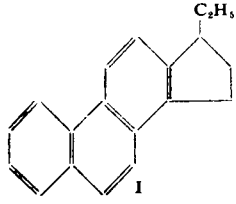
ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

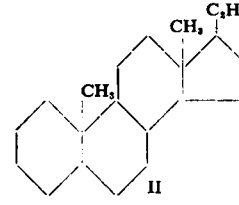
CHEMISTRY

ALKALOIDS

Conessine, Constitution of. R. D. Hayworth, J. McKenna and N. Singh. (Nature, 1948, **162**, 22.) Careful fractionation of the selenium dehydrogenation products of the hydrocarbon mixture $C_{21}H_{30}$, from pyrolysis of conessine dihydriodide, yielded a crystalline hydrocarbon C_{19} H_{18}, m.pt. 78° to 79°C., which showed many similarities with synthetic 3-ethyl*cyclo*-pentenophenanthrene (I), m.pt. 84·5° to 85·5°C., although the identity was not convincingly established.



I



II

Degradation of conessine by the Hofmann and Emde processes gave a hydrocarbon $C_{21}H_{30}$ which on reduction yielded approximately equal amounts of two isomeric hydrocarbons $C_{21}H_{36}$, m.pt. 56° to 58°C. and 83° to 84°C. The latter isomer is identical chemically and physically with *allo*pregnane (II) prepared from progesterone. The carbon atoms of conessine are therefore accounted for by the *allo*pregnane structure (II) and the three N-methyl groups, but the positions of the ethylenic linkage and the points of attachment of the basic centres are still uncertain. R. E. S.

Iodosalicylates of Alkaloids. M. Covello and A. Capone. (*Ann. Chim. appl., Roma*, 1948, **38**, 123.) 3-Iodosalicylic acid and 5-iodosalicylic acid were compared with picric acid and styphnic acid as reagents for the detection of alkaloids. In general the solubilities of the salts are greater than those of the corresponding picrates and styphnates, that is, the reaction is less delicate. Pilocarpine did not precipitate in 10 per cent. solution and codeine only in solutions stronger than 0·7 per cent; these salts may be useful for hypodermic use. The 3-iodosalicylates of brucine (m.pt. 224°C. decomp.), quinine (m.pt. neutral 164° to 164·5°C., basic 156°C. decomp.) cinchonine (m.pt. 167·5° to 168°C.) morphine (m.pt. 194° to 194·5°C. decomp.) and strychnine (decomposes at about 192°C.) were prepared and illustrations of the microscopic appearance of the crystals, which may be useful for identification of the alkaloids, are given.

H. D.

ANALYTICAL

Adrenaline, Determination of, with Iodine. J. Ehrlen. (*Farm. Revy*, 1948, **47**, 321.) The photometric determination is usually carried out at *p*H 4 to 7. At a higher *p*H the colour rapidly fades owing to further oxidation; at a lower *p*H the colour development is very slow. By using oxidising agents such as potassium ferricyanide, adrenochrome is produced with an absorption maximum at 485 mμ. With iodine, however, a mixture of adrenochrome and iodoadrenochrome is obtained and the absorption maximum may be anywhere

between 485 and 525 mμ. The more acid the solution, the greater the proportion of iodoadrenochrome. The mixed colour has sometimes been considered incorrectly as a variation of colour with the *p*H. In the method of Thorvik, carried out at *p*H 4·8, the adrenaline is converted almost quantitatively into iodoadrenochrome. Other oxidising agents simplify the course of the reaction; potassium ferricyanide is very suitable. At *p*H 6 the oxidation velocity is fairly high and nearly quantitative, corresponding to a calculated molar extinction coefficient of 4250 at 485 mμ. The reaction of the solution is then adjusted to *p*H 3 to 4, when the adrenochrome is very stable. An advantage of this method is that, in presence of procaine, no precipitate is formed. When iodine is used, the extinction curves for adrenochrome and iodoadrenochrome cut one another at 525 mμ and at this point the result is independent of the proportions of the two compounds formed. G. M.

Adrenaline, Fluorimetric Determination of. J. Ehrlen. (*Farm Revy.*, 1948, **47**, 242.) The method, which is applied particularly to procaine solutions, is a development of that recently published by the author, and the fluorescence is now measured photometrically, using a filter (maximum transmission at 405 mμ: cut-off at 480 mμ) in the incident light, and another filter (not transmitting below 500 mμ) between the sample and the photo cell. The fluorescence results from atmospheric oxidation in alkaline solution, but is rapidly destroyed by further oxidation. It is suggested that the fluorescent compound is 1-methyl-3 : 5 : 6-trihydroxyindol, formed directly from adrenochrome. Under the conditions given by the author, the oxidation of adrenaline to adrenochrome is quantitative, and in the next stage the addition of a reducing agent prevents the further oxidation of the fluorescent compound during the assay. Details are as follows. A sample containing 3 to 30 μg. of adrenaline and 10 to 50 mg. of procaine is diluted with water to 3 ml. and mixed with 0·1 ml. of 0.1M hydrochloric acid and 0·5 ml. of 0·15M (2 per cent.) sodium acetate solution. To this is added 1·0 ml. of a 0·5 per cent. solution of potassium ferricyanide. After two minutes the mixture is made up to 25 ml. with a mixture of 5 ml. of 5M sodium hydroxide, 5 ml. of alcohol (95 per cent.), 10 ml. of water, and 0·5 ml. of a 5 per cent. solution of ascorbic acid. The solution is transferred to a sample holder, and the fluorescence is read off after 15 minutes. A blank on the reagents is also done. The standardisation should be carried out on solutions and under conditions similar to those of the assay. G. M.

Alkyl Nitrates, Determination of, in Pharmaceutical Preparations. P. Lundgren and T. Canbäck. (*Svensk farm. Tidskr.*, 1948, **52**, 298, 313, 333.) Although the phenoldisulphonic acid method of determination of nitrates is in general satisfactory, it has certain limitations. In particular it is not suited for the determination of alkyl nitrates in oil solutions or in ointments. These limitations do not apply to *m*-xylenol-(4-hydroxy-1 : 3-dimethylbenzene), which is nitrated to *o*-nitroxylenol(5-nitro-4-hydroxy-1 : 3-dimethylbenzene). A photometric determination of the dissociation constant of the nitro compound showed that it had a value for pk_A of $7{\cdot}98 \pm 0{\cdot}04$. This indicates that to develop the full colour the *p*H of the solution must be not less than 11. The absorption curve has two peaks, at 268·5 and 396 mμ. A detailed examination of the reaction, as applied to the determination of glyceryl trinitrate, mannityl hexanitrate, sorbityl dinitrate, and pentaerythrityl tetranitrate showed that these compounds were quantitatively hydrolysed under the conditions chosen. The nitration of the *m*-xylenol gave an 82 per cent. yield of the nitro compound, and the recovery of the latter by steam distillation was 95 per cent. Thus

an accurate analysis may be obtained by using a standard curve prepared from potassium nitrate. For tablets it is necessary to adjust the quantities according to the following table.

