ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

***p*-Acetaminobenzaldehyde Thiosemicarbazone, Colorimetric Determination of.** J. Gootjes and W. T. Nauta. (*Pharm. Weekbl.* 1950, **85,** 869.) The method is based on the reaction of Grote for organic sulphur compounds. The reagent is prepared by dissolving 2 g. of sodium nitroprusside and 2 g. of hydroxylamine hydrochloride in 40 ml. of water, and adding 4 g. of sodium bicarbonate. When evolution of gas has ceased, the solution is filtered and diluted to 100 ml. The reagent may be kept for about 1 month in the ice chest. The reaction is carried out by adding to a solution, containing 1-20 μg. of the compound, 0·05 ml. of reagent. After 1 hour the colour is measured. The best results are obtained at *p*H 2·5 and the reaction may with advantage be carried out in a buffer solution. G. M.

Alum in Alum-Precipitated Biologicals, Determination of. M. B. Jacobs. (*J. Amer. pharm. Ass.*, 1950, **39,** 523.) The method is based on the solution of the alum-precipitated biological in a dilute acid-citrate solution, the buffering of the mixture with a tartrate buffer, the neutralisation of the test mixture with barium hydroxide and isolation of the aluminium by use of potassium fluoride with consequent liberation of 3 moles of alkali hydroxide for every mole of aluminium; the liberated alkali is finally estimated acidimetrically. Details are given for the determination. In 16 experiments on a standard alum solution the minimum value for mg. of alum per ml. obtained was 4·54, the maximum value was 4·91, and the average value 4·76. In comparison, 7 gravimetric determinations had a minimum value of 4·52, a maximum value of 4·84, and an average value of 4·65 mg. alum per ml. The calculated value was 4·74. 5 batches of alum-precipitated toxoid were determined by both the acidimetric and gravimetric method and in all instances the result for the gravimetric procedure was higher than that for the acidimetric procedure. It was considered that the acidimetric results were correct, the gravimetric results being high due to the co-precipitation of iron. Examples are given in which gravimetric estimations were corrected for the iron present after determination as thiocyanate. R. E. S.

Colchicine, Colorimetric Determination of. H. Mack and E. J. Finn. (*J. Amer. pharm. Ass.*, 1950, **39,** 532.) The method depends on the fact that, when hydroxylamine hydrochloride and sodium hydroxide in solution are added in slight excess to an aqueous solution of colchicine, an orange colour develops on standing and especially upon warming the solution. Standardisation of the reagent solutions and the reaction time allowed the development of a rapid quantitative reaction resulting in a stable colour which could be estimated photometrically at 500 mμ. In preparing a standard calibration curve, pure colchicine salicylate was used, and experimental work was conducted in subdued light. Recovery results of 96 per cent. were obtained on tablets of colchicine salicylate and potassium iodide. Difficulty was experienced in the recovery of colchicine from solutions in the absence of salicylates, the results being variable and constantly higher than with colchicine salicylate. The addition of sodium

salicylate, however, gave consistent recoveries and it is suggested that the determination should be conducted in the presence of salicylates before development of the colour. R. E. S.

Morphine in Opium, Determination of. B. Drevon and G. Lafitte. (*Ann. pharm. franc.*, 1950, **8**, 397.) In a colorimetric determination, greater accuracy can be obtained by determining extinctions at different concentrations and drawing a curve. Since, for reactions which obey Beer's Law, this should be a straight line, drawing such a line through the points obtained enables minor experimental errors to be eliminated. Details of the method, applied to opium, are as follows. Exactly 0·5 g. of opium is rubbed down with a small quantity of water until uniform, and 1 g. of calcium hydroxide is added. After standing for 15 minutes, with frequent mixing, the mixture is diluted with 15 ml. of water. After a further 15 minutes, with frequent stirring, a further 15 ml. of water is added, and the mixture is centrifuged or allowed to settle. The clear liquid is poured off through a small pleated filter into a 500 ml. measuring flask. The residue is extracted again 3 times, in each case with 25 ml. of water. This solution, made up to volume, is used for the colorimetric determination. A standard solution of morphine (0·1 mg./ml.) is made by dissolving 0·1318 g. of anhydrous morphine hydrochloride in 1 l. Three series of tubes (a, b, and c) are taken. In two series (a and c) are placed respectively 2, 4, 5 and 7 ml. of the opium solution, and the same volumes of the morphine solution are placed in series b. To each tube of a and b are added successively 0·1 ml. of concentrated hydrochloric acid, and 1 ml. of 10 per cent. solution of iodic acid. After 1 minute the tubes are treated with 1 ml. of a cold freshly-prepared saturated solution of ammonium carbonate, followed by 3 drops of a fresh 1·7 per cent. aqueous solution of crystalline ferric sulphate. The same reagents are added to the series c, but without the iodic acid. Finally the volumes are made up to 10 ml. and the extinctions are determined at 470 mμ in 1 cm. cells. The values found for series a, after deducting the corresponding blank values of series b, are plotted against volumes of the solution, and a straight line, passing through the origin and as near as possible to the points, is drawn. A similar line is drawn for the standard solution. From these curves the percentage of morphine in the sample is calculated. G. M.

