinine was active as an antimalarial, conessine and its isomers showed no similar activity. When tested by intracutaneous injection into guinea-pigs connessine and its isomers were shown to possess marked local anæsthetic potency, conessine being about twice as active as cocaine, *iso*conessine about 50 per cent. stronger than cocaine, and *neo*conessine being about equal to cocaine. The relative local anæsthetic potencies of conessine and its isomers and of cocaine, quinidine and procaine are very similar to their related activities in depressing the action of acetylcholine on the frog rectus muscle. This is a further addition to the evidence that the action of acetylcholine is concerned with the sensation of pain. Conessine also resembles quinidine in diminishing the action of acetylcholine on the isolated intestine, the rabbit auricle, the frog rectus and on denervated mammalian muscle, and in lengthening the refractory period of cardiac tissue, and the effect of vagal stimulation on the heart in the anæsthetised rabbit is temporarily abolished by conessine as by quinidine.

S. L. W.

Dimercaprol (B.A.L.), Effect of Environmental Temperature on. F. F. McDonald. (*Brit. J. Pharmacol.*, 1948, **3**, 116.) Variations of 15 to 85 per cent. in mortality occurred in groups of rats used as standard controls in assaying samples of dimercaprol. So wide a difference in response was greater than would be expected by chance and some other external factor was suspected of contributing to the toxic effects of dimer-

caprol. Temperature being the greatest variant to which the rats were subjected, experiments were conducted to see if this affected the mortality of rats caused by a standard dose of dimercaprol. Rats injected intramuscularly with 140 mg./kg. of Oxford Standard B.A.L. were kept in thermostatically controlled chambers at temperatures varying from 39°F. to 84°F. for 72 hours after injection. The results showed a quite remarkable effect of temperature on toxicity, the mortality rate varying from 20 to 100 per cent., with a minimum mortality at 63°F. Rats used for assays should therefore be kept at an even temperature or in a thermostatically controlled room if possible, and no estimation of the relative toxicity of samples should be made without reference to the results obtained from a dose of a standard preparation given at the same time. If propylene glycol is used as a vehicle for injection, the required amount should be distilled off on the same day.

S. L. W.

Dimercaprol. (B.A.L.) and its Glucoside, Effects of, in Acute Lead Poisoning. M. Weatherall. (*Brit. J. Pharmacol.*, 1948, **3**, 137.) In mice poisoned by repeated intraperitoneal injections of lead acetate the mortality was reduced slightly by dimercaprol and significantly by the glucoside, but it was difficult to produce lead poisoning suitable for experimental study in these animals. In suitable concentrations dimercaprol prevented the action of lead acetate on rabbit red blood cells *in vitro*. If it was added half or one hour after the lead acetate the effect was small and consisted chiefly in preventing the full effect of the lead, not of significantly reversing the established change in fragility. Mixtures of dimercaprol and plasma in certain proportions, and plasma from rabbits injected with dimercaprol, protected washed erythrocytes from the effect of lead acetate less than did equal amounts of dimercaprol or plasma alone. In rabbits poisoned by a single dose of lead acetate given by stomach tube dimercaprol and the glucoside each significantly decreased the subsequent anæmia and increased the coproporphyrinuria. The mortality was apparently unaffected by dimercaprol but was reduced by the glucoside, though the number of rabbits was too small for the difference in mortality to be significant. The action in lead poisoning appears to be one of inactivating lead ions not yet taken up by cells, rather than of actually de-leading cells or altering the cell lead so as to prevent its fragility effect. There is certainly no reversal of poisoning comparable to that seen with arsenicals. Clearly the drug prevents the acute hæmolytic anæmia as long as it is available in the circulation, but on the other hand certain features of lead poisoning are enhanced, notably the coproporphyrin excretion and possibly the speed of the reticulocyte response. The available evidence does not warrant its use in clinical plumbism, but it would perhaps be premature to reject all dithiols as useless or dangerous. S. L. W.

