ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Amylobarbitone and Pentobarbitone Sodium in Mixtures, Identification of. E. G. Brooker. (*Analyst*, 1957, **82**, 448.) These barbiturates are not easily separable by direct paper chromatography. Separation can be achieved by preliminary treatment with concentrated sulphuric acid at 100° for one hour. Amylobarbitone is unaffected while pentobarbitone can be separated into 5-ethylbarbituric acid and an unidentified hydrolysis product. The acid reaction mixture is diluted with water, extracted with ether, the ether evaporated and the residue dissolved in chloroform. An aliquot of this is used for chromatography with the water-poor phase of the system *n*-butanol-*n*-pentanol-ammonia (1 : 1 : 1) as mobile phase. The procedure can be used for quantities as small as 0·1 mg. and on mixtures containing as little as 10 per cent of pentobarbitone sodium in amylobarbitone. D. B. C.

Analgesics, Reactions of. M. Hädicke and M. Kuntze. (*Pharm. Zentralh.*, 1957, **96**, 152.) Reactions suitable for the identification of a number of analgesics are given in the table below:

Substance	with phosphomolybdic acid	with nitric-sulphuric acid	with Marquis' reagent
Methadone	weak blue, white precipitate	dark red	slow rose
Eucopon	bluish, turbid	do.	reddish brown
Pethidine	nil	nil	orange brown
Morphine	deep blue	pale yellow	purple
Eucodal	blue colour, crystalline precipitate	yellow	yellow-violet-blue
Codeine	weak blue	yellow	violet
Ethylmorphine	blue	yellow	yellow-violet
Dicodid	weak blue	yellow	red violet
Dilaudid	deep blue	pale yellow	violet
Papaverine	crystalline precipitate on standing	orange yellow	purple red

G. M.

Barbiturates, Microscopic Identification of. H. M. Romijn. (*Pharm. Weekbl.*, 1957, **92**, 397.) The reagents used consist of a 1 and 10 per cent solution of cupric acetate (monohydrate) in ammonia (25 per cent). By adding about 1 mg. of the barbiturate to a drop of each of these reagents it is possible to identify a number of barbiturates. Actually four types of crystals may be observed—violet, blue, colourless or yellow. The preliminary classification is made according to the following scheme):—(1) One or both reactions give both blue and violet crystals: heptobarbitone, allobarbitone, *iso*butylallylbarbitone, phenobarbitone, barbitone and aprobarbitone. (2) One or both reactions give blue but no violet crystals: cyclobarbitone, cycloheptenylethylbarbitone, propylbarbitone, butobarbitone, *iso*amylethylbarbitone, pentobarbitone, and *sec.*-butylbromoallylbarbitone. (3) No reaction in the cold; after boiling and addition of ammonia, violet or colourless, but no blue, crystals: hexobarbitone and methylphenobarbitone. Illustrations are given of the characteristic crystalline forms observed in each case. Crystals are also given by a number of organic acids and other compounds. G. M.

Ergotamine and Ergotoxine, Estimation of. D. D. Jones, H. Katyama and V. E. Tyler Jr. (*J. Amer. pharm. Ass., Sci. Ed.*, 1957, **46**, 426). When ergot alkaloids are submitted to chromatography on buffered paper under controlled conditions, the R_F value increases as the quantity of alkaloid applied to the paper is increased, presumably owing to a tendency for the alkaloidal base to overload the salt-forming capacity of the buffered paper. Within limits the increase in R_F value is proportional to the quantity of alkaloid applied to a spot on the paper, and this is the basis of the proposed method of assay. Strips of filter-paper are dipped in McIlvaine's buffer solution (pH 4) and allowed to dry. Fresh alcoholic solutions equivalent to 10 to 30 mg. of the alkaloids are placed in spots on the strips, which are developed with chloroform saturated with 0·1 M citric acid, by the ascending technique. Slight variations of R_F values are encountered, as a result of which a minimum of 4 experiments for each unknown and each concentration of standard is required to achieve an accuracy of $\pm$ 2·5 to 3 μg. The method is suitable for general laboratory use when high accuracy is not necessary. G. B.

