ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Cinchophen, Determination of, in the Presence of Aspirin, Sodium Bicarbonate, Caffeine, Hexamine and Lactose. W. Kamp and J. W. Kampman. (*Pharm. Weekbl.*, 1958, **93**, 545.) Since the official methods for the assay of cinchophen in the British Pharmaceutical Codex and Danish Pharmacopoeia are not applicable in the presence of the above-named substances, the following method is proposed:—The sample is extracted with an aqueous sodium carbonate solution and the filtrate evaporated to dryness on a water bath. The residue is then dissolved in a little glacial acetic acid, and after warming to almost boiling point, a known amount of 0·1N iodine solution is added with constant shaking. After cooling the liquid in the flask is made up to a known volume, and the excess iodine is determined in an aliquot portion of the filtrate by titration with 0·1N sodium thiosulphate solution. Cinchopen forms a black precipitate of formula $(C_{16}H_{11}NO_2)_2 \cdot HI \cdot I_3$ so that 1 g. atom of iodine is equivalent to 2/3 mol. phenylcinchoninic acid. Results are still on the high side (up to 2·8 per cent high), but the method seems the most satisfactory. D. B. C.

Digitalis Glycoside Mixtures, Quantitative Determination of, by Paper Chromatography. L. Fuchs, M. Wichtl and H. Jachs. (*Arch. Pharm. Berl.*, 1958 **291**, 193.) The authors report conditions suitable for a quantitative estimation by paper chromatography of the most important glycosides in digitalis leaves or extracts thereof using the Baljet reaction (i.e., using as the reagent a solution containing 95 volumes of 1 per cent picric acid in water and 5 volumes of 10 per cent NaOH solution in water). The molar extinction coefficients of different cardio-active glycosides and aglycones were determined using the pure substances for comparison, measurements being taken 20 minutes after the addition of the reagent to obtain the maximum colour intensity. For the separation by paper chromatography a solvent mixture of chloroform, tetrahydrofuran and formamide in the ratio 50 : 50 : 6·5 was used for the determination of the primary glycosides and mixture of xylene and methylethyl ketone, ratio 1 : 1, saturated with formamide was used for the determination of secondary glycosides. It was found necessary to add formamide to the glycoside solutions which were transferred to the paper to avoid certain disturbances in the separation. Examples are reported for the quantitative determination of lanatoside A, B and C, strospeside, acetyldigitoxin, acetylgitoxin, acetyldigoxin and digoxin besides small quantities of digitoxigenin and gitoxigenin and the sum of water-soluble glycosides (digitalinum verum, gitorin and lanatoside D, etc.) in the leaves of *Digitalis lanata* and purpurea glycosides A and B, glycogitaloxin, strospeside, verodoxin, gitaloxin, digitoxin, gitoxin besides a small amount of digitoxigenin and the sum of water-soluble glycosides in the leaves of *Digitalis purpurea*. The small amount of aglycone is attributed to the unfavourable drying conditions employed for both drugs. Two other examples are given. A control determination of the total cardiac glycosides, calculated as digitoxin, was performed on the starting solution before chromatographic separation, and this corresponded well with the result calculated from the sum of the extinction coefficients of the separated substances. D. B. C.

Polyoxypropylene Glycols, Analysis of. E. H. Vogelenzang and D. J. Stöver. (*Pharm. Weekbl.*, 1958, **93**, 550.) Determination of the hydroxyl content by acetylation with acetic anhydride and pyridine (used for polyoxyethylene glycols) gives very high results when applied to polyoxypropylene glycols due to hydrolysis of ether bonds adjacent to methyl groups. The following method using propionic anhydride and *p*-toluene sulphonic acid as catalyst was found to give more satisfactory results:—About ½ millimol of polyoxypropylene glycol, accurately weighed, is transferred to a dry conical flask with a ground glass stopper together with a known amount of a reagent containing propionic anhydride and *p*-toluene sulphonic acid. After standing 30 minutes at 20°, an accurately measured excess of a standard solution of aniline in dry benzene is added. After 15 minutes the excess aniline is titrated with standard perchloric acid in glacial acetic acid using a solution of crystal violet as indicator which changes from blue-green to green. The whole operation is repeated without the sample. It is also necessary to determine the water content of the material by the Karl-Fischer method and to apply a correction.