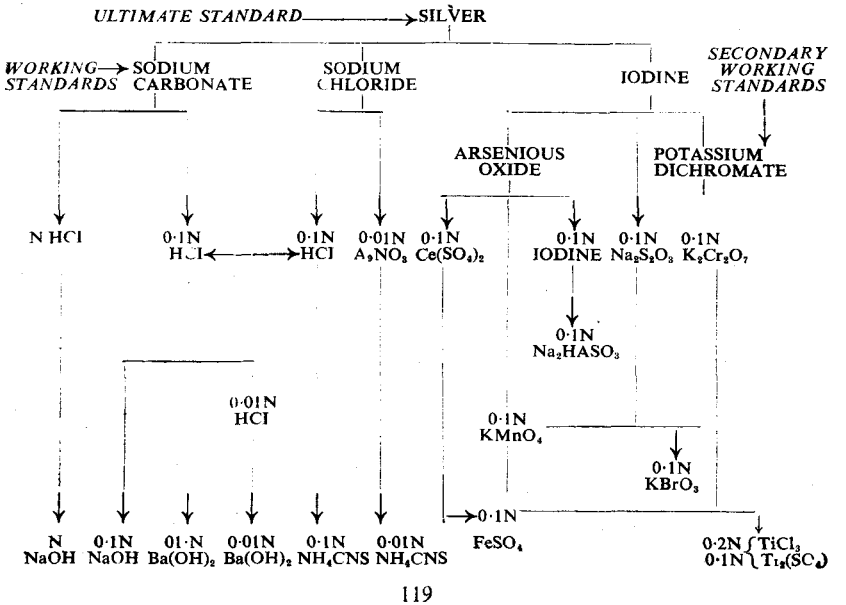
Morphine in Poppy Heads, Determination of. J. F. Reith and A. W. M. Indemans. (*Pharm. Weekbl.*, 1950, **85**, 309.) For the determination of morphine in poppy heads and poppy straw, preference was given to the photometric method using nitrosomorphine. A rapid method is as follows. 1 to 2 g. of the material, in B10 powder, is rubbed down with 2 ml. of 10 per cent. solution of sodium carbonate, and the mixture is allowed to stand for 1 hour, after which 2 ml. of 20 per cent. solution of sodium carbonate and 20 ml. of a mixture of equal parts of benzene and butanol are added. The mixture is shaken for 1 hour, and filtered on the pump through paper, the residue being washed twice with 10 ml. of solvent mixture. The combined extracts are shaken out with 10 ml. of 0·5N sulphuric acid, then with 10 ml. of water. After nearly neutralising, the aqueous extract is made up to 50 ml.; and 5 or 10 ml. is made up to 20 ml. with water and treated with 1 ml. of glacial acetic acid and 1 ml. of 10 per cent. solution of sodium nitrite. After exactly 5 minutes, 3 ml. of 15 per cent. ammonia solution is added. The absorption is then determined at 490 mμ. A corresponding mixture, without the addition of the sodium nitrite, is used as a blank. The results obtained were slightly higher than those of the gravimetric Mannich method, but

attempts to remove the interfering substance were unsuccessful. Although treatment with lead acetate decreases the amount of colouring matter in the solution, it does not affect the result of the photometric determination.

G. M.

Strychnine and Genostrychnine, Chromatographic Separation of. G. Tappi. (*Ann. Chim. applic., Roma.* 1950, **40,** 345.) That the toxicity of the amino-oxides of the alkaloids (genalkaloids) is so much less than that of the alkaloids from which they are derived, while the pharmacodynamic action is the same, makes it important to have a reliable method of separating the two substances. In the case of strychnine and genostrychnine, this can be done chomatographically. The author used a column 22 × 95 mm., with 20 g. of silica gel previously dried at 120°C., with the addition of a buffer of a M/15 solution of mono-potassium phosphate and bi-sodium phosphate (pH=6·8) (about 12 ml. is required to moisten the silica gel) and the chloroform used was previously shaken with the same buffer solution. 200 ml. of chloroform was run through the column and then a solution of 200 mg. of strychnine and 200 mg. of genostrychnine prepared by Oesterlin's method (*Ber. dtsch. chem. Ges.*, 1943, **76,** 224) in 25 ml. of chloroform poured on and the column developed by percolating with chloroform at the rate of about 4 ml. a minute. The chloroform was collected in fractions of 25 ml. and the whole of the strychnine was recovered in the first 7 or 8 fractions. The genostrychnine commenced to come in the twelfth fraction and was all recovered when 2,000 ml. had passed through. The strychnine was determined by 0·05N sulphuric acid and the genostrychnine by precipitation as iodo-mercurate and determining the mercury in the precipitate (*J. Pharm. Chim.* 1931, **14,** 328). H. D.