Salicylic Acid in Aspirin, Determination of. C. W. Strode, F. N. Stewart, H. O. Schott and O. J. Coleman. (*Analyt. Chem.*, 1957, **29**, 1184.) Spectrophotometric and visual techniques are described for the quantitative determination of salicylic acid in acetylsalicylic acid and in aspirin tablets (including those tinted with dyes) in amounts down to less than 0·005 per cent. Variables such as pH, temperature, rate of hydrolysis of acetylsalicylic acid are strictly controlled, a special correction being applied for this last variable which is proportional to the time elapsing during manipulation. A calibration curve is prepared by adding graded amounts of pure salicylic acid to a fixed amount of a solution of purified acetylsalicylic acid in ethanol and standard ferric alum solution and diluting to a suitable volume with water. The weight of test sample taken is such that the concentration of acetylsalicylic acid is the same as that in the solutions used for the calibration curve. Results of the spectrophotometric analysis of typical white, pink and green aspirin granulations containing 10 to 20 per cent starch show that the over-all precision is maintained. D. B. C.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Protein Component of High Molecular Weight in the Serum of Patients with Rheumatoid Arthritis. E. C. Franklin, H. R. Holman, H. J. Müller-Eberhard and H. G. Kunkel. (*J. exp. Med.*, 1957, **105**, 425.) In the sera of a number of patients with rheumatoid arthiritis an unusual high molecular weight protein could be detected by direct ultracentrifuge analysis of whole serum. The material sedimented more rapidly than the normal 19S component in the γ-globulin fraction and reached a concentration up to 340 mg. per cent. This high molecular weight material was also present in the γ-globulin fraction of serum and joint fluid. It had an $S_{20,w}$ of approximately 22S and could be dissociated into two fractions, one of which had a sedimentation coefficient of approximately 19S. The relationship between the unusual protein complex and various 19S γ-globulins and 19S antibodies is discussed. G.F.S.

Sphingosine as an Inhibitor of Blood Clotting. E. Hecht and D. Shapiro. (*Science*, 1957, **125**, 1041.) A powerful clot delaying substance, identified as sphingosine, has been isolated from brain tissue. It is a component of cerebrosides and sphingomyelins, it has been isolated from the liquid activator of pig brain and it seems to be the active principle of antithromboplastin, which appears in the blood of haemophiliacs in abnormally high quantities. Small quantities of sphingosine prolong the clotting time of chicken plasma to 40 hours or more but the inhibitory action is prevented by the liquid activator from pig brain. Sphignosine and certain derivatives have been synthesized, its structure is CH_3–$(CH_2)_{12}$–CH = CH–CHOH–CHNH_2–CH_2OH. The presence of the double bond as well as the free functional OH and NH_2 groups is essential for activity. The intensity of the reactions with sphingosine depend on its concentration, on the concentration of lipid activator and on the properties of the plasma. Two isomers of threoninol, which are the lowest homologues of dihydrosphingosine have been isolated and their oxalates found to have a powerful inhibitory influence on the clotting of chicken plasma. G. F. S.

BIOCHEMICAL ANALYSIS

Barbiturates in Biological Material, Separation and Identification of. L. G. Allgén. (*Scand. J. clin. lab. Invest.*, 1957, **9**, 71.) While spectrophotometric methods are used to differentiate between various barbiturates in some cases they are not satisfactory, particularly when low amounts are present and interfering substances are present. Paper chromatography has therefore been compared with spectrophotometric results in such cases. For paper chromatography of blood 10 ml. is extracted by shaking for 3 minutes with 50 ml. of chloroform, the chloroform is filtered and evaporated to dryness on a water bath. The residue is triturated with 0·1 ml. of ethanol for several minutes. For urine and gastric contents 50 ml. is acidified with dilute sulphuric acid and extracted with 100 ml. of chloroform and an aliquot (60 ml.) evaporated and the residue dissolved in 0·2 ml. of ethanol. Using Whatman No. 1 filter paper sheets the ethanol concentrates are applied as spots on the paper on a line about 7 cm. from one end, and one and three times 5 μl. of each solution applied by micropipette. Standards of diethylbarbituric acid are applied to each paper in amounts of 25 to 50 μg. in ethanol solution, and any barbiturate suspected is also applied as a standard. Descending paper chromatography is carried out using alkaline aqueous suspensions of various alcohols (ethanol, butanol, *iso*amyl alcohol, tertiary amyl alcohol, hexanol and benzyl alcohol). The time of running varies with the solvent used. The papers are air dried and the spots identified by ultra-violet illumination and by cutting out the spots, extracting with 4 ml. of 0·05 M pH 10 borate buffer followed by determination of the absorption curve at various wavelengths between 220 and 350 mμ in a spectrophotometer. Absorption curves were also obtained after adding 0·5 ml. of N sodium hydroxide to 3 ml. of eluate and then after adding 1 ml. of N sulphuric acid. A number of chemical spraying reagents have also been used including 0·02N potassium permanganate and 0·1N silver nitrate. The R_F values of a number of barbiturates are given and chromatographic findings from a number of patients suffering from barbiturate poisoning are surveyed. The paper chromatographic method takes too long for routine use, but it is useful in special cases. G. F. S.