D. B. C.

Reserpine, Deserpidine and Rescinnamine, Separation and Determination of, by Partition Column Chromatography. A. L. Hayden, L. A. Ford and A. E. H. Houk. (*J. Amer. pharm. Ass., Sci. Ed.*, 1958, **47**, 157.) The suggested method is suitable for determination of the purity of crystalline specimens of the alkaloids, and for the analysis of commercial mixed alkaloids. Separation is accomplished by chromatography on a column of diatomaceous silica (Celite 545), using formamide as immobile solvent, and eluting with a mixture of heptane 715, chloroform 110, morpholine 1. Deserpidine is eluted first, followed by reserpine and finally rescinnamine. The quantity of each alkaloid in solution can be estimated by measurement of the ultra-violet absorption of the appropriate fraction against a solvent blank, at the maxima at 272 mμ for deserpidine, 267 and 295 mμ for reserpine and 304 mμ for rescinnamine. The result is calculated by comparison with the absorption of standard solutions. The method is sufficiently sensitive to detect 1–5 per cent of one of the alkaloids occurring as an impurity in another. G. B.

Strychnine and Brucine, Separation of, by Paper Chromatography. G. Dušinský and M. Tyllová. (*Nature, Lond.*, 1958, **181**, 1335.) A new paper chromatographic procedure for the separation of strychnine and brucine is described, based on the finding that small amounts of brucine (but not of strychine) are quantitatively oxidised in 4N nitric acid to *o*-brucichinone. An aqueous or ethanolic solution (1 ml.) containing not less than 1 mg. of strychnine and brucine is mixed with concentrated nitric acid (d = 1·41; 0·3 ml.), the acid neutralised after 1 minute by addition of sodium hydroxide solution (2 ml., 15 per cent), and the pH finally adjusted to 4–5 with glacial acetic acid. The solution (equivalent to 30–100 μg.) is spotted on to strips of Whatman No. 1 filter paper, which have been impregnated with formaldehyde-methanol (1 : 1) and chromatographed (descending technique) with butanol-acetic acid-water (4 : 1 : 5) at 22° for about 6 hours. After drying the chromatogram, strychnine (R_F 0·76) is detected with Dragendorff's reagent, brucichinone (R_F 0·1) appearing as a red spot near the starting line. The method can be applied quantitatively as an assay for strychnine. J. B. S.

ORGANIC CHEMISTRY

Dihydro-6-desoxy Morphine, a New Preparation of. R. Bognár and S. Makleit. (*Arzneimitt.-Forsch.*, 1958, **8**, 323.) 3-Acetyldihydromorphine was first produced either by the hydrogenation of morphine in the presence of palladium to give dihydromorphine followed by acetylation of the phenolic hydroxy group with actic anhydride and sodium bicarbonate, or by acetylation as described to give 3-acetylmorphine and subsequent hydrogenation with a palladium catalyst. Both processes gave excellent yields. The 6-tosyl derivative was then formed by the reaction of 3-acetyldihydromorphine in pyridine at room temperature with *p*-toluene sulphonyl chloride. This, on reacting with lithium aluminium hydride in tetrahydrofuran solution, underwent deacetylation and removal of the tosyl group which was replaced by hydrogen giving the desired dihydro-6-desoxy morphine. In addition to ultra-violet data, this was characterised by methylation with diazomethane to give dihydro-6-desoxy codeine which was also produced by hydrogenation of the known compound α-chlorocodid. D. B. C.

