ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ALKALOIDS

Cinchona, Limit Test for Quinine Content of. R. Moers. (*J. Pharm. Belg.*, 1949, **4**, 219.) The following colorimetric modification of the thalleoquinine test may be used to ensure that samples of cinchona contain the required minimum of 1·0 per cent. of quinine. The powdered bark is extracted by the method of the Belgian Pharmacopœia, and the solution is made up to 50 ml. and filtered. Portions of 1, 0·5, 0·25 and 0·125 ml. of this solution are made up to 5 ml. and treated with 0·4, 0·3, 0·2 and 0·1 ml. respectively of one-fifth saturated bromine water. After shaking for 10 seconds, 10 drops of solution of ammonia are added, and, after a further shaking for 15 seconds, the mixtures are diluted to 10 ml. with methyl alcohol. With 1 per cent. of quinine in the original bark, the smallest quantity gives no visible reaction; the thalleoquinine colour is first visible in the tube containing 0·25 ml. of the original liquid. The colours may also be determined photometrically, using a 440 filter. G. M.

Quinine and Quinidine, Differential Colour Reaction of. L. David. (*Pharm. Acta Helvet*, 1949, **24**, 427.) Since quinine and quinidine are stereo-isomers, they give in general the same reactions. They may be distinguished by means of the following reactions. 0·01 g. of the alkaloidal salt is mixed thoroughly, in a small basin, with 0·25 ml. of bromine water, and the mixture is immediately transferred to a test tube, and washed in with 1 ml. of water; 1 ml. of chloroform is added, and the mixture is allowed to stand for 3 minutes, shaking occasionally; the mixture is then treated with 1 drop of 10 per cent. potassium ferrocyanide solution, shaken, treated with 3 ml. of 5 N sodium hydroxide, and shaken again; the colour of the separated chloroform is observed by transmitted light, with quinine the liquid is colourless; with quinidine bright red. The two alkaloids may also be distinguished by a solubility reaction. 0·01 g. of the salt and 2 ml. of water are brought to the boil and treated with 1 drop of ferrocyanide solution; with quinine the solution is a first clear, then becomes milky, and a deposit of minute spherical particles forms on the walls of the tube, with quinidine a precipitate of yellowish needle crystals appears; as the deposit from quinine is amorphous, the polarisation microscope may be used to distinguish these two deposits. G. M.

ANALYTICAL

Eserine Solutions, Determination of Decomposition Products in. H. Hellberg. (*Svensk Farm. Tidskr.*, 1949, **53**, 638.) The deterioration of eserine solutions is initiated by decomposition of the urethane chain, leading to the production of methylamine, carbon dioxide and eserinol. The latter is oxidised to rubreserine and other products. The decomposition may be followed either by colorimetric determination of the rubreserine, or from the methylamine. From a solution of eserine, which has undergone some decomposition in presence of air, the unchanged eserine, together with some methylamine, may be extracted by means of ether, since the eserinol will have been oxidised to rubreserine, which is not extracted. Three methods

are proposed for the examination of such solutions. 1. A solution, containing 20 to 100 mg. of eserine salicylate in 10 ml., is made alkaline with sodium carbonate and extracted immediately with pure ether, using in all about 100 ml. of ether. The ethereal solution is dried with sodium sulphate, and evaporated to dryness, then evaporated down with more ether. The residue is dissolved in 0·01 N sulphuric acid, and the alkaloid is determined by back titration with borax, using methyl red as indicator. 2. The solution, containing 0·5 to 5 mg. of eserine, is extracted as before, the residue is dissolved in a few ml. of water and 3 drops of M sulphuric acid. After hydrolysis of the eserine, the methylamine is separated by distillation and determined colorimetrically with ninhydrin. 3. The solution, containing 0·5 to 5 mg. of eserine, is extracted as before. To the filtered ether solution 0·01 N sulphuric acid is added, and the solution is then evaporated on a water-bath. The eserine is then determined photometrically as rubreserine by the method previously described by the author (*Svensk Farm. Tidskr.*, 1947, **51**, 560). G. M.

Local Anæsthetics, Colorimetric Determination of. K Steiger and F. Hippenmeyer. (*Pharm. Acta Helvet,* 1949, **24**, 443.) The method, based on the formation of reineckates, may be used for procaine, pantocaine and nupercaine, but not for panthesine. Adrenaline does not interfere. The reagent is prepared by shaking 1 g. of ammonium reineckate with 50 ml. of water for 10 minutes, and filtering. The determination is carried out as follows. The solution, containing 2 to 20 mg. of the local anæsthetic, is diluted to 8 ml., and treated with 1 ml. of 20 per cent. sulphuric acid and 4 ml. of reagent. After shaking vigorously, the mixture is allowed to stand for 1 hour, and then filtered through a sintered glass filter, the residue being washed with 5 ml. of water. After sucking dry on the pump, the precipitate is dissolved in acetone to 10 ml. and the colour is determined The absorption maximum is at 530 mμ, and a filter S 53 may be used.

G. M.

Morphine, Determination of, in Poppy Capsules. M. Mascré and C. Genot-Boulanger. (*Ann. pharm. franc.*, 1949, **7**, 493.) The following method is suitable for an accurate determination. Moisten 100 to 200 g. in coarse powder with 10 per cent. sodium carbonate solution or with methyl alcohol. Exhaust by percolation with methyl alcohol for 5 or 6 hours in a Soxhlet apparatus, concentrate to about 20 ml. and evaporate to a firm extract. The extract can be weighed and the proportion of morphine determined by the official method, but this involves measuring the moisture content of the lime extract and making corrections for it, which can be avoided as follows. Mix the extract with 1 g. of slaked lime and 20 to 25 g. of water, triturate carefully and transfer, with the aid of 3 quantities, each of 3 to 5 ml. of water, to a stoppered bottle. Allow to stand for 1 hour, shaking gently at frequent intervals. Filter with slight suction and, to the residue on the filter, add 2 to 3 ml. of lime water, and allow to stand for 10 to 15 minutes, stirring several times before filtering. Repeat the treatment of the residue on the filter twice and place the combined filtrates in a tared vessel. Take 25 g. of precipitate, titrate the morphine by the method of the French Codex and calculate the total quantity of morphine in the sample. Methyl alcohol is chosen as the menstruum to extract the capsules because it yields an extract which is compatible with milk of lime; chloroform, acetone, ethyl acetate and ethyl alcohol do not. For the purpose of selecting seed from plants of high morphine content, a quick, simple method giving an approximate assessment of morphine

content, and using a sample of as little as 5 g. is required. A suitable method is to remove the seeds, and extract 5 g. of powdered capsules by heating under reflux with methyl alcohol. An aliquot quantity of the extract, equivalent to 4 g. of capsules, is evaporated, and the morphine extracted with milk of lime or barium hydroxide solution. The solution is rendered acid by the addition of dilute acetic acid and treated with diluted Mayer's reagent to determine the quantity of reagent required to precipitate the alkaloid completely. The reagent is standardised in terms of morphine by repeating the experiment with graded quantities of morphine hydrochloride solution acidified with dilute acetic acid. The determination is only approximate, and is affected by changes in temperature. It is especially simple if it is only required to verify that the capsules contain at least, say, 0·5 per cent. of morphine. G. B.