Poliomyelitis Antibodies, Detection of. H. L. Hodes, H. D. Zepp, W. L. Henley and R. Berger. (*Science*, 1957, **125**, 1089.) A valuable screening test for distinguishing immune from non-immune persons is described. The upward spread of virus in strips of filter paper is decreased by serum containing specific antibody. Whatman filter paper No. 3 is cut into strips 12 by 1·75 cm. Each strip is marked off into 1 cm. spaces (numbered 1 to 12), suspended from a rubber stopper and autoclaved. Poliovirus cultivated in monkey kidney tissue is diluted to a concentration of 100 TCD50 per ml. in 0·85 per cent saline containing 10 per cent bouillon broth. Thirty ml. of the diluted virus is placed in a sterile bottle surrounded by ice. The serum to be tested (previously inactivated at 56°) is then distributed evenly over spaces 3 and 4 of the filter paper. The paper is placed in the bottle containing the virus with only the lower half of space 1 below the surface of the virus suspension. After 1 hour the strips of paper are removed, and each paper is cut off and placed in a monkey kidney tissue-culture tube. Tissue culture tubes are incubated and observed for virus cytopathogenic effects in the usual manner. Neutralising antibodies titres of the serums used in the paper tests are determined by standard tissue culture methods. In 52 successive duplicate tests with 14 human serums, virus was detected on every wet space of every paper strip on which the serum containing no antibody had been placed, while no virus was found above space 6 when the serum contained type-specific poliovirus antibody (usually not above space 4). Only 0·025 ml. of serum is required. G. F. S.

Protein in Biological Fluids, Microdetermination of. G. R. Kingsley and G. Getchell. (*J. biol. Chem.*, 1957, **225**, 545.) An investigation has been made to develop the most practical method for the microdetermination of protein in body fluids using tetrabromophenolphthalein ethyl ester (TBPEE) or its potassium salt. A simple accurate method is described for the estimation of total protein in spinal fluid and serum sensitive to 0·1 μg. For spinal fluid add 0·02 ml. of fresh spinal fluid to a standard photometer cuvette containing 4 ml. of water maintained at 25° in a water bath. Add 1 ml. of working indicator solution (a 1 in 10 dilution of a stock solution containing 134 mg. of TBPEE, both in methanol). Add 0·5 ml. of 0·004N acetic acid and mix, stand for 5 minutes at 25° and read the per cent transmittance of light at 600 mμ against a blank prepared with distilled water and set at 100 per cent transmission. For serum dilute 1 ml. of fresh serum to 100 ml. with saline, dilute 2 ml. of this mixture to 100 ml. with water, add 4 ml. of the final dilution to the cuvette and continue as for CSF. The accuracy of the new method compares very favourably with the biuret, phenol, Kjeldahl-nesslerization and turbimetric methods except with abnormal specimens where there was only good agreement in 1 out of 30 specimens. Apparently most abnormal spinal fluids contain protein which reacts as serum, and the method has been adapted satisfactorily for the determination of serum present in spinal fluid. The method was not satisfactory for the determination of urinary protein. G. F. S.

PHARMACOLOGY AND THERAPEUTICS

Antibiotic Treatment of Severe Bronchiectasis. Report by a Sub-Committee of the Antibiotics Clinical Trials (Non-Tuberculous) Committee of the M.R.C. (*Brit. med. J.*, 1957, **2**, 255). The trial was conducted at seven centres. Patients were between 15 and 55 years of age and all had had symptoms of bronchiectasis for at least three months. 112 patients were treated; 36 were treated with penicillin, 40 with oxytetracycline, and 36 with lactose. The drugs were provided as indistinguishable 0·25 g. capsules, two of which were given four times

a day on two days each week for a year. Regular measurements were made of the volume of a 24-hour sputum specimen and of the severity of cough, dyspnoea, haemoptysis and disability. Each of the groups showed a reduction in the sputum volume, the reduction being greater for the pus than for the mucus fraction, during the year. The reduction was rapid in the oxytetracycline group, and for pus to about half the pre-treatment level. The reduction in the penicillin and lactose groups was slower, and to about 70 per cent of the pre-treatment level in each. In each group there was some reduction in the severity of cough and dyspnoea and in the number of episodes of haemoptysis, the oxytetracycline group showing a slight advantage. During the period of treatment the patients receiving oxytetracycline suffered less severe interference with their lives. The number of days on which patients in this group were confined to bed was less than half the total for those receiving penicillin and a little over a quarter of those receiving lactose. The number of episodes of fever and the number of days off work was also less in the oxytetracycline group. The results as a whole indicated a definite benefit from oxytetracycline, and a probable but smaller benefit from penicillin. Even in the oxytetracycline group, however, the effect was not dramatic. It is clear that the response obtained and the expense entailed do not justify the widespread use of long-term oxytetracycline therapy in most patients with bronchiectasis, though for the relatively few advanced cases it offers a measure of relief not apparently obtainable by oral penicillin in the doses used. S. L. W.