***iso*Nicotinic Acid Hydrazide, New Method of Preparation.** H. B. Thomasen. (*Acta chem. scand.*, 1957, **11**, 1787.) A new synthesis of *iso*nicotinic acid hydrazide in 90 per cent yield is described in which *iso*nicotinic acid hydrazonium salt is submitted to azeotropic distillation with a suitable water entrainer, such as amyl alcohol or xylene. J. B. S.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Adrenal Cortical Hormones and Formation of Histamine and 5-Hydroxytryptamine. R. Hicks and G. B. West. (*Nature, Lond.*, 1958, **181**, 1342.) The effects of cortisone and certain of its analogues on the tissue levels of histamine and 5-hydroxytryptamine have been studied in rats. Histamine-levels in the skin areas of rats treated for 14 days with cortisone or hydrocortisone (50 mg./kg./day) fell to about half those of animals in control groups. Degranulation of skin mast cells was noticeable, but no disruption of the cell membrane. In the jejunum and spleen only histamine depletion was detected. Deoxycortone acetate failed to alter the tissue levels of either of the amines, or the morphology of the mast cells. The recovery rate of tissues depleted of histamine by treatment with Polymixin B was greatly retarded by administration of cortisone, whilst the effect on tissue 5-hydroxytryptamine was even more pronounced. Concentrations of the latter in the skin areas (only) fell to about 20 per cent of that in controls—a fall comparable with that found after treatment with reserpine. Deoxycortone acetate showed no such effect. It is suggested that cortisone and other glucocorticoids lower the activity of histidine decarboxylase and 5-hydroxytryptophan decarboxylase, the mineralocorticoids being devoid of such action. J. B. S.

Antigen-antibody Complexes, Soluble, Production of Anaphylaxis in the White Mouse with. S. Tokuda and R. S. Weiser. (*Science*, 1958, **128**, 1237.) A soluble antigen-antibody complex was prepared by adding heat inactivated rabbit anti-serum to excess of antigen (bovine serum albumin), the mixture then

being incubated and centrifuged. When injected intravenously into mice this complex produced death in 90 per cent of the animals with all the symptoms of anaphylaxis. One-fifth of this toxic dose of complex killed only about 28 per cent of the mice but was 100 per cent lethal to mice which had received *Haemophilus pertussis* vaccine 5 days previously. It is well known that such pertussis treatment renders mice highly susceptible to active and passive anaphylaxis induced by the usual methods. The fact that anaphylaxis produced with the soluble antigen-antibody complex was typical in all respects, suggests that the site of antigen-antibody action and the ensuing events leading to anaphylaxis are similar regardless of whether shock is induced in the usual manner by injection of antigen or by injection of the soluble preformed antigen-antibody complex. The speed and severity of the shock is probably determined by the rate at which the preformed complex reaches the site where antigen-antibody injury is produced. This work represents a fresh approach for investigating the mechanism of anaphylaxis in the mouse but care is necessary before applying these results to anaphylaxis in other species. W. C. B.

***m*-Methoxynoradrenaline, Presence, Formation and Metabolism of, in the Brain.** J. Axelrod. (*Science*, 1958, **127**, 754.) Chromatographic studies on extracts of the brains of rats indicated that noradrenaline is metabolised in the rat brain to *m*-methoxynoradrenaline (normetanephrine) and that this reaction requires *S*-adenosylmethionine as the methyl donor. The *m*-methoxynoradrenaline is then deaminated by the brain mitochondria and oxidised to form 3-methoxy-4-hydroxymandelic acid. W. C. B.

BIOCHEMICAL ANALYSIS

Adrenaline and Noradrenaline in Plasma, Fluorimetric Determination of. R. Robinson and F. D. Stott. (*Biochem. J.*, 1958, **68**, 28P.) The authors have modified the method of Euler and Floding, and using a fluorimeter constructed for high sensitivity were able to determine the two amines at concentrations as low as 0·2 μg./l. of adrenaline and 0·3 μg./l. of noradrenaline. By use of a differential oxidising procedure both adrenaline and noradrenaline in mixtures can be determined. The amines are isolated from plasma on micro columns of alumina. Aliquots of the eluate buffered to pH 3·5 and 6·0 are treated with potassium ferricyanide solution, when at pH 3·5 all the adrenaline but only about 4 per cent of noradrenaline is oxidised, while at pH 6·0 both amines are quantitatively oxidised to the corresponding chromes. Alkali and ascorbic acid convert the chromes to trihydroxyindoles and stabilise them, when the fluorescence can be measured. Prevention of the disintegration of platelets was found to lower the adrenaline and noradrenaline concentration, which is in harmony with the view that the platelets may act as vehicles for transport of the amines. J. R. F.