Orange Oils from Palestine. H. T. Islip and F. Major. (*Bull. imp. Inst.*, 1948, **46**, 213.) Continuing an investigation of Palestinian sweet orange oils (*Bull. imp. Inst.*, 1947, **45**, 15) the authors report upon an examination of 9 further samples. Analytical figures for these are compared with those given by Nicholls, Parry and the British Pharmaceutical Codex. Only two of the samples conformed to the requirements of the B.P.C. in all respects. Regarding the aldehyde content for which there are no limits in the B.P.C., the figures obtained were in good agreement with those found previously at the Imperial Institute for Palestinian oils but none reached the minimum of the limits of Parry or Nicholls. The method employed for this determination was that of the Essential Oils Sub-Committee of the Society of Public Analysts, while Nicholls used a more drastic method using N hydroxylamine hydrochloride at a temperature of 60°C. The authors are of the opinion that higher results would be expected under these more drastic conditions, but it is open to question whether they are more accurate.

	$d_{15.5}^{15.5}$	$\alpha_D^{20°}$	$n_D^{20°}$	Aldehydes as decylic per cent.	Non-volatile matter per cent.
Sample 1	0·8500	+97·77°	1·4739	1·04	2·94
2	0·8536	+94·47°	1·4750	1·37	6·68
3	0·8514	+94·76°	1·4749	1·34	4·78
4	0·8502	+97·84°	1·4741	1·04	2·87
5	0·8504	+97·10°	1·4740	1·13	4·18
6	0·8510	+97·37°	1·4741	1·24	4·21
7	0·8506	+97·32°	1·4742	1·26	4·20
8	0·8542	+95·55°	1·4749	1·34	6·47
9	0·8522	+96·35°	1·4741	1·29	5·53
Palestinian Oil (Nicholls) ...	0·850–0·852	+97° to +99°	1·473–1·4745	1·5–1·9	3·2–3·8
Sweet Orange Oil (Parry) ...	0·848–0·854	+94° to +99°	1·4725–1·4750	1·5–3·0	1·5–4·0
Sweet Orange Oil (B.P.C.)	0·848–0·852	+95° to +99°	1·472–1·474	—	2–4

G. R. A. S.

GLYCOSIDES, FERMENTS AND CARBOHYDRATES

***Adenium Hongkel*, new Digitalis Heteroside from.** M. Frèrejacque and V. Hasenfratz. (*C. R. Acad. Sci., Paris*, 1949, **229**, 848.) A number of species of *Adenium* are used by the natives of Africa for arrow poisons. From the wood there was obtained a new heteroside, Hongkeline, which gave the reactions of digitalis glucosides. The formula is $C_{30}H_{46}O_8$ and it has m.pt. 130° to 135°C., $[\alpha]_{20°}^{D}$ −10·3° (in methyl alcohol). It contains a methoxyl group and has a lactone function. By acetylation there was obtained a diacetyl derivative, m.pt. 207°C. Hydrolysis gave a reducing sugar and a genin which could not be crystallised. G. M.

Phenylosazones, Identification of, by Chromatography. P. F. Jørgensen. (*Dansk Tidsskr. Farm.*, 1950, **24**, 1.) Although the phenylosazones of hexoses, pentoses, methylpentoses and tetroses with unbranched carbon chains cannot be completely separated by means of a single chromatographic column, this is possible by using a series of columns. The adsorbents used consist of calcium carbonate of definite particle size, and talc, the solvents being either chloroform containing a small proportion of alcohol (94 per cent.) or a mixture of equal volumes of acetone and chloroform. The first separation from chloroform-alcohol (3 per cent.) on calcium carbonate (8μ) gives a series of distinct bands, comprising, from the top downwards: sorbose; glucose and galactose; altrose; xylose, arabinose and rhamnose; fucose; and erythrulose. The first band is reworked from chloroform-alcohol (5 per cent.) on calcium carbonate (8μ), and gives two bands, the first of sorbose and glucose, the second of galactose. Sorbose and glucose are reworked from acetone-chloroform on talc, and give an upper band of sorbose and a lower one of glucose. The arabinose-rhamnose mixture from the first column is treated, from chloroform-alcohol (2·5 per cent.), on a column of calcium carbonate (3·5μ), and gives an upper band of arabinose and a lower one of rhamnose. The method may be applied to glycosides as follows: the compound is dissolved in alcohol (60 per cent.) and refluxed for 5 hours under reflux with dilute sulphuric acid. The alcohol is removed by evaporation, and, after cooling, the mixture is neutralised with barium hydroxide (methyl red). After filtration and decolorisation with charcoal, equal part of phenylhydrazine hydrochloride and sodium acetate are added. The mixture is heated for 15 minutes on the water-bath, filtered and cooled. The separated phenylosazone is dried and subjected to chromatographic analysis. The method can be used as a micro method, in which case the phenylosazone must be extracted from the reaction mixture with chloroform. An example of this is the application to digitoxose, the phenylosazone of which appears between the bands of arabinose and of rhamnose and fucose.

G. M.

ORGANIC CHEMISTRY

C^{14} Uniformly Labelled Fructose, Preparation of, by means of Photosynthesis and Paper Chromatography. S. Udenfriend and M. Gibbs. (*Science*, 1949, **110**, 708.) Four trifoliate bean leaves were allowed to photosynthesise in the present of 2·8 mc. of $C^{14}O_2$, and extracted with 80 per cent. alcohol. Polar compounds were removed by ether extraction and by passing through ion exchange columns (Amberlite 100-H and Duolite A-4) and hydrolysis of the sucrose was accomplished by heating with sulphuric acid at 80°C. for 10 minutes. The acid was removed by ion-exchange columns, and most of the glucose was removed by crystallisation on the addition of carrier glucose and alcohol. The fructose was separated from the remaining glucose by paper chromatography on 72 strips of filter paper (14 inches × 1½ inches). The chromatograms were developed with phenol and the bands were located by their radio-autographs. The fructose bands were cut out and extracted with 80 per cent. alcohol in a Soxhlet apparatus. The alcohol was removed by vacuum distillation, water being added from time to time, and traces of phenol were removed from the aqueous solution by ether extraction. After adding 30 mg. of carrier fructose, the solution was purified by passing through ion exchange columns and evaporated to a syrup at 35°C. *in vacuo*. Crystallisation was carried out in a centrifuge tube, 30 mg. of carrier fructose being added during the process. The purity of

the fructose was verified chromatographically, and microbiological degradation showed it to be uniformly labelled. The specific activity of the final product was 1·2 mc. per mg. of fructose. G. B.