Volumetric Solutions, Standardisation of. Analytical Chemists' Committee of Imperial Chemical Industries, Ltd. (*Analyst,* 1950, **75,** 577.) A description is given of the method used for the standardisation of volumetric solutions; the system is a development of that outlined by Hinks (*Analyst,* 1930, **55,** 238). The procedure is based on pure electrolytic silver as an



ultimate standard, with iodine, sodium carbonate and sodium chloride as working standards and arsenious oxide and potassium dichromate as secondary working standards. The system depends on the adoption of a single ultimate standard of reference upon which the titre of all the principal laboratory standard solutions is based. The working standards are used as intermediaries between the ultimate standard and the volumetric solutions, but where the latter are not directly referable to the working standards, reference is made through the secondary working standards. The whole scheme is outlined in the diagram. Details are given for the preparation of the working standards sodium carbonate, iodine, sodium chloride, and for the standardisation of their solutions. Similarly the use of arsenious oxide and potassium dichromate as secondary working standards is described. The precautions necessary for the accurate volumetric procedures involved are outlined for acid-alkali titrations, for oxidimetry and for precipitation reactions. R. E. S.

BIOCHEMISTRY

BIOCHEMICAL ANALYSIS

***p*-Acetamidobenzaldehyde Thiosemicarbazone in Blood, Colorimetric Estimation of.** D. G. Moss. (*Lancet*, 1950, **259**, 570.) The method used depends on hydrolysis to the corresponding derivative of *p*-aminobenzaldehyde which is then diazotised and coupled with an aromatic amine. The serum, plasma, or whole blood, is mixed with water, trichloracetic acid solution is added slowly, with agitation, and the mixture, after standing for a few minutes, is centrifuged or filtered through a small filter-paper. An aliquot of the filtrate is placed in a graduated centrifuge tube, 0·2 N sulphuric acid is added, and the tube placed in a boiling water-bath for 45 minutes after which the tube is cooled and 0·02 per cent. sodium nitrite solution is added. After standing for 3 minutes, 0·5 per cent. dimethyl-α-naphthylamine solution is added and the mixture is adjusted to the final volume. The colour develops almost at once, having maximum absorption at 530 mμ, and is stable for some time if not exposed to direct sunlight. A standard solution is treated similarly during the determination and, if desired, a blank on the reagents can be performed. The method is satisfactory at concentrations as low as 0·4 mg./100 ml. of blood. R. E. S.

Barbiturates in Blood, Determination of. P. Hous. (*Acta Pharmacol. Toxicol.*, 1950, **6**, 227.) A simple spectrophotometric method for the clinical analysis of barbiturates in blood is described. 3 ml. of serum is shaken with 25 ml. of chloroform for 3 minutes. The chloroform layer is run off, filtered through paper and 20 ml. is shaken 5 ml. of borate-sodium hydroxide buffer solution (*p*H 10) for another 3 minutes. When it has separated the aqueous layer is centrifuged at 3,000 r.p.m. for 5 minutes and 3·5 ml. of it is examined in a Beckman spectrophotometer (model DU) at 240 mμ using the buffer solution as a reference blank. 0·25 ml. of 6N hydrochloric is then added to each photometer cell to bring the *p*H to 2 and the absorption is measured again. The difference in the two absorption values gives the concentration of barbiturates by reference to a special calibration curve. It is necessary to know the identity of the barbiturate to obtain an accurate result. The standard error is 7·5 per cent. on a single analysis and 6·5 per cent. on a duplicate. Errors may be due to the extraction of sulphamerazine and sulphadiazine with the barbiturates and by other substances extracted from blood which interfere with the absorption values, as well as the usual losses during processing. A. D. O.