3-Hydroxytyramine, Presence of, in Brain. A. Carlsson, M. Lindqvist, T. Magnusson and B. Waldeck. (*Science*, 1958, **127**, 471.) The study of 3-hydroxytyramine has been hampered by the lack of sensitive and specific assay methods. The authors have observed that if the pH of samples prepared essentially according to the fluorimetric method of Euler and Floding was adjusted to about 5 with acetic acid the fluorescence for 3-hydroxytyramine, weak with the original method, is enhanced. Further, the activation and fluorescent peaks were at much shorter wavelengths that those from adrenaline and noradrenaline, which therefore do not interfere. Using this method, together with ion exchange chromatography, 3-hydroxytyramine has been

found in the rabbit brain at a concentration of 0·4 μg./g., which is roughly equal to the noradrenaline content. Intravenous injection of reserpine (5 mg./kg.) caused almost complete disappearance of 3-hydroxytyramine from brain, and an intravenous injection of the precursor 3:4-dihydroxyphenylalanine (5 mg./kg.) caused a marked increase, accompanied by central excitation. Both phenomena were enhanced by iproniazid. J. R. F.

PHARMACOLOGY AND THERAPEUTICS

Aluminium Glycinate in Peptic Ulcer. T. Clark and J. N. Hunt. (*Practitioner*, 1958, **180**, 334.) A comparison *in vitro* of the antacid action of magnesium oxide and an aluminium glycinate preparation showed that the aluminium compound, even in gross excess, did not, in contrast to magnesium oxide, raise the pH of the gastric contents above that of the plasma. Tests in four patients with duodenal ulcers showed that the continuous sucking of four tablets of an aluminium glycinate preparation an hour raised the pH of the gastric contents to 4 but did not carry it beyond pH 7. On the other hand, intermittent doses of aluminium glycinate were less effective in maintaining the pH of the gastric contents above 4 continuously. In these experiments aluminium glycinate produced an acid deficit in the urine corresponding to not more than one-quarter of its antacid power measured to pH 4. This would allow a dose corresponding to 6 hours' effective antacid control per day without danger of alkalosis. On this basis patients with normal renal function have the power to excrete alkali corresponding to an oral intake of about 300 aluminium glycinate tablets daily. S. L. W.

Barbiturate and Tranquillizer Drugs, Comparative Sedative Effects of. T. A. Loomis and T. C. West. (*J. Pharmacol.*, 1958, **122**, 525.) In a series of controlled experiments, the comparative sedative effects of orally administered quinalbarbitone sodium (100 mg.), chlorpromazine hydrochloride (50 mg.), meprobamate (400 mg.), phenaglycodol (300 mg.) and a placebo consisting of 200 mg. of corn starch were evaluated on normal human male subjects. The subjects, all of whom had received previous training, were required to operate an automobile driving test apparatus which automatically recorded driving faults. Quinalbarbitone, chlorpromazine and meprobamate caused significant impairment of performance on the test apparatus. Phenaglycodol and the placebo were without effect. Quinalbarbitone produced the most intense impairment of function. Chlorpromazine produced impairment after a delayed onset of action. Meprobamate produced delayed impairment after the first dose and immediate impairment after the second. W. C. B.

Benactyzine in Patients with Violent Tempers and with Parkinsonism. P. W. Nathan. (*Brit. med. J.*, 1958, **1**, 926.) Twelve patients (10 of them epileptics) with violent tempers formed the subject of this investigation. Benactyzine was given orally in tablets containing 1 mg., and these were alternated with control tablets. In half the patients the first supply of tablets consisted of benactyzine, and in the other half it consisted of the control tablets; on subsequent occasions the tablets and the patients were reversed. The dosage of benactyzine varied between 3 and 12 mg. a day. In most of the patients the investigation lasted between one and two years. The results showed that benactyzine was of no greater value than the control tablets in reducing outbursts of temper. Benactyzine was also tested on 18 patients with Parkinsonism, in a dose varying from 3 to 10 mg. a day; control tablets were also employed in

this group. No patients were improved by the benactyzine who were not also improved by the control tablets, or who, on other occasions, received no benefit from benactyzine. S. L. W.

