ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ALKALOIDS

Ergot Alkaloids, Paper Chromatography of. A. M. Berg. (*Pharm. Weekbl.*, 1951, **86**, 900.) The six most important alkaloids of ergot can be separated by using buffered filter paper (*p*H 5) and ether as solvent. The best results are obtained by circular chromatography, which gives narrower bands than are obtained with the usual strip method. These bands represent, in order from the centre, ergometrine, ergometrinine, ergotamine, ergotaminine, ergocristine and ergocristinine. They are located by their fluorescence in ultra-violet light.

G. M.

Gelsemicine, Structure of. M. M. Janot, R. Goutarel and W. Friedrich. (*Ann. pharm. franc.*, 1951, **9**, 305.) Gelsemicine is relatively rare and owing to difficulties similar to those met in the elucidation of the structure of gelsemine, the formula is not yet certain. That adopted is $C_{19}H_{24}O_3N_2$. The alkaloid has been obtained by benzoylation and a laborious chromatographic purification on alumina followed by recrystallisation. The product melted at 262° C. and is considered to be an oxynorhydrogelsemine. J. R. F.

ANALYTICAL

Alkaloids, Paper Chromatography of. R. Munier and M. Macheboeuf. (*Bull. Soc. Chim. biol.*, 1951, **33**, 846.) In dealing with mixtures of alkaloids with unknown chromatographic characters, it is necessary first to determine the physicochemical conditions (*p*H) giving the most sharply defined spots, and then to find a solvent giving R_F values showing good separation. With a dissociation constant of the base not less than 10^{-2}, neutral or acid solutions should be used; at K = 10^{-3} to 10^{-7}, alkaline solutions; and at K = less than 10^{-12}, either acid, alkaline or neutral. Examples of the separation of groups of alkaloids are given; the figures given representing R_F values. *Atropine group: n*-butanol + 14 per cent. of glacial acetic acid: atropine, 0·71; hyoscyamine, 0·72; homatropine, 0·64; scopolamine, 0·60; tropine, 0·43. *Nicotine group: n*-butanol + 20 per cent. of hydrochloric acid (d = 1·19): nicotine hydrochloride, 0·27; pyrrolidine hydrochloride, 0·53; pyridine hydrochloride, 0·36. *Alkaloids of broom: n*-butanol + 20 per cent. of glacial acetic acid: genisteine, 0·84; sparteine, 0·73. *Pseudocinchona group: n*-butanol + 4 per cent. of hydrochloric acid (d = 1·19). Distinct spots are given by corynanthine, corynantheine cryst., corynanthidine, corynantheidine and yohimbine. For the development of alkaloidal spots two solutions are used: 0·85 g. of bismuth subnitrate with 40 ml. of water and 10 ml. of glacial acetic acid, and 8 g. of potassium iodide with 20 ml. of water. Equal volumes of these two solutions are mixed, and 10 ml. of the mixture is diluted with 20 ml. of glacial acetic acid and 100 ml. of water. The paper is dipped in this reagent for a few seconds, and dried between filter paper. The spots show up red on a pale orange ground.

G. M.

Ephedrine, Colorimetric and Chromatographic Determination of. A. Capone. (*Boll. chim.-farm.*, 1951, **90**, 465.) Ephedrine, 1 to 15 mg., is placed in a 25-ml. flask, with 4 ml. of 16 per cent. sodium chloride solution, 0·45 ml. of 0·1N sodium hydroxide, 6 drops of 33 per cent. hydrogen peroxide, and water to make 25 ml., and the flask is kept in a boiling water-bath for 5 minutes. A reddish-violet colour is produced and the reading is taken in a Hellige colorimeter. The amount of ephedrine present is read from a curve previously obtained by treating known quantities in the same way. Many drugs likely to be mixed with ephedrine, such as diethylbarbituric acid, calcium chloride, codeine, magnesium chloride, terpene hydrate cause only slight inaccuracies but many, such as lactic acid, calcium gluconate, chloral hydrate and potassium bromide and iodide hinder the reaction. The author therefore devised a chromatographic method. 0·01 ml. of the solution to be examined is placed on a sheet of Schleicher and Schull filter paper No. 597 36 cm. high, placing the drops 25 mm. apart for aqueous solutions and 30 mm. apart for oils and ointments. The solvent is allowed to ascend for 30 cm. in a suitable closed glass cylinder at room temperature. To develop the chromatogram the paper is kept immersed in an atmosphere saturated with iodine vapour for 12 hours. For aqueous solutions the solvent is 100 parts of water-saturated butanol with 25 parts of ethanol, for oils and ointments it is equal parts of butanol, ethanol and water. The quantity of ephedrine should be about 50 μg. H. D.

Hyoscyamine and Atropine, Decomposition of. W. Schneider. (*Arch. Pharm., Berl.*, 1951, **284**, 306.) The cause of the ease of racemisation of hyoscyamine lies in the character of the tropic acid fraction of the molecule, which has a enolisable hydrogen atom attached to the asymmetric carbon atom. The racemisation is favoured by the same factors as the enolisation. This also applies to hyoscine and homatropine. Hyoscyamine and atropine behave similarly with respect to hydrolytic decomposition. The proportion of atropine and tropine in a partially hydrolysed solution may be determined by shaking out the bases and determining their equivalent by titration against standard acid. Comparing the effect of sodium carbonate, ammonia and sodium bicarbonate on atropine, the greatest amount of hydrolysis is produced by sodium carbonate, less by ammonia, and only a small amount by sodium bicarbonate. In assaying drugs, using the ammonia method, high values are therefore due not only to traces of residual ammonia, but partially to tropine. G. M.

Hyoscyamine and Hyoscine, Separation of. G. Schill and A. Ägren. (*Svensk farm. Tidskr.*, 1952, **56**, 55.) A chromatographic method has been worked out for the separation of hyoscyamine and scopolamine. For the pure substances a solution in chloroform is added to a column of kieselguhr acidified with hydrochloric acid, and eluted with chloroform. The eluate contains the hyoscyamine as hydrochloride which is converted to base by passing the eluate through a kieselguhr column containing sodium carbonate; the alkaline column is washed with chloroform to remove the hyoscyamine. The scopolamine is eluted from the first column with chloroform saturated with ammonia; recovery experiments with known amounts of the alkaloids were satisfactory. The same principle is used for separation of belladonna alkaloids in pharmaceutical preparations; an amount of the preparation equivalent to about 0·15 g. of alkaloids is made alkaline with M sodium carbonate and extracted with 200 ml. of chloroform by percolation. The eluate in turn passes three columns; the first containing 4 ml. of M hydrochloric acid and 15 g. of kieselguhr retains the scopolamine, the second containing 4 ml. of M sodium carbonate and 15 g. of

kieselguhr will convert the hyoscyamine hydrochloride to base, while the third containing 4 ml. of 0·5M phosphoric acid and 15 g. of kieselguhr retains the hyoscyamine; the inert substances pass through the columns. The first column is then eluted with 250 ml. of chloroform and the eluate may pass the second and third columns; the scopolamine is eluted from the first column with 250 ml. of chloroform saturated with ammonia, and the solution may pass 10 g. of aluminium oxide. The second column is washed with 50 ml. of chloroform and the eluate is added to the third column. The hyoscyamine is eluted from the third column with 250 ml. of chloroform saturated with ammonia, and the eluate may pass 10 g. of aluminium oxide. The second column is necessary in order not to get low values since if it is omitted part of the hyoscyamine hydrochloride will pass the third column. Recovery experiments were satisfactory. R. E. S.

