ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Adrenaline and Noradrenaline, Fluorescence of, with Ethylenediamine. G. P. Burn and E. O. Field. (*Nature, Lond.*, 1956, **178**, 542.) Weil-Malherbe and Bone have estimated the relative proportions of adrenaline and noradrenaline in mixtures of the two by the different colours of fluorescence given by these substances when coupled with ethylenediamine and extracted into *iso*butanol. This work investigates further the mechanism of the reaction. The reaction proceeds in several steps and the relative rates of formation and decomposition depend on temperature, pH and concentration of the ethylenediamine. Optimum conditions for the formation of the fluorescent material are pH 9·5, ethylenediamine concentration 0·4 per cent; the yield being maximal in 15 minutes. At higher concentrations of ethylenediamine decomposition is rapid. It is possible to separate both the adrenaline and noradrenaline derivatives into two fractions; having different R_F values and fluorescing a different colour. Evidence from the emission spectrum of the noradrenaline derivative shows that the proportions of the two fluorescent products depend on the concentrations of noradrenaline and of ethylenediamine. As therefore there are at least two fluorescent derivatives of adrenaline and noradrenaline the conditions of the experiment must be very carefully controlled in order to obtain reproducible results. M. M.

Hexachlorophene in Liquid Soaps, Determination of. R. F. Childs and L. M. Parks. (*J. Amer. pharm. Ass., Sci. Ed.*, 1956, **45**, 313.) In alkaline solution, hexachlorophene exists mainly in an ionic form, which has a greater ultra-violet absorption than the unionised form, with shift of the absorption peaks to longer wavelengths. The authors describe a method of assay which depends on measurements of the difference in absorption at 312 mμ between acid and alkaline solutions. A 5 g. sample of hexachlorophene soap is dissolved in ethanol to produce 100 ml. 25 ml. of this solution is diluted to 100 ml. with methanol (90 per cent) and 15 ml. is placed in each of two flasks. To one flask is added 0·3M acetic acid to 50 ml., and to the other, methanol (90 per cent) to 50 ml. The difference between the ultra-violet absorption of these solutions is determined at 312 mμ, and the content of hexachlorophene is calculated from a standard curve showing the difference in absorption of solutions of pure hexachlorophene at pH 8 and pH 3. The absorption due to the presence of soap is the same in both solutions and so does not affect the result. G. B.

Ipecacuanha, Assay of. E. Brochmann-Hanssen. (*J. Amer. pharm. Ass., Sci. Ed.*, 1956, **45**, 344.) Ipecacuanha may be extracted by means of ion exchange resins, using the technique previously described (*J. Amer. pharm. Ass., Sci. Ed.*, 1956, **45**, 74). 0·2 g. of ipecacuanha is placed in an extraction tube with 1 g. of activated cation exchange resin (Dowex 50-X_2) and 20 ml. of water. After shaking for 15 minutes, the mixture is transferred to a suitable ion exchange tube and the exhausted drug removed by a backwash of distilled water. The alkaloids are eluted with 4N ammonium hydroxide in methanol (70 per cent) and the extract purified by passing it through a column of anion exchange resin

(Dowex 1-X_1) previously activated with N sodium hydroxide. The quantity of non-phenolic alkaloids in solution is determined by measuring the ultra-violet absorption at 285 mμ against a blank solution prepared by passing methanolic ammonia through the same column of Dowex 1-X_1. The result is calculated as emetine. For the determination of phenolic alkaloids the anion exchange resin is washed with water to remove ammonia and the alkaloids eluted with 0·1N acetic acid. After the addition of sodium hydroxide-sodium bicarbonate solution and a coupling agent, the colour intensity is determined at 495 mμ against a blank prepared similarly but without the coupling agent. The result is calculated in terms of cephaeline. Using this method, 15 minutes at room temperature is sufficient for complete extraction of the alkaloids from the drug. Results are appreciably higher than those obtained by the U.S. Pharmacopeia method, in which inefficient extraction appears to be responsible for the low results. The proposed method is simple, rapid and capable of high precision. G. B.