Benzylpenicillin, Rectal Absorption of. K. Backe-Hansen. (*Scand. J. Clin. lab. Invest.*, 1957, **9**, 170.) Sodium lauryl sulphate has been shown to increase the rectal absorption of benzylpenicillin from suppositories prepared with cocoa butter or Imhausen Base H. Determination of the penicillin serum concentration in fifteen patients after insertion of suppositories containing 500,000 units of benzylpenicillin showed the absorption was rapid and maximal blood concentrations were attained within 30 minutes. These were on the average about one third of the maximum following intramuscular injection.
G. F. S.

Cortisone: Influence on Teratogenic Effects of Hypervitaminosis-A. J. W. Millen and D. H. M. Woollam. (*Brit. med. J.*, 1957, **2**, 196.) An investigation was undertaken to explore the effect of cortisone administered to rats during pregnancy on the incidence of deformities of the brain and calvaria produced by hypervitaminosis-A. The pregnant rats were divided into three groups, each group consisting of 12 animals. Group I received 60,000 I.U. of vitamin A acetate daily from the 8th to the 13th day, inclusive, of pregnancy; Group 2 received 20 mg. of cortisone acetate daily from the 9th to the 12th day, inclusive; and Group 3 received 60,000 I.U. of vitamin A acetate daily from the 8th to the 13th day, inclusive, and 20 mg. of cortisone acetate from the 9th to the 12th day, inclusive. The rats were killed on the 20th day of pregnancy and the foetuses removed and inspected for abnormalities. In Group 1 the number of young with deformity of brain and calvaria was 6 out of 77 (7·8 per cent), in Group 2, there were none out of 73, and in Group 3 there were 15 out of 41 (36·6 per cent). These results suggest strongly that cortisone (while itself having no teratogenic action) potentiates the known teratogenic effect of hypervitaminosis-A. It may well be that the increased incidence of cleft-palate observed by Fraser and others in mice genetically susceptible to the condition was also due to the cortisone potentiating the expression of the inherent genetic weakness. S. L. W.

5-Hydroxytryptamine Antagonism by Lysergic Acid Diethylamide after Intracerebral Injection into Conscious Mice. T. J. Haley. (*J. Amer. pharm. Ass., Sci. Ed.*, 1957, **46**, 428.) Intracerebral injection of 5-hydroxytryptamine into conscious mice was shown to give rise to scratching and stupor, whereas lysergic acid diethylamide, its 1-acetyl and 1-methyl derivatives and (+)-lysergic acid dimethylamide gave rise to hyperexcitability, piloerection, muscle incoordination and sensitivity. In addition, lysergic acid diethylamide produced a sensitivity to sound, muscle twitch in the lumbar area and a peculiar alternating stamping of the feet. Mixtures of 5-hydroxytryptamine and lysergic acid diethylamide or its derivatives were injected to detect any antagonism between these substances: lysergic acid diethylamide, and its 1-acetyl and 1-methyl derivatives were shown to block the central effects of 5-hydroxytryptamine, whereas lysergic acid dimethylamide did not. G. B.

Hypoglycaemic Drug, Pharmacology of. G. Ungar, L. Freedman and S. L. Shapiro. (*Proc. Soc. exp. Biol. N.Y.*, 1957, **95**, 190.) From a series of 200 new mono- and disubstituted alkyl and aralkyl derivatives of formamidinyliminourea *N*-β-phenylformamidinyliminourea (DBI) has been found to be a highly active oral hypoglycaemic agent in both normal and alloxan-diabetic animals. In guinea pigs, rats, rabbits, cats and monkeys hypoglycaemia reached its maximum in five hours and was back to normal in twenty-four hours. The monkey was the most sensitive. DBI failed to cause hypoglycaemia in dogs, but it reduced the blood sugar in alloxan-diabetic rats, rabbits and monkeys and maintained it at normal level. DBI differs from other orally active hypoglycaemic agents in not causing a significant change in the glycogen content of liver and muscle. Apart from its hypoglycaemic action DBI has no acute pharmacological actions and if the blood sugar is maintained by the administration of glucose, animals can tolerate very high doses. G. F. S.