TOXICOLOGY

Morphine, Diamorphine, Codeine and Barbiturates, Separation and Determination of Mixtures of. A. Stolman and C. P. Stewart. (*Analyst*, 1949, **74**, 543.) Separation by adsorption on a florisil column was investigated. All three alkaloids could be adsorbed under the conditions given but differential elution was difficult. Selective solvents were sought, and it was found that acetone would elute codeine and diamorphine but not morphine, whereas ethyl acetate would elute codeine but not morphine or diamorphine when these alkaloids were present alone. When the three alkaloids were present on the column together or in pairs however, these solvents gave no differential elution. Under the varying conditions tried it was not possible to effect complete separation of the alkaloids. Experiments with barbitone and phenobarbitone using florisil columns and acid or alkaline solutions similar to the model tissue extracts from which the three alkaloids had been adsorbed, showed that there was no adsorption of these barbiturates, thus making it possible to separate a mixture of these alkaloids from barbiturates. Removal of the barbiturates from the eluate of the florisil column was obtained on a column of activated cocoanut shell charcoal ground to 60 to 100 mesh particle size. Barbitone and phenobarbitone added to model solutions containing water, salt, alcohol, and trichloracetic acid were adsorbed over a wide range of *p*H (5·5 to 8·5), but ethyl acetate, in concentrations of only 6 ml. /100 ml. completely inhibited the adsorption. The adsorbed barbiturate was eluted by refluxing for 1 hour with ethyl acetate, and the eluate carefully evaporated to dryness. The crystalline residue was taken up in 10 ml. of water acidified with hydrochloric acid and the barbituric acid extracted from this by ether, which was then evaporated to dryness and the residue used for colorimetric determination by the cobaltous acetate-*iso*propylamine reaction of Levvy. Almost complete recoveries of barbiturates from model solutions could be obtained but urine determinations were not attempted owing to the pigment interference. It is considered that more detailed work is needed before the method can be accepted as of general value in toxicological analysis, although such further work may be undertaken with reasonable hope of success. R. E. S.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

***Actinomyces griseus*, a new Antibiotic from.** F. Grumbach, P Goret, E. Arquié, F. Boyer, C. Flachat and P. Villmin. (*C.R. Acad. Sci., Paris*, 1949, **229**, 787.) While acid extraction of the mycelium of *Actinomyces griseus* gives an antibiotic having the properties of streptomycin, alkaline extraction gives, in large yield, another substance which is very active towards Gram-positive organisms and streptomycin-resistant *Staphylococcus aureus*, but inactive towards *E. coli*, and only slightly active towards *Klebsiella pneumoniæ*. This substance is only found in certain strains of the organism and is not present in any quantity in the

culture medium. It has no activity, *in vivo*, on mice infected experimentally with streptococcus or pneumococcus; and *in vitro* the inhibitory action is destroyed by the addition of serum to the culture medium. This antibiotic does not dialyse to any extent, will not pass through an L3 candle, and does not diffuse into gelose; thus it has a high molecular weight. G. M.

Aureomycin Hydrochloride, Adsorption on Aluminium Hydroxide Gel. F. E. Di Gangi and C. H. Rogers. (*J. Amer. pharm. Ass., Sci. Ed.*, 1949, **38**, 646.) When aluminium hydroxide gel is added to a solution of aureomycin hydrochloride and allowed to settle, the supernatant liquid is colourless and the golden yellow colour is associated with the aluminium hydroxide gel. 5 ml. of aluminium hydroxide gel is capable of adsorbing almost all the aureomycin hydrochloride from 50 ml. of a 0·1 per cent. w/v solution. Experimentally, the solution before and after treatment with aluminium hydroxide gel, can be assayed bacteriologically, or colorimetrically using a Fisher electrophotometer with a filter having a band of approximately 425 mμ. Discrepancies between the two methods are due in part to deviation from the Lambert-Beer law in concentrations below 20 μg. per ml. 0·1 per cent. solutions of aureomycin hydrochloride are stable when stored for 8 weeks in a refrigerator, but weaker solutions lose some of their activity.

G. B.

BIOCHEMICAL ANALYSIS

Androsterone and Testosterone, Spectrophotometric Determination of. P. E. Hilmer and W. C. Hess. (*Anal. Chem.*, 1949, **21**, 822.) The method is based on the determination of the absorption spectra of the 2:4-dinitrophenylhydrazones of the hormones after treatment with 0·1N alcoholic potassium hydroxide. For the preparation of the hydrazones, 30 mg. was dissolved in 50 ml. of redistilled aldehyde-free ethyl alcohol and refluxed for 2 hours with 10 ml. of a saturated alcoholic solution of 2:4-dinitrophenylhydrazine, 1 ml. of concentrated hydrochloric acid was added and refluxing was continued for 2 minutes more. Distilled water was added until cloudy, the solution was cooled to room temperature, and was then placed in the icebox until precipitation was complete, the crude hydrazone being filtered off and washed with 95 per cent. ethyl alcohol and water. The hydrazone was dissolved in a minimum amount of benzene, adsorbed on a column (100 × 15 mm.) of alumina and treated with approximately 100 ml. of a 12 per cent. solution of chloroform in benzene, which resulted in the formation of two bands, the band of unreacted hydrazine being eluted by this solvent. The other band (hydrazone) was eluted with approximately 150 ml. of chloroform. Solutions of the hydrazones in chloroform, 2·5 ml. containing approximately 120 and 104 μg. of hydrazone or 74 and 64 μg. of hormone per ml. respectively, were treated with 5 ml. of 0·1N alcoholic potassium hydroxide, diluted to a volume of 50 ml. with alcohol (95 per cent.) and the ultra-violet absorption spectrum examined in a photoelectric spectrophotometer. The hydrazone of androsterone showed maximum absorption at 430 mμ.; the maximum for testosterone hydrazone was at 460 mμ. As an experiment in the separation of androgens from œstrogens a benzene solution containing *ca.* 20 μg. of each of the hydrazones of androsterone, testosterone, œstrone, and progesterone was adsorbed on a 100 mm. column of alumina, the column was washed with 10 ml. of benzene, 50 ml. of 1 per cent. acetone in light petroleum, and finally with chloroform until the washings were colourless. After evaporation of the solvent, the residue was dissolved in benzene, adsorbed on a 300-mm. column of florisil, washed with 5 ml. of benzene and then eluted with approximately

150 ml. of 20 per cent. solution of acetone in light petroleum. The androgens were eluted in the first portion of the acetone-petroleum washing, the solvent was evaporated, the residue was dissolved in 1·25 ml. of chloroform and made to 25 ml. with alcohol (95 per cent.). A 2 ml. aliquot portion of this solution was treated with 8 ml. of 0·1N alcoholic potassium hydroxide and the absorption taken at 430 and 460 mμ; standard solutions of androsterone and testosterone hydrazones were also treated with alcoholic alkali and the absorption taken at 430 and 460 mμ. The concentration of androsterone and testosterone in the "unknown" solution were then calculated from the formulæ of Knudson (*Ind. Engng. Chem. Anal. Ed.*, 1940, **12**, 715). Relatively good recovery of the hormones was obtained in five experiments by this method; the procedure was also used for preliminary studies on the determination of androgens in blood. R. E. S.