Benzchlorpropamide in Epilepsy. D. S. Sharpe, G. Dutton and J. R. Mirrey. (*Brit. med. J.*, 1958, **1**, 1044.) Twenty-five cases of epilepsy in mental defectives were treated over a period of six months with the anticonvulsant benzchlorpropamide (Nydrane). Irrespective of what other drugs were being used, 0·5 g. of benzchlorpropamide daily was added to the patients' treatment for the first 7 days. Following this, other anticonvulsants were gradually withdrawn and substituted by 0·5 g. of benzchlorpropamide weekly until the maximum dose was reached—usually, from 3 to 4 g. a day given in three equal parts. With grand mal convulsions, 68 per cent improved, 20 per cent showed no change, and 12 per cent were worse. General improvement in behaviour was shown in 32 per cent. It was not possible to control the epilepsy with benzchlorpropamide alone; in all except 3 cases a maintenance dose of barbiturates had to be given in addition. There was a notable freedom from signs and symptoms of toxicity, except that transient renal disturbances were observed in some cases. S. L. W.

Captodiame, Pharmacology and Toxicology of. R. Kopf and I. Møller Nielsen. (*Arzneimitt.-Forsch.*, 1958, **8**, 154.) It has already been reported that captodiame (*p*-butylmercaptobenzhydryl-β-dimethylaminoethylsulphide) has marked sedative and spasmolytic actions. In rats and mice it has been found to potentiate the anaesthetic effect of *n*-methylated barbiturates and thiobarbiturates as well as the analgesic effect of ketobemidone, pethidine, 1-*iso*-methadone and morphine. Whereas captodiame has no effect on leptazol- or strychnine-induced convulsions it does have a certain protective effect against electric shock treatment. In rats it causes a moderate fall in body temperature. It has no neuromuscular blocking action in the rat and no ganglion blocking effect in the cat. Oedema of the rat's foot was inhibited by 50 mg./kg. of captodiame. The thyroid gland, adrenals and ovaries of rats were not morphologically or functionally affected by moderate doses of captodiame. Subtoxic doses caused ascorbic acid depletion of the adrenal gland which appeared to be mediated via the pituitary gland. Administration of up to 100 mg./kg. orally, daily for 3 months did not have adverse effects as judged by the general condition, body weight, blood picture and histology of the essential organs in rats and cats. M. M.

Chlorophenols, Biological Action of. M. E. Farquaharson, J. C. Gage and J. Northover. (*Brit. J. Pharmacol.*, 1958, **13**, 20.) Chlorination of phenol produces a series of nineteen compounds comprising mono-, di-, tri- and tetrachloro-isomers and one pentachloro-form. The lower compounds are used as antiseptics, the high as herbicides, fungicides and insecticides. A study of the effects of progressive chlorination of phenol on toxicity has shown that changes in toxicity occur in correlation with the dissociation constants. The higher chlorinated phenols interfere with oxidative phosphorylation and this property may be attributed to the chlorophenate ion. The lower compounds have a convulsant action probably due to the undissociated molecule. The higher chlorinated phenols produce a contracture of the isolated phrenic nerve diaphragm and a stimulation of *in vitro* oxygen uptake in rat brain homogenate. G. F. S.

Ciba 10870 in Parkinsonism. W. Hughes, J. H. Keevil and I. E. Gibbs. (*Brit. med. J.*, 1958, **1**, 928.) A controlled trial of a parasympatholytic drug, 3 - phenyl - 3(β-diethylaminoethyl) - 2:6 - dioxopiperidine hydrochloride (Ciba 10870) was made in 16 cases of Parkinsonism. Patients were given six 2·5 mg. tablets daily, the drug being alternated with a placebo every 4 days. The preparation relieved some of the most troublesome symptoms in every case, and in some cases produced very good results. The general impression was that it was equal, if not superior, to any therapy in current use. The best effect was on salivation in post-encephalitics; on rigidity the results on the whole were good; its effect on tremor was no better than that achieved by current therapy. Mental confusion occurred in one case and disappeared when the drug was stopped. No effects on bowel function were observed and no pupillary changes were seen. No blood dyscrasias were observed. S. L. W.