Digitoxin and Gitoxin, A Polarographic Method for the Determination of. J. G. Hilton. (*J. Pharmacol.* 1950, **100,** 258.) Digitoxin gives an average half wave potential of −1·965 volts, and gitoxin gives a half wave potential of −1·960 volts. Both substances give height of polarographic break versus concentration curves of such a type that low concentrations of the order of 2 to 20 μg. per cent., or lower, may be determined. A method for the assay of tincture of digitalis, based on the solubility and polarographic properties of these two glycosides is described. The assay requires only 1 ml. of tincture and will determine as little as 10 μg. per cent. of either substance in the original solution. Errors due to the possible presence in the tincture of other compounds, having the same solubility and polarographic properties as either digitoxin or gitoxin, are considered to be so small as to be negligible. When digitoxin is added to whole blood, it is not all recoverable; some is retained in the cells. This may help to explain the long duration of activity of digitoxin in the body. G. R. B.

Magnesium in Blood, Determination of. P. Pignard. (*Bull. Soc. Chim. biol.*, 1950, **32,** 401.) For the determination in serum, 1 ml. of the freshly prepared serum is dried and ignited carefully to a white ash, which is taken up in 1 ml. of hydrochloric acid, and the solution is evaporated to dryness. The residue is extracted with 1 ml. of 0·5 per cent. acetic acid, the extraction being repeated three times with 0·5 ml. quantities of the acid. The solution is treated with 0·5 ml. of 0·1 N ammonium oxalate solution and, after waiting one minute, with 0·15 ml. of a 2 per cent. alcoholic solution of 8-hydroxyquinoline and 0·5 ml. of 20 per cent. solution of piperazine. After heating at 80° to 90°C. for 20 minutes, the mixture is centrifuged, the clear liquid being syphoned off. The residue is washed 3 times with 3 ml. of ammonia solution (strong solution diluted 1 : 10). The residue is dissolved in 5 ml. of 3 per cent. hydrochloric acid and transferred to a 50-ml. graduated flask, being rinsed in with 30 ml. of water. To this is added a solution of diazotised sulphanilic acid, prepared from 10 ml. of a solution of 1 g. of sulphanilic acid and 5 ml. of concentrated hydrochloric acid in 1 l. of water, and 0·5 ml. of 0·5 per cent. solution of sodium nitrite. After 30 seconds, the excess of nitrite is destroyed by the addition of 1 ml. of 1 per cent. solution of ammonium sulphamate. After mixing, 5 ml. of 8 per cent. sodium hydroxide is added and the volume is made up to the mark. The colour is then determined. For the determination of magnesium in red blood cells, the blood, mixed with sodium oxalate, is centrifuged; 1 ml. of the sediment is added to 10 ml. of water in a centrifuge tube, and allowed to hæmolyse for at least 30 minutes. Protein is removed by the addition of 4 ml. of 10 per cent. trichloracetic acid, and the mixture is centrifuged: 5 ml. of the clear liquid is evaporated on the water-bath to remove trichloracetic acid, and the residue is then ashed and the analysis completed as before. The determination in blood is made in the same way, taking 1 ml. of blood collected in oxalate, and using 10 ml. of the deproteinised liquid for the assay. The colour standardisation curve is prepared from pure 8-hydroxyquinoline (100 μg. corresponds to 8·38 μg. of magnesium). It is important to clean all glassware used with chromic acid, and to use double distilled water. G. M.

Penicillin, Iodimetric Determination of. K. Ilver, O. I. Johansen and F. Reimers. (*Dansk Tidsskr. Farm.*, 1950, **24,** 253.) From a study of the conditions for the iodimetric titration of penicillin, the following conclusions were drawn. It is more satisfactory to use 0·05 N iodine, rather

than 0·01N, as in the latter case the concentration of potassium iodide is too low, blank values are greater, and the determinations are less consistent, while with the higher concentration of iodide the procaine salt can be titrated at higher *p*H value. The most satisfactory and reproducible blank titrations are obtained at *p*H about 5. The results are very dependent on the temperature, and it is desirable that this should be exactly specified. The conditions given in the Norwegian Pharmacopœia for sodium penicillin are very satisfactory, and may also be used for the procaine salt. Methods in which the titration is carried out in acid solution at *p*H not less than 2 (e.g., U.S.P. XIV) and the blank is done at *p*H 5, may also be expected to give satisfactory results, if the iodide concentration is about 0·05 N. A lower concentration gives a high blank value, while too much iodide retards the oxidation of the penicilloic acid. G. M.