Aureomycin in Serum, Fluorimetric Determination of. J. C. Seed and C. E. Wilson. (*Science*, 1949, **110**, 707.) Silica gel, in No. 200 powder is washed with a current of distilled water to remove the very small particles, giving a suspension of particles of fairly uniform size which is used to prepare the adsorption columns. 1 ml. of the serum under test is passed through a column, followed by 1 ml. of isotonic saline solution to wash out the serum, and 1 ml. of alcohol to intensify the fluorescence. When the column is viewed in radiation from an argon-mercury lamp with a filter absorbing all wavelengths greater than 400 mμ, a band of yellow fluorescence due to the aureomycin is observed. The concentration of aureomycin in the serum may be assessed by comparing the width and intensity of the yellow fluorescent band with that in other columns, prepared in the same way, from serum to which measured quantities of aureomycin hydrochloride have been added. The presence of sulphonamides, penicillin, dicoumarol, salicylates, vitamins, streptomycin or chloramphenicol does not interfere with the determination. The fluorimetric method gives higher results than a bacteriological test, indicating that there is probably a substance present which is allied to, and associated with, aureomycin and which is fluorescent, but inactive bacteriologically. G. B.

Benzylpenicillin, Colorimetric Determination of. G. E. Boxer and P. M. Everett. (*Anal. Chem.*, 1949, **21**, 670.) A colorimetric method for the determination of benzylpenicillin in samples of any purity and in fermentation liquors is described and is based on the analytical separation of the active penicillin followed by the colorimetric determination of the phenylacetyl side chain of penicillin G. The substances used to stimulate the production of penicillin G in fermentation liquors are usually either basic or neutral phenylacetyl derivatives and extraction of the penicillins from the broth at low *p*H into an organic solvent and then re-extraction into a neutral aqueous phase, will effectively separate them from the precursor material. Two types of phenylacetyl derivatives (a) benzylpenicilloic acid and (b) various degradation products, are encountered in addition to benzylpenicillin itself. Penicillin G can be separated by chloroform extraction at *p*H 2 when the dicarboxylic acids (penicilloic acids) are not extracted. A blank obtained by conversion of the penicillin to penicilloic acid by treatment with either alkali or penicillinase gives a quantitative measure of any phenylacetyl-like substance other than benzylpenicillin extracted by chloroform at *p*H 2. In determinations of benzylpenicillin, the recrystallised sodium salt is extracted with chloroform and a glycine buffer at *p*H 2. The dried chloroform solution is evaporated and the residue nitrated with sulphuric acid containing 10 per

cent. of potassium nitrate (1 ml.) for 30 minutes on a steam bath. Following nitration and cooling, 2 ml. of water followed by 2 ml. of ammonia solution (sp.gr. 0·9) are added. The colour is developed by the addition of 2 ml. of a 15 per cent. aqueous solution of hydroxylamine and the optical density measured at 580 mμ in a suitable spectrophotometer using distilled water as a blank. A plot of the optical density against the amount of penicillin is linear. Fermentation broths should be diluted to contain 25 to 150 μg. of penicillin per ml. and extracted with amyl acetate and glycine buffer solution. The amyl acetate solution is extracted with ice-cold sodium phosphate solution (0·15 M) and the active solution is prepared by extracting the phosphate solution with hydrochloric acid (0·35 N) and ice-cold chloroform and treating it as above. The blank is prepared by heating the phosphate extract with (1·3 N) sodium hydroxide solution for 1 minute, adding hydrochloric acid (2 N) and extracting with chloroform. The recovery of penicillin added to unfermented broth was 95·5 ± 3·0 per cent. from fermented broth containing penicillin and at various stages of fermentation the analytical recovery of added penicillin over the amount already present was 97 ± 5 per cent. with largest deviation of -13 and +12 per cent. Total penicillins and penicillin G can be determined simultaneously. In the blank sample, penicillin is destroyed with penicillinase, hydroxylamine solution is added to both samples followed, after 3 minutes, by 1 ml. of a 20 per cent. solution of ferrous ammonium sulphate in (3·5 N) sulphuric acid and the developed colour read on a suitable spectrophotometer at 515 mμ with the blank as zero reading. Beer's law is obeyed over the entire range. The colour is essentially constant within the first 5 minutes and then decreases at the rate of 8 per cent. every 10 minutes. The hydroxamic acid formation is completed in 2 minutes and the compound is stable for as long as 2 hours. The recovery at 2 different levels of penicillin was 97±5 per cent. and the largest deviation −13 and +11 per cent. For intermediates in the purification, the accuracy was 99·4±4·4 per cent. with deviation of +6·3 and −8·4 per cent. R. E. S.

Citric Acid, Fluorimetric Determination of. E. Leininger and S. Katz. (*Anal. Chem.*, 1949, **21**, 810.) The method proposed is based on the fact that acontyl chloride is formed when anhydrous citric acid and anhydrous sodium carbonate are refluxed with thionyl chloride; after excess of thionyl chloride is volatilised, aconitamide is formed by exposure of the acontyl chloride to ammonia gas at room temperature followed by treatment of the aconitamide residue with 76 per cent. sulphuric acid at 165°C. to produce citraxinic acid. After neutralisation with ammonia an intense blue fluorescence is shown in ultra-violet light. A solution (1 ml. or less) of the sample containing 10 to 75 μg. of citric acid in a 25-ml. reaction flask is heated for 2 hours in a vacuum oven at 65° to 70°C. in order to obtain an anhydrous residue, and approximately 15 mg. of anhydrous sodium carbonate and 2 ml. of thionyl chloride are added to the sample. A combined reflux condenser and drying tube containing dehydrite is attached to the reaction flask which is heated in an oil bath at 95° to 100°C. After refluxing for 20 minutes, the reaction flask with the tube attached is removed from the oil bath and the excess of thionyl chloride is volatilised and evacuated through a three-way stopcock attached to the top of the condenser. The reaction flask is evacuated for 4 minutes after the residue appears dry and then air is allowed to flow into the flask by means of a capillary inlet through the three-way stopcock. The evacuation and introduction of dry air are repeated 3 times and the flask and condenser are introduced into an ammonia chamber. After removal of the condenser the residue in the

flask is exposed to ammonia for 10 minutes and then moistened with 2 ml. of 76 per cent. sulphuric acid. The flask is then heated for $6 \pm 0{\cdot}5$ minutes at 162° to 168°C. in an oil bath; after removal from the oil bath, the solution is diluted with 5 ml. of water and transferred quantitatively to a 100-ml. glass stoppered volumetric flask, the solution is made alkaline to litmus with dilute ammonium hydroxide (6N), made up to volume and the fluorescence intensity is measured in a fluorimeter at $24° \pm 0{\cdot}5$°C. The effect of changes in various operating conditions at each step in the procedure is discussed and a detailed description of the apparatus is given. It is claimed that the method is applicable to the determination of 10 to 75 μg. of anhydrous citric acid; sulphate ions and hygroscopic substances interfered with the determination, although tartaric acid and malic acid up to 100 μg. did not. The application of the method to the determination of citric acid in citrus juices is described and the results are compared with those obtained by the A.O.A.C. method. R. E. S.