Substance	Wt. per tablet	*a* mg.	*b* ml.	*c* ml.	*d* ml.	*e* mg.	Solvent
Glyceryl trinitrate	0·00025—0·001	1·5—4	10	50·0	5·00	0·15—0·40	ether
Mannityl hexanitrate	0·005 —0·015	7·5—20	20	100·0	2·00	0·15—0·40	ether
Pentaerythrityl tetranitrate	0·030	15—40	20	100·0	1·00	0·15—0·40	acetone
Sorbityl dinitrate	0·002—0·010	6—15	10	50·0	2·00	0·25—0·60	ether

A weight of powdered tablets corresponding to *a* mg. of alkyl nitrate is extracted with *b* ml. of solvent for some minutes, and the solution is decanted through a filter paper, the extraction being continued with three more quantities of solvent, and the combined solution is made up to *c* ml. An aliquot of *d* ml. (corresponding to *e* mg. of alkyl nitrate) is transferred to a 250-ml. beaker, evaporated in a current of cold air, and treated with 1·0 ml. of a 2 per cent. solution of *m*-xylenol in acetone and 10·0 ml. of 72 per cent. sulphuric acid. The beaker is covered and left for 30 minutes, after which time the reaction is stopped by adding 50 ml. of water. The mixture is then distilled into a cylinder containing 5 ml. of N/1 sodium hydroxide, the distillation being carried out slowly, taking in all about 5 to 8 minutes, and stopped when 15 ml. have distilled over. The product is made up to 50 ml. and the extinction determined at 447 mμ. The percentage of nitrate is determined from a standard curve obtained with potassium nitrate. If necessary, the ether solution may be washed with sodium sulphate solution before the hydrolysis to remove interfering substances. In the case of sorbityl dinitrate, white flecks may appear in the receiver and it is necessary to filter the solution before making up to volume. For ointments the method is similar, but it is necessary to agitate the mixture from time to time during the hydrolysis. Ointment bases such as soft paraffin or lanoline do not interfere. G. M.

Bismuth, A New Reaction of. M. Jean. (*C.R. Acad. Sci., Paris*, 1948, **226**, 85.) To 1 ml. of a slightly acid solution of bismuth nitrate (containing about 0·2 mg. of bismuth) is added 10 ml. of a solution containing 0·32 g. of rubianic acid and 6·5 g. of silicotungstic acid per l. A white turbidity is produced. On heating for 10 minutes in a water-bath a brown colour appears, proportional to the amount of bismuth. The optimum acidity for the reaction corresponds to 0·1N nitric acid; the limits being from 2N to *p*H3. A distinct reaction is obtained with 20 μg. of bismuth at a dilution of 1 in 100,000. Interference is produced by metals which react with rubianic acid (copper, nickel, cobalt, ruthenium and platinum) or with silicotungstic acid (caesium), also by silver, mercury, zinc, cadmium and antimony. Chlorides weaken the reaction; acetates and tartrates prevent it. The reaction may be used for colorimetric determination. G. M.

Calcium and Magnesium, in Solutions for Hypodermic and Intravenous Use, Determination of. R. Vigni. (*Ann. Chim. appl., Roma*, 1948, **38**, 133.) Solutions of calcium and magnesium thiosulphates are used parenterally. To determine the amounts of the bases present in these solutions, the calcium is precipitated by adding a large excess of ammonium chloride, heating to boiling, making alkaline with ammonia and adding ammonium oxalate; the precipitate

is washed 8 or 10 times with ammoniacal water, heated to 40°C. for 2 hours to remove free ammonia, dissolved in dilute sulphuric acid and titrated with permanganate. The precipitate is free from magnesium, which will all be in the filtrate and washings. These are mixed, heated to 80°C. and a slight excess of the reagent recommended by Autenrieth added, which precipitates the magnesium as ammonio-magnesium phosphate. After 3 or 4 hours, the precipitate is washed by decantation with 2·5 per cent. ammonia, dried at 40°C. for 2 hours to remove excess of ammonia, and titrated with N/1 hydrochloric acid, using methyl orange as indicator, until an orange colour is obtained; 1 ml. of N/1 hydrochloric acid equals 0·01216 g. of magnesium. H. D.

Diamidines, Amperometric Microtitration of. J. B. Conn. (*Anal. Chem.*, 1948, **20,** 585.) A number of diamidines were observed to give highly insoluble red alizarinsulphonates in neutral solutions, but attempts to use the reaction colorimetrically or gravimetrically failed; an amperometric titration procedure was successful. Alizarinsulphonic acid is polarographically reducible, the half-wave potential being −0·67 volt (against the saturated calomel electrode) and at −0·90 volt a steady diffusion current is reached. When a solution of diamidine salt in neutral buffer was titrated with a solution of sodium alizarinsulphonate a plot of the diffusion current at −0·90 volt against reagent volume could be resolved into two straight lines intersecting at a 1 to 1 equivalence point. The diamidines studied were (1) 4:4′-stilbenedicarboxyamidine diisethionate (stilbamidine), (2) 4:4′-oxydibenzamidine dihydrochloride (phenamidine), (3) *p,p*-(trimethylenedioxy) dibenzamidine dihydrochloride (propamidine), and (4) 4:4′-(pentamethylenedioxy) dibenzamidine dihydrochloride (pentamidine). Graphs are given for the titration of these compounds, and also for their decomposition under sterilisation conditions. The overall reproducibility found was ±0·5 per cent., the greatest spread of results being 1·5 per cent. for phenamidine.

R. E. S.

Digitoxin, Colorimetric Assay. A. T. Warren, F. O. Howland and L. W. Green (*J. Amer, pharm. Ass., Sci. Ed.*, 1948, **37,** 186.) In alkaline solution digitoxin gives a purple colour with sodium-β-naphthaquinone-4-sulphonate which changes to yellow on acidification. The yellow colour is stable and can be measured photometrically. Procedures are described for detecting digitoxin and for estimating it in powder and tablets. Interfering substances include lanatoside A and lanatoside C, which give strongly positive tests and lanatoside B and gitoxin, which give weakly positive tests; digitonin gives a negative result. The intensity of the colour is increased by aldehydes, necessitating the use of aldehyde-free alcohol. The effect of lactose in inhibiting the formation of the purple colour was avoided in the assay of tablets by extracting with chloroform; no other excipient interfered. Results of the assay of 5 samples of digitoxin powder and 8 samples of tablets, indicate the repeatability of the method, which should be useful for rapid routine analysis. G. R. K.

Fatty Acids of Intermediate Chain Length, Estimation by Partition Chromatography. M. H. Peterson and M. J. Johnson. (*J. biol. Chem.*, 1948, **174,** 775.) The partition chromatograms used consisted of tubes packed with a coarse diatomaceous earth moistened with water or aqueous sulphuric acid as the non-mobile phase. As the developing solvent, thiophene-free benzene alone and mixed with Skellysolve B, and butanol-

chloroform mixtures were used. Sulphuric acid (27 to 35N) was found to be a better solvent and a better non-mobile phase than water; using both these solvents quantitative separation of formic, acetic, propionic, *n*-butyric, caproic, caprylic, and capric acids is possible. Detailed procedure is given for the quantitative analysis of fatty acids in biological materials. Fatty acids, in known mixtures or fatty acids added to butter fat, were recovered with a maximum error of 8 per cent. R. E. S.