Cinnamic Acid, Action of Esters of, on Capillary Permeability. J. J. Pocidalo and M. Chaslot. (*Thérapie*, 1958, **13**, 72.) A 20 per cent preparation of the ester under examination in a sodium alginate emulsion base was applied to a rectangular patch of the skin of a rabbit's abdomen, the hair having been removed 24 to 48 hours previously. Similar rectangles were treated with the base alone, and with soft paraffin. Application was followed by gentle massage for 3 minutes, and after an interval of 15 minutes, a 1 per cent solution of trypan blue (1 ml./kg.) was injected. Five minutes later, chloroform was applied to the skin with the aid of cotton wool, and left in contact for 1 minute. The delay in appearance of a blue colour on the skin was used as a measure of the reduction of permeability of the capillaries. Neither the soft paraffin nor the sodium alginate emulsion base appeared to have any effect in these experiments. Methyl cinnamate showed a marked effect in reducing permeability, but the most powerful ester was ethyl cinnamate. Higher homologues showed progressively less effect, the hexyl and higher esters being ineffective. The allyl and phenylethyl esters were also ineffective. G. B.

Dieldrin Poisoning in Man. T. B. Patel and V. N. Rao. (*Brit. med. J.*, 1958, **1**, 919.) An account is given of 20 cases of poisoning by dieldrin among spray teams in filaria and malaria control work in India. A 50 per cent dieldrin wettable powder was used, the strength of the final diluted suspension being 1·25 per cent for malaria control and 2·5 per cent for filaria control work. The rate of spraying in both cases was the same, and the deposits were 28 and 56 mg./sq. ft. (290 and 580 mg./sq. metre) respectively. There were 10 cases of poisoning among 105 sprayers in the filaria unit, and 10 cases among 192 workers in the malaria unit. In the filaria unit poisoning was seen from 14 to 154 days (average 57 days) after the first exposure to dieldrin. In the malaria unit the cases occurred from 60 to 116 days (average 99 days) after exposure. No protective clothing or masks were used and washing with soap and water was not done. The symptoms started with giddiness, headache and twitching of muscles, going on to convulsive attacks occurring up to several times a day, with loss of consciousness for periods of up to 2 hours. There were no deaths. Most of the cases of poisoning occurred during a second period of exposure. The teams were in the habit of using their bare hands for transferring the powder from the containers to the water and for stirring the suspensions prepared from the powder. The incidence of poisoning will probably be reduced by the introduction of suitable precautions. S. L. W.

4-Diphenylmethyl-(±)-tropyltropinium Bromide, a new Ganglion-blocking Agent. K. Nádor and L. Gyermek. (*Arzneimitt.-Forsch.*, 1958, **8**, 336.) In an attempt to find a ganglion-blocking agent with little parasympatholytic effect the authors examined some simple alkyl quaternary derivatives of tropine esters which possessed both actions. Ganglion-blocking action was considerably increased and parasympatholytic action decreased by substituting aralkyl instead of alkyl groups, especially *para*-substituted aralkyl groups. Among the best of the compounds examined from a therapeutic point of view, the 4-diphenylmethyl quaternary derivative of atropine combined marked ganglion-blocking action with slight parasymptholytic action. A detailed description of the pharmacology of this compound is given. D. B. C.

Framycetin in Infantile Gastro-enteritis. R. Louwette and A. Lambrechts. (*Brit. med. J.*, 1958, **1**, 868.) Framycetin has a very favourable action on gastro-enteritis due to pathogenic *Escherichia coli* in premature babies and infants. Twenty-five infants, with ages ranging from 7 days to 7 months, were successfully treated; 14 were premature babies and 8 others were undernourished. Framycetin is well tolerated and in a dosage of 50 mg./kg. daily by mouth for 5 days does not appear to be toxic. The framycetin was administered in the form of a flavoured water-soluble powder, the daily dose being divided into two portions. It acts with the same speed and potency as neomycin. Diarrhoea, dehydration, and vomiting disappear very rapidly, often within two days after establishing treatment; stool cultures usually become negative within three days. S. L. W.

