ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ALKALOIDS

Desmethylcolchicine, a Constituent of U.S.P. Colchicine. R. M. Horowitz and G. E. Ullyot. (*Science*, 1952, **115**, 216.) A batch of U.S.P. colchicine was purified by adsorbing on alumina and then eluting the pure colchicine with chloroform. Upon further elution with methanol-chloroform (1 : 99), desmethylcolchicine was obtained (up to 4 per cent. based on the weight of impure colchicine). The evidence for the structure of this compound, of formula $C_{21}H_{23}O_6N$, which is similar to colchicine but with one of the methoxyl groups in ring A demethylated, is as follows: (*a*) contains three methoxyl groups, (*b*) yields colchicine on treatment with diazomethane, and (*c*) gives a colour with ferric chloride only after it has been heated in dilute hydrochloric acid (presence of an enol ether). It is obtained as yellow prisms from ethyl acetate-ether containing a trace of chloroform. It turns to a glass at *ca* 176° to 190° C., recrystallises at *ca* 200° to 210° C., and melts finally at 275·5° to 277° C. No chemical changes are involved in these transitions. A comparison is made of the physical constants of this desmethylcolchicine, and one obtained (designated "Substance C") from the seeds of *Colchicum autumnale* by Santavý and Reichstein (*Helv. chim. Acta.*, 1950, **33**, 1606), and the two compounds are assumed to be identical. A. H. B.

Ergot Alkaloids, Paper Chromatography of. L. Fuchs and M. Pöhm. (*Scientia pharm.*, 1951, **19**, 232.) The composition of the ergotoxine group of alkaloids was determined by paper chromatographic separation of the amino-acids obtained after hydrolysis with concentrated hydrochloric acid; ergocristine gives phenylalanine, ergocornine valine, and ergokryptine leucine, in addition to proline which is formed from all three. Suitable solvents with the corresponding *R* values, are given below:

	n-butanol 4 acetic acid 1 water 5	*n*-butanol 1 benzyl alcohol 1 water 2
Proline	0.34	0.10
Valine	0.50	0.15
Leucine	0.66	0.30
Phenylalanine ..	0.63	0.40

The composition of the ergotoxine group of alkaloids varies greatly. Any one of the three alkaloids mentioned above may predominate. In some cases (individual sclerotia) ergocristine or ergocornine were absent, in others all three were present in equal quantities. G. M.

Tropine, Paper Chromatographic Separation of, from Esters. P. Mathes and W. Klementschitz. (*Scientia pharm.*, 1951, **19**, 235.) Tropine derivatives may be separated and differentiated by paper chromatography, using as solvent a mixture of 70 parts of β-ethoxyethanol with 30 of water. The operation is carried out in an atmosphere of ammonia to avoid the formation of "tails," and either the free bases or their hydrochlorides may be used. *R* values

are as follows: tropine, 0·75; lactyltropine, 0·85; atropine, 0·90; *l*-hyoscyamine, 0·90; homatropine, 0·90. The spots are developed with a 0·5 per cent. ethanolic solution of diphenylcarbazone. Quantities may be estimated by measuring the area of the spots. G. M.

ANALYTICAL

Amidines, Volumetric Assay of. F. H. Stephan. (*Anal. Chem.*, 1951, **24**, 180.) Two new volumetric methods are given for the amidines lomidine dimethane sulphonate, lomidine diisethionate, hexamidine diisethionate, benzamidine hydrochloride, *p*-sulphamidobenzamidine, stilbamidine diisethionate, 2-hydroxystilbamidine diisethionate and *p*-arsonobenzamidine. In the first method the amidine is precipitated with an excess of iodine, rendered alkaline, and the residue is separated by filtration. The filtrate is acidified and the iodine not consumed by the amidine is liberated and titrated with standard thiosulphate; the equivalent weight is equal to the molecular weight of the product divided by double the number of amidine groups in the formula. A table is given of the precision and accuracy of various methods. The second method depends on the fact that at room temperature and at a *p*H between 5·2 and 7·0, mercuric acetate interacts with the amidines to form voluminous gelatinous white insoluble derivatives which are termed "mercuriamidines." Under these conditions the reaction is quantitative and can be applied to the volumetric determination of the amidines, the solution used being 0·1 N mercuric acetate buffered with crystalline sodium acetate. Most accurate results were obtained at 18° to 22° C.; below 12° C. results were low while above 28° C. results were high due to increased mercuration. The mercuriamidines were white, bulky and gelatinous, insoluble in water and ethanol, but soluble in dilute acids. R. E. S.

Belladonna Preparations, Assay of, by Partition Chromatography. G. Schill and A. Ågren. (*Svensk farm. Tidskr*, 1951, **55**, 781, 797, 825.) By using an organic solvent as mobile phase and an acid buffer solution as immobile phase it is possible to separate the alkaloids of belladonna completely from neutral ballast substances. The first stage of the assay varies with the preparation: *Extractum belladonnae*, 10 g. is mixed with 10 ml. of M sodium carbonate and 10 g. of kieselguhr: *Extractum belladonnae liquidum* (1 : 1), 10 g. is mixed with 10 ml. of M sodium carbonate and 20 g. of kieselguhr: *Belladonnae folium*, 30 g. of the powder is mixed with about 30 ml. of M sodium carbonate to give a homogenous and rather dry mixture. The mixture is packed in a column and eluted with 200 ml. of chloroform at about 2 ml. per minute. The eluate is allowed to flow directly on to a column containing 15 g. of kieselguhr previously mixed with 4 ml. of 0·5 M phosphoric acid, and packed by forming into a slurry with chloroform. This second column is washed with 100 ml. of chloroform and the alkaloids are then eluted with 250 ml. of chloroform which has previously been shaken with half its volume of concentrated ammonia, and filtered. The eluate is passed through 10 g. of alumina, concentrated to 10 ml. and the optical rotation is determined. It is then evaporated to dryness, the residue being re-evaporated with 10 ml. of chloroform twice, and the residue is titrated with 0·1N hydrochloric acid. For satisfactory results a suitable kieselguhr must be used. This should correspond to the United States Pharmacopoeia specification, and pass a number of other tests which are described. It is important that it should be free from chlorides and nitrates. G. M.

Diethylstilbœstrol and Related Œstrogens, Spectrophotometric Assay of. C. A. Kelly and A. E. James. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41**, 97.) The assay depends upon the formation of a stable red colour from stilbœstrol by diazotisation and coupling with *m*-nitraniline. The method is applicable to tablets and pharmaceutical preparations and to benzœstrol, hexœstrol, mestilbol and dienœstrol, with slight variations in the wavelength of maximum absorption. The diazotisation solution is prepared by dissolving 50 mg. of *m*-nitraniline in 2 ml. of dilute hydrochloric acid, cooling and adding 1 ml. of 5 per cent. w/v sodium nitrite solution followed after 2 minutes by 95 ml. of cold water, 1 ml. of a 5 per cent. w/v solution of sulphamic acid and sufficient water to produce 100 ml. A solution containing 20 to 80 μg. of stilbœstrol in 5 ml. of ethanol (50 per cent.) is mixed with 1 ml. of 5 per cent. sodium borate solution and 2 ml. of cold diazotisation solution and allowed to stand for 10 minutes. 1 ml. of 10 per cent. sodium hydroxide solution is added, and sufficient water to produce 10 ml. The transmission is measured at the absorption maximum of 510 mμ, and read against a standard curve. Beer's Law applies with quantities up to 80 μg. of stilbœstrol in 10 ml. G. B.