Nicotinic Acid in Pharmaceutical Products, Determination of. A. Mueller and S. H. Fox. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 513.) When nicotinic acid reacts with cyanogen bromide in the presence of ammonia, a bright yellow colour is produced. The intensity of the colour is proportional to concentration when absorption at the maximum wavelength is plotted against concentration. The maximum wavelength is 408 mμ and the colour reaches its maximum intensity after two to two-and-a-half minutes. The maximum wavelength for nicotinamide is at 389 mμ, reaching its maximum intensity after 6 minutes. Since the rate of reaction with nicotinamide is slower than with nicotinic acid, it is better to hydrolyse the amide; either acid or alkaline hydrolysis may be used. The method of determination is to heat a suitable number of capsules, tablets, etc., with water on a steam-bath until the sample is dispersed; if a fatty basis is present, 3 to 5 ml. of ethylene dichloride is added to dissolve the fat. After cooling, the solution is made up to volume and filtered. If hydrolysis is necessary an aliquot part of the filtrate is evaporated to low bulk with hydrochloric acid, diluted with water and the *p*H adjusted to 2 to 12 with potassium hydroxide; alternatively the filtrate may be heated with 0·5 N sodium hydroxide. The test solution is then treated with a buffered ammonia solution and a 10 per cent. solution of cyanogen bromide in water, and the absorption measured. The experiments are repeated using a standard solution of nicotinic acid, and the result calculated from a given formula. With coloured solutions, a blank determination is also carried out and the absorption of the blank subtracted from the total. Data given showing results obtained with multivitamin capsules with or without ferrous sulphate, ferrous gluconate, liver concentrate, whole dried liver, yeast, and mixtures of these indicate that the method is precise in the application to pharmaceutical preparations.

G. R. K.

Phenol, Bromination of, in Assays. R. Reimschneider. (*Chim. et Ind.*, 1951, **66**, 806.) A number of assay processes depend upon the treatment of phenol with bromine in acid solution, tribromophenol bromide being formed. Methods which measure only the amount of free bromine absorbed in the reaction give results in good agreement with theory. Such methods involve treating phenol with an excess of bromine and reducing the excess with standard arsenious acid or thiosulphate. Methods which depend upon a determination of the quantity of bromide ions remaining in solution after the reaction of the phenol with bromine, estimated by titration after removal of the precipitate and excess of bromine, yield high results, whereas those which depend on weighing the tribromophenol bromide or estimation of bromide in the precipitate, yield low

results. The errors appear to be due to the solubility of the bromo-derivative in acid solutions and possibly also to secondary reactions. G. B.

Sulphonamides, Identification of, on Paper Chromatograms. A. E. Steel. (*Nature, Lond.*, 1951, **168**, 877.) A solution of *n*-butanol, acetic acid and water in the proportions of 50:15:35 by volume has been found a satisfactory solvent for developing sulphonamides on paper chromatograms. R_F values found range from 0·55 (sulphaguanidine) to 0·85 (sulphamerazine). Detection of the spots, carried out in alcoholic solution to minimise spreading, is by spraying the dried paper with nitrous acid solution, a mixture of 0·1 g. of sodium nitrite in 1 ml. of water shaken first after adding 10 ml. of *n*-butanol, and again after the addition of 0·3 ml. of concentrated hydrochloric acid. This is followed after 1 minute, by a 1 per cent. solution of dimethyl-α-naphthylamine or a similar coupling reagent, red or pink indicating a positive result. 1 μg. is detectable by this method, which has also been used for quantitative measurements. J. R. F.

Zinc, Identification and Volumetric Determination of. H. Wachsmuth and J. Cornelis. (*J. Pharm. Belg.*, 1951, **6**, 389.) The addition of a few drops of 0·5 per cent. solution of potassium ferricyanide to a solution containing a small amount of zinc and adrenaline gives a pink colour (sensitivity 1 in 10,000), with diphenylamine a violet colour (sensitivity 1 in 10,000), with benzidine a bluish-violet (blanks should be tried in this case) (sensitivity 1 in 50,000), and with potassium iodide and starch a blue colour (sensitivity 1 in 1,000,000). Nickel, cobalt, copper and manganese interfere giving different colours. For volumetric determination a standard solution containing 32·935 g./l. of potassium ferricyanide and another containing 16·615 g./l. of potassium iodide are used. To 5 ml. of ferricyanide solution add 5 ml. of potassium iodide and an exactly measured volume of the solution to be tested. Titrate the liberated iodine with 0·01N sodium thiosulphate. 2 atoms of iodine are liberated for 3 atoms of zinc. The solution should be neutral or slightly acid with hydrochloric acid, it will have a yellow colour at the end of the titration owing to the excess of ferricyanide. Bismuth, mercury, barium, magnesium, chromium, tin and boric acid have no influence on the reaction, but nickel and cobalt hinder it, as well as copper, but it is easy to determine the latter and then titrate the zinc in the same sample. Add some crystals of potassium iodide and a little starch, wait a quarter of an hour and titrate the copper with sodium thiosulphate and then titrate the zinc as described. Iron must be removed as follows. If necessary, neutralise with 10 per cent. solution of sodium carbonate and then add 10 per cent. acetic acid until the precipitate disappears. Heat to 70° to 80° C. and saturate with hydrogen sulphide. Allow to stand for 10 minutes and centrifuge; wash the precipitate with 10 per cent. acetic acid. If there is much iron repeat the operation. Dissolve the precipitate in 1 ml. of concentrated hydrochloric acid, dilute to 40 ml. and boil off the hydrogen sulphide. Cool and determine the zinc as above. H. D.

ESSENTIAL OILS

***Lippia carviodora* from Somaliland, Oil from.** H. T. Islip and W. S. A. Matthews (*Colonial Plant and Animal Prod.*, 1951, **2**, 96.) A sample of dried leaves from the Somaliland Protectorate yielded on steam distillation 3·15 per cent. of a pale yellow oil having an odour reminiscent of caraway. The characters and composition of the oil were compared with oils distilled in Kenya from the same species in 1944 and 1945 respectively. Sample A was distilled

from a mixture of 36-lb. flower heads and 1-lb. each of leaves and twigs which yielded only 0·99 per cent. The composition of the three oils is summarised in the table. Although the oils from the two localities were similar the yield from the Somaliland leaves was much greater than that from flower heads or leaves from Kenya. It is considered that the oil should find a market in the United Kingdom especially as a source of carvone.