Local Anaesthetics, Determination of, in Non-aqueous Media. B. Salvesen, S. Kristoffersen and A. Aasbø. (*Medd. Norsk. Farm. Sels.*, 1956, **5**, 88.) Cocaine, amylocaine, pseudococaine, phenacaine and cinchocaine hydrochlorides were titrated in a mixture of equal volumes of glacial acetic acid and dioxan, in the presence of mercuric acetate. Perchloric acid in acetic acid was used as the titrating agent, and a sharp end point was observed when crystal violet was used as indicator. Results close to the theoretical figure were obtained. Procaine, larocaine and amethocaine hydrochlorides gave two inflections of the potential curve, both of which could be used as end points of the potentiometric titration, but the indicator change, corresponding to the second potentiometric end point, was not sharp. The compounds were acetylated by heating to boiling a solution of the local anaesthetic agent in a mixture of 5 volumes of acetic acid with 1 of acetic anhydride, after which the solutions could be titrated as above, and a sharp colour change (violet to blue) obtained with crystal violet as indicator. G. B.

Thiamine and Riboflavine in Mixtures, Fluorimetric Determination of. W. E. Ohnesorge an L. B. Rogers. (*Analyt. Chem.*, 1956, **28**, 1017.) This method was designed to eliminate the necessity for chromatographic separation of the vitamins before analysis. The thiamine (aneurine) is converted to thiochrome by alkaline ferricyanide, the pH is adjusted to such a value that both the riboflavine and thiochrome fluoresce. The exciting radiation consists of a monochromatic source at 365 mμ, and the fluorescence at 450 mμ (chiefly due to the thiochrome) and at 530 mμ (chiefly due to the riboflavine) is measured. The fluorescent spectra overlap but calibration charts are prepared using known mixtures of the vitamins from 0·5 to 4·0 p.p.m. of each and a quinine standard for arbitary comparison. The standard deviations are of the order of $\pm$ 5 per cent for each vitamin. The effect of a number of variables such as pH, temperature, time of irradiation and the effect of alkaline ferricyanide and light on riboflavine fluorescence are considered. D. B. C.

GLYCOSIDES, FERMENTS AND CARBOHYDRATES

Digitalis Leaves, Biological Standardisation of. K. B. Jensen. (*Acta pharm. tox., Kbh.*, 1956, **12**, 136.) An investigation has been made of the efficiency of the most commonly employed glycoside extraction procedures used in the standardisation of digitalis, namely maceration with 70 per cent ethanol, soxhlet extraction with absolute ethanol for six hours and maceration with

absolute ethanol for 24 hours followed by boiling on a water bath for 30 minutes. Paper chromatographic and fluorimetric determinations were made of the individual cardio-active glycosides and aglycones, and the results were compared with a percolation procedure using 70 per cent ethanol previously shown to give total extraction. It was found that maceration with 70 per cent ethanol gave total extraction of the cardio-active substances, but the two methods with absolute ethanol gave very incomplete extraction. G. F. S.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Adrenaline and Noradrenaline Concentrations in Rat Tissues, Seasonal Variations of. K. A. Montagu. (*Nature, Lond.*, 1956, **178**, 417.) Variations of catechol amine concentration in tissues from male rats were studied over a period of 12 months. Adrenaline and noradrenaline were estimated fluorimetrically in the heart, kidneys, liver, diaphragm, leg muscles, brain and spleen, using a modification of the method of Weil-Malherbe and Bone. The adrenaline and noradrenaline concentrations and the percentage of adrenaline in the mixture usually showed two maxima and two minima in the year, often of very unequal size. Both the amines showed a 2–5 fold variation in the different months, the maximum concentrations being in the summer and winter and the minimum in spring and late summer. The percentage of adrenaline showed 1·5–3 fold variations, being maximum in March and July. These fluctuations were true of all the tissues except brain. The variations in the heart, liver, leg muscles and spleen were statistically significant. Experiments with bilaterally demedullated rats indicated that the variations are not dependent on the adrenal medulla. They cannot be due to seasonal differences of environmental temperature or diet, nor solely to differences of light nor to interconversion of the two amines. They might have been caused in part by differences in the weight of tissues expressed as percentages of body weight; seasonal metabolic changes might account for changes of weight and of the adrenaline and noradrenaline contents of tissues. M. M.