Mecamylamine in the Management of Hypertension, Use of. F. H. Smirk and E. G. McQueen. (*Brit. med. J.*, 1957, **1**, 422.) The use of mecamylamine in the management of hypertension over a period of four to eight months is described. The drugs were given orally or by subcutaneous or intravenous injection to forty patients, many of whom had proved difficult to control with other ganglion-blocking agents. In contrast with the quaternary ammonium compounds mecamylamine was well absorbed from the alimentary tract so that the oral dose was little more than the parenteral dose. Tolerance to mecamylamine was slight and insufficient to cause difficulty in fixing the maintenance dose. Duration of action was longer than that of pentolinium or chlorisondamine: consequently control over blood pressure was easier. For the management of hypertension two doses a day are recommended, the evening dose being 30 per cent higher than the morning one. The average daily dose used was 33 mg. Adequate control of the blood pressure was in some instances hindered by the occurrence of side effects caused by parasympathetic ganglion block; these appeared to be rather more prominent than with pentolinium. There were, however, individual differences in patients, so that with equal falls in blood pressure, side effects were less in some patients when they were treated with mecamylamine and less in others when the drug used was pentolinium. Combinations of mecamylamine with rauwolfia alkaloids was also satisfactory. No delayed toxicity with the ganglion-blocking agent was encountered during the eight months' trial. G. P.

Muscarine Chloride, Pharmacological Actions of. P. J. Fraser. (*Brit. J. Pharmacol.*, 1957, **12**, 47.) The action of chromatographically pure crystalline muscarine chloride, prepared from *Amanita muscaria*, was compared with acetylcholine on a number of different organs from various species. Muscarine caused contraction of the smooth muscle of the gut, uterus, urinary bladder, and bronchi, both *in vivo* and *in vitro*. Isolated preparations of the ureter and carotid artery of the horse were also contracted, and the isolated auricles of the guinea pig and rabbit and frog's heart were slowed. The alkaloid caused a drop in blood pressure, although on the isolated rabbit's ear it produced either constriction or dilatation of the blood vessels. All the actions were qualitatively similar to the parasympathomimetic actions of acetylcholine, though muscarine was usually more potent, and, as with acetylcholine, the effects were readily prevented with atropine. In high concentration the drug had some contractural action on the frog's isolated rectus abdominis muscle, but had no neuromuscular blocking action on the rat diaphragm or on the cat gastrocnemius. Muscarine was destroyed neither by pepsin nor by boiling at any pH. It was inactive by mouth in a monkey in a dose many times that which would have been toxic in man. With true- or pseudo-cholinesterase, no hydrolysis or enzyme inhibition were seen. G. P.

Nalorphine, Analgesic Activity and Morphine Antagonism of Compounds related to. C. A. Winter, P. D. Orahovats and E. G. Lehman. (*Arch. int. Pharmacodyn.*, 1957, **110**, 186.) The analgesic and antimorphine properties of 70 compounds have been compared. Analgesic activity was determined in rats using the radiant heat method applied to the tail. For analgesic activity comparisons were made with morphine and for antimorphine activity with nalorphine. The results showed that length of the *N*-substituent chain had an important influence upon both analgesic activity and morphine antagonism. In the morphine series, compounds with 3-carbon chains, allyl, propyl, *iso*butyl and methallyl had some degree of antimorphine activity, with the *N*-propyl compound exhibiting activity of the same order as the *N*-allyl. Substitution of other elements or groups for hydrogen in the chain destroys the antimorphine activity without conferring analgesic properties. Lengthening the side chain beyond *N*-butyl yields potent analgesic agents. None of the morphine derivatives with aromatic side chains were antimorphine agents, but one of them, *N*-phenylethylnormorphine was an extraordinary potent analgesic. Both the *N*-allyl and *N*-propyl substituents yielded potent antimorphine compounds not only with morphine, but also with diacetylmorphine, dihydromorphine, desoxymorphine and dihydromorphinone. Both the *N*-allyl and *N*-propyl derivatives of dihydromorphinone were exceptionally potent antimorphine agents. Neither *N*-propylnorcodeine, *N*-propyldesoxynorcodeine nor *N*-propyldihydrodesoxynorcodeine was as active an antagonist as the corresponding *N*-allyl derivative. Neither the *N*-allyl nor the *N*-propyl derivative of either dihydrocodeine or of dihydrocodeinone was active. Tripropionylnormorphine and the *N*-allyl derivatives of *iso*morphinan and 6-methyl-$\triangle^{6}$-desoxynorcodeine had moderate antimorphine activity, while the 1-*N*-allyl-3-hydroxy-morphinan (levallorphan) was as active as nalorphine. *N*-Allylnorpethidine was an active analgesic like pethidine. G. F. S.