	Sample from Somaliland	Sample A from Kenya	Sample B from Kenya
	per cent. w/w	per cent. w/w	per cent. w/w
Ketones, mainly *d*-carvone	67·3	67·9	60·2
Free alcohols as linalool	2·9	2·4	3·5
Acids, as acetic	Negligible	0·1	0·1
Esters as linalyl acetate	0·7	1·3	4·1
Terpenes (mainly *d*-limonene) sesquiterpenes and undetermined	29·1	28·3	32·1

G. R. A. S.

FIXED OILS, FATS AND WAXES

Niger Seed Oil from Tanganyika. R. W. Pearman, W. D. Raymond and J. A. Squires (*Colonial Plant and Animal Prod.*, 1951, **2**, 101.) Three samples of seed of *Guizotia abyssinica* Cass., grown in Tanganyika yielded to extraction with light petroleum from 35 to 38 per cent. of fixed oil. The characters of these oils are tabulated and compared with published figures. Niger seed oil being a drying oil finds application in paints and can also be used for the manufacture of soap. As an edible oil it is satisfactory when fresh, but has the disadvantage that it deteriorates rather rapidly. G. R. A. S.

GLYCOSIDES, FERMENTS AND CARBOHYDRATES

Sapote Gum, Composition of. E. Anderson and H. D. Ledbetter. (*J. Amer. pharm. Ass. Sci. Ed.*, 1951, **40**, 623.) Crude Peruvian sapote gum is the exudate which flows from the wounds of trees which have been tapped for the latex from which chicle is prepared. It contains 6 to 10 per cent. of resin which may be separated by heating with water and filtering. The water-soluble gum may be purified by decolorising with bromine and precipitating with ethanol. It contains calcium and magnesium salts of a methoxyuronic acid containing about 2 uronic acid and 7 anhydropentose groups to each methoxyl. The pentosan material (64·7 per cent. of the crude gum) is derived from D-xylose and L-arabinose in the ratio 8·5:1. Most of the L-arabinose is liberated by hydrolysis in dilute acid at 80° C. for 2 hours, and heating for 4 hours removes most of the D-xylose, 2 sugar units remaining attached to each uronic acid group. Drastic hydrolysis (autoclaving) fails to remove all the D-xylose from combination with the uronic acid. G. B.

GUMS AND RESINS

***Podophyllum emodi* Wall, New Compounds from.** M. V. Nadkarni, P. B. Maury and J. L. Hartwell. (*J. Amer. chem. Soc.*, 1952, **74**, 280.) In the search for tumour-necrotising components of the resin from different species of *Podophyllum*, the resin from *P. emodi* Wall was investigated using chromatography with activated alumina. Three colourless crystalline compounds were isolated, their order of decreasing strength of absorption being podophyllotoxin (36 to 39 per cent. yield), demethylpodophyllotoxin (I) (1·7 per cent.) and

1-O-(β-D-glucopyranosyl)-picropodophyllin (II) (1·8 per cent.). Compounds I and II are new. Compound I crystallised in colourless transparent prisms, m.pt. 250·0° to 251·6° C., from ethanol, and methylation of this substance with diazomethane produced podophyllotoxin. Compound II crystallised in long, thin, colourless needles from 75 per cent. methanol or water, m.pt. 237·0° to 238·2° C. Hydrolysis of II with dilute hydrochloric acid gave D-glucose and picropodophyllin. The glucoside II was shown to be probably a β-glucopyranoside. Compound I is active in producing hæmorrhage and necrosis in Sarcoma 37 in mice, while II is inactive even in high doses. A. H. B.

TOXICOLOGY

Arsenic in Hair, A Method of Localisation for Use in Toxicology. H. Griffon and J. Barbaud. (*Ann. pharm. franç.*, 1951, **9**, 545.) Hairs are cut off at the scalp, fastened together keeping the cut ends level, washed in acetone, ethanol, water and again in acetone and dried, before being submitted to neutron bombardment to induce radioactivity. By means of a Geiger-Muller counter and a lead slit, the activity is determined over each 2 mm. portion along the length of the bundle of hairs. Radioactivity induced in the natural constituents of the hair decreases in a regular manner from the cut end to the tip, on account of the decrease in thickness of the hair and of the decay in radioactivity during measurement. For normal hair the graph relating radioactivity to length is a straight line, and undulations indicate the presence of adventitious arsenic which can be confirmed by study of its radioactive period (26 hours 8 minutes). From the rate of hair growth and position of the arsenic deposits, the time of arsenic intoxication can be calculated, and this generally accords more exactly with the facts than do the results of chemical methods which do not localise the arsenic along the length of the hair with such great accuracy. G. B.

β-*p*-Hydroxyphenylpropionic Acid in Viscera, Identification of. G. Roche Lynch. (*Analyst*, 1951, **76**, 610.) The crude isolate is purified by grinding with light petroleum (40° to 50° C.) and recrystallised from benzene. The crystals are soluble in water and benzene but not in light petroleum. The mol. wt. is 166 and the empirical formula $C_9H_{10}O_3$. The crystals, a pure sample of the acid and a mixture of the two, melt at 126·5° to 127·5° C., thus confirming the nature of the isolate. The acid when treated with bromine in acetic acid yields a crystalline bromo derivative m.pt. 112·5° to 113·5° C. ex water. Also it gives a very strong brownish red colouration on coupling with diazotised sulphanilic acid in alkaline solution. J. R. F.

β-*p*-Hydroxyphenylpropionic Acid in Viscera, Note on the Occurrence of. L. C. Nickolls. (*Analyst*, 1951, **76**, 609.) An extraction of the viscera from an exhumed body, subjected to anærobic conditions, with the purpose of isolating a suspected barbiturate fraction, yielded yellow crystals the m.pt. of which was raised by purification to 128° C. This crystalline compound gave results similar to barbiturates with a series of chemical reactions, but sodium fusion and microanalysis showed a negative result for nitrogen, and mixed m.pts. with the common barbiturates were much lower. A pure sample of β-*p*-hydroxyphenylpropionic acid gave all the reactions for the unknown material and had m.pt. and a mixed m.pt. with the unknown of 128° C., thus confirming identity. It is suggested that the mixed m.pt. should always be employed in the identification of suspected barbiturates in viscera. J. R. F.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Adrenaline, Inhibition of Oxidation by Borate. E. M. Trautner and M. Messer. (*Nature, Lond.*, 1952, **169**, 31.) When dilute solutions of adrenaline, M/500 to M/2000 were allowed to oxidise in phosphate and borate buffers, it was found that the oxygen uptake in phosphate-buffer increased rapidly as the *p*H was increased above 7·0, but with borate buffer remained very low and almost unchanged up to a *p*H of just above 9·0. Above *p*H 9·5 the oxidation-rates increased markedly, though they were still lower than in other buffers at the same *p*H. Adrenaline was also allowed to oxidise in phosphate buffer in the presence of varying concentrations of borate. About 50 per cent. inhibition occurred when adrenaline and borate were present in equimolar proportions, at *p*H 7·8, 37·5° C., the concentrations of each being M/500. It is assumed that the borate forms complexes with the adrenaline, blocking the hydroxyl groups and hindering the onset of oxidation. Apparently borate also forms complexes with the oxidation products of adrenaline. The complexes are apparently unstable above *p*H 9 and on dilution. When adrenaline-borate mixtures were injected intravenously into an anæsthetised cat, they showed neither inhibition nor intensification, nor prolongation of the adrenaline effect on the blood pressure and the nictitating membrane. A. H. B.