Frangula Bark, Assay of. K. Erne. (*Svensk farm. Tidskr.* 1948, **52**, 345, 377.) The method adopted for determining the biological activity of frangula bark was as follows: White mice were starved for 15 hours, and varying doses of the bark mixed with soft cheese, malt extract and water (8+8+1) were given. Observations were made after 4 hours. A positive reaction was shown by diarrhœa with copious yellowish-brown excretions. Each sample was tested on 3 groups of about 20 animals, each group receiving a different dose. The results were compared with those obtained with a sample which was taken as standard. Chemical tests were as follows. Total anthraquinones: 0·1 g. of the bark was refluxed with 30 ml. of M/2 sulphuric acid for half an hour. The mixture was then extracted in a separating funnel with successive 25-ml. quantities of ether until all the colour was extracted. The ether solution was filtered, and shaken out with 20-ml. quantities of M/2 sodium hydroxide. The alkaline solution was acidified with sulphuric acid and re-extracted with ether. The filtered ethereal extract was shaken with M/4 lead acetate until no more dark precipitate was formed, then extracted with M/2 sodium hydroxide, and the extract was made up to 50 ml. with the alkali. Ten ml. of this solution was diluted to 50 ml. with M/2 sodium hydroxide and, after 20 minutes, the extinction was determined at 530 mμ. The extinction coefficient for emodin is 3·88. Free anthraquinones: These were determined as above with the omission of the acid hydrolysis. Anthranols: 0·1 g. of the bark was refluxed with 10 ml. of M/2 sulphuric acid for 15 minutes, and the mixture extracted with 10-ml. quantities of ether until all the colour was extracted. The ether solution was dried with sodium sulphate, filtered, and passed through an alumina column (Brockmann) containing 5 g. of alumina. After developing the chromatogram with 50 ml. of dry ether, the yellow fluorescent zone was separated and treated with a few drops of a solution of 0·5 g. of selenious acid in concentrated sulphuric acid. A greenish black colour showed the presence of anthranols. The approximate percentage was determined by acid hydrolysis of the glycosides, extraction with benzene and petroleum ether, and chromatographing on calcium and magnesium carbonates, the anthranols being finally isolated and oxidised to anthraquinones which were determined photometrically. The results of the chemical and biological tests were not closely parallel, but it is considered that the chemical test is able to estimate the clinical value of the bark within about 20 per cent. The results obtained do not show any definite relation between bark thickness and physiological activity, although for a thickness below 0·7 mm. the activity was proportional to the thickness, and above this value the activity appeared to be constant, although for one sample of bark there was a marked peak at 2·5 mm. Thus the view that there is a maximum activity in bark from stems of 3 to 4 years old is not confirmed. There was in general no inequality between barks of the official thickness (1·5 mm.) and thicker ones. Anthranols may be present even in samples which have been heated at 100°C and then stored for one year. An official

test for anthranols would appear to be desirable. Heating at 100°C. for one hour had no deleterious effect on the potency, but stabilised the anthraquinone content. Such a treatment might well be substituted for that of storage for one year. G. M.

Morphine, Electrophotometric Determination of. Laura Nicolini. (*Ann. Pharm., Fr.*, 1947, **5**, 528.) The official colorimetric method of the British Pharmacopœia for the determination of morphine is criticised. In the search for a reaction specific for morphine, which allows determination of the alkaloid without previous extraction, the author adapted the colorimetric method of Guarino. A solution, containing from 5 to 10 mg. of morphine, was placed in a 50 ml. flask and 10 ml. of N/10 hydrochloric acid added. The mixture was shaken, while 10 ml. of a 1 per cent. solution of iodic acid was added, followed after exactly 30 seconds, by 15 ml. of a saturated solution of ammonium carbonate. The mixture was allowed to stand for a short while with occasional shaking. The volume was adjusted with the solution of ammonium carbonate and several drops of a 0·2 per cent. solution of ferric chloride, acidified with N/5 hydrochloric acid, were carefully added drop by drop, till no further colour change took place. Excess of ferric chloride must not be added, since it causes precipitation of a hydrate or the iodide, which colours the violet solution yellow and would interfere with the electrophotometer reading. The assay was continued by Guarino's method, and colour intensity was estimated photometrically. Opium had first to be extracted by triturating with N/10 hydrochloric acid, and shaking for 20 minutes, before using this method. The photometer readings plotted against the content of morphine in mg., gave a straight line and obeyed Lambert-Beer's law. L. H. P.

Senna Glycosides, Colorimetric Estimation of. By W. Kussmaul and B. Becker. (*Helv. chim. Acta.*, 1947, **30**, 59.) A satisfactory and reproducible colour for the estimation of the glycosides sennoside A and B can be produced as follows: the aglycone is obtained by heating 10 ml. of a 0·5 to 1·0 per cent. alkaline solution of glycoside with 5 ml. of concentrated hydrochloric acid on a steam bath for about 15 minutes, when precipitation should be complete. After cooling, the precipitate is redissolved in concentrated sodium hydroxide, and the solution is extracted with 80 ml. of ether in a separating funnel, and then acidified with 50 per cent. sulphuric acid. The yellow ethereal layer is run off, any further precipitate in the aqueous layer is dissolved with more sodium hydroxide and the solution is shaken with 40 ml. of ether. The ether-fraction is next shaken with 3 or 4 quantities, each of 5 ml., of sodium bicarbonate solution. The mixed sodium bicarbonate solution is then extracted with 60 ml. of ether and acidified with 50 per cent. sulphuric acid. The aqueous layer is twice extracted with 20 ml. quantities of ether. Any deposit should be redissolved by the addition of alkali before shaking with ether. The mixed ether extracts are then filtered and the filtrate should be used within 10 hours. 5 ml. of the filtered solution is then extracted with 10 ml. of N/1 caustic soda. It is then treated with 0·2 ml. of 3 per cent. hydrogen peroxide and gently heated for about 4 minutes. A standard colorimeter curve is prepared by dissolving 30 mg. of pure sennoside B (dried in vacuo at 80°C.; equivalent to 18·75 of aglycone) in about 50 ml. of water with aid of a few drops of alkali. 10 ml. of this solution is hydrolysed with hydrochloric acid as above and 5 ml. of the resulting solution is oxidised as above. This solution is estimated in either a Zeiss-Pulfrich Photometer or a " Weka " Havemann photoelectric

colorimeter and the readings are transferred to a graph which for both sennoside A and B is a straight line passing through zero. A. D. O.