Ephedrine in Pharmaceutical Preparations, Colorimetric Assay of. L. G. Chatten and L. I. Pugsley. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41**, 108.) The determination depends upon the reaction of ephedrine with picryl chloride in benzene solution to produce a yellow colour which is measured in a colorimeter with a filter transmitting at 400 mμ, the wavelength of maximum absorption of the coloured compound. There is a linear relationship between light absorption and amount of ephedrine, when quantities between 0·1 and 0·6 mg. in 9 ml. of benzene are treated with 1 ml. of a 0·3 per cent. solution of picryl chloride in benzene. Heating the mixture at 75° to 77° C. for 20 minutes, while insufficient to complete the reaction, gives satisfactory sensitivity. The intensity of the colour tends to increase after removal of the solution from the hot water bath; consequently the procedure described must be followed in detail, the colour being read after 3 minutes at room temperature. Under such conditions, optical density = 0·0415 + 0·8667 × quantity of ephedrine in mg. Methods are described for the extraction of ephedrine from aqueous sprays, water-soluble jellies, syrups, capsules, tablets and ointments, for which the colorimetric method gives good results whereas results of gravimetric assays tend to be too high. G. B.

Gentisic and Salicylic Acids, Simultaneous Spectrophotometric Determination of. L. J. Kleckner and A. Osol. (*J. Amer. pharm. Ass. Sci. Ed.* 1952, **41**, 103.) Solutions adjusted to *p*H 5·0 to 8·0, containing a total of 15 to 35 mg. of the acids in 1000 ml. of water are examined in the spectrophotometer at 296 mμ (absorption maximum for salicylic acid) and 320 mμ (absorption maximum for gentisic acid). The result is calculated from the absorption at these wavelengths, by means of the given equations derived from absorption data for the acids. The total quantity of the acids is checked by measurement of the absorption at 306·5 mμ, at which wavelength salicylic and gentisic acids exhibit equal absorption. An assay may be considered satisfactory if the sum of the results for salicylic and gentisic acids is within 0·7 mg. of that for total acids calculated from the absorption at 306·5 mμ. Small amounts of lactose or sucrose do not interfere, but ether-insoluble interfering substances have to be removed by extracting the acid solution with ether, evaporating the extract and preparing the solution for assay from the residue. G. B.

Local Anæsthetics, Analytical Characters of. K. Steiger and E. Kühni. (*Acta Pharm. Internat.*, 1951, **2**, 1.) The reactions of a number of local anæsthetics towards halides, cyanide, thiocyanate, alkali, oxidising agents and alkaloidal reagents are described. The following values are given for the melting points (Thiele block) of the picrates, after drying for 48 hours over phosphorus pentoxide:—Procaine monopicrate, 131·5° to 132·5° C.; procaine dipicrate, 147° to 148° C.; larocaine picrate, 163° to 165° C.; monocaine picrate, 164° to 165·5° C.; pantocaine picrate, 115° to 118° C.; farmocaine picrate, 91° to 93° C.; amylocaine picrate, 111° to 114° C.; alypin monopicrate, 130° to 132° C.; alypin dipicrate, 187·5° to 190·5° C.; metycaine picrate, 119·5° to 121·5° C.; intracaine picrate, 114·5° to 116° C.; diocaine picrate, 115·5° to 117·5° C.; tropacocaine picrate, 223·5° to 234° C.; xylocaine picrate, 218° to 222° C.; surfacaine picrate, 89·5° to 92·5° C.; stadacaine picrate, 118° to 120° C.; cocaine picrate, 158° to 161° C. G. M.

Methanol, Assay of and Content in Brandy. M. St. Mokranjac and S. Radmić. (*Acta pharm. Jug.*, 1951, **1**, 97.) The best conditions for the quantitative determination of methanol by Denigés method are obtained when the solution contains 5 per cent. of ethanol; higher percentages reduce the sensitivity of the test. The test is most sensitive when carried out in aqueous solution, but the curves obtained do not then obey Beer's law. In carrying out the assay, the ethanol content should be adjusted to 5 per cent., the solution should be allowed to stand for 1 hour at 30° C. before the absorption is measured, and sulphuric acid diluted with an equal volume of water should be used. The methanol content of various brandies ranged from 0·108 to 1·455 per cent., expressed as ml. per 100 ml. of absolute ethanol. The lowest percentage was found in a plum brandy in the manufacture of which the first runnings of the distillation were rejected. A limit of 1 ml. of methanol per 100 ml. of absolute ethanol is suggested for all brandies. G. R. K.

Morphine in Opium, Determination of, by Paper Chromatography. A. B. Svendsen. (*Pharm. Acta Helvet.*, 1951, **26**, 323.) About 0·25 g. of morphine is rubbed down with 0·5 ml. of concentrated formic acid, transferred with the aid of 2·5 ml. of water to a 3G3 glass filter, and filtered, the residue being washed by rubbing with 0·5 ml. of formic acid (5 per cent.) for 2 minutes, this operation being repeated until there is, in all, 5 ml. of extract. Of this solution 0·01 ml. is chromatographed, using a mixture of ethyl acetate, formic acid and water (10:1:3). A further 0·01 ml. of solution is applied, so that the spot corresponds to 0·02 ml. It is necessary to have 6 spots on the paper: 5 for the quantitative series, and 1 in order to determine the position of the morphine. The latter is done by cutting off a strip of the paper, containing one spot, and developing it by spraying with 2 per cent. sodium nitrite solution: after 2 minutes the paper is placed in an ammoniacal atmosphere. Each spot is then cut out and placed in a test tube, where it is treated with 2 ml. of 1 per cent. hydrochloric acid and 2 ml. of sodium nitrite solution (0·5 per cent.). After exactly 10 minutes, 1 ml. of 5 per cent. ammonia is added. If necessary, the mixture is filtered on a sintered glass filter, and the extinction is determined at 450 mμ. The amount of morphine is then derived from a standardisation curve obtained with pure morphine. G. M.

Quinine and Quinidine, Identification of. D. Barković. (*Acta pharm. Jug.*, 1951, **1**, 73, 91.) Solutions of quinine or quinidine containing sodium acetate,

calcium carbonate, magnesium oxide, or similar substances, and warmed to 60° C. yield a red colour with bromine water. In the presence of sodium bicarbonate or an excess of sodium acetate, the red product is soluble in chloroform. On the addition of hydrochloric acid to the red solution, the colour becomes yellow but is restored to red by the further addition of sodium acetate. The yellow product yields the reactions of peroxides with potassium iodide. The red colour of the original solution also becomes yellow on the addition of zinc and sulphur dioxide or sodium pyrosulphite, and eventually disappears, but returns when the mixture is allowed to stand or is treated with an oxidising agent. If the yellow mixture is treated with dilute sulphuric acid, it gives with ferric chloride a colour similar to that given by pyrocatechol. To distinguish between the two alkaloids about 5 mg. is dissolved in 2 to 3 ml. of very dilute acetic acid (the salts are dissolved in water) by warming to 60° C. and treated with a drop of a 5 per cent. solution of sodium acetate, and, without mixing, 2 drops of bromine water. After 30 to 60 seconds, a red to violet-red colour develops on mixing. 2 to 3 minutes later, 3 ml. of 2N sodium hydroxide is added and after a further 1 to 2 minutes, the mixture is shaken with 1 to 2 ml. of chloroform. In the presence of quinidine the chloroform becomes red or violet-red, whereas in the presence of quinine it remains colourless or becomes only pale red. If the quinine solution is made slightly alkaline with sodium hydroxide and shaken with chloroform, the red or violet-red colour develops fully. In the presence of an excess of alkali the chloroform layer gradually becomes red or violet-red in the presence of quinidine but remains colourless or becomes only pale red in the presence of quinine. G. R. K.