Antibiotics, Microscopic Identification of. O. Landgren. (*Farm. Revy.*, 1951, **50**, 781.) The crystal characters of antibiotics may be determined by the following scheme. For the test a series of liquid mixtures of *iso*-amyl *iso*-valerate, α-bromonaphthalene, liquid paraffin and methylene iodide are prepared, showing a range of refractive index at 0·01 intervals. The observations are made as follows:—The solid substance is observed microscopically in a liquid having about the expected refractive index. After focusing, the tube is raised, when a bright line is observed following the contour of each crystal. On raising the tube this line wanders towards the medium (crystal or liquid) which has the highest refractive index. By a series of trials with different liquids the refractive index of the crystal is determined. The preparation is observed in polarised light, without analyser: if all crystals are equally bright, the material is monochroic; if there are varying colours, it is pleochroic; and if some are light and

	Crystal character	Refractive index
Chloramphenicol	monochroic anisotropic	1·52 to 1·53
Dihydrostreptomycin sulphate	isotropic, glassy	1·54 to 1·55
do.	dichroic, anisotropic, microcrystalline	1·55 to 1·56
Streptomycin sulphate	isotropic, glassy	1·54 to 1·55–1·56
Streptomycin-calcium chloride	isotropic, glassy	1·55 to 1·56–1·57
Penicillin-potassium	pleochroic, anisotropic	1·57 to 1·58
Procaine-penicillin	monochroic, anisotropic	1·57 to 1·58
Penicillin-sodium	anisotropic laminae	1·59 to 1·61
Aureomycin base	pleochroic, anisotropic, tabular	1·70 to 1·74
Aureomycin hydrochloride	monochroic, isotropic, glassy	1·66 to 1·67
Penicillin-calcium	isotropic, glassy	1·57 to 1·58
Bacitracin	isotropic, amorphous	1·54 to 1·55
Polymyxin B sulphate	isotropic, amorphous	1·53
Terramycin hydrochloride	monochroic, anisotropic	1·55 to 1·56
Tersavin (ephedrine-penicillin)	dichroic, anisotropic, laminae	1·56 to 1·57
Usnic acid	dichroic, anisotropic, columns	1·61 to 1·62

others dark, it is dichroic. Between crossed Nicols, if all crystals are dark they are isotropic; if they are light or coloured in certain positions, they are anisotropic. With the latter there is more than one refractive index, and if the form of the crystals is such that they lie in different positions these can be determined. Observed characters of antibiotics are as shown in the table (where 3 values are given for the refractive index, the last figure represents a higher value which was noted after several hours). G. M.

Fungicides, Organic, A New Class of. A. R. Kittleson. (*Science*, 1952 **115**, 84.) *N*-trichloromethylthio derivatives of imides, hydantoins, 2:4-oxazolidinediones and sulphonamides were prepared as follows. Disperse 1 mole of the sodium derivative in 1000 ml. of benzene and add during 2 to 3 hours, by dropping funnel, 1 mole of perchloromethyl mercaptan, stirring and heating gradually and continuing to boil under a reflux condenser for 4 to 6 hours. Filter to remove sodium chloride, concentrate, cool and collect the precipitated *N*-trichloromethylthio derivative on a filter. *N*-trichloromethyl-thiomorpholine was prepared similarly from perchloromethyl mercaptan and an excess of morpholine. Derivatives were stable compounds, obtained in good yield and had LD50 less than 10 parts per million against *Alternaria solani* and *Sclerotinia fructiola* by the slide germination technique. G. B.

Riboflavinyl Glucoside. L. G. Whitby. (*Biochem. J.*, 1952, **50**, 433.) A new derivative of riboflavine is described, prepared by incubation of riboflavine with an enzyme obtained from rat liver. An aqueous solution is stable at 100° C., but N sodium hydroxide at 100° C. rapidly destroys the flavine by attacking the *iso*alloxazine nucleus; the compound is hydrolysed by strong acids, with the production of riboflavine, the reaction being completed in 2·5 hours in N hydrochloric acid at 100° C. The molecular absorption coefficient at 450 mμ and the positions of the maxima and minima are the same as reported for riboflavine by Singer and Kearney, although in the region 440 to 310 mμ the absorption of the new flavine is consistently 2 to 3 per cent. less intense. The elementary composition of the substance was found $C_{23}H_{30}O_{11}N_4$; the structure of the compound is discussed and is identified as 5′-D-riboflavine-D-glucopyranoside (riboflavinyl glucoside). It is suggested that the glucosidic linkage has the α-configuration. Preliminary investigations of the enzymic reaction indicate that the enzyme catalyses a transglycosidation of D-glucose from maltose or glycogen to riboflavine. R. E. S.

BIOCHEMICAL ANALYSIS

Aneurine, Microbiological Assay of. S. C. Fang and J. S. Butts. (*Proc. Soc. exp. Biol., N.Y.*, 1951, **78**, 463.) The test organism used is *Lactobacillus fermenti* 36 and the extent of growth is determined by measurement of the turbidity by means of a Klett-Summerson photo-colorimeter using a 54 filter after 16 hours at 37° C. The medium contains takadiastase-digested starch which has a stimulant effect on the growth of the test organism; it also contains filbert nut meal extract which appreciably increases the rate of growth. In the assay of foodstuffs the sample is digested with a mixture of takadiastase and papain, and it is likely that any starch will break down into dextrin and maltose which stimulate the growth of the organism. The authors believe that enzyme-digested starch is one of the many stimulants which may be responsible for erratic results in the assay of the B vitamins of some natural products, and recommend its addition to the assay medium. H. T. B.