Sodium Diethyl- and Phenylethylbarbiturates, Acidimetric Titration of. H. Baggesgaard-Rasmussen and F. Reimers. (*Dansk Tidsskr. Farm.*, 1948, **22**, 166.) Determination of the acidity exponents for diethylbarbituric acid and phenylethylbarbituric acid in aqueous alcohol gave the following figures. Diethylbarbituric acid, *p*k8·96 (alcohol 50 per cent.); 9·54 (alcohol 75 per cent.); phenylethylbarbituric acid *p*k8·61 (alcohol 50 per cent.), 9·20 (alcohol 75 per cent.). Since the barbituric acids are weaker in dilute alcohol than in water, the end point is sharper and there is no precipitation of the free acid during titration. The titration of the sodium salts is carried out as follows. 0·100 g. of sodium diethylbarbiturate or 0·1250 g. of sodium phenylethylbarbiturate is dissolved in a mixture of 10 ml. of alcohol (86 per cent. by weight) and 5 ml. of water, and titrated with aqueous N/10 hydrochloric acid to a green colour, using bromophenol blue as indicator. G. M.

Sulphonamides, Microscopic Identification of. G. L. Keenan. (*J. Amer. pharm. Ass., Sci. Ed.*, 1948, **37**, 202.) Optical crystallographic data and microchemical tests are described for sulphanilamide, sulphadiazine, sulphapyridine, sulphathiazole, sulphaguanidine and sulphamerazine, together with optical crystallographic data of certain of the complexes obtained in the microchemical tests. The tests described are based upon complexes formed with the following reagents: for sulphanilamide, aromatic aldehydes and silver nitrate; for sulphadiazine, gold bromide and hydrochloric acid; for sulphapyridine, gold chloride; for sulphathiazole, picrolonic acid; for sulphaguanidine, nitric acid; and for sulphamerazine, gold chloride and sodium bromide, and picrolonic acid. G. R. K.

Sulphur in Organic Compounds, Microdetermination of. A. Steyermark, E. Bass and B. Littman. (*Anal. Chem.*, 1948, **20**, 587.) Sulphur-containing organic compounds which gave low results by some micro-analytical methods were analysed satisfactorily by burning, following the Carius method, after which the resulting sulphate was titrated with barium chloride by the tetrahydroxyquinone indicator technique. R. E. S.

Tragacanth, Powdered, Evaluation of. Report No. 1 of the Tragacanth Sub-Committee of the Analytical Methods Committee of the Society of Public Analysts. (*Analyst*, 1948, **73**, 368.) This report deals with the measurement of the viscosity of mucilages made from the powdered gum. The falling sphere method and the U-tube method were rejected as being unsuitable or difficult to apply, and a method is recommended using a Redwood No. 1 viscometer. The principle of determining the concentration of the dry gum that would be required to produce a mucilage with a corrected efflux time of 100 sec. for 50 ml. of mucilage at 20°C. was adopted. Details of preparation of the mucilage, determination of viscosity and method of calculation are given. The moisture content is determined by drying about 1 g. of the powder in an open dish to constant weight in a steam-heated oven. R. E. S.

Water, Detection of. P. Boymond. (*Pharm. Acta Helvet.*, 1948, **23**, 207.) A powder which may be used for the detection of water is composed as follows: bromophenol blue, 5 parts; sodium carbonate, anhydrous, 15 parts; starch, 40

parts; tragacanth, 40 parts. This is dusted on the concave face of a watch-glass which has previously been smeared with a thin layer of soft paraffin. The watch-glass is placed on a crucible containing the material to be tested. On heating the bottom of the crucible with a small flame, the presence of water is shown by a violet colour appearing on the watch-glass. The method will detect 2 mg. of water. The reaction is not given by organic liquids, and it may be used to detect water in pomades and other galenical preparations. G. M.

GLYCOSIDES, FERMENTS AND CARBOHYDRATES

Potato Starch, Fractionation of. Part IV. Absorption Spectra and Colour Intensities of the Starch-Iodine Complexes. L. H. Lampitt, C. H. F. Fuller and N. Goldenberg. (*J. Soc. chem. Ind., Lond.*, 1948, **67**, 97.) Over the range 2400 to 7500 Å, the absorption spectra of the starch-iodine complexes of potato starch and its cold-water-soluble and hot-water-soluble fractions are very similar qualitatively to those of wheat starch fractions, the visible part of the spectrum (4300 to 7500 Å) being most sensitive to any changes in the starch. Depolymerisation by grinding lowers absorption only at the longer visible wave-lengths; at 5700 Å the effect, if any, is very small and disappears over the range 4300 to 5300 Å. Depolymerisation by grinding appears to consist in disruption of the unbranched parts of the amylopectin molecules and of the unbranched parts of the amylose molecules. The cold-water-soluble fractions of potato starch are richer in amylose and poorer in amylopectin than the hot-water-soluble fractions; in wheat starch fractions, the reverse is the case. The greater solubility of potato starch amylose in cold water is attributed to its lower molecular weight. The different behaviour of wheat starch is due either to the absorption by the amylose of the lipids present in the starch or to increased association between the amylose and amylopectin by means of hydrogen bonding, or to a combination of these factors. G. R. K.

INORGANIC

Clays, Effect of the Absorption of Sulphur on the Colloidal Properties of. A. Malquori. (*Ann. Chim. appl., Roma*, 1948, **38**, 137.) The thixotropic index of clays, measured by Winkler's method, is increased by heating them with sulphur. The clay is thoroughly mixed with flowers of sulphur and heated in a tube for one hour at 130° to 140°C. For comparison the original clay is similarly treated without sulphur. The index increases up to a point with increased quantities of sulphur and then falls off, but the behaviour varies greatly with different clays. A sample of bentonite, which consisted of montmorillonite, increased up to 30 per cent. of sulphur, one of kaolin, consisting of kaolinite, up to 5 per cent., and one of Gavi clay (sericite) up to 15 per cent. The author discusses the relation of these different behaviours with the crystalline structures of the different types of clay, and connects it with the content of hygroscopic moisture. H. D.

Hydrogen, Evolution from Ferrous Hydroxide. U. R. Evand and J. N. Wanklyn. (*Nature*, 1948, **162**, 27.) Ferrous hydroxide, pure enough to be almost colourless, was precipitated by mixing ferrous chloride and potassium hydroxide solutions in an atmosphere of hydrogen. After precipitation the ferrous hydroxide and supernatant liquid were left in a flask connected to a manometer, but no hydrogen evolution was detected under these conditions even with ferrous chloride in excess. Further experiments

following those of Schikorr also failed to yield hydrogen even when the reactants were heated to 100°C. Hydrogen was, however, evolved at room temperature with excess of ferrous sulphate if platinum chloride, colloidal platinum, nickel sulphate, nickel powder, copper powder or sodium sulphide was added. Manganese sulphate yielded no hydrogen under these conditions. R. E. S.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Antimalarial Agents and Their Action on the Glucose Metabolism of Plasmodia. P. B. Marshall. (*Brit. J. Pharmacol.*, 1948, **3**, 1.) Using blood from chicks heavily infected with *Plasmodium gallinaceum*, the authors show that quinine and mepacrine exert inhibitory activity at several points in the glucose metabolism of plasmodia. Quinine inhibits hexokinase and phosphoglyceraldehyde dehydrogenase moderately, and possibly lactic dehydrogenase and pyruvate oxidation. Mepacrine inhibits hexokinase strongly, phosphoglyceraldehyde dehydrogenase moderately, and probably pyruvate oxidation. Further studies are necessary to find what proportion of the total inhibitory action takes place at the different points in the carbohydrate metabolism, and, indeed, whether the greater part of the inhibition does take place against the carbohydrate metabolism, or against other metabolic functions. S. L. W.