Pregnanediol in Urine, Determination of. S. L. Tompsett. (*J. clin. Path.*, 1950, **3**, 287.) The entire 24-hour collection is heated on a water-bath for 15 minutes under a reflux condenser with one-tenth its volume of concentrated hydrochloric acid and 200 ml. of toluene. The mixture is cooled rapidly and the toluene layer separated, the aqueous layer being washed with two further 200 ml. quantities of toluene. The mixed toluene extracts are washed twice with 100 ml. of 10 per cent. sodium hydroxide and twice with 100 ml. quantities of water, and then evaporated to dryness *in vacuo*. The dry residue is dissolved in 10 ml. of dehydrated alcohol, the solution transferred to a 100-ml. conical flask and 40 ml. of 0·1N sodium hydroxide is added at about 70°C. The mixture is cooled, placed in a refrigerator overnight and filtered through a 7 cm. No. 42 Whatman filter paper. The filter is washed with 40 ml. of water at 5°C. and returned to the conical flask, adding 10 ml. of dehydrated alcohol. When solution of the pregnanediol is effected, 40 ml. of water at about 70°C. is added and the liquid again cooled, stored in a refrigerator overnight, filtered and the residue washed as before. Finally, the residue on the filter paper is dissolved in 40 ml. of dehydrated alcohol, the solution is transferred to a tared 50 ml. beaker, evaporated in the oven at 100°C., cooled and weighed.

H. T. B.

Salicylate in Serum, Determination of. A. L. Tarnoky and V. A. L. Brews. (*J. clin. Path.*, 1950, **3**, 289.) The following is suggested as a simple method suitable for the control of salicylate therapy. It depends on the use of acetone to precipitate proteins, dissolve the salicylate and, possibly, free any salicylate held by protein, followed by transfer to an aqueous-acetone phase by addition of water, extraction with a solvent and determination by means of the colour reaction with ferric chloride. 1 ml. of the sample is added slowly to 5 ml. of acetone and the mixture shaken vigorously for 3 minutes, allowed to stand 20 minutes and centrifuged for 5 minutes. The clear supernatant liquid is added to a centrifuge tube containing 1 ml. of methylene chloride and 3 ml. of 0·05 per cent. ferric chloride solution. After shaking for 1 minute the mixture is centrifuged for 5 minutes. The purple layer is removed by a Pasteur pipette and the colour compared with a standard prepared from sodium salicylate. The method gives an average recovery of salicylate added to serum of 90 per cent. or more. It is not applicable to whole blood nor to oxalated plasma.

H. T. B.

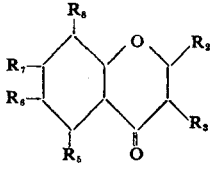
Vitamin A, Estimation of Free and Esterified. E. Eden. (*Biochem. J.*, 1950, **46**, 259.) A micro method was developed for the separation of vitamin

A alcohol and ester. A small column of alumina was used on which vitamin A alcohol was adsorbed from a light petroleum solution, whereas the ester passed straight through and could be collected as a first fraction. A second fraction was collected by washing the column with light petroleum and the vitamin A alcohol was then eluted with a solution of 20 per cent. of acetone in light petroleum. The amounts of vitamin A in each fraction were estimated using the antimony trichloride reaction. The separation proved to be satisfactory either for artificial mixtures or biological extracts fortified with vitamin A alcohol or ester. R. E. S.

CHEMOTHERAPY

Phenols, Fluorine-Substituted, Anthelmintic Activity of. M. F. W. Dunker. (*J. Amer. pharm. Ass., Sci. Ed.*, 1950, **39**, 437.) The compounds tested were 2-*n*-propyl-4-fluorophenyl, the corresponding 2-*iso*-butyl-, 2-*n*-amyl- and 2-*n*-hexyl- derivatives, 4-*iso*-amyl-2-fluorophenol, fluoro- and chlorothymol. Their activities were determined by the Lamson technique of immersing a number of worms in solutions of the compounds and observing the number surviving after a given time. Suspensions (1 in 1000) in phenol of the 2-*n*-amyl- and 2-*n*-hexyl- compounds and 4-*iso*-2-fluorophenol were as active as 2-*n*-hexyl-4-chlorophenol, which was used as an arbitrary standard, but they had little activity in the absence of phenol. The preparation of fluorothymol was attempted, but the product had little activity. A. D. O.

Pyrones, Relation between Constitution and Physiological Activity of. G. Jongebreur. (*Thesis, University of Utrecht*, 1950.) The chief active constituent of Ammi visnaga is khellin, an α-pyrone derivative (5:8-dimethoxy-2-methylfuranochromone). Its action was compared with that of related synthetic derivatives by two methods: spasmolytic action on the cæcum of the fowl; and dilatation of the coronary vessels of the surviving heart of the rat. In all 40 synthetic compounds were examined, of which 8 had a greater activity than khellin. The following general rules for the effect of substitution in the chromone molecule were derived. Starting from the structure given



activity is increased by: successively replacing the hydrogen in R_2 by methyl, longer alkyl groups, 2′-furyl, 3′-pyridyl, 3′-aminophenyl, or phenyl: replacing the lactone oxygen by sulphur: replacing hydrogen in R_3 by methyl: introduction of methoxy groups in the benzene nucleus, in the order R_6, R_5+R_7, $R_5+R_7+R_8$, R_7+R_8, R_7, R_5+R_8: replacing the hydrogen in R_7 in the order, methoxy, ethoxy, allyloxy, isopropoxy. G. M.