Aneurine Salts, Titration of, with Perchloric Acid. C. W. Pifer and E. G. Wollish. (*J. Amer. pharm. Ass. Sci. Ed.*, 1951, **40**, 609.) Aneurine in glacial acetic acid solution may be titrated with perchloric acid. Halogen ions must be removed by the addition of mercuric acetate before titration. The following method is suggested for the assay of aneurine hydrochloride. Dissolve about 0·6 g. by warming with 80 ml. of glacial acetic acid, cool, add 10 ml. of 6 per cent. mercuric acetate reagent and titrate with 0·1N perchloric acid. The end-point is detected potentiometrically or by using crystal violet as indicator; each molecule of aneurine neutralises 2 equivalents of acid. Mercuric acetate need not be added when aneurine mononitrate is being assayed. The reaction is not specific and a number of compensating or limit tests for specific impurities is suggested. For example, 2-methyl-5-ethoxymethyl-6-aminopyrimidine, 4-methyl-5-β-(hydroxyethyl)thiazole and 2-methyl-5-bromoethyl-6-aminopyrimidine can be extracted with ether from aneurine in alkaline solution, dissolved in glacial acetic acid and titrated with perchloric acid; 6-amino-5-aminoethyl-2-methylpyrimidine may be estimated by the red colour (absorption maximum, 560 mμ) which it gives with ninhydrin. G. B.

Calcium in Biological Fluids, Determination of. I. J. Greenblatt and S. Hartman. (*Anal. Chem.*, 1951, **23**, 1708.) The determination depends on the fact that calcium in an ionic state, in the presence of ammonium purpurate produces a pink colour and when titrated with a solution of disodium dihydrogen ethylenediamine tetra-acetate dihydrate, the calcium is firmly bonded in an ionised soluble complex which turns orchid-purple. The biological fluid is pipetted into a suitable vessel, the *p*H adjusted with sodium hydroxide and ammonium purpurate is added to produce a salmon-pink colour. The mixture is then titrated with disodium dihydrogen ethylenediamine tetra-acetate dihydrate, until a stable orchid-purple colour is obtained, which, upon the addition of another drop of disodium dihydrogen ethylenediamine tetra-acetate dihydrate, will not alter; a standard calcium solution is treated similarly. Excellent agreement was obtained in comparison with potassium permanganate methods in which the calcium was precipitated as an oxalate. In hæmolytic serum with a marked increase of ionic iron, and in jaundice serum with a marked increase in bile pigments, a blurring of the sharp, distinct end point ordinarily obtained in titrating clear serums was experienced. R. E. S.

Phenylpyruvic Acid in Urine, Estimation of. J. P. Berry and L. I. Woolf. (*Nature, Lond.*, 1952, **169**, 202.) Urine from phenylketonurics contains an ether-soluble acid, phenolic in nature which gave false high results in Penrose and Quastel's method (*Biochem. J.*, 1937, **31**, 266) for phenylpyruvic acid, and the following method was therefore worked out. The urine is acidified (*p*H 1) and extracted with ether; the ether is evaporated in a stream of nitrogen at room temperature and the residue dissolved in a glycine-sodium chloride-hydrochloric acid buffer at *p*H 2·2. Ferric chloride is added and the resulting colour read at its maximum (2 to 3½ minutes after mixing) in a photoelectric colorimeter using Ilford 607 filter ($\lambda_{max.}$ = 600 mμ); fading was rather slow. A straight line graph is given, obtained with pure phenylpyruvic acid; recovery of phenylpyruvic acid added to normal urine varied from 98 to 100 per cent. The results are quoted for several urines in which phenylpyruvic acid was estimated (*a*) by this method and (*b*) by the dinitrophenylhydrazone method (modified for photoelectric colorimetry); in all cases method (*a*) gave results considerably lower than those obtained by method (*b*). *p*-Hydroxyphenylpyruvic acid and homogentisic acid

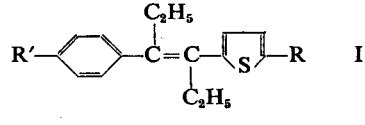
do not interfere in the proposed method, since the blue-green colour they give fades completely within 1 minute. By the dinitrophenylhydrazone method, *p*-hydroxyphenylpyruvic acid gives, mole for mole, 1·3 times the colour intensity given by phenylpyruvic acid. The nature of the interfering substance is unknown. R. E. S.

Propylthiouracil in Urine, Determination with 2:6-Dichloroquinone-chloroimide. R. A. McAllister. (*J. clin. Path.*, 1951, **4**, 432.) Take 100 ml. of urine and adjust the *p*H to 6·0. Transfer 50 ml. or an aliquot containing up to 5 mg. of propylthiouracil, to a small separating funnel. Extract 3 times with 100 ml. amounts of peroxide-free ether. Pool the extracts and wash once with 100 ml. of water. Evaporate the pooled extracts to dryness and dissolve the residue in 2 ml. of aldehyde-free absolute ethanol. Wash the solution into a flask and make up to 100 ml. Take, in 2 tubes, aliquots of 2 and 1 ml. and adjust the volume of each to 5 ml. with water, add 5 ml. of borate buffer *p*H 8 and 0·1 ml. of 0·4 per cent. chloroimide reagent. Mix the contents in each tube and allow to stand during 45 minutes. Add 10 ml. of chloroform to each, and shake until the yellow colour is extracted. Allow to settle and remove the aqueous supernatant liquid by suction. Filter through a small No. 42 Whatman paper and read in a Spekker absorptiometer against chloroform using the violet filter. Prepare a standard reference graph by applying the colour reaction to 10, 20, 30, 40, 50 and 100 μg. of propylthiouracil, each in 5 ml. of water, and extract the colours with 10 ml. of chloroform. J. R. F.

CHEMOTHERAPY

Barbituric Acid, Thiocyanate and *iso*Thiourea Derivatives of. G. S. Skinner and W. H. Waitz. (*J. Amer. chem. Soc.*, 1952, **74**, 498.) A series of thiocyanate and *iso*thiourea derivatives of barbituric acid of type $RR'C(CONH)_2CO$ where R = C_2H_5–; *n*–C_3H_7–; *n*–C_4H_9–; *i*–C_5H_{11}; *n*–C_5H_{11}; and R′ = $NCSCH_2CH_2$–; $(H_2N{=}C(NH_2)SCH_2CH_2$–$)^+Br^-$; $HN{=}C(NH_2)SCH_2CH_2$–, were prepared and subjected to pharmacological testing. Both the thiocyanates and the *iso*thiouronium salts were easily prepared in good yields by the action of potassium thiocyanate and thiourea, respectively, on the β-bromoethylbarbituric acid derivates in ethanol. The *iso*thiouronium salts were converted to the *iso*thiourea derivatives by treatment of their warm aqueous solutions with a slight excess of ammonia. The thiocyanates resisted hydrolysis without cleavage of the ring but the *iso*thiourea derivatives were smoothly hydrolysed to the mercaptobarbituric acids. None of the compounds produced hypnosis or anæsthesia, but the *iso*thiouronium bromides exhibited some anticonvulsant activity. A. H. B.