Rutin, Determination of, in Presence of Quercitin. L. Hörhammer and R. Hänsell. (*Arch. Pharm. Berl.*, 1951, **284**, 276.) Both rutin and quercitin give colours with zirconium oxychloride, the maxima of absorption being at about 430 and 475 mμ respectively, but that with rutin is destroyed almost completely by citric acid. For the detection of quercitin in presence of rutin, 20 ml. of an absolute acetone extract is treated with 1 ml. of a 2 per cent. solution of aluminium chloride in methanol. Quercitin gives a strong green fluorescence, visible in daylight, and generally increased by dilution with methanol. It is possible to detect 0·5 mg. of quercitin in presence of 5 g. of rutin. For the determination of rutin in presence of quercitin, the preparation is extracted in a micro-Soxhlet extractor with methanol. Aliquots of the solution are transferred to two 50-ml. measuring flasks. To one is added 1 ml. of a 2 per cent. methanolic solution of zirconium oxychloride ($ZrO(Cl_2),8H_2O$). After making up to the mark with methanol and waiting for 20 minutes, the extinction coefficient is determined (filter S43). The other flask is treated with so much methanol that, after filling to the mark with water, the concentration of methanol will be 20 per cent. The contents are then treated with 1·0 ml. of 2 per cent. aqueous solution of citric acid, and 1 ml. of zirconium oxychloride solution. After making up with water, and waiting for 20 minutes, the absorption is again determined as before. A blank is used to compensate for any colour in the extract. The results are calculated according to the formulæ, which hold for the range of 5 to 90 per cent. of quercitin in presence of 95 to 10 per cent. rutin:

$$C_Q = \frac{E'_m - 0{\cdot}03}{0{\cdot}508}; \quad C_R = \frac{E_m - C_Q\,0{\cdot}481}{0{\cdot}384}$$

G. M.

Sulphanilamides in Mixture, Spectrographic Determination of. J. Thomas and G. Lagrange. (*J. Pharm. Belg.*, 1951, **6**, 355.) A spectrophotometric method for the identification and determination either alone or in mixture of sulphadiazine, sulphamerazine, sulphathiazole and sulpha-2-ethyl thiodiazol is described. The principle consists of first determining the absorption of the mixture at 440 mμ (sulphadiazine) and at 320 mμ (sulphamerazine) after extraction and dilution with acetone so that 2 ml. contains 0·8 mg. of the drug present in greatest quantity. Evaporate 2 ml. to dryness *in vacuo*, add 5 drops of ethanol and evaporate again. To the residue in a tube add 2 ml. of concentrated sulphuric acid and 1 ml. of a fresh, colourless, aqueous 5 per cent. solution of resorcinol drop by drop, shaking and cooling in iced water. Cover the tube with tinfoil and place for 30 minutes in a water-bath at 80°. Cool immediately and make up to 10 ml. with a mixture of equal parts of a 40 per cent. v/v sulphuric acid solution and glycerol (A). Cool in iced water, shake and make the determinations 10 minutes after leaving the bath in a 5-mm. cell for sulphadiazine and after 15 minutes in a 1-cm. cell for sulphamerazine. A blank of 2 ml. of concentrated sulphuric acid, 1 ml. of water and solution (A) to 10 ml. is used. The absorption of a 1 mg. per cent. solution in N hydrochloric acid in a 1-cm. cell is measured at 280 mμ for sulphathiazole and at 268 mμ for sulpha-2-ethyl thiodiazol. H. D.

Zinc Oxide in Ointments, Assay of. J. Deltombe. (*J. Pharm., Belg.*, 1952, **7**, 93.) The following method gives accurate and reproducible results in about 30 minutes on ointments containing 5 to 10 per cent. of zinc oxide. Dissolve 5 g. of ointment by shaking with 30 ml. of chloroform, add 30 ml. of dilute sulphuric acid and shake for 10 minutes. Add 3 drops of mixed methyl orange-bromocresol green indicator and 5 drops of phenolphthalein solution, add 9 ml. of a 20 per cent. solution of sodium hydroxide and titrate with 0·25N sodium hydroxide until the orange-red colour disappears (i.e., the solution is almost colourless when shaken and yellowish on standing). Titrate with 0·25N sodium hydroxide to the phenolphthalein end-point (purple-violet). Each ml. of 0·25N sodium hydroxide used between the two end-points is equivalent to 0·0101725 × 4/3 g. of ZnO. A long, but accurate, method is to weigh the zinc oxide on a sintered-glass filter after removal of the ointment base by repeated washing with chloroform. The U.S.P. XIII method gives low, and the B.P. 1948 variable, results. The method of titration as sulphate in chloroform gives high results in the presence of starch unless the technique is suitably modified. G. B.

ORGANIC CHEMISTRY

Rutin and Related Flavonols, Preparation of Water-soluble Metal Complexes of. C. F. Krewson and J. F. Couch. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41**, 83.) A number of metallic compounds were tested for their power to increase the solubility of rutin, which is soluble only in about 10,000 parts of cold water. Rutin (0·7 g.) was dissolved in 150 ml. of boiling water, the metallic compounds added and the mixture boiled, cooled and filtered. The residue of insoluble rutin was weighed, and the quantity in solution calculated. The following compounds were effective in solubilising the rutin:—ferrous ammonium sulphate, ferrous lactate, ferric chloride, ferrous gluconate, ferric pyrophosphate, saccharated iron oxide and cuprous chloride. With some of these substances stoichiometric complexes appeared to be formed, for example, 2 moles of rutin reacted with each mole of ferrous gluconate whereas equimolecular complexes were formed with ferric chloride and ferrous ammonium sulphate. A preparation made with ferrous gluconate contained 28 mg. of rutin and 1·16 mg. of

iron in 5 ml. and had the *p*H 4·2. Saccharated iron oxide preparations contained up to 550 mg. of rutin and 2 g. of iron in 5 ml. at *p*H 6·8 to 9·3, and could be diluted with water without the formation of a precipitate. Saccharated iron oxide, but not ferrous gluconate, increased the solubility of quercitin and quercitrin in addition to rutin. G. B.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Amylase and Maltase in Urine. P. F. Fleury, J. E. Courtois and D. Ramon. (*Bull. Soc. Chim. biol. Paris*, 1951, **33**, 1762.) Samples of human urine, preserved with chloroform were mixed with phosphate buffer at *p*H 7 and maltose solution and incubated for 22 hours at 37°. The solution was boiled to remove chloroform and to inactivate the enzyme, and glucose was estimated by the yeast fermentation method of Ramon. Control experiments were carried out with urine previously boiled for 10 minutes to inactivate the enzyme. Urine samples showed a faint maltasic activity, and the urinary maltase appeared to be identical with the α-glucosidase of certain tissues. Attempts were made to obtain urinary amylase free from maltase by fractionation with ammonium sulphate and by chromatography on cellite-alumina columns. A satisfactory purified amylase was prepared by precipitation with 40 to 70 per cent. of acetone, maltase being inactivated by acetone treatment. Reducing sugars produced by the action of this amylase contained about 2 per cent. of glucose. G. B.