Vitamin K, *in vitro* Tuberculostatic Effect of Analogues of. (A. Kimler. (*J. Bact.*, 1950, **60**, 469.) The *in vitro* effect of four analogues of vitamin K, chemically related to phthiocol, on *M. tuberculosis*, var. ***hominis*** strain H37Rv was investigated. The medium used contained asparagin, 0·5 per cent.; potassium dihydrogen phosphate, 0·5 per cent.; $Mg_3(C_6H_5O_7)_2$, 0·25 per cent.; potassium sulphate, 0·05 per cent.; and glycerol, 2 per cent., in water. The *p*H was adjusted to 7·1; sterilisation was effected by autoclaving at 10 pounds pressure for 20 minutes. The critical concentrations (the lowest concentration in μg./ml. giving 50 per cent. inhibition) were: for 4-amino-2-methyl-1-naphthol hydrochloride 1μg./ml.; for 2-methyl-1, 4-naphthoquinone sodium bisulphite 2 μg./ml.; for tetrasodium 2-methyl-1,4-naphthoquinone diphosphoric acid ester 100 μg./ml. It is suggested that

the analogues of vitamin K act as inhibitory competitive analogues of the metabolite phthiocol, the structural formula of which differs from 2-methyl-1,4-naphthoquinone (the active nucleus about which the vitamin K analogues are constructed) in the presence of a hydroxyl group on the third carbon atom. The presence of a free amino group appears to increase the tuberculostatic property of a compound. G. R. B.

PHARMACY

DISPENSING

Adrenaline, Stabilisation of, by Trichloracetic Acid. M. Zâîir. (*Folia Pharm.* 1950, **1**, 93.) In view of the poisoning action of halogenated acetic acids on oxidation-reduction systems, an attempt was made to use these acids for the preservation of dilute adrenaline solutions. The results were unsatisfactory. G. M.

Morphine Salts, Hypodermic Tablets of. J. A. Scigliano, W. A. Purdum and N. E. Foss. (*J. Amer. pharm. Ass. Sci. Ed.*, 1950, **39**, 627.) Moulded tablets of morphine sulphate, morphine and atropine sulphates and the Schlesinger formula, prepared with lactose as diluent, become discoloured on storage. The discoloration can be prevented by using as diluent, lactose to which 0·1 per cent. of sodium metabisulphite has been added, or mannitol, or by storing the tablets in a desiccator. A suitable moulding solution contains alcohol (3 per cent. v/v) and sucrose (5 per cent. w/v) in distilled water. Tablets containing the above diluents retain their solubility satisfactorily, although tablets stored in a desiccated atmosphere dissolve rather more slowly than those stored under ordinary conditions. The decrease in alkaloidal strength is small in all the tablets, regardless of storage or discoloration. G. B.

PHARMACOLOGY AND THERAPEUTICS

Analgesics, an Estimation of the Activity of. W. W. Bonnycastle and C. S. Leonard. (*J. Pharmacol.* 1950, **100**, 141.) This report describes a procedure which will discriminate between various analgesics and is relatively simple in principle. The method is based on the amount of stimulus, applied in the form of a beam of radiant heat to the tails of male rats which have previously received intraperitoneal injections of various analgesics, which causes the rats to react by withdrawing their tails. The rats are previously trained (without analgesics) so that groups of rats are selected which give uniform responses. If it is assumed that the action of the rats to analgesic drugs is parallel in all cases and that the dosage response curve ranges without change of shape from the normal reaction time to lack of reaction under a constant stimulus, then by considering only the number of animals which failed to react at any given dose an estimate of potency can be made, and, assuming that the method is sensitive enough, a basis for comparison of various analgesics is provided. Estimated on the basis of an all-or-none response, and giving morphine an arbitrary value of 100, the value for methadone (amidone) was 114, codeine 9·5, meperidine (pethodine) 5·1, amidopyrine 1·3 and aspirin 0·98. Alternatively the results may be assessed from a graded response. S. L. W.