Panthenol, Microbiological Assay of. E. De Ritter and S. H. Rubin. (*Anal. Chem.*, 1949, **21**, 823.) The microbiological assay method for the determination of panthenol (αγ-dihydroxy-*N*-(3-hydroxypropyl)-ββ-dimethylbutyramide, the biologically active hydroxy analogue of pantothenic acid) due originally to Walter (*Jubilee Vol., Emil Barell* (Hoffman-La Roche, Inc., Basle) 1946, 98) has been modified to permit rapid assays of panthenol in the presence of pantoyl lactone as well as pantoic acid. The lactone is removed quantitatively from an aqueous test solution by continuous extraction for 1 to 2 hours with ethyl ether. The remaining aqueous solution is assayed for pantoic acid before and after alkaline hydrolysis the results indicating respectively, preformed and total pantoic acid; the difference represents pantoic acid formed by hydrolysis of panthenol. To correct for slight losses in the ether extraction a standard solution of panthenol is subjected to the same treatment. Pantothenic acid if present in relatively small amounts (up to 10 per cent. of the panthenol) will not interfere seriously with the panthenol assay since a partial correction for the pantothenate is provided by assay before hydrolysis. The assay medium of Sarett and Cheldelin (*J. biol. Chem.*, 1945, **159**, 311) using *Acetobacter suboxydans* was modified by the introduction, among other ingredients, of untreated liver concentrate, enzyme-digested casein, tween 80, and lactate. With the modified medium turbidimetric readings could be taken after 40 hours in stationary 50-ml. conical flasks or after 20 to 24 hours in colorimetric tubes if the latter were shaken continuously. Good agreement with bio-assays in rats was shown. R. E. S.

Vitamin B_1, Determination of. H. Utiger. (*Bull. Soc. Chim. biol.*, 1949, **31**, 238.) The determination of vitamin B_1 by its effect on the growth of the fungus *Phycomyces bl.* (by weighing the mycelium) does not give satisfactory results owing to interference by other compounds. The method proposed by the author is based on his observation that there is optimal accumulation of pyruvic acid at a concentration of vitamin of 0·04μg. per 20 ml., this being independent of time under the conditions given. Thus it is only necessary to determine the amount of an extract which gives the optimum production of pyruvic acid in order to determine the vitamin content. The culture solution consists of 20 ml. of a solution containing 3 per cent. of glucose, 0·1 per cent. of asparagin, 0·15 per cent. of potassium dihydrogen phosphate, and 0·05 per cent. of magnesium phosphate. The glucose solution is first treated with active carbon. The material to be examined is heated for 1 hour in an autoclave with 5N hydrochloric acid, the extract being then

filtered and adjusted to *p*H 6·5. Various amounts of the extract are added to 20 ml. of the nutrient solution, the mixture is sterilised, and finally inoculated with the spores of the fungus, and kept at 26°±1°C. for 96 hours. In order to determine the pyruvic acid the solution is filtered, and made up to 20 ml. A portion of this solution is made up to 2·0 ml. and treated with 1 ml. of a 0·1 per cent. solution of 2:4-dinitrophenylhydrazine in warm 2N hydrochloric acid. After standing for 10 minutes, the liquid is extracted with ethyl acetate 3 times, using only 1 ml. of the latter. The ethyl acetate is extracted with 3 quantities, each of 2 ml., of 10 per cent. sodium carbonate solution, the latter being washed with ethyl acetate. Five ml. of the aqueous solution is treated with 4 ml. of N sodium hydroxide and, after 10 min., the colour is determined photometrically using filter S50 and a 1 cm. cell. The quantity of pyruvic acid in μg. is then equal to Ek × 75·0. For the determination of the vitamin, a series of such tests are carried out with varying quantities of the extract under examination. At a certain concentration of extract, there is a maximum concentration of pyruvic acid, and this corresponds to 0·04 μg. of vitamin B per 20 ml. of nutritive solution. G. M.

PHARMACY

DISPENSING

Calcium Gluconate and Saccharate, Injection of. H. Siegrist. (*Pharm. Acta Helvet.*, 1949, **24**, 430.) Comparative trials of calcium lævulinate and calcium saccharate showed that the latter was the more effective means for increasing the solubility of calcium gluconate. Formulae are given for two solutions. Calcium gluconate injection: 80 ml. of freshly distilled water is boiled, and first 0·36 g. of calcium *d*-saccharate and then 9·5 g. of calcium gluconate is dissolved in it. After cooling, the solution is made up to 100 ml. with freshly boiled and cooled water, filtered, and filled into previously sterilised ampoules of hard glass. The ampoules are sterilised in the autoclave at 120°C. for 20 minutes. The sterilisation is repeated twice at 24-hour intervals. During the sterilisation the ampoules are laid on their sides. Strong injection of calcium gluconate: this is made similarly, and contains 0·72 g. of calcium *d*-saccharate and 19·0 g. of calcium gluconate in 100 ml. G. M.

Eserine Solutions, Stability of. H. Hellberg. (*Svensk farm. Tidskr.*, 1949, **53**, 658.) Although solutions of eserine readily assume a strong red colour, this does not necessarily indicate any considerable amount of decomposition. The first stage of the decomposition is a hydrolysis with formation of eserinol, which then oxidises to rubreserine. Thus even in the absence of air the solution decomposes, although it does not show any red colour. The addition of sulphite prevents the development of colour, but not the decomposition, since the sulphite merely converts the coloured products to substances which are colourless at an acid *p*H value. Solutions of eserine are fairly stable if the *p*H is not above 6; a solution in 2 per cent. boric acid may be kept for several weeks without any appreciable amount of decomposition other than a slight pink colour. The addition of sulphite, to prevent discolouration, is liable to lower the *p*H value, and is therefore undesirable for eye drops. Solutions of eserine must not be sterilised by heat, whatever the *p*H value. G. M.