Penicillin, Radioactive, Chromatography of. E. Lester Smith and D. Allison. (*Analyst*, 1952, **77**, 29.) Radioactive penicillin of high specific activity (up to 600 millicuries per g.) was prepared by fermentation of a synthetic medium containing sulphur-35 as sulphate. The resulting mixture of penicillins was then subjected to paper chromatography, being spotted out on buffered strips, which were developed with ether in the special apparatus described by Goodall and Levi (*Analyst*, 1947, **72**, 277; *Quart. J. Pharm. Pharmacol.*, 1948, **21**, 85). Quantitative assessment was made by the bio-autographic method on agar plates inoculated with *B. subtilis* and also by two radiometric methods; sections containing individual penicillins were cut from the paper chromatograms, radio-autographs being used as guides, and either they were "counted" directly under a thin end-window Geiger-Müller tube or aqueous extracts were evaporated on planchettes for counting. Details are given of modifications of the chromatographic procedure. Attempts to utilise the ^{35}S-penicillin in an isotope dilution assay specifically for benzylpenicillin were unsatisfactory since the *iso*propyl-ether complex method was inadequate as a means of purification. R. E. S.

Quinine and Quinidine, Action of on Cholinesterase. E. Bach, B. Robert and L. Robert. (*Bull. Soc. Chim. biol. Paris*, 1951, **33**, 1805.) Quinine or quinidine was dissolved in 9 ml. of recently boiled water and mixed with 1 ml. of 0·1M acetylcholine chloride or bromide, 1 drop of cresol red solution and 0·5 ml. of horse serum as a source of cholinesterase. Control solutions were prepared without the inhibitor. Experiments were carried out at 37° C., hydrolytic action being determined by a titrimetric method. Results were corrected to 40° C. (optimum for the reaction) and the rate of hydrolysis interpreted according to the equations of Goldstein and Strauss. Inhibition commenced at a

concentration of about 10^{-5} mol./l. for quinine and about one-tenth that concentration for quinidine. In a horse serum containing 4·76 per cent. of enzyme at 40° C. the competitive system with quinine was observed in the zone A_SB_I (substrate in great excess relative to enzyme-substrate complex; free enzyme and enzyme-inhibitor complex in comparable amounts) and quinidine in the zone A_SA_I (substrate and inhibitor in great excess relative to enzyme-substrate and enzyme-inhibitor complexes). The dissociation constant of the cholinesterase-quinine complex was $8{\cdot}55 \times 10^{-6}$ and of the cholinesterase-quinidine complex, $2{\cdot}23 \times 10^{-6}$. The concentration of non-specific (blood serum) cholinesterase in horse serum estimated from the maximum rate of hydrolysis was of the order of 10^{-8} mol./l. G. B.

Vitamin B_{12}, New Form of. U. J. Lewis, D. V. Tappan and C. A. Elvehjem. (*J. biol. Chem.*, 1952, **194**, 539). The isolation of a vitamin B_{12}-active material present in the fæcal matter of rats is reported. Dried fæces were extracted with boiling water, the resulting extract being filtered and evaporated to a syrup under reduced pressure; after precipitating proteins with ethanol, the active fraction was adsorbed on charcoal, from which it was eluted with hot ethanol (65 per cent.). The extract was then purified by alumina adsorption and chromatography on a silica column using *n*-butanol-water as the solvent system; a crystalline product was obtained. The compound had growth-promoting properties for *L. leichmannii* but was inactive for the rat; the growth response of the chick to the material was comparable to that of crystalline vitamin B_{12}. The feeding of inorganic cobalt to the rats brought about an increased production of the new factor although the amount of activity present in the liver, kidney, spleen, muscle tissue and urine remained essentially the same whether extra cobalt was present or absent. Details of the paper chromatography of the new vitamin B_{12}-active form are given using a bioautographic technique and *n*-butanol-water as the solvent; the behaviour differed from that of vitamin B_{12} itself. The absorption spectrum in water differed considerably from that of vitamin B_{12}, the peak at 278 mμ being absent. R. E. S.

BIOCHEMICAL ANALYSIS

Acetic Acid, Micro-analytical Estimation of. E. Ciaranfi and A. Fonnesu. (*Biochem. J.*, 1952, **50**, 698.) A method is presented for the micro-estimation of acetates and acetic acid in blood and tissues. The sample (1 g. of tissue, 5 ml. of blood) is mixed with excess of methanol and distilled under conditions such that the methyl esters of the fatty acids are produced; the acetate (b.pt. 57° C.) boils at a lower temperature than methanol (b.pt. 65° C.), whereas the methyl esters of the other members of the homologous series have a higher boiling point; thus by esterification of the fatty acids and subsequent distillation a considerable separation of acetic acid from the remainder can be effected. By repeated distillations the C_3 to C_7 fatty acid esters are removed from the resulting methyl acetate; the ester is then saponified and the resulting sodium acetate brought to dryness. Formic acid and hydrogen sulphide are removed by oxidation with potassium dichromate-sulphuric acid, the acetic acid remaining unchanged; the acetic acid is then oxidised by increasing the sulphuric acid concentration and by adding silver ions. The dichromate reduction is measured photometrically (450 mμ) and the acetic acid is estimated by the difference in the extinction. The method permits the estimation of acetic acid in blood and tissues (0·1 to 2·3 mg.) with sufficient accuracy for biological

purposes, the error being less than ± 10 per cent. Tables showing the concentrations of acetic acid under physiological conditions, in human blood and in the blood, liver, kidney and muscle of the guinea-pig and rat are given.

R. E. S.

Glucose in the Presence of Maltose, Estimation of. D. Ramon. (*Bull. Soc. Chim. biol. Paris*, 1951, **33**, 1756.) A mixture of 27 ml. of sugar solution with 3 ml. of phosphate buffer at *p*H 7 is warmed and mixed with 0·3 g. of baker's yeast at 37° C. The mixture is allowed to ferment at 37° C. for 30 minutes and centrifuged. Ethanol is removed from the supernatant liquid by distillation and estimated by treatment with nitric acid-potassium dichromate solution and titration of the excess of reagent iodimetrically. A duplicate experiment is performed using distilled water in place of sugar solution and any necessary allowance made. The result is calculated from the datum that for solutions containing 0·025 to 0·040 per cent. w/v, the yield is 54 per cent. of the theoretical 2 molecules of ethanol per molecule of glucose. Maltose does not yield ethanol under these conditions and the accuracy of the method is fairly high for a reaction of such complexity. During 30 minutes' fermentation the whole of the glucose is destroyed but in spite of the low yield of ethanol other possible products such as acetone or acetaldehyde do not appear in the distillate. When fermentation continues for more than 45 minutes the yield of ethanol from glucose is not increased but maltose undergoes slight fermentation. Toluene should be avoided as it interferes with the hydrolysis of the glucose, but sugar solutions may be preserved with chloroform, which is removed by heating before making an estimation of the glucose content. G. B.