Laminarin Sulphate, Antilipaemic Activity of. S. Mookerjea and W. W. Hawkins. (*Canad. J. Biochem. Physiol.*, 1958, **36**, 261.) The antilipaemic activity of heparin is reflected in its effects upon the concentrations of glyceride, phospholipid and cholesterol. In addition, there is a splitting off of lipid from β-lipoprotein, the protein particularly involved in the transport of cholesterol. There is also evidence that heparin, presumably because of this property, inhibits the development of atherosclerosis in hypercholesterolaemic rabbits. A number of compounds of relatively high molecular weight, most of them sulphated, have been shown to have antilipaemic activity. Among them, a preparation of laminarin sulphate, with a low sulphate content and a low anticoagulant activity, has been shown to reduce hyperlipaemia and correspondingly to affect the β-lipoprotein. In this paper a sample of laminarin sulphate is used which was obtained from *Laminaria digitata*. It contains 1·7 sulphate groups per glucose unit, somewhat less than does heparin. Its molecular weight is about 10,000, also less than that of heparin. It has about one-third of the anticoagulant activity of heparin and appears to act like it, principally as an antithrombin. It reduces alimentary lipaemia in dogs and rats. The experiments described in this paper concern the antilipaemic activity of this compound in comparison with that of heparin. Rabbits were chosen because of the high levels of blood lipids, particularly of cholesterol, which can be induced in them by dietary means. It was found that when the rabbits were fed on a diet containing 1 per cent cholesterol the blood serum levels of neutral fat, phospholipid, free and esterified cholesterol and β-lipoprotein were greatly increased. After the parental administration of laminarin sulphate or of heparin, all these were decreased and the electrophoretic mobility of the β-lipoprotein was increased. Laminarin sulphate showed the same effect as heparin on the hyperlipaemia. There was no definite relationship between the magnitude of dosage of either compound and the degree of its antilipaemic effect. M. M.

2-Methyl-3-*o*-tolylquinazol-4-one, a New Hypnotic Drug, Pharmacology of. J.-R. Boissier, C. Dumont and C. Malen. (*Thérapie*, 1958, **13**, 30.) The toxicity of 2-methyl-3-*o*-tolylquinazol-4-one was determined in mice, rats, rabbits and guinea pigs, using various routes of administration. The hypnotic action was determined by experiments using fish, mice, guinea pigs and rabbits. The compound was shown to have a suitable hypnotic action and a relatively low toxicity, the ratio of hypnotic to lethal doses being of the order of 4, compared with 2 to 2·5 for phenobarbitone. Onset of hypnotic action was rapid, and the drug antagonised the effect of leptazol, but not of strychnine or picrotoxin. It opposed the effects of amphetamine and other stimulants, and potentiated the action of pentobarbitone, methylpentynol, chlorpromazine and reserpine. It appeared to be free from objectionable side-effects. G. B.

Morphine; Treatment of Side-effects. G. Christie, S. Gershon, R. Gray, F. H. Shaw, I. McCance and D. W. Bruce. (*Brit. med. J.*, 1958, **1**, 675.) Provided the sensitivity of the patient is first ascertained to small doses, morphine is not a dangerous drug. All the side-effects can now be controlled. The most frequent side-effect is not respiratory depression but nausea and vomiting, of which the incidence may be as high as 30 per cent. Large doses of morphine (up to 200 mg. four times daily) may be required to control chronic pain. The patient should not be denied the benefit of complete analgesia on the score of side-effects or addiction. The results in over 400 cases show such fears to be groundless when the appropriate antagonists are employed. These are nalorphine, which is used for the control of respiratory depression; amiphenazole which combats central depression and is essential for the long-term treatment of intractable pain with large doses of morphine; and cyclizine which completely controls the nausea and vomiting. Both amiphenazole and cyclizine are completely harmless. Larger doses of amiphenazole (40 to 100 mg. four times daily) than hitherto used are now employed, and wide experience shows the drug to be one of the safest in medicine. S. L. W.

Noradrenaline in Artery Walls; Dispersal by Reserpine. J. H. Burn and M. J. Rand. (*Brit. med. J.*, 1958, **1**, 903.) It has been shown that noradrenaline is present in artery walls but hitherto it has not been thought to affect vascular tone. The vasoconstriction caused by certain substances, such as nicotine, in the vessels of the rabbit ear has now been shown to be due to the release of noradrenaline from the artery wall, since the vasoconstriction was absent in the ears from rabbits treated with reserpine. On extracting the skin of rabbit ears a noradrenaline-like substance was found which was not present in ears from reserpine-treated rabbits. Chromaffin cells, present in the ears of normal rabbits, are absent in the ears of reserpine-treated rabbits. Strips of aorta from normal rabbits, suspended in a bath, contracted on addition of nicotine; they were found to contain noradrenaline in a mean amount of 0·5 μg./g. Strips of aorta from rabbits treated with reserpine did not contract on addition of nicotine, contained only traces of noradrenaline and were highly sensitive to this amine, indicating that the store of noradrenaline in the vessel wall must normally reduce the effect of noradrenaline, and probably the effect of sympathetic impulses also. Conditions such as Raynaud's disease may be due to a release of noradrenaline from the store in the artery wall and might therefore benefit from treatment with reserpine. S. L. W.