Diethylstilbœstrol, Some Thiophene Analogues of. W. R. Biggerstaff and O. L. Stafford. (*J. Amer. chem. Soc.*, 1952, **74**, 419.) Although compound Ia (R′ = H, R = H) had previously been shown to possess only a low order of œstrogenic activity, compounds Ib (R′ = OH, R = H) and Ic (R′ = OH, R = Br) were prepared because the introduction of a 4-hydroxyl group into the α:α′-diethylstilbene nucleus greatly enhanced the œstrogenic activity.



I

Compound Ib was much more active than Ia and produced 50 per cent. œstrus (rats) in 100-μg. doses and 100 per cent. at 250 μg. It also appears to be much more active than its benzene analogue, 4-hydroxy-α:α'-diethylstilbene. The introduction of a bromine atom in the thiophene ring (compound Ic) results in a decided lowering of the activity. The synthesis of the above compounds is described. A. H. B.

***N*-Substituted Diallylbarbiturates, Antipyretic and Analgesic Activity of.** F. Sandberg. (*Svensk farm. Tidskr.*, 1951, **55**, 698.) A number of derivatives were tested for antipyretic and analgesic action. These were 1-(*N*-phenylcarbamylmethyl)-5:5-diallylbarbituric acid; 1-(*N*-*p*-ethoxyphenylcarbamylmethyl)-5:5-diallylbarbituric acid; 1-(*N*-*p*-allyloxyphenylcarbamylmethyl)-5:5-diallylbarbituric acid; 1:3-di (*N*-phenylcarbamylmethyl)-5:5-diallylbarbituric acid; 1:3-di(*N*-*p*-ethoxyphenylcarbamylmethyl)-5:5-diallylbarbituric acid and 1:3-di(*N*-*p*-allyloxyphenylcarbamylmethyl)-5:5diallylbarbituric acid. Their action was very slight. This result was unexpected, since it would be expected that the metabolism for these compounds would be similar to that of other aniline derivatives such as acetanilide or phenacetin. It was also found that a molar mixture of diallylbarbituric acid with acetanilide, phenacetin or *p*-allyloxyacetanilide produced a greater antipyretic and analgesic effect than the chemical compounds of these components, owing to an additive synergism. There was, however, one exception—there was no synergism between the analgesic effect of diallylbarbituric acid and *p*-allyloxyacetanilide. It was also noted that the latter compound, unlike acetanilide and phenacetin, appreciably shortened the duration of the anæsthetic action of diallylbarbituric acid.

G. M.

PHARMACY

DISPENSING

Calcium Gluconate Solutions, Stabilisation of. S. Balasundaram and V. Subrahmanyan. (*Indian J. Pharm.*, 1951, **13**, 179.) Solutions containing 10 per cent. of calcium gluconate were stabilised by the addition of 0·6 per cent. of boric acid; 15 per cent. solutions required 0·9 per cent. of boric acid. Adjustment of the *p*H to 6·8 to 7·0 resulted in a slight decrease in the amount of boric acid required. The following concentrations of other stabilisers were necessary to prevent crystallisation in 10 per cent. solutions of calcium gluconate: calcium saccharate, 0·8 per cent.; calcium galactonate, 0·8 per cent.; and calcium lactobionate, 0·6 per cent. 1 per cent. of calcium lactate stabilised a 9·6 per cent. solution of calcium gluconate. The following substances were unsatisfactory as stabilisers: lactic acid, glucose, fructose, sucrose, sodium chloride, sodium bromide and sodium iodide. G. R. K.

NOTES AND FORMULÆ

Antiseptic Power of Some Ointments, Influence of Excipients on. A. Mirimanoff and F. Ducommun. (*Pharm. Acta Helvet.*, 1951, **26**, 387.) Bacteriostatic power against *Staphylococcus aureus* was determined for a number of substances. The most powerful bacteriostatics tested were phenylmercuric borate (merfen), domiphen (bradosol) and désogène, a mixture of methosulphates of quaternary trimethylammonium bases. The bacteriostatic power of certain substances was increased in the presence of cationic detergents, for example, formaldehyde, mercurochrome and boric acid with bradosol and phenol with désogène. This exaltation could not be confirmed with anionic

detergents. No exaltation or bacteriostatic power was observed with the non-ionic detergents crillex 11, carbowax 1500 and tween 20. Ointments were tested against *S. aureus* by a cylinder-plate method. Zones of inhibition were measured after 36 hours' incubation with ointments prepared from the following bases: (1) soft paraffin/lanolin (water in oil), (2) glyceryl monostearate and paraffins (oil in water) and (3) bentonite. Formaldehyde, boric acid, mercuric oxycyanide, silver proteinate, merfen, mercurochrome and penicillin were incorporated. In general the antiseptics diffused most readily from the bentonite base and least from the water in oil base. It was not possible to give a general rule, but it was frequently observed that anionic detergents increased the diffusion of the antiseptic while non-ionic detergents decreased it. The method of testing was not suitable for cationic detergents. G. B.

Chlorcyclizine Hydrochloride (Di-Paralene Hydrochloride). (*New and Non-official Remedies, J. Amer. med. Ass.*, 1952, **148**, 286.) Chlorcyclizine hydrochloride is 1-*p*-chlorobenzhydryl-4-methylpiperazine hydrochloride and occurs as a white, odourless, bitter, crystalline solid, m.pt. 222° to 227° C., soluble in water (1 in 1·6), ethanol (1 in 10·4) and chloroform (1 in 3·6) and almost insoluble in benzene and ether; a 1 per cent. solution has *p*H 5·0 to 5·5. The picrate obtained by treating a 1 per cent. solution with picric acid melts at 215° to 219° C., with decomposition. Chlorcyclizine hydrochloride loses not more than 2 per cent. of its weight when dried for 3 hours at 120° C., and yields not more than 0·20 per cent. of residue on ignition. A 0·001 per cent. w/v solution in ethanol exhibits an ultra-violet absorption maximum at 2300 Å. ($E^{1\ \text{per cent.}}_{1\ \text{cm.}}$, 443 ± 10) and a minimum at 2180 Å. It is used as a histamine antagonist in a dose of 50 mg. 2 or 3 times daily. G. R. K.

PHARMACOGNOSY

Agar-yielding Seaweeds from the Philippines. M. Cantoria, G. T. Velasquez and P. Valenzuela. (*J. Philipp. pharm. Ass.*, 1951, **38**, 295). A survey of the red seaweeds growing near the Philippines and likely to yield agar has been made. The identification and characters of the three most promising plants *Hypnea musciformis* var. *hipporoides* (Kuetz.) Web. v. B., *Gracilaria canaliculata* (Kuetz.) Sond. and *Gracilaria lichenoides* (L.) Gmel. are discussed. The appearance of transverse sections of the thallus, drawings and photographs of which are given, together with the staining effects of ruthenium red solution B.P. were found useful in identifying the plants. J. W. F.