Benzimidazole, The Folic Acid Activity and Antagonism of Two Structurally Related Derivatives of. P. C. Edwards, Dorothy Starling, A. M. Mattocks and H. E. Skipper. (*Science*, 1948, **107**, 119.) Substances having an action like folic acid have previously been reported, and so have compounds which are antagonistic to folic acid. The authors have studied two benzimidazole derivatives for their folic acid activity or antagonism, because the benzimidazole nucleus closely resembles the purine nucleus and shows competitive action with amino-purines. The first compound examined was N-(4-[{(2-benzimidazoyl)-methyl} -amino]-benzoyl)-glutamic acid in which the pterin nucleus (pyrimido-4 : 5-pyrazine) of pteroylglutamic acid had been substituted by the benzimidazole nucleus; it retained a certain degree of folic acid activity, as measured by the growth stimulating effects on *Streptococcus fæcalis*. The other compound investigated was N-(4-[(2-benzimidazolyl)-methyl-amino]-benzenesulphonyl) glutamic acid, which had a sulphonyl group in place of the ketonic group of the first compound; the substance reversed the biological activity of folic acid on *S. fæcalis* and became a metabolite antagonist. This reversal of activity is reminiscent of the essential metabolite antagonist theory for the sulphonamides, and throws some doubt on the specificity of the pteridin nucleus for the folic acid system. L. H. P.

Heparin, a New Extraction Procedure for. O. Snellman, R. Jensen and B. Sylven. (*Nature*, 1948, **161**, 639.) Solutions of potassium thiocyanate exert a pronounced power of extracting the mast cell granular substance from liver tissue fairly quickly and completely. Using M/1 potassium thiocyanate solution for 24 hours, the authors obtained about 90 per cent. extraction of the metachromatic material in ox liver. Histochemical examination of the tissue residues showed only insignificant amounts of metachromatic substances left after such extraction. After extraction the potassium thiocyanate was readily removed by dialysis, leaving the following fractions to be analysed: tissue residue, precipitate, supernatant and dialysate. These fractions were

treated by tryptic digestion, and the heparin contents assayed by estimating the anticoagulating effects by means of the thrombin method of Jaques and Charles. The yield of heparin, expressed in mg. of " standard heparin," was 61·8 mg./kg. of liver, the tissue residue yielding 5·5 mg./kg., the precipitate 56·3 mg./kg., and the supernatant and dialysate nil. S. L. W.

Penicillin Standards. C. R. Bond. (*Analyst*, 1948, **73**, 254.) The development and history of British standard penicillins is described, with details of a new working standard consisting of a crystalline sodium salt with an appreciably higher potency and containing only 0·4 per cent. of penicillin F in addition to penicillin G. A comparison of the composition of various penicillin standards is given, the determinations being made by Goodall and Levi's micro-chromatographic method. R. E. S.

BIOCHEMICAL ANALYSIS

Mercury in Organic Material, Determination of, by Polarographic Methods. G. Costa. (*Ann. Chim. appl., Roma*, 1948, **38**, 157.) By the destruction of the organic matter by suitable means and conversion of the mercury to iodide the metal may be determined polarographically. For urine, pass a strong current of chlorine through 250 ml. at 80°C. for 1 hour; then pass a strong current of air in the cold for 1 hour, filter and concentrate on the water-bath to about 100 ml. Pass hydrogen sulphide through the liquid and, whether mercury is present or not, a brown precipitate is obtained. Set aside for 24 hours. Decant the clear liquid and centrifuge the remainder, washing the precipitate with a little water saturated with hydrogen sulphide. Then dissolve the precipitate in chlorine water, passing chlorine gas if necessary for a few minutes. The liquid remains turbid owing to the separation of sulphur. Filter into a graduated 20 ml. flask and make up to volume. This may be added to Schwartz's solution (potassium iodide, 4 g.; sodium acetate, 4·22 g.; gelatin (or, better, tylose) 0·2 g. in 100 ml. of water). Curves are given showing the results with different quantities of mercury and also the results of the presence of other heavy metals. The results are accurate within about 10 per cent. and 2 mg. of mercury per litre can be determined. H. D.

Œstrone, Equilin and Equilenin, Determination of, by Infra-red Spectrophotometry. J. Carol, J. C. Molitor and E. O. Haenni. (*J. Amer. pharm. Ass., Sci. Ed.*, 1948, **37**, 173.) Mixtures of these ketosteroids were analysed by measuring the optical densities of solutions of their benzenesulphonyl esters in carbon disulphide at selected wave-lengths for each component in the infra-red region. The concentration of each component was calculated from graphs prepared by plotting optical density against concentration for each substance at the selected wave-lengths. The selected wave-lengths were 10·45 μ, at which equilenin shows maximum absorption, 10·88 μ, at which œstrone shows the maximum, and 10·96 μ, at which equilin shows the maximum. The benzenesulphonyl esters were chosen because they are readily prepared, show the greatest differences in absorption at the selected wave-lengths, and are sufficiently soluble in carbon disulphide. The method gave satisfactory results with 20 prepared samples, and with mixtures recovered from commercial oily solutions of natural œstrogens. G. R. K.

Penicillin, Assay by the Dilution Method. C. G. Pope. (*Analyst*, 1948, **73**, 247.) A full description of this assay has already been published (Pope

and Stevens, *Bull. Health Org., L. of N.*, 1946, **12**, 274.) and reference is made to essential details only. Growth curves are given from the practical results obtained, the purpose being to indicate the reason for the sharp end-point shown in this assay procedure. Figures are given of results obtained in comparative determinations of various standard penicillins and the advantages and disadvantages of the assay are tabulated. A method is outlined for the assay of penicillins G and K in commercial samples, depending on the fact that penicillins G and K give different values in terms of I.U./mg. when assayed against *Staphylococcus aureus*, while more nearly equal weights of each are adsorbed on charcoal. R. E. S.

Penicillin, Investigation on the Iodimetric Method of Estimation of. A. M. Wild, (*J. Soc. chem. Ind., Lond.*, 1948, **67**, 90.) The method depends upon measuring the amount of iodine absorbed by the penicilloates produced by alkaline hydrolysis (Alicino, *Industr. Engng. Chem., Anal. Edit.*, 1946, **18**, 619; *Quart. J. Pharm. Pharmacol.*, 1947, **20**, 59.) The results are shown to vary with temperature, concentration of potassium iodide in the iodine solution, *p*H, and the purity of the penicillin. The original suggestion that the effects of the impurities could be overcome by performing the blank titration immediately after addition of the iodine supposed that the impurities absorbed iodine immediately and that they were unaffected by alkali. Both suppositions are shown to be in error, and it seems doubtful whether the method can be used for the estimation of low-grade penicillin. For reasonably pure samples, the errors introduced are not large, and by strict control of conditions results are obtained which are more consistent and reliable than those from the usual bioassay. Using the modified procedure described, results have compared favourably with triplicate bioassays on the same samples. For samples of high penicillin G content, with potencies over 1000 units/mg., differences greater than 3 per cent. have been rare and the error progressively decreased as the samples tended to absolute purity. The repeatability of the method has been found to be of the order of $\pm$ 1·5 per cent. G. R. K.