Amine Contents of the Two Adrenal Glands of the Cat, Relation between. K. R. Butterworth and M. Mann. (*Nature, Lond.*, 1956, **178**, 363.) Since frequently there is a difference in the weight of the left and right adrenal glands of the cat a statistical investigation is carried out into the relation between the two glands of each animal. The following facts were investigated: (1) the relative percentages of noradrenaline in the two glands of each animal and (2) whether the total amine content is the same for both glands or whether the heavier gland contains more amine. The glands from each of 36 adult cats were dissected out and 50 mg./ml. extracts prepared in 0·1 N hydrochloric acid. The adrenaline and noradrenaline content of each extract was determined biologically, using the cat blood pressure and nictitating membrane as separate test preparations and calculating the results by the formula of Bülbring. It was found that the percentages of noradrenaline in the left and right glands of each animal were the same. The mean percentage of noradrenaline in the left gland was 44·5 per cent and in the right gland 44·0 per cent. This correlation between the pairs of glands was independent of the degree of methylation and of any difference in the weight of the two glands. There was found to be a much closer agreement between the amount of amine in the two glands when the results were expressed as per gland than when expressed as per unit weight

of gland. This was true whether the difference in the weight of the two glands was small or large. Differences in the weight of the two glands were as large as 36·4 per cent. These results are of value in experiments where one gland of the animal is used as a control and the effects of drugs on the other are studied.

M. M.

BIOCHEMICAL ANALYSIS

Barbitone in Blood, Quantitative Determination of. R. Askevold and F. Løken. (*Scand. J. clin. lab. Invest.*, 1956, **8**, 1.) A simple extraction method for the determination of barbitone in blood serum is described. It is based on the extraction of the barbiturate from the serum into chloroform through simultaneous removal of water and proteins by addition of sodium sulphate. Pipette 15 ml. of chloroform into a test-tube, add 2 g. of sodium sulphate, 0·1 ml. of concentrated hydrochloric acid and 3 ml. of serum. Shake, add another 2 g. of sodium sulphate and shake again. The chloroform layer should now be free from water. Prepare also a blank in the same way omitting the serum. Filter both sample and blank, pipette 5 ml. of the filtrate into glass stoppered test-tubes and add 5 ml. of borate buffer (pH 10). Shake for 3 minutes, centrifuge and transfer about 3 ml. of the aqueous phase of the sample and the blank into quartz cells. Read in a spectrophotometer at 239 mμ. Add 0·05 ml. concentrated hydrochloric acid to the two, mix and read again.

If spectrophotometer reading at 239 mμ alkaline $= D_1$
and at 239 mμ acid $= D_2$

$(D_1 - D_2) \times 10{\cdot}6 =$ mg. barbitone sodium/100 ml.

The recovery of barbitone sodium averaged 96 per cent. G. F. S.

Magnesium in Serum, Estimation of. D. W. Neill and R. A. Neely. (*J. clin. Path.*, 1956, **9**, 162.) The titan yellow method for estimating serum magnesium has been modified by the addition of calcium to the standard solution to eliminate any calcium effect, and by the use of gum ghatti in place of hydroxylamine as a colour stabilizer. For the assay, 1 ml. of serum is diluted with 5 ml. of water and proteins are precipitated by the addition of 2 ml. of 10 per cent sodium tungstate and 2 ml. of 0·67N sulphuric acid. After centrifuging take 5 ml. of the supernatant and add 1 ml. of water, 1 ml. of 0·1 per cent gum ghatti solution, 1 ml. of 0·05 per cent titan yellow and 2 ml. of 4N sodium hydroxide solution. Read the optical density in a colorimeter with a 624 filter and determine the magnesium concentration by reference to a standard curve. A blank is run alongside, using 1 ml. of calcium chloride solution (equivalent to 0·05 mg. $CaCl_2$). The normal adult magnesium level in serum by this technique was 2·3 mg. per 100 ml. (range 1·9 to 2·7). G. F. S.