Penicillin and Lanoline Ointments, Stability of. N. Å. Diding and E. Sandell. *Svensk farm. Tidskr.* 1949, **53,** 617.) The stability of penicillin ointment, prepared with anhydrous lanoline, depends on the state of oxidation of the latter. The formula used gave a product containing 1000 units of sodium penicillin per g., in a base of 9 parts of soft paraffin with 1 part of anhydrous lanoline. Eight samples of lanoline were used, these having peroxide values (ml. of 0·01 N sodium thioulphate per g.) ranging from 0·71 to 8·2. With 5 samples, where the peroxide value was not more than 1·24, the loss of penicillin activity was about 24 per cent. in 3½ months. the others (peroxide values 4 to 8) showed a loss averaging 58 per cent.

G. M.

Penicillin G, Pharmaceutical Applications of Aqueous Solutions of. G. Schuster, M. Dessus, J. Roux-Delimal and A. Morel. (*Ann. pharm. franc.*, 1949, **8,** 535.) The stability of ointments prepared by absorbing aqueous solutions of penicillin in lanolin, soft paraffin or benzoinated lard is not materially improved by the inclusion of formalin or buffering salts in the solutions. The following is the formula of an ointment containing a synthetic wax (polyethylene glycol ester). Formalin-treated, buffered penicillin solution, 10 ml. (1,000 Units), liphax 49, 10 g., sterilised liquid paraffin, up to 100 ml. This preparation has been found to retain 90 per cent. of its potency for at least 2 months. G. B.

Suppositories, Calculation of Quantities for Preparation of, by Cold Compression. V. G. Jensen and E. Jørgensen. (*Dansk Tidsskr. Farm.*, 1950, **24,** 9.) If it is necessary to prepare N suppositories of volume *a* ml., and assuming the average weight of suppositories made with the base only is A g., then a provisional mass (total weight C g.) is made containing the required amount of prescribed substance and less than the full amount of base, and the average weight of suppositories made from this is determined (B g.). The amount of base which it is necessary to add to the total mass is then given by the formula $\frac{(N \times B - C)\,A}{B}$. Of the 2247 suppositories which were made in the course of this investigation, only 11 deviated by more than 5 per cent. from the required dose. Of these 9 were of chlorbutol and caffeine, which is always difficult. The maximum error in weight of suppositories prepared according to the above calculation was 3·4 per cent., and was in all cases considerably less than when an empirical calculation was used. G. M.

NOTES AND FORMULARIES

Doxylamine Succinate. (*New and Nonofficial Remedies. J. Amer. med. Ass.*, 1950, **142,** 33.) Doxylamine (decapryn) succinate, 2[α-(2-dimethylaminoethoxy)-α-methylbenzyl] pyridine succinate is a cream to white powder, with a characteristic odour. It is very soluble in water, freely soluble in alcohol and in chloroform and slightly soluble in benzene. The free base is obtained as an oil on the addition of sodium hydroxide solution. The melting-range is 100° to 104°C., and the *p*H of a 1 per cent. aqueous solution is 4·9 to 5·1. A 1 per cent. aqueous solution gives, with picric acid solution, a yellow gummy precipitate and with ammonium reineckate, a pink precipitate. 50 mg. mixed with 1 ml. of sulphuric acid gives a clear yellow to light orange solution which persists on standing. Succinic acid (melting-range 188°

to 190°C.) may be obtained from a solution by addition to ammonia, shaking out the base with ether and acidifying. Standards : $E_{1\ cm.}^{1\ per\ cent.}$ 260 mμ, 107 to 113; nitrogen by semi-micro Kjeldahl, 7·00 to 7·30 per cent., doxylamine succinate, by electrometric titration with alkali, 98·5 to 100·5 per cent.; limit of loss on drying *in vacuo* over phosphorus pentoxide for 5 hours, 0·5 per cent., and sulphated ash limit, 0·1 per cent. Doxylamine succinate is a histamine-antagonising substance with a marked sedative effect. G. B.

PHARMACOGNOSY

Anthraquinones and Anthraquinone glycosides. H. Muhlemann. (*Pharm. Acta Helvet*, 1949, **24**, 343, 356.) Reduction products of the anthraquinone glycosides appear to be the active substances present in anthraquinone drugs, though so far anthranol glycosides in a pure state have been isolated only from senna. Certain anthraquinone glycosides were therefore reduced to the corresponding anthranols and their chemical, physical and physiological properties were investigated. Reduction was effected in aqueous sodium hydroxide solution at room temperature using catalytic hydrogen and palladium-charcoal. Anthranols were first formed and later converted into anthrones. These hydrogenated compounds were very readily oxidised in air and could be isolated only with the utmost difficulty. They would not crystallise except after oxidation to the anthraquinone form. These facts may explain why, apart from the sennosides, no anthranol glycosides have been prepared in a crystalline form from plant material. The purgative activity of these glycosides was not much stronger than that of the original anthraquinone glycosides. Details are given for the preparation of the following compounds, chrysazin-anthrone-galactoside, chrysazin-anthrone-cellobioside, chrysazin-anthranol-cellobioside-acetate, emodin-anthranol-glucoside-A-heptacetate, and 1:7-dihydroxy-5-methylanthranol-glucoside-hexacetate. As a preliminary to the synthesis of various anthraquinone compounds, the author was able to prepare isocochinillic acid (4-methyl-6-hydroxy-1:2:5-benzoltricarbonic acid) by a relatively simple condensation. Full details of the method are given. On the basis of this method various derivatives of anthrone and anthraquinone have been prepared, e.g., 1-hydroxy-3-methyl-9-anthrone, 1-hydroxy-3-ethyl-9-anthrone, 1-hydroxy-3-carboxy-9-anthrone, 1-hydroxy-3-methyl anthraquinone, 1:5-dihydroxy-3-methyl anthraquinone. J. W. F.

***Hyoscyamus muticus*, Botanical and Phytochemical Studies of.** Z. F. Ahmed and I. R. Fahmy. (*J. Amer. pharm. Ass.*, 1949, **38**, 479.) The formation of alkaloid during the development of the plant has been studied by the use of Wagner's reagent which precipitates hyoscyamine iodide within the cell in the form of characteristic crystals, and by alkaloidal assays of different parts of the plant and at different stages of development. Alkaloids first appear in the aerial parts and do not appear in the roots till about the fortieth day of growth. The highest alkaloidal percentage in the mature plant occurs in the floral parts, then the leaves, the stems and finally the roots which contain the lowest percentage. The best yield of alkaloid is obtained from the overground portions, in the flowering stage. The appearance of anthocyanin pigments in certain tissues seems to be followed by increased alkaloidal content. J. W. F.