Penicillin, Microbiological Assay by the Turbidimetric Method. C. R. Bond and O. L. Davies. (*Analyst*, 1948, **73**, 251.) The various factors affecting this assay method are discussed and a nutrient broth formula for *Staphylococcus aureus*, with details of the inoculum, is given. The following results of experimental work are quoted: small deviations in optimum temperature (37°C.) caused appreciable depreciation in growth; measurements over a period of $2\frac{1}{2}$ to $4\frac{1}{2}$ hours incubation showed a continuous increase in growth; the greatest rate of growth occurred at *p*H 7·5 while at *p*H 6·0 to *p*H 6·5 the growth rate was markedly retarded; the best bacteriostatic used to stop the growth of the test organism at the end of the incubation period was formalin. The advantages and disadvantages of the method are compared with those of the serial dilution and cylinder-plate methods. The standard errors found were: serial dilution, 10 per cent.; cylinder-plate, 4 per cent.; turbidimetric, 4 per cent. R. E. S.

CHEMOTHERAPY

Curare-like Action of Polymethylene *bis*-Quaternary Ammonium Salts. R. B. Barlow and H. R. Ing. (*Nature*, 1948, **161**, 718.) Tubocurarine chloride is a *bis*-tetrahydro*iso*quinoline alkaloid containing 2 quaternary nitrogen atoms, and its potency in blocking neuromuscular transmissions compared with that

of simple quaternary ammonium salts might be partly due to the presence of 2 such cationic groups at some optimum distance apart. The authors therefore prepared and tested for curare-like activity a number of simple *bis*-quaternary ammonium salts in which the nitrogen atoms were separated by polymethylene chains of different lengths. Among the salts prepared were polymethylene *bis*-trimethyl- and *bis*-triethyl-ammonium bromides, with chain-lengths of from 2 to 5 and 7 to 13 carbon atoms, and a smaller group of polymethylene *bis*-quinolinium and *bis*-strychninium dibromides; the drugs were tested on the phrenic nerve-diaphragm preparation of the rat. In the *bis*-trimethyl-ammonium series none of the compounds was more than 2/5 as active as tubocurarine chloride; on the other hand, using the rabbit head-drop test, the C_{10} member of this series was found to be about 3 times as potent as tubocurarine chloride, 0·08 mg./kg. being required to produce head-drop compared with 0·26 mg./kg. of *d*-tubocurarine chloride. Thus, the relative activities, and their variation within a homologous series, may be quite different in the rat diaphragm and the rabbit head-drop tests. As the augmentation of the contractions of the rat diaphragm produced by nearly all the *bis*-quaternary ammonium salts resembled superficially the effect of anticholinesterase drugs, the authors tested representative members on the cholinesterase of caudate nucleus (dog), with acetylcholine as substrate, and found that they all showed some inhibition of the enzyme at concentrations slightly lower than those needed to reduce the contractions of the rat diaphragm. S. L. W.

Curare-like Action of Polymethylene *bis*-Quaternary Ammonium Salts. S. D. M. Paton and E. J. Zaimis. (*Nature*, 1948, **161**, 718.) In a pharmacological study of a series of straight-chain aliphatic ω-*bis*-trimethyl-ammonium iodides, it was found that in the rabbit head-drop test for curare-like activity, the potency increased from the ethylene derivative to the octamethylene derivative, and the decamethylene derivative (C_{10}) was more potent still, 0·11 mg./kg. of the iodide being required to produce head-drop compared with 0·25 mg./kg. of *d*-tubocurarine chloride. The potency in relation to *d*-tubocurarine chloride varied however with the test object; thus, the approximate ratio of an effective dose of the C_8 derivative to an equipotent dose of *d*-tubocurarine chloride was, on the cat's tibialis, 1/3; on rabbit's head-drop, 3; on frog-nerve-sartorius preparation, 3; on rat's diaphragm preparation, 50 to 100. The curarine-like action was not antagonised by neostigmine in doses adequate to antagonise the effect of *d*-tubocurarine chloride either in the cat's tibialis or in the rabbit's head-drop test. Comparison of potency with *d*-tubocurarine chloride was complicated by the finding that while *d*-tubocurarine chloride is unaltered in potency when given after these *bis*-quaternary salts, the converse is not true; thus, following the injection of two-thirds head-drop dose, approximately twice as much of the C_{10} derivative was required to produce head-drop as was normally needed. The authors stress the importance of pharmacological testing of possible substitutes for *d*-tubocurarine chloride on more than one test object and suggest that before clinical application can be considered it is desirable to find some satisfactory antagonist to their effects. S. L. W.

Streptomycin, Sulphetrone and Promin; Chemotherapeutic Action in Experimental Tuberculosis. G. Brownlee and C. R. Kennedy. (*Brit. J. Pharmacol.*, 1948, **3**, 37.) This report describes a comparison between the chemotherapeutic antituberculous activity of streptomycin, sulphetrone, promin, and combined streptomycin and sulphetrone. Four groups of 18 guinea-pigs, and one control group of 11, infected with a human virulent strain of *M.*

tuberculosis, were treated 22 days after infection with drugs for 168 days. One group received 0·5 per cent. of promin in the diet, one 2 per cent. of sulphetrone in the diet, one 10 mg. of streptomycin parenterally daily, and a fourth 2 per cent. of sulphetrone in the diet and 10 mg. of streptomycin parenterally daily; the control group of 11 animals remained untreated. On the basis of survival time, change in weight, response to tuberculin tests, macroscopic evidence of gross tuberculosis *post mortem* or microscopic examination, all presented a uniform picture of degrees of protection. The order of efficiency of the drugs was streptomycin with sulphetrone, streptomycin, sulphetrone, and promin. The protection given by the combined streptomycin and sulphetrone treatment was so marked as to be clearly synergistic. The authors express the opinion that the disease was progressive in all groups, though at a much suppressed rate in those groups where protection was greatest. Nevertheless, the experimental effects produced by the combined streptomycin and sulphetrone therapy are considered to justify a careful clinical evaluation in selected cases. S. L. W.

PHARMACY

GALENICAL PHARMACY

Strophanthus, Preliminary Report on the Extraction of. C. L. Huyck. (*J. Amer. pharm, Ass., Sci. Ed.*, 1948, **37**, 191.) Tinctures were prepared by percolation with alcohol (95 per cent.) and alcohol (65 per cent.) and assayed colorimetrically by a modification of the picric acid method of Knudson and Dresbach. The results given show there is little to choose between the solvents or the methods, except that the tinctures prepared with the weaker alcohol showed a somewhat greater loss of activity after 6 months and formed a precipitate. G. R. K.