Pacatal and Chlorpromazine in Schizophrenia. J. Lomas. (*Brit. med. J.*, 1957, **2**, 78.) Fifty schizophrenic patients were treated with Pacatal and 50 with chlorpromazine. The usual dosage of either drug was 300 mg. daily. Assessment of results was made on a five-point scale by an independent observer

after 13 weeks treatment or when treatment had to be discontinued. Chlorpromazine was shown to be much more effective than Pacatal; only 8 of 50 patients receiving Pacatal were more than moderately improved as against 23 of those on chlorpromazine. Pacatal would appear to be less toxic than chlorpromazine. Dryness of the mouth occurred in almost all patients taking Pacatal; cycloplegia was also common, and constipation was occasionally troublesome, but less so than with chlorpromazine. Jaundice does not seem to be a risk in using Pacatal but, as with chlorpromazine, agranulocytosis is a dangerous complication. S. L. W.

Phenothiazine Derivatives, Central Depressant Activity of a New Series of. J. Schmitt, J. Mercier, M. Aurousseau, A. Hallot and P. Comoy. (*C.R. Acad. Sci., Paris*, 1957, **244**, 255.) Four derivatives of chlorpromazine in which the chlorine atom was replaced by an acyl radical were prepared and the pharmacological activity of one, 3-acetyl-10-(3-dimethylaminopropyl) phenothiazine (1522CB) examined. This derivative had high central depressant and antiadrenaline activity in the dog. The vasopressor response to 1 to 4 μg./kg. of adrenaline was abolished by 10 μg./kg. of 1522CB, and reversed by larger doses of the antagonist. A hypnotic action in mice was seen with subcutaneous injection of 1 to 3 mg./kg., a dose of 0·5 to 1 mg./kg. prolonging barbiturate sleeping time some two to three times. The analgesic action of morphine was also potentiated by these doses of 1522CB. Convulsions induced by direct cortical stimulation in the dog and EEG arousal responses with peripheral nociceptive stimuli were diminished, by 0·5 to 1 mg./kg. of the drug. These central actions could be explained by the depression the drug exerts on the brainstem reticular activating system. In addition 1522CB had a powerful anti-emetic action against apomorphine in the dog and reduced the body temperature in the mouse and rat. Cardiovascular reflexes such as the pressor response to anoxia or carotid occlusion were very sensitive to the action of the drug. Other actions included local anaesthetic activity comparable with cocaine, feeble atropine-like effects on the salivary glands and moderate antispasmodic and antihistamine actions. Intravenous injection in the dog caused hypotension and diminished cardiac output. Neuromuscular block in the rabbit with gallamine was increased by 1522CB. The LD50 in mice was 70 mg./kg. intravenously and 130 mg./kg. orally. Chronic toxicity tests in the rat revealed no untoward effects on hepatic or renal function or on blood formation. G. P.

Plastic and Red Rubber Giving-sets; Thrombophlebitis following Intravenous Transfusions. (*Lancet*, 1957, **272**, 595.) This is a report to the Medical Research Council on an assessment of the incidence of thrombophlebitis long-continued intravenous infusions in two series of recipients. In one series the infusions were given through red rubber sets often supplied by the National Blood Transfusion Service, in the second series the infusions were given through sets made of plastic (polyvinyl chloride with added "plasticiser" and "stabiliser"). In other respects the two series were closely comparable. Seven hospitals took part in the trial and 700 reports were received. The investigation showed that in the series in which plastic tubing was used the incidence of thrombophlebitis was approximately half of that in which red rubber tubing was used; the proportions of very severe and severe reactions were 32 out of 180 (18 per cent) for the plastic sets, and 64 out of 189 (34 per cent) for the rubber sets. It would be unwise to conclude that the cases of major thromophlebitis following infusion through plastic tubing were necessarily due to harmful substances contained in that tubing. S. L. W.

Quinine, Potentiating Effects of. P. D. Orahovats, E. G. Lehman and E. W. Chapin. (*Arch. int. Pharmacodyn.*, 1957, **110**, 245.) Studies in animals have shown that quinine potentiates analgesics, hypnotics and anaesthetics. In rats, quinine itself had no analgesic action in doses up to 1000 mg./kg., but it strongly potentiated the analgesic effect of morphine. It also potentiated methadone, pethidine, codeine and 6-methyl-δ-desoxymorphine. After quinine, nalorphine showed an analgesic action. Potentiation was only seen when the quinine was given before or with the analgesic, never when given afterwards. Quinine pretreatment in doses up to 200 mg./kg. did not increase the acute toxicity of morphine. The potentiating effect of quinine on analgesics was also seen in dogs, but it antagonised the excitant action of morphine in cats. Quinine itself did not produce signs of CNS depression, hypnosis or sedation, but it enhanced the hypnotic effect of pentobarbitone without increasing its toxicity. Quinine was also found to prolong the action of a variety of chemically non related hypnotic agents in rats, cats and rabbits. G. F. S.