***Hysocyamus muticus*, Effect of Environment on the Growth and Alkaloidal Content.** Z. F. Ahmed and I. R. Fahmy. (*J. Amer. pharm.*

Ass., Sci. Ed., 1949, **38**, 484.) In order to produce the highest vegetative and alkaloidal yields, the following conditions of growth should be observed. Loamy soil with moderate irrigation, as excessive irrigation is detrimental. Application of nitrogenous fertilisers, especially inorganic. Ample sunshine which promotes the formation of hairs, calcium oxalate and colouring matter as well as alkaloids. Spring or summer sowing of the seeds. The plant is liable to attack by the root-knot nematode (*Heterodera marioni*); such infestation leads to low alkaloidal yields. J. W. F.

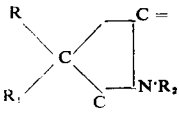
PHARMACOLOGY AND THERAPEUTICS

Bis-3:3′-(4-oxycoumarinyl) ethyl acetate (B.O.E.A.). A New Coumarin Substance. C. C. Burt, H. P. Wright and M. Kubik. (*Brit. med. J.*, 1949, 2, 1250.) In anticoagulant action, bis-3:3′-(oxycoumarinyl) ethyl acetate, has about one-fourth the activity, weight for weight, of dicoumarol. After a single dose, the minimal prothrombin level was reached between 8 and 24 hours and equally rapidly returned towards normal. With dicoumarol, the minimal level was not reached for 32 hours and was maintained for a comparatively long period. Clinical tests on 126 subjects treated therapeutically led to the conclusion that this compound is a step forward towards the production of an ideal anticoagulant, but prothrombin estimations must be carried out daily before the desired level is reached and at least every other day while the patient is under treatment. The cases included post-operative thrombosis and pulmonary embolism, spontaneous venous thrombosis, puerperal thrombosis, arterial thrombosis or embolism. In the majority of cases, 0·9 to 1·2 g. was given on the first 2 days, and thereafter dosage was regulated by response to treatment, 0·3 to 0·6 g. usually being sufficient. In over 80 per cent. of the patients the prothrombin level of the blood fell to under 50 per cent. of normal within 36 hours after the first dose and returned to over 50 per cent. of normal within the same period. The majority of patients were under treatment for 5 to 14 days, but in some cases treatment was continual for 3 to 4 weeks, 2 months and 10 months respectively. G. R. B.

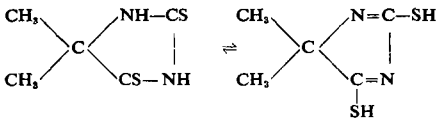
Decamethonium Iodide and Bromide; Effects on Neuromuscular Function and Induced Convulsions in Man. D. Grob, D. A. Holaday and A. M. Harvey. (*New Engl. J. Med.*, 1949, **241**, 812.) Intravenous administration of 2·5 to 3 mg. of C10 diiodide or of 2 to 2·75 mg. of C10 dibromide over a period of 5 seconds to 2 minutes produced complete relaxation of the muscles of the neck, arms, legs, shoulder girdle and pelvic girdle, and the degree of paralysis produced by this dosage could be maintained at a uniform level by further injections of 0·5 mg. every 4 or 5 minutes or 1 mg. every 8 or 10 minutes. If electric shock therapy was administered after C 10 at the height of the resulting paralysis the severity of both the tonic and clonic phases of the convulsion was lessened by as much as 50 per cent., without any apparent diminution of the therapeutic effect, and with no prominent subjective or objective effects except on neuromuscular function. The advantages of C 10 for the production of muscular relaxation prior to electrically produced convulsions, as compared with *d*-tubocurarine are shorter duration of action, and more rapid recovery of motor power, less pronounced effects on the pharyngeal, laryngeal, facial, and, in some cases, respiratory muscles, and the absence of any histamine-like effects. In the treatment of overdosage the intravenous injection of pentamethonium iodide

(C 5) did not result in a more rapid return of strength than occurred spontaneously, but the production of a high local concentration by the intra-arterial administration of 5 mg. did result in a slightly more rapid return of strength in the injected extremity. Neostigmine was ineffective. S. L. W.

Dimethyldithiohydantoin, a New Antiepileptic. R. Hazard, J. Cheymol, P. Chabrier and K. Smarzewska. (*Ann. pharm. franc.*, 1949, **7**, 569.) An examination of 40 compounds of the type depicted



showed that the maximum of anti-convulsive efficiency towards toxic crises, with the minimum toxicity, was obtained with dimethyldithiohydantoin. A new method of synthesis of this compound consists in treating a solution of 1 molecule of α-hydroxybutyronitrile in benzene with 2 molecules of carbon disulphide and 1 molecule of ammonia, dissolved in alcohol. After 24 hours, the mixture is filtered, the solution is evaporated, and the residue is taken up in 10 per cent. sodium hydroxide solution. The compound is then precipitated by the addition of sulphuric acid. After recrystallisation from benzene or hot water, it has m.pt. 142°C. It reacts in two forms:—



The calcium salt, which appears to be most suitable for clinical use, is prepared by treating the compound with excess of lime, in presence of water. After filtering, the solution is evaporated to dryness, and the residue is extracted with alcohol to remove excess of lime. This salt is stable (in the absence of carbon dioxide), but aqueous solutions decompose slowly in the cold, more rapidly on heating. Tests of toxicity, with mice and rabbits, indicate that the toxic dose for man is much greater than the useful therapeutic dose. The hypnotic dose (for mice) is 3 times that for phenobarbital. Therapeutic trials have been carried out on 190 epileptic hospital cases, and it is claimed that the compound offers the following advantages. Against phenobarbital: absence of hypnotic action in anti-convulsant doses. Against phenytoin: absence of vertigo, ataxia, nausea, etc. It therefore permits of ambulatory treatment. A dose of 1 g. is of value for facial neuralgia. A possible action on the thyroid has been noted; any considerable reduction in basal metabolism necessitates cessation of treatment, or the use of thyroid medication. G. M.

Procaine Penicillin and Sulphonamide Antagonism. H. Fischbach, H. Welch, E. Q. King, J. Levine, C. W. Price and W. A. Randall. (*J. Amer. pharm. Ass.*, 1949, **38**, 544.) The breakdown of procaine, derived from procaine penicillin, in the body to *p*-aminobenzoic acid and its possible antagonism to sulphonamide drugs has been studied. 36 male adults were injected intramuscularly with 1·5 million units of procaine penicillin (aqueous) representing 0·62 g. of procaine; 3 hours later, samples of blood were collected and immediately analysed for their penicillin content and for procaine or its derivatives. A new method was developed for the estimation of procaine and its metabolic products, a separation into three groups