NOTES AND FORMULÆ

Polyvinyl Alcohol as an Emulsifying Agent. G. F. Biehn and M. L. Ernsberger. (*Ind. Engn. Chem.*, 1948, **40**, 1449.) Commercial polyvinyl alcohols (partially or completely hydrolysed polyvinyl acetates) were examined for their interfacial tension and emulsifying properties. The most effective polyvinyl alcohols were found to be high-viscosity products hydrolysed to the extent of 75 to 80 per cent. At a concentration of 0·5 per cent. or higher (based on the total emulsion) these emulsifying agents compared favourably with other agents in giving emulsions of small droplet size, foaming was less, and where present the foam was unstable. Results on the stability of emulsions showed that the effectiveness of emulsifying agents generally varied greatly with different water-immiscible liquids. Comparisons with the polyvinyl alcohols showed that these agents and sodium dodecyl sulphate gave the most stable emulsions of trichloroethylene; for dibutyl phthalate, polyvinyl alcohols, sodium oleate and methyl cellulose were equally effective; for linseed oil, sodium alginate and sodium oleate were good, while two polyvinyl alcohols tested were fairly effective. The emulsion stabilities were measured by a method involving the measurement of the rate of separation of the internal phase under a constant centrifugal force. For emulsions containing sodium chloride, magnesium chloride or calcium chloride, the latter in concentrations corresponding to hard waters, a high viscosity 76 to 79 per cent. hydrolysed polyvinyl acetate gave stable emulsions, but other polyvinyl alcohols unexpectedly proved

less effective even than some of the common ionic agents. Certain of the polyvinyl alcohols were effective over a wide *p*H range. Methods of preparation of emulsions using dry powdered polyvinyl alcohol as well as viscous aqueous solutions are given. R. E. S.

PHARMACOGNOSY

***Datura metel*, Effect of Colchicine Treatment on the Alkaloidal Content of.** A. E. Beesley and G. E. Foster. (*Nature*, 1948, **161**, 561.) In contrast to the results reported by J. M. Rowson (*Quart. J. Pharm. Pharmacol.*, 1945, **18**, 175) that the treatment of seeds of *D. metel* and other solanaceous plants with a 0·4 per cent. aqueous solution of colchicine produced polyploid plants with a higher alkaloidal content than untreated seeds, a batch of *D. metel* seeds, similarly treated, produced plants which showed no evidence of polyploidy and no significant increase in alkaloidal content when compared with plants grown from a control group of seeds under conditions as far as practicable identical. G. R. K.

Ergot and Preparations, Alkaloidal Content of. S. A. Schou, P. F. Jorgensen and V. G. Jensen. (*Dansk Tidsskr. Farm.*, 1948, **22**, 161.) An examination was made of the alkaloidal content of 35 samples of ergot of varying geographical origin and harvests from 1938 to 1947. The content of ergometrine alkaloids was nil in 14 cases, while in 15 samples it was over 0·025 per cent., the maximum being 0·060 per cent. Five samples contained no ergotoxine alkaloids, 21 contained 0·100 per cent. or over, and the maximum was 0·217 per cent. For the new Danish Pharmacopœia it is recommended that the minimum limit for ergot should be 0·025 per cent. of ergometrine alkaloids and 0·100 per cent. of ergotoxine alkaloids: for the liquid extract the corresponding figures are 0·020 and 0·060 per cent. respectively. If 1 per cent. of ascorbic acid is added to the extract, and it is made from a drug containing the minimum proportion of alkaloids, the extract will still meet the requirements after storage for 6 months. G. M.

Morphine Content of Poppy Capsules. H. Baggesgaard-Rasmussen and O. Lanng. (*Dansk Tidsskr. Farm.*, 1948, **22**, 203.) A number of methods of assay were tried, the most satisfactory being a polarographic one, as follows. 2 g. of powdered capsules is moistened with 1 ml. of 1·2 M sodium carbonate solution and heated at 70°C. in a flask provided with a reflux condenser for 1 hour with 20 ml. of a mixture of butyl alcohol (7 volumes) and benzene (3 volumes). The mixture is then filtered through a sintered glass filter, the residue being pressed down and then washed with about 50 ml. of the mixed solvent. The extract is shaken out with 10 ml. of N/1 hydrochloric acid, and washed 3 times with 10 ml. of water. The aqueous extracts, which are practially colourless, are evaporated to 10 ml., treated with hydrochloric acid and potassium nitrate, then with excess of potassium hydroxide and the morphine is determined polarographically. The method was applied to experimental crops from seed of capsules tested the preceding year. The morphine content of the capsules of the second year (1947) was much higher than that of the preceding year, but this is probably due to the very different weather conditions. The distribution of morphine in the capsule was investigated by cutting the capsules into three equal parts by horizontal cuts,

the placenta and stigma being examined separately. Typical results were as follows:—

	Weight per cent. of total	Morphine (anhydrous) per cent. of total	Morphine per cent.
Upper part	16·5	0·31	11·8
Middle part	26·4	0·43	26·5
Lower part	34·1	0·52	41·0
Placenta	14·0	0·50	16·0
Stigma	9·0	0·24	4·7

G. M.

Opium from Greece. P. G. Kritikos. (*Pharm. Acta. Helvet.*, 1948, **23**, 196.) A certain amount of opium is produced in Greece. Examination of a number of samples from different districts gave the following figures :—

	Sample						
	1	2	3	4	5	6	7
Moisture (100°C.) ...	6·38	3·48	4·03	3·68	6·01	3·54	5·78
Ash	2·90	3·35	2·97	2·65	2·08	4·98	3·60
Meconic acid ...	4·81	5·81	4·92	5·29	5·56	5·18	5·05
Narcotine	4·18	4·02	4·03	3·92	5·17	3·79	4·25
Codeine	1·50	1·27	1·27	1·17	1·22	1·25	1·57
Morphine	15·61	10·25	14·50	14·43	15·40	15·74	15·59

All the above percentages, other than the moisture content, are calculated on the dry material. G. M.

PHARMACOLOGY AND THERAPEUTICS

Amidone, Pethidine and Morphine; Analgesic Effects in Human Subjects. E. N. Christensen and E. G. Gross. (*J. Amer. med. Ass.*, 1948, **137**, 594.) A comparison in 11 volunteer subjects, employing the Wolff, Hardy and Goodell technique, showed amidone to be about three times as potent as morphine and many times more potent than pethidine when given subcutaneously, but that it lacked the sedative action of either of these drugs. Nausea and vomiting were not experienced by any of the subjects. With all three drugs the duration of analgesia following subcutaneous injection is much longer than that following intravenous injection. The simultaneous injection of a dose of 0·3 mg. of atropine decreased both the intensity and duration of the analgesic effects of both amidone and morphine, and the duration but not the intensity of pethidine. When atropine was given with any of the drugs administered intravenously the only consistent change was a shortening of duration of effect of amidone. The undesirable side-effects of morphine and pethidine, such as nausea and vomiting, were absent when atropine was given simultaneously. Sedation was more marked when atropine was injected with each analgesic. Simultaneous injection of 0·5 mg. of neostigmine increased both the intensity and duration of the analgesic action of all the drugs. From these studies, combined with the study of the clinical results in 69 patients to whom amidone combined with atropine was given as a pre-anæsthetic agent, the authors conclude that amidone is an unsatisfactory pre-medication agent, but is most useful as a post-operative analgesic and in pain from many other causes. S. L. W.