Rauwolscine, Pharmacological Action of. J. D. Kohli, J. H. Balwani, C. Ray and N. N. De. (*Arch. int. Pharmacodyn.*, 1957, **111**, 108.) Rauwolscine is a stereoisomer of yohimbine isolated from *Rauwolfia canescens* Linn. which is closely related to *R. serpentina* Benth. Its adrenergic blocking activity has been compared with yohimbine and tolazoline by a number of methods. In inhibiting the adrenaline induced spasm on the guinea pig seminal vesicle, rauwolscine was about as active as yohimbine and about twice as active as tolazoline. It also markedly antagonised histamine and acetylcholine on this tissue. Rauwolsine was also as active as yohimbine in shortening the strychnine convulsion time of rats. In anaesthetised cats and dogs doses of 0·1 mg. to 2 mg/kg. caused a fall in blood pressure with recovery in 5 to 30 minutes and partial blocking of the blood pressure response to adrenaline was observed with 0·2 mg./kg. In 2 mg. doses it completely blocked the pressor effect of 10 to 20 μg. of adrenaline but not to 40 μg. so that it does not appear to be highly effective. Like dibenamine it blocks the influence of generalised sympathoadrenal stimulation. The blood pressure effects and adrenergic blockade of rauwolscine were the same as with yohimbine. Rauwolscine blocks the contracting effects of injected adrenaline and preganglionic stimulation on the cat nictitating membrane. In the cat perfused hind legs rauwolscine counteracts the vasoconstrictor effect of adrenaline. G. F. S.

Reserpine, Adrenergic Block by, in Man. B. Åblad. (*Acta pharm. tox. Kbh.*, 1957, **13**, 213.) A study is made of the mechanism of action of reserpine in man. Its effects on the reflex discharge of the sympathetic nervous system on the blood pressure, pulse frequency and muscle blood flow in healthy young adults are studied. The reflex discharge of the sympathetic nervous system was provoked by the subject immersing his feet in water at 12° for one minute. This rapidly caused a constriction of the blood vessels in the hand and forearm. To determine whether the sympathetic blockade is central or peripheral, the action of reserpine on the effects of an intravenous infusion of adrenaline or noradrenaline was studied. It was found that reserpine, 10 μg./kg. intravenously, partly inhibited the effect of small doses of adrenaline and noradrenaline on the peripheral resistance in skin and muscle, from 1 hour to 48 hours after its administration. The reflex vasoconstriction in skin and muscle was also partially inhibited by reserpine and to approximately the same degree as the effect of noradrenaline was inhibited. These results indicate that a considerable part of the decrease in peripheral resistance after reserpine depends on adrenergic block. M. M.

Senna Preparations, Clinical and Laboratory Assessment of. J. C. McC. Browne, V. Edmunds, J. W. Fairbairn and D. D. Reid. (*Brit. med. J.*, 1957, **1**, 436.) Controlled clinical trials designed to measure the relative clinical effectiveness of different senna preparations are described. In the trials comparison was made between results obtained for two B.P. preparations of syrup of senna and a dry granular preparation of senna pod (Senokot) and estimates of the potencies of the preparations by biological and chemical assay methods. Two groups of constipated patients were chosen: short-stay obstetric and long-stay chronically sick patients. In preliminary tests two criteria of potency were used: (i) the per cent of "satisfactory" results, one or more bowel movements occurring within a set period, and (ii) the total number of movements occurring within the time limit. The first criterion was found to be very subjective and was subsequently discarded in favour of the second. From the results obtained it was concluded that laxatives could be graded by the simple clinical trial described. Also, clinical results were in general agreement with those of both chemical assay of sennoside content and biological assay on mice. However, not only did apparently identical B.P. preparations of syrup of senna differ widely in their therapeutic effect, but, with average doses, the B.P. syrups tested were no better than inert controls. Deterioration of the B.P. preparations was confirmed by chemical assay. The dry granular preparation of senna pod was chemically stable and in doses usually prescribed had a potent laxative effect.

G. P.

Serotonin and Reserpine, Effects of Drugs on the Potentiation of Hexobarbitone Hypnosis produced by. G. C. Salmoiraghi and I. H. Page. (*J. Pharmacol.*, 1957, **120**, 20.) Small doses of lysergic acid diethylamide (LSD), a potent serotonin-blocking agent on isolated organs, has been shown to enhance rather than to block the potentiating effect of serotonin on hexobarbitone hypnosis in mice. A similar enhancing effect was also produced by small doses of other drugs which cause hallucinations in man (bufotenine, mescaline, and ibogaine) and also by small doses of brom-LSD (BOL), a lysergic acid derivative which does not cause mental changes in man when giving orally. The potentiating action of reserpine on hexobarbitone hypnosis is blocked by all these hallucinogen compounds in large and small doses. These results suggest that potentiation of the central effects of serotin rather than blockage may be responsible for the hallucinogenic effects of certain drugs, and that the effect of reserpine is not directly mediated by free serotonin released from body depots. G. F. S.