being made by extraction with immiscible solvents at different *p*H values. Those fractions containing *p*-aminobenzoic acid derivatives are hydrolysed to liberate free *p*-aminobenzoic acid which is determined by diazotization and coupling with *N*(1-naphthyl)ethylenediamine to form a highly coloured derivative. Concentrations of less than 0·1 μg./ml. of *p*-aminobenzoic acid may be detected by this method. Results indicated that the greater proportion of the procaine is converted to *N*-acetyl-*p*-aminobenzoic acid. A small amount is converted to *N*-acetyl procaine, while in 7 out of 36 cases very low concentrations of free *p*-aminobenzoic acid were found; 6 cases showed a concentration of 0·1 μg./ml. or less and the remaining one 0·3 μg./ml. The molar ratios of various sulphonamides required to overcome the antagonistic action of *p*-aminobenzoic acid were: sulphanilamide 4000-1, sulphaguanidine 4000-1, sulphacetamide 500-1, sulphapyridine 400-1, sulphadiazine less than 100-1, and sulphathiazole 50-1; thus only 0·02 μg. of *p*-aminobenzoic acid per ml. of blood would neutralise 100 μg. per ml. sulphanilamide. The experimental findings coupled with the above ratios indicate therefore that procaine penicillin may be safely administered with sulphadiazine, sulphathiazole, and sulphapyridine, but may be antagonistic towards sulphanilamide.

R. E. S.

Streptomycin in Treatment of Tuberculosis and Other Infections. S. Kallner. (*Acta med. scand.*, 1949, **134**, 146.) Results obtained with streptomycin in about 50 cases are described. The cases treated were of 2 types, namely, acute tuberculosis, and infections proving resistant to sulphonamide and penicillin treatment. In fresh tuberculosis of the lungs with high fever a rapid effect was achieved, resembling the effect achieved with sulphonamide or penicillin treatment of acute infection. There was a rapid drop in temperature which was accompanied by detoxication. The patients felt better and their appetites and general health improved. In acute pulmonary tuberculosis the process was suspended so that a pneumothorax could be produced or thoracoplasty performed. Tuberculosis of glands, tuberculous osteitis and tuberculous fistulæ were successfully treated. Good results were frequently obtained with streptomycin (often where sulphonamide and penicillin had proved ineffective) in pyelitis and cystopyelitis, ulcerative colitis, chronic respiratory tract infections, especially when associated with bronchiectasis, and bronchial asthma complicated by purulent respiratory tract infection.

S. L. W.

Thephorin Ointment in Pruritic Dermatoses. C. S. D'Avanzo. (*New Engl. J. Med.*, 1949, **241**, 741.) Thephorin (2-methyl-9-phenyltetrahydro-1-pyridindene), applied locally in the form of a 5 per cent. ointment in a carbowax vehicle was employed in the treatment of 74 cases of pruritic dermatoses. It was found of very little use in neurodermatitis disseminata; indeed, many of the patients became definitely worse. On the other hand, it was found of distinct therapeutic value in lichen chronicus simplex (neurodermatitis circumscripta) and chronic dermatoses associated with pruritus, approximately 50 per cent. being improved. About half the patients with initial improvement became refractory to continued use of the ointment. Four of the patients developed sensitisation to the ointment.

S. L. W.

Thiourea Compared with Propylthiouracil in Thyrotoxicosis. G. T. Kent, R. A. Shipley and K. D. Rundell. (*Amer. J. med. Sci.*, 1949, **217**, 627.) The early decline in popularity of thiourea as an anti-thyroid drug was due

to its supposed low potency as indicated by animal assay and its high incidence of side-reactions in the dosage originally employed (1 to 2 g. daily). The object of the clinical investigation reported was to compare the usefulness of thiourea in small doses with that of propylthiouracil. Iodine (15 m. of Lugol's solution daily) was given with the thiourea in almost all cases and in a minority of cases with propylthiouracil. Both thiourea and propylthiouracil gave effective control in doses as low as 0·1 g. daily, though a daily dose of 0·2 or 0·3 g. daily of either drug gave more rapid improvement. Of 49 cases treated with thiourea, side-reactions, chiefly fever, occurred in 16 per cent.; no dangerous toxicity was encountered. In 51 cases treated with propylthiouracil there was one instance of fever, one of mild leukopenia and one of nausea, complete control of thyrotoxicosis occasionally required doses in excess of 0·3 g. daily. Iodine did not interfere with the efficacy of the drugs.

S. L. W.

Tolserol in the Treatment of children with Cerebral Palsy. E. Denhoff, R. H. Holden and C. M. Silver. (*New Engl. J. Med.*, 1949, **241**, 695.) Sixteen children, with ages ranging from 3 to 8 years, suffering from cerebral palsy, were treated with tolserol (3-*o*-toloxy-1:2-propanediol) for two 3-week periods. The average dose was 33 mg./lb. of bodyweight per 24 hours. The tolserol was administered in the form of a mixture with aqueous propylene glycol and syrup of cherry, so that 30 ml. of the mixture contained 1 g. of the drug. The mixture was administered to each child 6 times a day. There was no outstanding general improvement as a result of the treatment, but there was evidence that the drug caused a diminution of exaggerated reflexes and some improvement in co-ordination. Improvement was primarily in the neurologic category: 56·2 per cent. of the children showed diminution of exaggerated reflexes, and 12 per cent. became worse. There were no observable toxic effects, although for the first few days a few children complained of nausea and abdominal pain. S. L. W.

***d*-Tubocurarine Iodide, Dimethyl Ether of, as an Adjunct to Anæsthesia.** V. K. Stoelting, J. P. Graf and Z. Vieira. (*Proc. Soc. exp. Biol. N.Y.*, 1949, **69**, 565.) The dimethyl ether of *d*-tubocurarine iodide ($C_{40}H_{48}O_6N_2I_2,3H_2O$), referred to as M-curare, was administered to 100 anæsthetised patients of both sexes, ranging in age from 10 to 84 years. The drug was dissolved in distilled water and the curare adjusted to 0·5 mg./ml., the *p*H varying from 4·0 to 5·0. Injections were given intravenously, the initial dose consisting of 1 mg. or more of the drug. An average of 2 mg. of M-curare produced satisfactory relaxation in patients receiving cyclopropane anæsthesia; an average of 2·25 mg. was required with ether anæsthesia, and 3 mg. with nitrous oxide anæsthesia. The dosage was given in one or more injections within a period of 10 minutes. Adequate relaxation was not noted in any patients receiving less than 1 mg. of M-curare. Relaxation produced by the initial dose sufficed for surgical procedures lasting for 60 to 90 minutes; after this, supplementary injections of 0·5 to 1 mg. were infrequently required. No cardiovascular changes were noted in any of the patients and mild respiratory depression was observed in 9 out of the 100 patients, in 7 of which it existed before surgery. The relaxation obtained with M-curare in this study was comparable with that obtained with *d*-tubocurarine chloride. The drug appears to have a selective action on skeletal muscle similar to that of *d*-tubocurarine chloride, but seldom affects the muscles of respiration. Less M-curare than *d*-tubocurarine chloride is needed on a weight for weight basis. S. L. W.