CHEMOTHERAPY

Antibacterial Substances in Seeds. L. Ferenczy. (*Nature, Lond.*, 1956, **178**, 639.) During investigations of the physiology of germination, it was observed that micro-organisms occurring on some species of seeds proliferated during germination whilst seeds of other species remained sterile. It was inferred that antibacterial substances must be released from the seeds during germination. Further investigations were made by the agar diffusion method using the following test organisms: *B. mycoides, B. megaterium, B. subtilis, Staph. aureus, A. aerogenes, Shig. flexneri, Erwinia carotovora* and *Xanthomonas malvacearum.* All were rapidly growing strains, so that sterilisation of the seeds was unnecessary.

Bouillon agar (pH 7·0) plates of 5 mm. thickness were seeded with freshly prepared suspensions, the surfaces of the plates dried and the seeds sunk into the medium. Zones of inhibition were measured after incubation for 20 hours at 30°. Entire seeds were tested with the exception of seeds of species of *Fraxinus*, which were cut transversely in order to ascertain whether germination inhibiting compounds known to be released under these conditions possessed antibacterial properties. Of 400 species examined, the seeds of 36 plant species gave positive results. In most cases the effect was selective, only the Gram-positive bacteria being inhibited. Substances released from *Fraxinus* species were effective against all the test organisms. Seeds of several species of *Kniphofia* were highly active against Gram-positive organisms and the authors report that the active substance from this genus has been isolated. Isolation of antibacterial substances from other seeds has been commenced. B. A. W.

PHARMACY

Cyanocobalamin in the Presence of Aneurine and Nicotinamide, The Stability of. J. Dony and J. Conter (*J. Pharm. Belg.*, 1956, **11**, 186). Solutions containing cyanocobalamin (5 μg./ml.) alone and with various quantities of nicotinamide, aneurine, and both nicotinamide and aneurine together, were prepared and adjusted to pH 5. Samples were kept in sealed ampoules and stoppered bottles, protected from light, while others were subjected to heat treatment. The cyanocobalamin content was then determined by microbiological assay. At ordinary temperatures, this vitamin was stable for up to 2 months, alone or in the presence of aneurine, nicotinamide or both. At 37° it was stable in the presence of either aneurine or nicotinamide, but when both were present together, the stability decreased as the proportion of aneurine was increased. Cyanocobalamin was stable to heat at 100° for 4 hours in the presence of nicotinamide or of up to 10 mg./ml. of aneurine. On autoclaving solutions of cyanocobalamin alone or with nicotinamide at 120° for 20 minutes, a very slight decomposition occurred. Solutions containing cyanocobalamin, nicotinamide and aneurine could not be autoclaved without considerable loss of vitamin B_{12}. G. B.

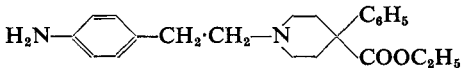
PHARMACOLOGY AND THERAPEUTICS

Acenocoumarin as an Anticoagulant. F. J. Schilling and O. R. Kruesi. (*Amer. J. med. Sci.*, 1956, **231**, 558.) Acenocoumarin (Sintrom) is nitro-phenyl-acetyl-ethyl-4-hydroxycoumarin. It is a white, crystalline, tasteless powder which is administered by mouth as tablets or capsules. This report is based on observations made on 65 patients with thromboembolic conditions who were treated with acenocoumarin for an average period of 27 days. The effective doses were found to be 20 mg. the first day, 8 to 16 mg. the second day, and an average of 4 to 6 mg. daily for maintenance therapy. All the patients developed adequate hypoprothrombinaemia as a result of this therapy. The administration of a single daily oral dose produced an adequate hypoprothrombinaemia which appeared to be well sustained according to daily prothrombin values. On single daily doses of acenocoumarin the 65 patients were within the therapeutic range of hypoprothrombinaemia for about 75 per cent of the time. Excessive hypoprothrombinaemia developed in 3 patients during maintenance therapy, but was successfully treated with vitamin K_1. After cessation of acenocoumarin administration the dilute prothrombin time rapidly

approaches normal within 30 hours. There was no evidence in the series that the drug caused gastrointestinal irritation, or hepatic, renal or haemopoietic toxicity. S. L. W.