***Hyoscyamus muticus* L. Morphology and Histology of the Flowering Tops.** A. H. Saber and S. I. Balbaa. (*Reports Pharm. Soc., Egypt*, 1951, **33**, 29.) A detailed description of the inflorescence and of the macroscopical and microscopical characters of the flower are given, as well as a table comparing the characters with those of the flower of *Hyoscyamus niger* L. J. W. F.

***Myroxylon pereirae* Klotzch, a Source of Nerolidol.** R. Cortesi. (*Bull. Soc. Pharm., Bordeaux.*, 1951, **89**, 141.) Portions of the trunks of healthy and of wounded trees of *Myroxylon pereiræ* from San Salvador were examined anatomically and chemically. The heart wood is distinguished chiefly from the sap wood by the presence of a reddish-brown secretion; this secretion appears to originate in the medullary rays and passes into the neighbouring fibres and finally into the vessels in which it resinifies and blocks up the lumen. The amount of volatile fraction of the secretion in the wounded trunk was

30 per cent. higher than in the healthy one, thus confirming the general rule that pathological conditions increase the flow of secretion. The most important constituent of this volatile fraction is nerolidol which is a valuable source material for the synthesis of α-tocopherol. Nerolidol is obtained from balsam of Peru (the commercially prepared oleoresin from *Myroxylon pereiræ*) but is present only in traces, whereas the volatile fraction secreted in the heart wood of this tree contains up to 70 per cent. Probably, during the stages of burning, boiling in water, etc., involved in the preparation of balsam of Peru, the bulk of the volatile nerolidol is lost. The author suggests that by taking these facts into account the tree could be used as a valuable source of natural nerolidol.

J. W. F.

PHARMACOLOGY AND THERAPEUTICS

Aconitine and Lappaconitine, Toxicity of. F. Dybing, O. Dybing and K. B. Jensen. (*Acta Pharmacol. Toxicol.*, 1951, 7, 337.) Lappaconitine is the chief alkaloid in *Aconitum septentrionale*, a plant common in parts of Scandinavia, which occasionally causes poisoning in cattle; the dried root contains up to 5·8 per cent. of total alkaloids of which about 80 per cent. is lappaconitine. Experiments on mice showed lappaconitine to have 1/20 to 1/40 the toxicity of aconitine, according to the method of administration. Both aconitine and lappaconitine are relatively stable to heating in aqueous solutions at *p*H 3, whereas they are easily hydrolysed in neutral solutions. Lappaconitine and its hydrolytic products—picrolappaconitine and lappaconine—can be identified by their R_F values in paper chromatography. Picrolappaconitine shows blue fluorescence in ultra-violet light and can be diazotised and coupled with β-naphthol to produce a red colour. Lappaconitine and picrolappaconitine can be isolated from and chromatographically identified in urine from rats given sub-lethal doses of lappaconitine. A method is described for the isolation of aconitine from organic material, and its biological demonstration by a vomiting-like reflex produced in mice by subcutaneous injection. S. L. W.

Adrenaline and Noradrenaline, Concentrations in Adrenal Glands at Different Ages. G. B. West, D. M. Shepherd and R. B. Hunter. (*Lancet*, 1951, **261**, 966.) The amine content of the adrenal glands of adults and babies has been examined. The total pressor activity in exhausted adrenal glands of 36 cases was 0·303 mg./g. About 14 per cent. of this was noradrenaline. In 9 cases of hypertension the relative amount of noradrenaline in the gland was not significantly different from that found in other conditions. Lack of methylation was not considered the cause of hypertension in these patients. The activities of the medullary and cortical components of the glands were compared in 9 cases. 14 per cent. of the total activity in the medulla but only 3 per cent. in the cortex was found to be due to noradrenaline. This suggests that noradrenaline is formed in the medulla. Extracts from glands of children under 70 days old showed incomplete methylation, about 90 per cent. of noradrenaline being present. Large quantities were also found in the organs of Zuckerkandl. In one case of Addison's disease 50 per cent. of the total catechol amines was noradrenaline. J. R. F.

Adrenaline and Noradrenaline; Elimination of. A. Lund. (*Acta Pharmacol. Toxicol.*, 1951, 7, 297.) The destruction of adrenaline and noradrenaline in the rabbit has been studied on intact animals and isolated organs; both substances behaved in a similar manner. In the intact organism either substance disappeared from the blood circulation at a rate of about 10 μg./kg./minute. In

the perfused liver there was a maximum rate of destruction of 10 mg./kg./minute. In the perfused hind limb the maximum rate of destruction was about 3 μg./kg./minute. The prompt elimination of adrenaline and noradrenaline would appear to be due to a combination of the following processes: (1) complete destruction, consisting chiefly in oxidative deamination of adrenaline and noradrenaline in the blood passing through the liver; (2) prompt diffusion from the blood circulation into the muscular tissue; followed by (3) a slower oxidation through the adrenochrome stage, effected by the cytochromoxidase; and possibly (4) excretion of adrenaline and noradrenaline, partially transformed (esterified), through the kidneys. S. L. W.

Adrenocorticotrophic Hormone in Slow Release Medium. H. M. Bruce and A. S. Parkes. (*Lancet*, 1952, **262**, 71.) The clinical use of adrenocorticotrophic hormone is probably highly inefficient due to over-rapid absorption after the parenteral injection of a rapidly absorbed preparation. It remains in the circulation for less than 30 minutes and adrenal stimulation may be ended within an hour of its absorption. In practice this short duration of the action is counteracted by the frequent injection of small doses. With the object of eliminating the need for frequent injection experiments were carried out on nestling rats to compare the effectiveness of different media in prolonging the activity of the hormone, assays being based on the decrease in weight of the thymus glands of the experimental animals. Suspension in a medium consisting of 5 per cent. of beeswax in arachis oil increased the effectiveness of daily injections by at least 10 times as compared with solution in saline solution or suspension in oil alone. Large doses given as a single injection in the oil-wax medium produced an effect for several days. A preparation containing aluminium stearate was less effective. No work has yet been done on the effect if any of the particle size of the suspended hormone. H. T. B.

Alkyl Sugar Derivatives, Absorption and Excretion of. F. R. Skelton, H. M. McConkey, J. K. Souch and G. A. Grant. (*J. Amer. pharm. Ass. Sci. Ed.*, 1951, **40**, 626.) In rats, the 3-ethyl, 3-propyl and 3-butyl derivatives of glucose, and the 3-methyl and 1-methyl derivatives of fructose are almost quantitatively excreted after they have been administered intraperitoneally. Under the same conditions, about 70 per cent. of 3-methylglucose is excreted. Varying amounts are excreted after a single oral administration and similar results are obtained when alkyl sugars are added in a proportion of 20 per cent. to a synthetic diet. 3-methylglucose appears to be completely absorbed from the gut. Diuresis is most pronounced following administration of 3-methylglucose and 3-ethylglucose. No toxicity or metabolic adaptation is observed when 20 per cent. of 3-methylglucose is included in the diet for 1 year. In dogs, diuresis and loss of sodium are most marked for 3-methylglucose and 3-ethylglucose. In repeated administration the former is the more effective diuretic.