Vitamin B_{12}, Selective Assay of by Chromatography. F. Patte. (*Ann. pharm. franç.*, 1951, **9**, 660.) The following method is suitable for the determination of vitamin B_{12} (cyanocobalamin) in the presence of desoxyribonucleosides and desoxyribonucleotides which interfere in the ordinary microbiological assay. Solutions of the vitamin B_{12} standard containing 0·8, 1·6, 3·2 and 6·4 g. per ml. are prepared in distilled water, and suitable solutions of the preparation under test are also prepared. Using a special pipette delivering 0·0025 ml. drops, a row of drops of these solutions is placed on the filter paper and developed by ascending chromatography until the solvent (butanol saturated with water) has risen 7 cm. This takes about 45 to 60 minutes. The chromatogram is allowed to dry and placed on a seeded agar plate for incubation at 37° C. for 16 hours. The maximum diameter of the circles of growth stimulation due to vitamin B_{12} is displaced about 2 mm. above the origin of the chromatogram. Diameters of the circles are plotted on log-linear graph paper and should yield straight lines of equal slope from which the potency is calculated. Areas of growth stimulation due to the desoxyribonucleic matter are generally separated completely from the areas due to cyanocobalamin and its analogues. To obtain truly circular areas for measurement, the samples have to be diluted with water and not buffer solution as excessive amounts of salts disturb the chromatography. In samples containing much desoxyribonucleic material, flattening of the part of the growth-stimulation zone which is in contact with the desoxyribonucleic derivatives may occur. Some samples contain growth-stimulating factors which are not separated from the vitamin B_{12} by this method. The method was shown to be accurate with prepared mixtures of vitamin B_{12} and desoxyribonucleosides. This method is also useful for the qualitative detection of desoxyribonucleosides in samples of vitamin B_{12}. G. B.

CHEMOTHERAPY

Aminoalkyl Morphine Ethers. J. Cheymol, R. Giudicelli, P. Chabrier and K. Kristensson. (*Thérapie*, 1952, **7**, 21.) Diethylaminoethylmorphine was prepared by warming morphine in sodium hydroxide solution with the hydrochloride of diethylaminoethyl chloride. Piperidylethylmorphine was prepared in a similar manner. When injected intravenously into mice, diethylaminoethylmorphine and piperidylethylmorphine were more toxic than codeine while morpholinoethylmorphine was less toxic. The compounds exhibited a respiratory depressant action similar to codeine, but had a smaller convulsive effect. Piperidylethylmorphine and codeine showed about the same analgesic effect, which was absent in the case of the morpholinoethyl and diethylaminoethyl compounds. The dibromomethylates, prepared by reaction with methyl bromide in ethanol, exhibited a curare-like action, the ratio of curarising dose (rabbit head-drop method) to LD50 in mice being greater than for D-tubocurarine chloride. G. B.

Dithiocarbamic Esters, Antibacterial Activity of *N*-disubstituted. A. Quevauviller, P. Chabrier, G. Nachmias and G. Maillard. (*Ann. pharm. franç.*, 1951, **9**, 638.) Derivatives of dithiocarbamic acid dissolved in acetone were mixed with melted agar medium, which was poured into Petri dishes and allowed to set. The proportion of acetone was kept below 5 per cent. v/v to prevent inhibition of growth by the solvent. The plates were seeded in layers with 24-hour broth cultures of *Staphylococcus pyogenes aureus*, *Escherichia coli*, *Bacillus mesentericus* and *Pseudomonas æruginosa*, and incubated for 24 hours at 37° C. before comparison with similarly prepared agar plates to which the same quantity of solvent had been added. Derivatives of dithiocarbamic acid were more active against Gram-positive than against Gram-negative organisms. The sodium salts of the *N*-substituted derivatives, dimethylamino, morpholino and piperidino carbodithioic acids were of high antibacterial activity, the piperidino derivative being the most active and the morpholino derivative the least active. Esters of these substances having alcohol, nitrile or carboxylic acid groups were practically without antibacterial action, but the ketonic esters had a certain amount of activity against *B. mesentericus*. β-Dimethylaminoethyl *N*-dimethyldithiocarbamate had an activity similar to that of the sodium salt of the parent acid, but the corresponding quaternary ammonium salt was inactive. G. B.

Salicylamide, Analgesic Properties of Certain Derivatives of. M. Carron, J. Tabart and Mme. Jullien. (*Thérapie*, 1952, **7**, 27.) The analgesic effect of 42 substances administered orally to mice was examined by the application of a pain stimulus in the form of radiant heat applied to the tails of the mice. Analgesia was assessed by absence of movement of, or delay in moving, the tail when the radiation was applied to the base of it. All compounds were submitted to a screening test, a fixed dose of the drug being administered and the animal examined for analgesia after 30, 60, 90, 120 and 150 minutes. For the more active compounds, the minimal active dose and the toxicity on oral administration were determined in mice, and the therapeutic index calculated. *N*,*N*-diethylsalicylamide had the highest therapeutic index. Substitution in the phenolic group:—the introduction of hydrophilic functions, $-CH_2 \cdot CO_2H$, $-CH_2NH_2$, $-CH_2 \cdot CH_2OH$, $-CH \cdot CH(OH) \cdot CH_2OH$ decreased analgesic potency compared with salicylamide. Methylation increased the activity while ethylation decreased it. Substitution in the amido group:—*N*-dimethyl

and *N*-butyl derivatives were inactive, while *N*-diethyl and *N-iso*propyl derivatives were active. When two salicylamide molecules were joined at the amido groups by a 3-carbon atom chain the compound was active; corresponding compounds joined by 1 or 2 carbon atoms were inactive. 3 derivatives of gentisamide were inactive, but *o*-cresotinamide was more active than salicylamide. The therapeutic indices, $\left(\frac{\text{LD50}}{\text{MAD50}}\right)$, of some compounds were found to be as follows:—*o*-ethoxylbenzamide, 3·5; *N-iso*propylsalicylamide, 2·6; *N*-methylolsalicylamide, 3·54; trimethylene *bis*-salicylamide, 3·65; *N*-diethylsalicylamide, 5·66; *O*-acetylsalicylureide, 1·5; cresotinamide, 1·97; salicylamide, 2; amidopyrine, 2·8; acetylsalicylic acid, 2·07. G. B.

PHARMACY

DISPENSING

Neostigmine Methylsulphate, Decomposition of Solutions of. A. W. M. Indemans and J. A. C. Pinxteren. (*Pharm. Weekbl.*, 1951, **86**, 773.) Hydrolysis of solutions of neostigmine may be detected from the dimethylamine formed. About 0·1 ml. of the solution (= 50 μg.) is distilled with buffer solution of *p*H 8 in a microdistillation apparatus, the dimethylamine being collected in a drop of 0·1 N hydrochloric acid. The acid solution is evaporated to dryness, the residue taken up in 0·02 ml. of water and transferred to a micro tube. After making alkaline with sodium hydroxide, the mixture is distilled. The dimethylamine is detected by a piece of filter paper in the vapour, soaked in a solution of 1 g. of sodium nitroprusside in 10 ml. of freshly distilled and neutralised acetaldehyde. It is possible to detect 0·5 μg. of dimethylamine. G. M.