Cortisone Acetate; Smaller Maintenance Doses in Rheumatoid Arthritis. E. W. Boland and N. E. Headley. (*J. Amer. med. Ass.*, 1950, **144**, 365.) From this study of 42 patients treated with cortisone acetate it appears that

some severe cases and most moderately severe, moderate and mild cases of rheumatoid arthritis may be kept under adequate clinical control for long periods and with relative safety with smaller maintenance doses, provided larger doses are employed initially to suppress the disease. Subjective response in rheumatic symptoms and improvement in constitutional reactions were most striking within the first 7 to 10 days of cortisone administration. The improvement was very marked in 50 per cent. of severe cases, 93 per cent. of moderately severe cases, 89 per cent. of moderate cases and 100 per cent. of mild cases. Once the disease was suppressed by administration for a few days of initial large doses (100 mg. daily preceded in more severe cases by an initial injection of 200 or 300 mg.), and the dose gradually reduced, it was possible to maintain satisfactory improvement with daily amounts ranging from 32 to 65 m.g. in 32 of the 42 patients, the best results being obtained in the less severe cases. It was not necessary to give these smaller amounts every day, as larger doses every other day or 3 times weekly provided equally good antirheumatic effects. The incidence of adverse side-effects was much reduced with these smaller doses, occurring in only 8.3 per cent. of patients with average daily doses of 65 mg. or less compared with 33 per cent. with daily doses of 100 mg. S. L. W.

Digitalis, Methods of Assay of. G. Zöliner, A. Diekmann and F. Neuwald. (*Arch. Pharm. Berl.* 1950, **283,** 265.) Chemical assay of digitalis by the Neuwald modification of the Knudson-Dresbach methods gave results in good agreement with those of biological assay, using guinea-pigs and cats. The determination of genins, by the Neuwald method, gave however entirely different results, much lower than those obtained for the total glycosides. Comparison of the results of the two chemical methods shows that only about 20 per cent. of the value obtained for total glycosides is due to the presence of heart-active glycosides. It is known that the oral therapeutic action of digitalis is only 20 per cent. of the biological cat-effect, and that there is present a parenterally toxic fraction, without typical digitalis action, which gives a positive chemical reaction. It would appear that the relatively good agreement between the biological methods and modified Knudson-Dresbach method depends on the presence of this fraction, which represents about 80 per cent. of the toxic effect in the usual assay. The usual biological methods of assay should therefore be rejected. These latter methods give no information regarding the value of the determination of genins for the standardisation of digitalis. G. M.

Heparin in Pitkin's Menstruum, Activity of. J. D. Muir. (*Lancet,* 1950, **259,** 671.) Pitkin's menstruum is a mixture of gelatin, glucose, acetic acid and water, which is solid at room temperature but melts readily when warmed to 45° to 50°C. Ampoules containing 2 ml. of the menstruum with 200 mg. (200,000 I.U.) of heparin were employed. The optimum preliminary dose of heparin is usually 200 to 400 mg. In 6 volunteers 300 mg. of heparin and Pitkin's menstruum was given by deep subcutaneous injection and the coagulation times taken after 9, 15 and 21 hours. The 9-hour coagulation time was prolonged to 15 to 30 minutes in 5 of the cases, but in the 6th the effect was much greater and lasted up to 21 hours. Slight discomfort was felt at the site of injection but there were no untoward reactions. When an autocoagulant is required the need is urgent and a rapid effect is best obtained by injecting 8,000 to 10,000 I.U. of aqueous heparin intravenously, followed by 300 to 400 mg. of heparin-Pitkin subcutaneously. A further dose of aqueous heparin may be required after

3 hours if a low coagulation time reveals that absorption from heparin from the Pitkin's menstruum has not yet become effective. At the end of 12 hours a decision is made on further dosage of heparin-Pitkin. Usually after 12 hours the initial dose is repeated if coagulation time is less than double and half this dose if it is between two and three times the initial coagulation time. The dosage is reviewed again after 24 hours. S. L. W.

Hexamethonium Bromide in Treatment of Severe Hypertension. A. Campbell and E. Robertson. (*Brit. med. J.*, 1950, **2**, 804.) Eight cases of severe hypertension with papillœdema were treated with a marked lowering of blood pressure and relief of symptoms. Headache was abolished, the papillœdema showed marked regression, vision improved in every case, and the patients became ambulant. A dose of 100 mg. intramuscularly every 4 hours was found to give a progressive reduction of blood pressure in all cases. Subsequently oral treatment was shown to produce a more constant fall of blood pressure and the drug was administered in solution formed by dissolving a tablet containing 0·5 g. in 20 ml. of water. On the first day of treatment 0·25 g. should be given twice, followed by 0·25 g. 3 times daily for the next 2 days, the dosage being progressively increased until by the 10th day 0·5 g. is being given 4 to 6 times a day. The drug is more effective if given before meals. Side effects such as blurring of vision, dry mouth, nausea and heartburn were encountered in every case from the beginning of treatment; these were not severe and disappeared during the first two weeks, but recurred and disappeared with any significant increase in dosage. Apparent paralytic ileus was encountered in 2 patients, necessitating withdrawal of the drug for 24 hours and treatment by administration of a high enema, full dosage being subsequently resumed without complication. Treatment should always commence with a small dose; administration of a full dose initially produced a circulatory collapse in 2 patients. S. L. W.