Iron, Intravenous, in the treatment of Anæmia. H. G. B. Slack and J. F. Wilkinson. (*Lancet*, 1949, **256**, 11.) A stable iron-sucrose preparation suitable for intravenous administration was prepared as follows. Dissolve anhydrous ferric chloride 5.8 g. in distilled water 50 ml. on a water-bath at 95°C, add sucrose 28 g. and heat until dissolved; dissolve anhydrous sodium carbonate 1.8 g. and sodium hydroxide 5 g. in 25 ml. of water each; add the carbonate solution to the ferric chloride solution with stirring; add the sodium hydroxide solution, stir for 15 minutes, filter into rubber-capped vials or into ampoules and autoclave for 20 minutes. After autoclaving, a clear, dark brown solution is obtained, with a *p*H of about 10.5, which remains stable at room temperature for at least 12 months. The solution contains

2 per cent. of iron and 200 mg. is therefore contained in 10 ml. The scheme of dosage adopted in the treatment of 60 cases of iron-deficiency anæmia was 25 mg. on the first day, 50 mg. on the second day, 100 mg. on the third, and 200 mg. on the fourth and subsequent days, the injections being given into the antecubital veins at the rate of about 2 ml. per minute; the treatment was usually complete in 10 out-patient visits. Reactions, if any, were mild. In almost all cases the hæmatological and clinical responses were often as dramatic as those obtained when patients with pernicious anæmia in relapse receive adequate doses of a potent intramuscular liver extract, a reticulocyte peak of 10 to 18 per cent. developing within 7 to 10 days from the beginning of treatment. The calculated iron deficit given in this manner is utilised almost quantitatively and does not appear to require the addition of trace elements, ascorbic acid or folic acid. With a further 60 patients treated with a commercial iron-sucrose preparation there was no detectable difference in tolerance or response. S. L. W.

Paludrine, Activation of. F. Hawking and W. L. M. Perry. (*Brit. J. Pharmacol.*, 1948, **3**, 320.) Experiments with exo-erythrocytic forms of *Plasmodium gallinaceum* grown on tissue culture showed that paludrine in concentrations of 2 mg./l. exerts no apparent antimalarial action on the parasites *in vitro;* similarly, a concentration of paludrine of 20 mg./l. has no action *in vitro* on the endo-erythrocytic form of *P. cynomolgi;* these concentrations are higher than those commonly reached in the blood during human therapy. If, however, paludrine has been previously exposed to the action of body cells, either by injecting it into a monkey or fowl and collecting the serum, or by incubating it with minced rat liver, it exerts marked antimalarial action, preventing the development of the parasites. These results suggest that paludrine itself is not active against plasmodia, but that it undergoes some chemical modification by the body or by liver which converts it into a compound with plasmodicidal activities. S. L. W

Phthioic Acid and Synthetic Analogues, Pathogenic Effect of. J. Ungar, C. E. Coulthard and N. Dickinson. (*Brit. J. exp. Path.*, 1948, **29**, 322.) A number of synthetic acids closely related chemically to phthioic acid were tested by intraperitoneal injection into the guinea-pigs. The doses given ranged from 10 to 200 mg. and the animals were examined at various intervals of time after the injection. One of the more active substances, 3:12:15-trimethyldocosanoic acid, produced waxy deposits in various abdominal organs within 8 days of the injection of 25 mg., and white rounded nodules within 14 days. Intradermal injection produced erythema within 24 hours and nodule formation within 3 days. The changes were similar to those produced by an irritant foreign body of lipoid nature and often similar to those due to tubercular lesions. The pathogenic properties of the acids tested do not appear to be related to chemical structure. H. T. B.

Posterior Pituitary Extract, Standardisation. Modification of Dale and Laidlaw Method. P. Holton. (*Brit. J. Pharmacol.*, 1948, **3**, 328.) The Dale and Laidlaw method suffered from three defects, namely, that suitable guinea-pigs were relatively scarce, that the assay often required many hours, and that the error was about 20 per cent. Schild's null hypothesis (*J. Physiol.*, 1942, **101**, 115) was applied to an assay employing a modification of the Dale and Laidlaw method. A rat's uterus was used as the test preparation, since rats are cheaper and more easily obtained. One assay is described, and the

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