Adrenaline and Noradrenaline in Adrenal Autografts. O. Eränkö. (*Nature, Lond.*, 1956, **178**, 603.) Both cortical and medullary cells survive in adrenal grafts after transplantation into the anterior chamber of the eye. An investigation is carried out into whether adrenaline and noradrenaline are present in separate cells in these transplants as is so in the adrenal medulla. Using adult rats, a piece of adrenal medulla is inserted into the anterior chamber of the eye. 5 months later the animals are killed and the grafts removed. The adrenaline and noradrenaline contents of these grafts are estimated chemically after separation of the two amines by paper chromatography. Both amines were detected in the grafts, the adrenaline content being 5–10 times the noradrenaline content. Histological examination of the grafts showed chromaffin cells attached to both the cornea and iris. The cells were closely packed but regular cell acini, such as is present in the adrenal medulla, were replaced by irregular groups of cells. The iodate reaction, which stains the noradrenaline-containing cells brown, was positive in some graft cells but the majority, although showing the chromaffin reaction, remained colourless after iodate treatment, thus indicating the presence of adrenaline-containing cells. This is in good agreement with the chemical observations made and suggests that the grafted adrenomedullary cells have retained their ability to make and secrete the same catechol amine which they were making and secreting in the adrenal before grafting. M. M.

Analgesic, A New Synthetic. J. Weijlard, P. D. Orahovats, A. P. Sullivan, G. Purdue, F. K. Heath and K. Pfister, 3rd. (*J. Amer. chem., Soc.*, 1956, **78**, 2342.) Ethyl 1-(4-aminophenylethyl)-4-phenylpiperidine-4-carboxylate (I) was prepared by condensing *p*-aminophenylethyl chloride hydrochloride with ethyl 4-phenylpiperidine-4-carboxylate "carbonate" in



(I)

ethanol in the presence of sodium bicarbonate. It is a potent analgesic with high oral activity and relatively mild side reactions. Mild anti-acetylcholine and antihistaminic activity has been observed both with isolated organs and in intact animals. In animals the compound approaches morphine in analgesic potency, and does not produce nausea, vomiting or constipation. The acute oral and subcutaneous toxicity in mice is simillar to that of pethidine. The synthetic *N*-acetyl derivative has analgesic activity in rats of the same order as I. Preliminary results on man by oral and parenteral administration indicate an analgesic potency for I at least twice that of pethidine. A. H. B.

Atropine-like Compounds, Relation between the Structure and Action of. M. Ya. Mikhel'son, A. S. Artem'ev, I. V. Dardymov, É. V. Zeĭmal, F. V. Pevzner, E. K. Rozhkova, R. S. Rybolovlev, N. V. Savateev, Ya. R. Savinskiĭ, E. P. Uspenskaya, N. V. Khromov-Borisov, K. G. Tsirk and A. M. Yanovitskaya. (*VIII Vsesoyuznyi s'ezd fiziologov, Biokhimikov, farmakologov*, 1955, 424–426; *Sovetskoe Med. Referat. Obozrenie*, 1956, No. 26,

131–132.) Results of studies on the hydrochlorides, methiodides and ethiodides of diethylaminoethyl phenyl*cyclo*pentancarboxylate ("Pentafen") and diethylaminoacetylphenothiazine phenyl*cyclo*pentancarboxylate ("Difazin") are reported. All exhibited a marked nicotine and a weak muscarine antagonism. The intravenous doses needed to reduce the depressor effect due to excitation of the vagus nerve were one-fifth to one-twentieth of the doses that reduce the depressor effect following intravenous administration of acetylcholine. When the nitrogen of Pentafen or Difazin is converted to the quaternary form, the blocking action on the peripheral acetylcholine receptors is increased ten-fold. Difazin and Pentafen methiodides reduce the depressor action due to stimulation of the vagus nerve in doses of 0·05 mg./kg.; the corresponding dose of the hydrochlorides is 1·5 to 2 mg./kg. In addition, the alkyl iodide compounds show an enhanced capacity for blocking conduction at sympathetic ganglia; they also block the acetylcholine receptors of the suprarenal and carotid synapses; and they reduce the effect of acetylcholine on the blood pressure of the cat, on the isolated frog heart and on the isolated cat gut. The capacity for reversing neostigmine bronchospasm in cats is increased 20 to 50 times by quaternisation.