Tranquillising Drugs in Psychoneurosis. M. J. Raymond, C. J. Lucas, M. J. Beesley, B. A. O'Connell and J. A. F. Roberts. (*Brit. med. J.*, 1957, **2**, 63). This is the report of a controlled trial of five drugs, claimed to reduce tension, on psychoneurotic out-patients selected as having a tension component in the symptomatology. Seventy-nine patients were included in the trial, but of these 4 returned faulty records, and 24 defaulted. Each patient received each drug for 2 weeks, and a placebo (lactose) for 2 weeks and recorded his assessment of the drug on a five-point scale daily. A randomised design was used. The dosage for all of the drugs was two tablets three times daily. The drugs employed (with dose per tablet) were as follows: amylobarbitone, 50 mg.; benactyzine, 1 mg.; chlorpromazine, 25 mg.; meprobamate, 400 mg.; "Sedaltine" (carbromal, 195 mg., bromyaletone 65 mg., aluminium hydroxide 100 mg., rauwolfia 0·25 mg., mephenesin 100 mg.). The average score for the placebo was close to a nil response, neither good nor bad. Amylobarbitone was highly significantly superior to the placebo. There was no significant difference between the other four drugs and the placebo. S. L. W.

APPLIED BACTERIOLOGY

Bacteria, Preservation of, by Drying on Cellulose and Alginate Fibres. D. I. Annear. (*J. appl. Bact.*, 1957, **20**, 17.) The author reports the recovery of viable organisms from dried films of suspensions of *Salmonella ndolo* on fibres of calcium alginate and cellulose (absorbent cotton). Organisms grown on nutrient agar were suspended in a preserving medium (10 per cent peptone, 10 per cent glucose) and this suspension was used to inoculate tufts of sterile absorbent cotton wool or calcium alginate. Ampoules of the tufts were connected to a vacuum pump and were sealed after drying for 24 hours. Bacteria were recovered from the fibres by shaking with 1 per cent sodium hexametaphosphate in the case of calcium alginate or with nutrient broth in the case of cellulose fibres. Viable counts were made on blood agar. A very high recovery of organisms (nearly 100 per cent) was obtained from either of the fibres. High recoveries were also obtained after the organisms had been dried on cellulose fibres and stored for a period of six months at room temperature. The method of drying was rapid and freezing, if it occurred at all, must have been very transient. The author considers that the films on the fibres, although very thin, are firm in structure, the fibres acting as shock absorbers when the ampoules are jarred.

B. A. W.

***Escherichia coli*, Measurement of Thermodynamical Quantities in the Disinfection of.** W. Kondo. (*Bull. med. dent. Univ., Tokyo*, 1957, **4**, 81.) The author gives an account of the thermodynamical interpretation of results obtained on the effects of temperature on the disinfection of *E. coli* by phenol. A temperature range of 30–42° was used over a range of phenol concentration of 0·021–0·055 M. Survivors were estimated by a colony counting method after an exposure to the bactericide of 4 hours. No regular relationship between the concentration exponent and temperature was found. It was calculated that the amounts of variation in resistance of individual bacteria to the treatment were independent of temperature. The rate constant of phenol disinfection increased exponentially with temperature in accordance with the Arrhenius equation. The value of total energy of activation was calculated as 52,520 cal., and the activation energy per mol. phenol in disinfection as 8,120 cal. Values of entropy of activation calculated by statistical theory of reaction rate were very high (near 100 cal./deg.), this being suggestive of a protein denaturation. A quantitative relation is suggested between phenol concentration, exposure time, percent survival in probability scale and temperature of exposure.

B. A. W.

Fungi, Cultivation and Identification of, with the aid of Membrane Filters. S. Funder and S. Johannessen. (*J. gen. Microbiol.*, 1957, **17**, 117.) A method of cultivating fungi on a membrane filter was found usually to give more rapid growth than could be obtained on solid media. A sterile absorbent pad was placed in a petri dish and was evenly moistened with about 2 ml. of sterile yeast water. A sterile membrane filter was placed over the pad with care not to entrap air. Filter discs were inoculated from cultures of the fungi and the dishes incubated at room temperature for 2–3 days. The filter disc, or a part of it, was dried at room temperature for 3–4 hours and placed on a few drops of immersion oil on a microscope slide. The membrane was rendered transparent within a few seconds and was then examined microscopically. The method makes the use of plate or slide cultures unnecessary.

B. A. W.