GALENICAL PHARMACY

Disintegrating Agents, A Comparative Study of. H. M. Gross and C. H. Becker. (*J. Amer. pharm. Ass. Sci. Ed.*, 1952, **41**, 157.) Tablets were prepared by mixing lactose with a suitable quantity (generally 17 per cent.) of disintegrating agent and granulating with the aid of a solution containing 5 per cent. of zein, in a mixture of syrup, ethanol and water. For disintegrating agents which react with water, 5 per cent. of zein in *iso*propanol was used. Granules were lubricated with leucine (2 per cent.), and in an alternative procedure, some of the disintegrating agent was added with the lubricant. Tablets were tested for hardness with a Monsanto Hardness Tester, and for disintegration by the U.S.P. XIV method, results being extrapolated to a standard hardness of 7 kg. A variety of disintegrating agents, such as aveeno, pectin, corn starch, locust bean gum, methyl cellulose, magnesium peroxide, sodium carbonate-peroxide, citric acid-calcium carbonate and pectin-calcium carbonate, gave successful results, in many cases comparing favourably with commercial tablets prepared by precompression. Some gums such as algin, sodium alginate, veegum, tragacanth and karaya gave tablets which did not disintegrate within 10 minutes and often remained covered with a water-impervious gum layer. Tablets which disintegrated readily were prepared with dried citrus pulp and powdered dried sponge, but the former gave grainy, and the latter, tan-coloured tablets. Storage at room temperature for 500 hours did not increase disintegration times, except for tablets prepared with pectin. Similarly storage at 4° C. had little effect, but deodorised some tablets. Exposures to 45° C. for 500 hours had a deleterious effect in most cases. G. B.

PHARMACOGNOSY

Belladonna Leaves, Phosphatase of. J. E. Courtois, C. Anagnostopoulos and M. Khorsand. (*Bull. Soc. Chim. biol., Paris*, 1951, **33**, 1813.) The phosphatase occurs in two fractions, the greater part soluble in water, and the remainder insoluble and firmly bound to the cell tissues. The following three preparations were tested:—(1) the soluble enzyme prepared by extraction of the powdered leaves with water followed by precipitation with acetone, (2) the insoluble material after removal of the water-soluble material, washed with acetone and dried and (3) (2) after treatment with sodium cyanide to remove metallic ions. There was little difference in action between the different preparations, when incubated at 37° C. for 48 hours in contact with 0·04M glycerophosphate solution and a suitable buffer solution. The phosphatases present belonged to types II and III, and hydrolysed a number of phosphorus compounds, but not phytic acid. A distinctly greater proportion of the type II phosphatase occurred in the samples purified by a process of fractionation with ammonium sulphate, and the phosphatase was not significantly different from others of the same type. The type III phosphatase was markedly different from those obtained from sources other than leaves. It was strongly activated by the bivalent ions Mg^{++}, Sn^{++}, Ni^{++} and Co^{++}. G. B.

***Datura stramonium*, Location of Alkaloids in.** R. Hegnauer. (*Pharm. Weekbl.*, 1951, **86**, 935.) *Datura stramonium* was grafted on roots of tomato, previously tested for the absence of mydriatic alkaloids. It was possible to demonstrate a translocation of alkaloids in the plant in all directions and towards all organs, including the tomato root. When the grafted tops were cut off and immersed in alkaloidal solutions, the latter accumulated in greater concentration (calculated on the dry matter) in the midribs of the leaves than in the laminae of the leaves. Neither the demonstration of the presence of alkaloids in all organs, not the typical manner of accumulation of the alkaloids in the leaf, can be considered as a definite indication of alkaloid synthesis taking place in the underground organs. G. M.

Digitalis, Relation of Biological Activity to Time of Collection of. F. Neuwald. (*Arch. Pharm., Berl.*, 1951, **284**, 382.) It is generally assumed that digitalis leaves should be harvested in the afternoon, owing to the glycosides being synthesised in sunlight and broken down in the dark. Actually the differences in values found in the original experiments which were supposed to prove this fact were not significant. The author has re-investigated the problem, taking samples of leaves at 5 a.m. and 5 p.m. respectively, and testing the activity both biologically on cats, guinea-pigs and frogs, and chemically. The results show that there is no significant difference either in biological activity or in content of heart-active glycosides within a period of 24 hours. Similar results were also obtained with *D. lutea* and *D. ambigua*. There is therefore no reason to specify that the leaves should be collected in the afternoon. G. M.

***Scilla maritima*, Vegetative Reproduction.** I. Z. Devetak. (*Acta pharm. Jug.*, 1951, **1**, 83.) Pieces of bulb consisting of 2 or 3 scales joined to a small piece of the base were either set aside on the laboratory shelf or buried in sand. At the same time a number of scales were completely separated from the bulb and set aside either whole or cut into 2, 3, or 4 portions. After 3 months all the specimens had produced small bulbs weighing 5 to 15 g. When planted

in March, the bulbs began to grow normally in October. By this means one parent bulb weighing 3 kg. can be made to yield about 100 new plants in one season. G. R. K.

PHARMACOLOGY AND THERAPEUTICS

Aconite, Biological Assay of. R. Paris and J. Vavasseur. (*Ann. pharm. franç.*, 1951, **9**, 718.) A biological test is necessary because of wide variations in toxicity of aconite powders which cannot be distinguished microscopically. The method of the French Pharmcopœia 1949, using a guinea-pig is open to criticism because (1) only one animal is used and (2) only a minimum potency requirement is given, and consequently highly toxic aconites are not excluded. Upper and lower limits of potency are recommended, as in the U.S.P.X. A simpler and more precise method is based upon subcutaneous injection into mice, and it can be made more exact by making the determination of LD50 in comparison with a standard aconitine. The LD50 for pure aconitine varies between 8 and 9 μg./kg. according to the strain of mouse used. In a series of 10 commercial tinctures containing about 0·05 per cent. of total alkaloids and tested in mice, wide variations in potency were observed. In 3 of the tinctures, potency was similar to that of a control prepared from genuine *Aconitum napellus*, and 3 other tinctures had lower potencies, presumably having been prepared from old aconite roots. One specimen was highly toxic, resembling a control tincture prepared from *A. deinorrhizum*. G. B.