E. H.

Azacyclonol (Frenquel) in Chronic Schizophrenia. J. T. Ferguson. (*Antibiotic Med.*, 1956, **3**, 146.) The effects of administration of azacyclonol were observed on 264 chronic, hospitalised women mental patients, predominantly schizophrenics. Beneficial reports recorded by other investigators were confirmed. In those schizophrenic patients helped by the drug the primary effect appeared to be on the delusional system, and increases or decreases in psychomotor activity appeared to be secondary to the changes in delusional activity. Quiet, withdrawn patients became more active, while overactive patients became less active. Early in the course of treatment there may be cyclic changes in behaviour, but with continued treatment a return to the old behaviour pattern becomes less frequent. The clinical course was frequently found to be improved when reserpine or methyl phenidate (Ritalin) was administered concurrently with azacyclonol. The optimal oral dose of azacyclonol varies with different patients, but is usually about 100 mg. daily; the intravenous dose is 100 mg. three times daily. The most rapid response is obtained by giving azacyclonol intravenously for 1 to 3 days followed by oral therapy. Encouraging preliminary results were obtained with the drug in the treatment of psoriasis and arthritis occurring in psychotic patients. In this series of 264 patients no gross change in pulse, respiration, temperature or blood pressure was observed with oral doses up to 360 mg./day and intravenous doses up to 300 mg./day. No significant changes were found in non-protein nitrogen values, cephalin-flocculation tests, blood-sugar levels and urinalyses; no abnormalities of the total blood picture were reported.

S. L. W.

Carbutamide (BZ55) – Experimental and Clinical Studies. (*Canada med. Ass. J.*, 1956, **74**, 957–998.) This is a series of preliminary reports on work carried out on this oral antidiabetic in the laboratories and clinics of Toronto and presented during recent months at meetings of the Toronto Diabetes Association. The symposium, which consists of 7 experimental and 10 clinical reports, is prefaced by a short article by C. H. Best on insulin adjuvants or substitutes in which he concludes that while carbutamide would appear to be therapeutically effective in selected cases its widespread clinical use should only be considered after prolonged experimental and clinical research. In the experimental

reports, evidence is presented to show that carbutamide stimulates the islets of Langerhans, reduces the rate of absorption of glucose from the gut, and reduces the hexose-6-phosphatase activity of the liver, influencing glucose liberation from that organ. Each of these three changes would tend to reduce the blood-sugar level. Carbutamide is shown to be effective in lowering the blood-sugar level in depancreatised and in Houssay dogs, maintained with exogenous insulin, thus indicating that neither the pancreas nor the pituitary gland is essential for the action of the drug; carbutamide appeared to potentiate the action of insulin. On the other hand, on withdrawal of insulin, carbutamide did not prevent glycosuria in the pituitary-diabetic dog, nor did it prevent glycosuria, polyuria, ketonuria, and the rapid onset of severe upset in the depancreatised dog. No large-scale series of trials are included in the clinical reports, a total of only 41 cases being dealt with in the 10 papers. These preliminary trials seem to indicate that carbutamide has a limited value in controlling mild cases of diabetes, that is, in those cases which may be presumed to have reasonable amounts of endogenous insulin, but that it is unlikely to be of value in severe cases. It was of no value in lowering the blood sugar level in a patient with pancreatic diabetes following pancreatectomy, who had been successfully controlled for 5 years by insulin injections. Neither was it found of value in any one of 5 children whose diabetes was successfully controlled by insulin injections. Three of the children treated with carbutamide developed a blotchy, erythematous rash with pruritus, and one developed a mild febrile reaction as well. One other case in this series of trials developed an erythematous, pruritic rash, but no other toxic effects are reported. S. L. W.