Hexamethonium Salts, Effect on Gastric Secretion. A. W. Kay and A. N. Smith. (*Brit. med. J.*, 1950, **2**, 807.) Hexamethonium iodide was given orally to 10 patients with duodenal ulcer, a single dose of 500 mg. being administered by stomach tube; 5 of the patients were rendered achlorhydric, 3 had a substantial fall in gastric acidity, and in 2 there was no significant difference between control and test observations. Comparable results were obtained for each individual when the drug was given on repeated occasions; the effect was not prolonged from one day to the next. The depression of acid secretion from oral administration of the drug is less consistent than when it is administered intramuscularly. All the hexamethonium halides were found to be active in controlling spontaneous gastric secretion, the iodide and bromide being found to produce a greater fall in gastric acidity than the chloride. Side-effects observed included impairment of accommodation with blurring of vision after 12 out of 36 administrations, though this was severe only in 2 cases; and there was a tendency to constipation in several patients. The most notable side-effect is postural hypotension, but this can be controlled by muscular activity or recumbency; it is more likely to occur in fasting patients. S. L. W.

Lysivane Therapy for Parkinsonism. H. Palmer and D. J. A. Gallacher. (*Brit. med. J.*, 1950, **2**, 558.) Of the 16 patients observed in this study complete alleviation of symptoms was obtained in 1, a good result in 10, improvement in 4, and no change in 1. The drug was supplied in tablets

[*Continued on p. 128*

kindly supplied by Mr. F. J. Bolton, of J. F. Macfarlan and Co. The absorption data of the natural and synthetic materials were identical.

TABLE I

EFFECT OF *p*H ON THE ULTRA-VIOLET ABSORPTION OF PAPAVERINE HYDROCHLORIDE

*p*H of solution	Wavelength of maximum absorption	$E^{1\text{ per cent.}}_{1\text{ cm.}}$
9	238 mμ	1700
6·3	245 mμ	1285
3·95	251 mμ	1595

Wellcome Chemical Works,
Dartford, Kent.
February 12, 1951.

G. E. FOSTER
JEAN MACDONALD.

REFERENCES

1. Steiner, *C.R. Acad. Sci., Paris*, 1922, **175**, 1146.
2. Kitasato, *Acta Phytochim.*, 1927, **3**, 246.
3. Pruckner and Witkop, *Liebigs Ann.*, 1943, **554**, 134.

ABSTRACTS (*Continued from Page* 126)

containing 0·05 g. and the effective dose varied from 4 to 10 tablets daily. Rigidity was found to respond better than tremor when the two occurred in combination, but tremor alone responded best. One of the advantages of lysivane therapy is that the drug can be combined with other forms of treatment, such as stramonium. In two cases the effect achieved by the combination of the two drugs was far superior to that achieved by either separately. The chief toxic effects from the drug are drowsiness and lassitude, with or without vertigo, appearing half an hour after dosage and lasting 1 or 2 hours. Dryness of the mouth, transient diplopia, and vasomotor reactions occur rarely and disappear spontaneously. The drug should never be withdrawn suddenly. S. L. W.

Phenylindanedione, Clinical Trials with. A. Blaustein. (*Canad. med. Ass. J.*, 1950, **62**, 470.) The drug was investigated in 20 patients, 16 of whom had thrombotic episodes in the form of coronary heart disease and thrombophlebitis of the lower limbs. With an initial dose of 100 mg. in the morning and 100 mg. at bedtime the prothrombin concentration was altered from its initial value to 25 or 30 per cent. in from 23 to 28 hours. To lower the prothrombin level to 15 per cent. of concentration a dosage schedule of 50 mg. in the morning, 50 mg. at noon and 100 mg. at bedtime is employed. Maintenance requirements depend on the daily prothrombin time; in this series 51·4 mg./day represented the maintenance dose required to keep the prothrombin concentration between 25 and 30 per cent. On cessation of the drug the prothrombin time returns to normal in 48 to 72 hours. The drug can be safely given. Three of the patients were clinically overdosed, as evidenced by prothrombin times of infinity. Only one of the patients bled; he had hæmaturia, which ceased when the drug was discontinued. There was no evidence of any interference with liver function, and the sedimentation rate and white blood cell counts were not appreciably altered by the treatment. The actions of the drug would appear to place it somewhere between heparin and dicoumarol, though its properties are more closely allied to the latter. S. L. W.