Adrenaline and Noradrenaline; Release from the Suprarenal Gland. A. Lund. (*Acta Pharmacol. Toxicol.*, 1951, **7**, 309.) This investigation was carried out to show the course of the release of adrenaline and noradrenaline from the glands in circumstances, e.g. blood-letting and electrical stimulation, known by experience to give rise to a pronounced release of adrenaline. Venous blood from the left suprarenal gland of dogs was collected continuously from the suprarenal vein, while at the same time a corresponding amount of donor blood was infused through the jugular vein. In other words, the suprarenal gland was perfused *in situ*. The concentrations of adrenaline and noradrenaline in the blood samples were estimated fluorimetrically. Under gentle anæsthesia no adrenaline or noradrenaline is released to the blood. As blood pressure falls, from electric stimulation of the splanchnic nerve and at the time of death, a mixture of adrenaline and noradrenaline is released, of which from 25 to 50 per cent. is noradrenaline. In each experiment the concentration of noradrenaline to adrenaline remained constant, irrespective of the duration of the experiment or the nature of the stimulant. The suprarenal glands from non-anæsthetised animals contained on an average 1·56 mg. of adrenaline and 0·48 mg. of noradrenaline per g. The glands from anæsthetised animals contained only about half these amounts. S. L. W.

Digitoxoside and Gitoxoside, Some Comparative Pharmacological Data. R. Jequier, M. Peterfalvi and C. Plotka. (*Ann. pharm. franç.*, 1951, **9**, 730.) Pigeons were anæsthetised with ether and fitted with a cannula in the alar vein. Test solutions of the glycosides, purified by chromatography, were injected in 1·5 ml. quantities every 5 minutes until death of the animal by cardiac arrest occurred. The concentration of glycoside was adjusted to cause death in 65 to 95 minutes as described in the U.S.P. XIV. The average lethal dose showed a wide difference between the glycosides, being 0·40 mg./kg. for digitoxoside and 0·80 mg./kg. for gitoxoside, whereas in cats gitoxoside is only

slightly less toxic than digitoxoside. The dose necessary to produce cardiac irregularities, determined by the electrocardiograph in pigeons is 0·20 mg./kg. for digitoxoside and 0·25 mg./kg. for gitoxoside. It is pointed out that this variation in the ratio of toxicities of the glycosides according to the animal used and the method of testing may be the reason for the discrepancies in the results obtained by different biological methods of assay of digitalis preparations. In experiments in the isolated rabbit or guinea-pig heart, digitoxoside was found generally to increase the coronary output, and gitoxoside to diminish it. This effect was confirmed in experiments with a rat heart connected to the circulatory system of a living rat, this method having the advantage of using blood as perfusion fluid, a pulsating pressure instead of the constant pressure in the isolated organ method, and an animal of low sensitivity to the toxic action of digitalis on the heart. The opposing action of the two glycosides may serve to explain conflicting results previously reported in experiments on the coronary effect of digitalis preparations. G. B.

Hetrazan in the Treatment of Human Ascariasis. E. H. Loughlin, I. Rappaport, A. A. Joseph and W. G. Mullin. (*Lancet*, 1951, **261**, 1197.) A comparison was made on three groups of patients with ascariasis, whose ages ranged from 3 to 70 years, of the efficacy of different dosages of a syrup of hetrazan, containing 30 mg. of the dihydrogen citrate per ml., with that of the 6 mg./kg. given in tablet form. It was shown that the tablets given in this dosage three times daily for 5 days expelled numbers of ascaris comparable to those removed by the syrup given in single doses of 13 mg./kg. on the first day and 20 mg./kg. on the second and third days, or in single doses of 13 mg./kg. for 4 days; the syrup, however, possesses the advantage that it obviates multiple daily doses and is easier to administer to small children. The authors conclude that syrup of hetrazan, because of its excellent anthelmintic efficiency (91 to 94 per cent. of ascaris removed), its almost complete lack of toxicity in doses not exceeding 20 mg. daily, and its ease of administration, is the anthelmintic of choice for the treatment of ascariasis and would be useful for mass treatment. S. L. W.

Hexamethonium Bromide in Hypertension. E. A. Murphy. (*Lancet*, 1951, **256**, 899.) Encouraging results were obtained in 43 cases of hypertension of different degrees and in patients of different ages treated with hexamethonium bromide either orally or subcutaneously, some of whom had previously been treated without success by sympathectomy or with potassium thiocyanate. All cases with clinical or electrocardiographic evidence of coronary disease or evidence of cerebral thrombosis were excluded and the sensitivity of the patients to hexamethonium was established by the Freis test. The initial dose was 0·25 g. by mouth 3 times daily, gradually increased to a satisfactory level, a total dose of 1 g. 4 times daily being regarded as a maximum. If this failed, hypodermic injections were given, beginning with 25 mg. twice daily, and increasing gradually to a maximum of 200 mg. 3 times daily. The minimum effective dose was 0·5 g. twice daily by mouth or 25 mg. twice daily by injection. The most common side-effects, in the order of their frequency, were constipation, light-headedness, drowsiness, dry mouth, visual disturbances, nausea, diarrhœa and vomiting. All these side-effects responded to symptomatic treatment. The risk of bromism is small. The most dramatic improvements were in patients with severe retinopathy and placid temperament. The results in this series of patients seem to indicate that it is possible by this treatment to maintain a lowered blood pressure for a considerable period. As there is no correlation

between the serum-bromide level and the fall in blood pressure the theory that the long-term improvement is due solely to the bromide ion is ruled out; moreover, other salts of hexamethonium (especially the bitartrate) are also effective.

S. L. W.

Isotonic Saline Solution, Diuretic Effect of, Compared with that of Water. G. Blomhert, J. Gerbrandy, J. A. Molhuysen, L. A. de Vries and J. G. G. Borst. (*Lancet*, 1951, **261**, 1011.) The diuretic effects were observed in normal men, big meals and excessive intake of fluids being avoided for at least 7 hours before the experiments, which were preceded by a control period. During the experiments the subjects lay with the body slightly elevated. Following the ingestion of 2 l. of water at night, only 70 per cent. was excreted within 4 hours. The administration of 2 l. of isotonic saline solution during the day, either by mouth or by intravenous injection during 1 hour was followed by a diphasic diuresis. The first phase was similar to that after drinking plain water during the day, about 750 ml. of urine of low chloride content being excreted in the first 2 hours. A protracted mild saline diuresis followed. At night only a brief water diuresis averaging 630 ml., followed the drinking of 2 l. of isotonic saline solution, and when the solution was given by intravenous injection it was retained in the body. The intake of isotonic saline solution was followed by a temporary increase in the volume of circulating blood plasma and in the central venous pressure. It is suggested that the secretion of the antidiuretic hormone depends on both the osmotic pressure of the body fluids and on the circulation.

G. B.

Phenobarbitone Narcosis, Effect of Iodides on. J. C. Krantz, Jr. and M. J. Fassel. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 511.) Organidin, a substance obtained by the interaction of glycerin and iodine, significantly increased the duration of narcosis of phenobarbitone sodium when both were administered intraperitoneally in rats. Similar effects were produced by the administration of an equivalent amount of iodine as sodium iodide and also by glycerin, sucrose and sorbitol, although in each instance the increase was smaller than with organidin. A mixture of glycerin and sodium iodide of similar composition to organidin, however, produced an equivalent increase. Oral administration of organidin produced only a slight increase. The intraperitoneal administration of organidin and an otherwise non-narcotic dose of phenobarbitone sodium produced narcosis in all of nine rats, indicating that the threshold for narcosis was diminished by the presence of organic iodide; oral administration of organidin, sodium bromide and sodium iodide produced a similar effect. That the presence of iodide in the tissues appears to lower the threshold of narcosis was shown by adding 0·5 per cent. of sodium iodide to the drinking water for seven days and then giving a dose of 9 mg./100 g. of body weight of phenobarbitone sodium; narcosis lasting for an average of 75 minutes was produced in 6 out of 10 rats whereas without the iodide the same dose of phenobarbitone sodium had failed to produce narcosis in any of the rats. The potentiating action of the substances with high osmotic pressure when given intraperitoneally may be due to osmotic pressure changes in the animal since fluid will be drawn from the extracellular spaces, tissues, and blood, thereby increasing the concentration of the narcotic in the blood. G. R. K.