Carbutamide (BZ55) in Diabetes, Clinical Trial of. J. A. Hunt, W. Oakley and R. D. Lawrence. (*Brit. med. J.*, 1956, **2**, 445.) Carbutamide was tried in a representative group of 21 patients selected to cover a wide range of age, weight, severity and duration of diabetes; on the basis of the result a group of 17 were selected for treatment as out-patients. Diet control consisted of measured carbohydrate with free protein and fat. The patients were first studied for a control period of two weeks during which they were given dummy tablets. On the first and second days of the trial they were given 2·5 g. and 1·5 g. of the drug; subsequently the dose was 1 g. daily. If a satisfactory response was not obtained in 7 days, the maintenance dose was increased. In the representative group, glycosuria disappeared completely in 9, decreased in 6 and was unaffected in 6. Of the 15 who showed a response, the age at onset of diabetes varied from 45 to 75; only 4 of them had required insulin. Patients with heavy ketonuria did not respond to the drug. In the selected group the diabetes developed after the age of 40; none showed significant ketonuria without insulin. Glycosuria was not controlled by diet alone but in all cases it was reduced or eliminated when carbutamide was given. In the 8 patients who had previously been receiving insulin, the dosage varying from 12 to 88 units, the response was good in 4 and moderate in 4. From the results in the representative group it was concluded that young diabetics and those requiring more than small amounts of insulin show little or no response and there was no reliable evidence that carbutamide reduced the insulin requirement; in two young diabetics the glycosuria increased when the carbutamide was given in addition to their normal dose of insulin. Toxic reactions included giddiness in 8 patients, in 5 of whom it occurred only after the first dose of the drug. In 2 cases there was an irritant erythematous rash which disappeared on stopping treatment. One patient had a sulphonamide rash and one had a sulphonamide drug fever. H. T. B.

Hyperfibrinogenaemic Action of (+)- and (−)-Adrenaline. F. Mandelbaum, O. B. Henriques and S. B. Henriques. (*Nature, Lond.*, 1956, **178**, 363.) Studying the hyperfibrinogenaemic effect of several sympathomimetic amines, it was found that adrenaline, when given subcutaneously to rats, had the highest activity in increasing the blood plasma fibrinogen. Comparing the activity of (+)- and (−)-adrenaline, 40 rats were randomly distributed into 4 groups and given suitable doses of either isomer. 24 hours later the animals were bled under suitable conditions and the fibrinogen content determined by the standard technique of Cullen and Van Slyke. The relative potency of the two isomers was calculated by standard statistical methods. The results indicate that the *dextro* isomer has 2·8 per cent of the activity of the *laevo* isomer. This ratio is comparable to the ratio found for the pressor response in dogs. M. M.

Isopromedol, Pharmacological Properties of. M. D. Mashkovskii and P. N. Abramova. (*Farmakologiya i Toksikologiya*, 1956, **19**, No. 3, 26–32.) A pharmacological study of isopromedol, a stereoisomer of promedol (1 : 2 : 5-trimethyl-4-phenyl-4-piperidyl propionate) is reported. Isopromedol has m.p. 181° to 182·5° and the m.p. of its piperidol is 102° to 103°; the m.p. of the piperidol corresponding to promedol is 107° to 108°. Using white rats, rabbits and dogs, isopromedol was shown to be 2 to 3 times as analgesic as promedol, with similar properties; its effect is more prolonged. It is more powerful than promedol in relaxing smooth muscle. The toxicity of the two isomers is about the same. Isopromedol has been tried in 600 various gynaecological-obstetric patients; it is given subcutaneously in 1 to 2 per cent solution in 1 ml. doses or, less frequently, in oral doses of 0·025 to 0·05 g. The preparation has been approved for clinical use by the Scientific Council of the USSR Ministry of Health. E. H.

Lysergic Acid Diethylamide, Some Serotonin-like Activities of. E. Shaw and D. W. Woolley. (*Science*, 1956, **124**, 121.) Lysergic acid diethylamide (LSD) has been shown on the isolated heart of the clam (*Venus mercenaria*), and on the blood pressure of the dog, to have a serotonin-like action preceding an antagonism. In the anaesthetised dog, LSD showed, like serotonin, both pressor and depressor effects. The pressor effect was 1 to 3 times as powerful as serotonin and could be prevented by the new powerful antagonist of serotonin, 1-benzyl-2:5-dimethylserotonin. It is suggested that LSD, because of its structural resemblance to serotonin, combines with the receptors causing an initial stimulation prior to an antagonistic block. G. F. S.