***para*-Aminosalicylic Acid in Experimental Tuberculosis.** W. T. McCloskey, M. I. Smith and J. E. G. Frias. (*J. Pharmacol.*, 1948, **92**, 447.) Tests in rats, guinea-pigs and rabbits showed a relatively low toxicity in all these animals, but chronic toxicity tests on guinea-pigs indicated a cumulative action. The compound is well absorbed from the gastro-intestinal tract and is well retained for several hours. Analysis of the urine of rabbits showed that during the 24 hours following ingestion, from 10 to 20 per cent. of the dose administered was excreted as the free compound and about 80 to 90 per cent. as the conjugated compound. It was found to have little therapeutic activity in rabbits infected with a bovine strain and in guinea-pigs infected with a human strain of tubercle bacilli. When given in combination with streptomycin the chemotherapeutic efficacy was no greater than the sum of effects from the two drugs: there was no evidence of potentiation as with the sulphones and streptomycin.

S. L. W.

Diisopropyl Fluorophosphate; Effect on Anoxic Survival. A. F. Freedman and H. E. Himwich. (*Science*, 1948, **108**, 41.) It has been found that the use of diisopropyl fluorophosphate (D.F.P.) prolongs the survival period of medullary centres subjected to a complete arrest of circulation. If this increased resistance to anoxia observed in the isolated head should be found to apply also to the intact organism then it might be valuable in minimising the effects of anoxia. For this investigation the authors undertook a series of experiments under a variety of conditions, which included a comparison of the survival periods of animals previously injected with the drug with untreated controls, using (1) rats subjected to hypoxia, (2) the decapitated heads of new-born rats (length of gasping-time of head), (3) rats receiving excessive doses of pentobarbitone or of morphine. Only with morphine was there any suggestion of a beneficial effect from the previous use of the drug and on statistical analysis even this might be imputed to chance variation.

S. L. W.

Dimercaprol (B.A.L.), Influence of, on the Toxicity and Therapeutic Activity of Mapharsen. N. Ercoli and W. Wilson. (*J. Pharmacol.*, 1948, **92**, 121.) The influence of dimercaprol on the therapeutic activity of mapharsen was studied in relation to its toxicity in mice infected with *Trypanosoma equiperdum*. It was found that the curative or sterilising action of mapharsen is influenced much more readily by dimercaprol than the trypanocidal action, while the toxicity is the least affected. Thus, while the curative effect of mapharsen disappears with doses of dimercaprol as low as one-eighth to one-half the mapharsen dose, from 1·0 to 2·7 times more dimercaprol than mapharsen is required to interfere with toxic mapharsen doses. In other words the " therapeutic index " for the combined treatment is lower than for mapharsen alone, since the curative activity is more reduced than the toxicity by the same proportional dose of dimercaprol. In general, the higher the dose of the arsenical the more dimercaprol proportionately is required for inhibition. These findings preclude the possibility of combined chemotherapy with dimercaprol and mapharsen.

S. L. W.

Rutin, Effect on Anaphylactic and Histamine Shock. R. H. Wilson and F. De Eds. (*Science*, 1948, **107**, 369.) The conclusions drawn by Raiman, Later and Necheles (*Science*, 1947, **106**, 368) from their observation that rutin protects guinea-pigs from anaphylactic shock but not from histamine shock were that either histamine is not the direct cause of anaphylactic shock or rutin prevents the liberation of histamine. These conclusions are untenable in the light of results by other workers that rutin has a slight protective action

against histamine, that death from histamine can be prevented by compounds closely related to flavonols and that scorbutic guinea-pigs have an increased sensitivity to histamine which is counteracted by a mixture of *d*-catechin isomers. Rutin affords protection against histamine shock in an indirect way and is not a true antihistaminic. The evidence that it protects against anaphylactic shock supports the theory that symptoms of anaphylaxis are produced by histamine. G. R. K.

Thiouracil-treated Rats, Diffuse and Nodular Hyperplasia of the Thyroid Gland in. W. C. Kuzell, H. B. Tripi, G. M. Gardner and G. L. Laqueur. (*Science*, 1948, **107**, 374.) 58 albino rats were fed on a basic diet containing 0·1 per cent. of thiouracil for periods of 34, 51, 120, 142 and 233 days. Comparison of the thyroid glands at the end of these periods with those from a control group of rats showed extreme hypertrophy in the glands from those animals fed on the thiouracil diet for a long time (the glands from male rats which had received thiouracil for 233 days averaged an increase in weight above normal of 489·3 per cent.). Histologically, the glands from animals removed from the thiouracil diet after 34 and 51 days showed no hyperplasia, whereas those from rats fed on the diet for 120 days or more were distinctly hyperplastic with areas of nodular hyperplasia; the number of nodules was related to the amount of thiouracil ingested. Since this experiment was part of a study designed to show the effect of thiouracil-induced hypothyroidism on experimental polyarthritis, all animals were inoculated at varying times with a broth culture of pleuropneumonia-like organisms, but there was no evidence that this had any effect on the thyroid glands. G. R. K.

BACTERIOLOGY AND CLINICAL TESTS

Sodium *p*-Aminobenzoate, Bacteriostatic Properties of. R. Lecoq and and J. Solomides. (*C.R. Acad. Sci., Paris*, 1948, **226**, 846.) At dilutions of 1/130 to 1/250, sodium *p*-hydroxybenzoate has a bacteriostatic action, not only towards *Bact. coli* and the bacillus of Eberth, but also towards cultures of Gram-negative organisms—*B. dysenteriæ* Shiga and *Vibrio Choleræ*. On the other hand it has no action on Staphylococci, Streptococci, *B. subtilis* and *B. diphtheriæ*, even at 1/100. The development of *B. tuberculosis* (human and bovine) is inhibited even at a dilution of 1/1000. The action on moulds is variable: the growth of *Actinomyces griseus* is stopped at 1/250 while *Aspergillus niger* is resistant. G. M.

Vitamin K, Antibacterial Analogues of, Effect on *Mycobacterium tuberculosis*. C. N. Iland (*Nature*, 1948, **161**, 1010.) During a search for chemically defined growth-factors for *M. tuberculosis*, it was decided to investigate vitamin K, which is present in many organisms and is probably of nutritional importance. A pigment, 'phthiocol' (2-methyl-3-hydroxy-1:4-naphthoquinone), isolated from a laboratory strain of tubercle bacillus, has vitamin K-like activity, and it has been suggested that phthiocol is derived from vitamin K during the extraction of the bacteria. It has long been known that *M. paratuberculosis*, when freshly isolated, will grow only on media containing extracts of other acid-fast bacteria, notably *M. phlei*, and it has been claimed that phthiocol and 2-methyl-1:4-naphthoquinone can replace *M. phlei*, but the stimulant action is not so marked, hence it does not follow that the *M. phlei* growth-factor and these compounds are the same. The author concludes that the original hypothesis that vitamin K-like compounds are necessary for the nutrition of *M. tuberculosis* has not been proved, but that there are certain indications that similar substances play some part in the metabolism of the organisms. S. L. W.