Polymer-fume Fever. D. K. Harris. (*Lancet*, 1951, **261**, 1008.) Polytetrafluoroethylene ("Teflon," "Fluon") gives rise to toxic fumes when heated above 300° C. Exposure to the fumes produces toxic symptoms which may start with discomfort in the chest followed by an irritating cough. Within a few hours

there is a gradual increase in temperature, pulse-rate and possibly respiration rate, followed by shivering and sweating. Administration of oxygen is recommended. It appears that the fume consists of a fine sublimate with adsorbed hydrofluoric acid. Although the symptoms are similar to those of metal-fume fever, only traces of metal are present in the sublimate. G. B.

Sodium γ-Resorcylate in Rheumatic Fever. J. Reid, R. D. Watson, J. B. Cochran and D. H. Sproull. (*Brit. med. J.*, 1951, **2**, 321.) The chelate structure of salicylic acid is considered as a possible explanation of its activity in rheumatic fever, the *m*- and *p*-hydroxybenzoic acids being inactive. The pharmacological effects of increasing the chelate structure have been studied by investigating the antirheumatic action of the mono-sodium salt of γ-resorcylic acid. Oral administration of smaller doses was found to be as effective as salicylate in the 7 cases under treatment, and resulted in relief from acute arthritis in 1 to 4 days and a fall in temperature and pulse rate. The side effects accompanying the drug and the changes in fluid, nitrogen and chloride balances were similar to those reported with salicylate therapy, with the exception that profuse sweating, tinnitus and deafness were absent. The effect of the drug on the erythrocyte sedimentation rate is about the same as that of salicylate. Attention is drawn to the similarity in clinical and side-effects of salicylate, γ-resorcylate, adrenocorticotrophic hormone and cortisone. J. R. F.

Strophanthin, Heart Activity of, When Administered Gastro-enterically. G. Zöllner and K. Foth. (*Arch. Pharm., Berl.*, 1951, **284**, 253.) Experiments were carried out on 137 cats in order to determine the activity of strophanthin when administered by the gastro-enteric route. The materials used included a proprietary preparation "Strophoral," stated to be a derivative of strophanthin. The results were as follows. On the administration in the stomach of a simple intravenous toxic dose of g- or k-strophanthin or of strophoral, there was no absorption, while a similar test with digitoxin gave an absorption of 60 per cent. The upper parts of the intestine, and especially the ileum, are important in the action of strophoral. It was not proved whether the lower part took any share in the absorption. In the upper parts of the gastro-intestinal canal (stomach and duodenum), a reduction in the activity of strophanthins and of strophoral occurred. No proof could be obtained of any absorption from an isolated section of intestine, apparently because the length of the section was too small. Digestion of strophanthins or of strophoral in human gastric juice, followed by intravenous injection into cats, produced a reduction in heart activity of about 50 per cent. None of the experiments indicated any significant difference between g- and k-strophanthins and strophoral. G. M.

Veratrum Alkaloids, Depressor Action of. G. S. Dawes, J. C. Mott and J. G. Widdicombe. (*Brit. J. Pharmacol.*, 1951, **6**, 675.) From the results of comparative animal experiments using veratridine and veriloid, a mixture of veratrum alkaloids used clinically for producing a fall of blood pressure, it is concluded that the latter does not differ materially in its mode of action from the pure alkaloids. It elicits the Bezold reflex and sensitises or excites the pulmonary stretch receptors. The fall of blood pressure and heart rate caused by a slow infusion of veratridine in cats is abolished by cooling the vagi, and a similar result is obtained in some dogs under chloralose anæsthesia. In view of this apparent species difference it would be unwise to draw any conclusions about the precise mode of action of these drugs in man. There may be both a peripheral Bezold reflex and a central nervous action. S. L. W.

BOOK REVIEW

CLARK'S APPLIED PHARMACOLOGY. Eighth Edition, revised by Andrew Wilson and H. O. Schild. Pp. x + 670 (including 120 illustrations) and Index. J. and A. Churchill, Ltd., London. 1952. 37s. 6d.

There can be few pharmacologists who have not read and profited from the writings of the late Professor Clark. His book on the "Mode of Action of Drugs on Cells," published in 1933, was hailed at the time "as the most important contribution made to pharmacology in recent years." This book on "Applied Pharmacology" was first published in 1923, and 7 editions had appeared by 1940 shortly before Professor Clark's death. In preparing this new edition Professor Andrew Wilson and Dr. H. O. Schild have carried out a most commendable task. This could not have been easy, bearing in mind the rapid advances in pharmacology since 1942. They have painstakingly maintained the original broad foundations of the earlier editions, and yet have adequately included the new advances and new discoveries. This book was originally written in order to bridge the gap between the laboratory science of pharmacology and the clinical practice of therapeutics, so as to demonstrate as clearly as possible the connection between the two subjects. It consists of 31 chapters, giving a full and comprehensive account of pharmacology and chemotherapy based on a solid foundation of physiology. This is how pharmacology should be taught. There is a logical and systematic application of the principles of pharmacology in the treatment of disease, which gives the book a valuable place in therapeutics. Throughout, the book deals with the pharmacology of the various organs and physiological processes, rather than with the individual drugs themselves, the properties of which must be sought in several chapters. Inevitably, in a book of this size, space limits an adequate description of all the drugs and one might say "the book does not go far enough." However, the revisers have recognised this and included at the end of each chapter a list of general literature for supplementary reading. Here, too, there is selected list of official preparations, together with their dosage given entirely in the metric system. The chapter on the pharmacology of the autonomic nervous system seems all too short for such an important branch of pharmacology, and should be extended in subsequent editions. The chapter on the pharmacology of the heart is rather difficult to understand. There is certainly a need for a clear, concise and accurate account of the actions of the cardiac glycosides. This book offers to medical students, practitioners and pharmacists, a readable account of the principles and practice of pharmacology in relation to human disease. G. F. SOMERS.

ABSTRACTS (*Continued from page* 599.)

Veriloid (*Veratrum viride*), Treatment of Arterial Hypertension with. R. Kauntze and J. Trounce. (*Lancet*, 1951, **261**, 1002.) Veriloid is a mixture of ester alkaloids of *Veratrum viride*, standardised for hypotensive activity in dogs. It acts on the afferent vagus nerve and central nervous system direct. Administered by mouth or intravenous infusion, veriloid lowers the blood pressure in about 66 per cent. of hypertensive patients. Owing to its toxicity, the drug is useful in only 20 to 30 per cent. of cases, and dosage needs continuous supervision. Renal insufficiency is not adversely affected. Toxic symptoms which include nausea, recurrent vomiting and collapse are best treated with phenobarbitone. The same side reactions are observed with the pure alkaloids, germitrine and germidine. G. B.