Novobiocin in Pneumonia. B. M. Limson and M. J. Romansky. (*Antibiotic Med.*, 1956, **2**, 277.) Novobiocin was effective in the treatment of 30 patients with bacterial pneumonia, the results appearing comparable to those with other antibiotics. The fever subsided within 24 to 48 hours in 16 patients, 72 to 96 hours in 10, 5 days in 2, and 7 days in 2. Resolution of the pneumonia was noted within 3 to 4 days in 7 patients, 5 to 7 days in 13, 8 to 11 days in 9, and 14 days in 1. The total amount of antibiotic administered ranged from 6 to 24 g., the majority of patients receiving 12 to 16 g. High serum concentrations were obtained following cumulative oral administration of 500 mg. of novobiocin every 6 hours. Side reactions were limited to 2 cases of mild urticaria which cleared up within 48 hours after stopping the antibiotic. *In vitro* sensitivity tests of 18 strains of pneumococci isolated from patients showed all to be sensitive to less than 0·4 μg./ml. of novobiocin. S. L. W.

(ABSTRACTS *continued on p.* 144.)

muscle relaxant in the treatment of poliomyelitis (p. 227). The delightful story of the Countess of Chinchon's use of cinchona is given, but the author does not point out that recent historical research has shown the story to be false. Similarly, Dioscorides wrote about 100 A.D., not 77 B.C., and his work does not describe several thousand drugs. Perhaps rather naturally, I looked up the information on anthraquinone drugs and, though the author has published research work on this group, there are several serious errors. For instance, senna leaf (p. 97) is said to contain frangula emodin and chrysophanic acid; while it would be difficult to state categorically that this is untrue, so far no research work has proved their presence. Further, the author states that glycosides are only "believed to be present", sennosides A and B being merely "a glycosidal extract". Stoll and others isolated these substances as far back as 1942 and have since shown that they are pure chemicals whose structure has been completely elucidated. There is practically no information given on any recent work on the anthraquinone drugs.

While the author is to be congratulated on a modern approach to the subject, it is to be hoped that a further edition will correct the numerous errors, and give a more thorough treatment of important developments; in such circumstances the book will serve as a valuable guide to the study of one aspect of Pharmacognosy.

J. W. FAIRBAIRN.

(ABSTRACTS *continued from p.* 142.)

APPLIED BACTERIOLOGY

Bile Salts in Culture Media, a Substitute for. J. E. Jameson and N. W. Emberley. (*J. gen. Microbiol.*, 1956, **15**, 198.) The authors report on the use of the anionic detergent Teepol as a substitute for bile salts in culture media for organisms of the coli-typhoid group. It was found that Teepol was more selective against Gram-positive organisms than bile salts and it suppressed swarming of *Proteus* at lower concentrations. Investigation of the composition of Teepol from batch to batch revealed that variations in the relative amounts of alkyl sulphates of differing chain length were small. Teepol contains small residues of unsulphated organic matter, but saturated solutions of this residue in nutrient broth freely supported growth of *E. coli* and *Staph. aureus*. Media (liquid and solidified with agar) containing 0·1 per cent Teepol were compared with MacConkey medium. The Teepol medium tended to precipitate neutral red, and the best results were obtained when bromocresol purple was used as indicator. Plate counts by the Miles and Misra technique of cultures of 12 organisms of the coli-typhoid group were not significantly different when either Lemco, MacConkey or Teepol media were used. Mean colony diameters of 6 organisms were definitely larger when grown on Teepol medium. One or more strains of 12 serotypes each of *Shigella* and *Salmonella* grew freely on Teepol agar, whereas enterococci, micrococci and staphylococci did not grow. Teepol medium was shown to be as effective as MacConkey medium in the isolation of strains of *E. coli* from rectal swabs taken from babies with gastroenteritis and at least as effective for presumptive coli counts taken on 166 drinking waters and 162 sea waters. Colonies on Teepol agar did not readily go rough as on some batches of MacConkey agar and were at least equally suitable for slide-agglutination tests. The authors consider that Teepol is probably of far more constant composition than either sodium taurocholate or tauro-glycocholate and has the added advantage of being much cheaper. B. A. W.