Compound	Percentage excreted in the urine following oral administration	
	Rats	Dogs
3-methylglucose ..	85	85
3-ethylglucose ..	25	68
3-methylfructose ..	20	17
1-methylfructose ..	60	75
3-propylfructose ..	27	
3-butylfructose ..	35	

G. B.

p-Aminosalicylic Acid and m-Aminophenol, Antithyroid Effect of. K. Kjerulf-Jensen and G. Wolffbrandt. (*Acta Pharmacol. Toxicol.*, 1951, **8**, 376.) *p*-Aminosalicylic acid given to rats in a daily dose of 10 mg. for 10 days caused a moderate cellular thyroid hyperplasia which was prevented by the simultaneous administration orally of dried thyroid tissue, but not of sodium iodide. Feeding with *p*-aminosalicylic acid also caused thyroid hyperplasia in mice and rabbits, but not in guinea pigs. *m*-Aminophenol, one of the degradation products of *p*-aminosalicylic acid in the body, also caused thyroid hyperplasia in rats. The thyroid hyperplasia induced by either of these substances is qualitatively comparable with that produced by thiouracil; quantitatively, however, the effect of *m*-aminophenol in rats as a maximal thyroid blocking agent was found to be only about 1 per cent. of that of 6-methyl-2-thiouracil. The degree of antithyroid activity may be compared with that of *p*-aminobenzoic acid. These experiments, together with clinical observations, indicate that the development of artificial myxœdema and goitre may, although reversible and rare, be a possible side-effect of *p*-aminosalicylic acid therapy. S. L. W.

Benzilic Acid Derivatives, Pharmacology of. O. C. Forbes and P. B. Marshall. (*Brit. J. Pharmacol.*, 1951, **6**, 634.) 11 benzilic acid derivatives structurally related to diphenhydramine and trasentin were found to possess varying degrees of general spasmolytic, antihistamine and local anæsthetic properties. Their antihistamine properties were low compared with diphenhydramine and mepyramine, but anti-acetylcholine activity was higher in several of the compounds than that of trasentin. Two compounds, namely diethylaminoethyl diphenyl-(β-morpholinoethoxy)-acetate (3–0257) and β-diethylamino*iso*propyl diphenyl-(β-dimethylaminoethoxy)-acetate (3–0281)), are more potent local anæsthetics than procaine, being more than twice as active. All the compounds lower arterial blood pressure in the cat, and this effect is not abolished by atropine. The presence of a morpholino group in the molecule was found to diminish all types of pharmacological action. S. L. W.

Boric Acid, Phagocyticidal and Antibacterial Action of. M. Novak and W. I. Taylor. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 428.) Using blood drawn aseptically from healthy adult male donors, phagocytosis was found to be inhibited by concentrations of boric acid higher than 2 per cent. at temperatures of 37° or 40° C. It was partially inhibited by a 2 per cent. concentration, and totally inhibited by higher concentrations, at 34° C. Using a suspension of *Micrococcus pyogenes* var. *albus* a 4 per cent. boric acid concentration was not toxic to 100 per cent. of the cocci but was toxic to 100 per cent. of the phagocytes. Boric acid is soluble at room temperature to the extent of about 5 per cent. and this concentration is often used as a so-called mild antiseptic. The solubility of boric acid at 0° C. is 1·95 per cent. and it is recommended that refrigerated boric acid solutions only should be employed to ensure non-phagocyticidal concentrations. S. L. W.

Chloramphenicol Palmitate; Use in Pædiatrics. V. de P. Larkin. (*Proc. Soc. exp. Biol., N.Y.*, 1951, **78**, 191.) A suspension of chloramphenicol palmitate containing 125 mg. of chloramphenicol in 4 ml. was used in the treatment of 17 patients, whose ages ranged from 11 days to 9 years, with a variety of diseases. The dosage was 50 mg./kg. of body weight in 24 hours, divided in 4 or 6 equal doses and continued until the patient was clinically cured, from 3 to 7 days. All the patients responded promptly, the suspension being taken without difficulty. No instances of nausea, vomiting, diarrhœa, drug fever or drug eruption were observed in this series of cases. S. L. W.

LETTER TO THE EDITOR

The Determination of Santonin in Artemisia—Solubility Correction

SIR,—Many methods of assay for santonin in artemisia depend, in their final stages, upon the weight of santonin crystallised from ethanol (15 per cent. w/w). In a method recently described by Qazilbash[1] a solubility correction of 0·0064 g./90 ml. is applied, whereas published solubilities[2,3] for santonin in this solvent vary from 0·04 to 0·06 g./100 ml. When his method was applied to a santonin-free sample of herb to which a known quantity of santonin had been added low results were obtained, whereas a recovery of 99 per cent. was obtained using a correction based on a solubility of 0·044 g./100 ml. of solvent determined in this laboratory. Furthermore, in the assay the ultra-violet absorption spectrum of the mother liquor left after removing the crystals agrees with such a correction.

On the basis of the solubility determined in these laboratories, a correction of 0·04 g. would be valid and, therefore, any artemisia containing less than 0·4 per cent. of santonin would yield no crystals and the assay figures would be reported as nil. On the other hand, if Qazilbash's correction is valid, it should be possible to obtain crystals from artemisia containing as little as 0·07 per cent. of santonin. Reference to his Table II shows that the 24 samples examined fall into two groups, the smaller group containing more than 0·5 per cent. of santonin and the larger group reported as nil, but which on the basis of our suggested correction may have contained up to 0·4 per cent. of santonin. It would, therefore, be of interest to workers in this field if the data on which the 0·0064 g. correction is based, were brought forward.

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J. ISAACS.

April 16, 1952.

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ABSTRACTS (*Continued from page* 422)

Dihydrostreptomycin Sulphate, Toxicity for Auditory Nerve. C. Don and J. Gregory. (*Lancet*, 1952, **262**, 72.) An extensive review of published reports of the toxicity of dihydrostreptomycin for the auditory nerve suggests that the hydrochloride is more toxic than the sulphate, possibly because its chemical purity is lower. A follow-up investigation was carried out on 26 patients who had been treated for more than 6 weeks with 1 g. daily of dihydrostreptomycin sulphate of a minimum purity of 88 per cent. No cases of miliary or meningeal tuberculosis were included since auditory effects are known to occur in these patients without any form of chemotherapy. 4 cases showed auditory impairment: 1 with audiometric loss only, 1 with slight deafness, 1 with moderate deafness and 1 with severe deafness. The results obtained suggest that the purest form of dihydrostreptomycin sulphate at present available is toxic to the auditory nerve. H. T. B.