Raunescine and *iso*Raunescine, Effects of, on Behaviour and on the 5-Hydroxytryptamine and Noradrenaline Contents of Brain. M. K. Paasonen and P. B. Dews. (*Brit. J. Pharmacol.*, 1958, **13**, 84.) Raunescine and *iso*raunescine are rauwolfia alkaloids which reduce the adrenaline and noradrenaline content of the heart of rats. A study of the behaviour effects of these alkaloids in trained pigeons has shown that both alkaloids in sufficient dosage have effects very similar to reserpine but both were much less potent. In rats both raunescine and *iso*raunescine, like reserpine, caused a reduction in the concentration of both 5-hydroxytryptamine and noradrenaline in the brain. The results of these studies are compatible with the postulated indirect effect of the rauwolfia alkaloids on the brain through the release of noradrenaline and 5-hydroxytryptamine. G. F. S.

Sulphamerazine: Toxicity in Children. G. C. Arneil. (*Lancet*, 1958, **1**, 826.) Over a period of 10 years, a total of 29 patients have been treated at the Royal Hospital for Sick Children, Glasgow, for haematuria associated with taking sulphonamides. In 27 of the 29 children the preparation administered contained sulphamerazine. Most of the children were aged from 1 to 6 years, and the sulphonamide was given for periods of from 1 to 6 days in daily doses of from 100–400 mg./kg. bodyweight. The haematuria lasted from one to six days, and albuminuria persisted a few days longer. Anuria, hypertension, encephalopathy, and uraemia were seen in some patients but all subsequently recovered under conservative treatment. To justify giving a drug potentially noxious in therapeutic doses it must be shown to have significant advantages over other preparations. Sulphamerazine seems to have no such outstanding virtue and it is doubtful whether its use is justified. S. L. W.

Tienmulilminine, Hypotensive Effect of. K. Kuo-Chang and H. Bin. (*Acta physiol. Sinica*, 1958, **22**, 71.) Tienmulilminine is a new alkaloid isolated from the root of Chinese *Veratrum schindleri Loes. f.* Being a tertiary amine, this alkaloid yields alkamine by hydrolysis in acidic or alkaline medium. In anaesthetised cats, intravenous injections of tienmulilminine at the dosage of 0·45–0·6 mg./kg. produced a prompt fall of artial pressure, which, after 1½–3 minutes, decreased 50–130 mm. Hg below the original level (a reduction of 32–75 per cent). In the lapse of 15–60 minutes, the pressure gradually recovered. During the period of hypotension, the pressor reflex from temporary occlusion of common carotid artery was diminished. Repeated administrations showed no tachyphylaxis. The fall of blood pressure was, as a rule, accompanied by bradycardia, respiratory depression or sometimes apnoea. The hypotensive effect was very much reduced or even abolished in vagotomised cats, significantly reduced after previous injection of procaine-HCl mg./kg., but did not change remarkably in atropinised cats. A minute quantity of tienmulilminine (50–90 μg./kg.), ineffective by intravenous injection, produced a significant hypotension by injection into left ventricle. It appears, therefore, that the vagus is an important afferent pathway for the hypotension. The isolated carotid sinus was prepared according to Aviado's method. Injection of 30–50 μg./kg. into thyroid artery exhibited some hypotensive effect, but administrations of 80–400 μg./kg. raised the arterial pressure 40–140 mm. Hg. Thus, the carotid sinus was demonstrated as a secondary sensory region for the hypotensive effect of tienmulilminine. Its acute LD50 for intravenous and subcutaneous injections in mice was 3·2 and 26 mg./kg. respectively.