ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

11-Desmethoxyreserpine, Fluorometric Determination of. J. A. Gordon and D. J. Campbell. (*Analyt. Chem.*, 1957, **29**, 488). The method described uses the fluorescence resulting from the reaction of ceric salts with 11-desmethoxyreserpine. To a solution of the latter containing 0·5 to 4·5 μg. in 5N acetic acid is added 1·0 ml. of a solution of 0·001N ceric sulphate in 0·1N sulphuric acid and the solution made up to 10 ml., the tube is immersed in a boiling water bath for 1 hour, cooled, the volume readjusted to 10 ml. and the fluorescence measured against a quinine standard (0·25 μg./ml. of quinine sulphate in 0·1N sulphuric acid). To an aqueous extract prepared from tablets or to parenterals and elixirs, sodium bicarbonate is added to retain 3:4:5-trimethoxybenzoic acid or 11-desmethoxyreserpic acid before extraction of the 11-desmethoxyreserpine with chloroform. An aliquot part of the chloroform solution is evaporated to dryness under nitrogen and the residue taken up in 5N acetic acid. The process is being applied to mixtures of 11-desmethoxyreserpine and reserpine. The activation and fluorescent spectra of 11-desmethoxyreserpine and the fluorescent spectrum of cerate-treated 11-desmethoxyreserpine are given. D. B. C.

Morphine-Marmé Complex. L. Levi. (*Analyt. Chem.*, 1957, **29**, 470). A complex of formula $(C_{17}H_{19}NO_3)$ (CdI_2) is formed when morphine hydrochloride reacts with aqueous cadmium iodide or cadmium iodide-potassium iodide solution. Since the sensitivity of the reaction varies with the amount of potassium iodide in the reagent and the reagent-reactant ratio of the final system, conditions have been worked out to ensure maximum sensitivity which enables 0·1 mg. of morphine to be readily detected. The reagent solution contains 0·2M CdI_2 and 0·8M KI, and the morphine hydrochloride solution under test was 0·0053M, the best result being obtained when three volumes of the morphine solution interacted with one volume of reagent. Any deviation from these conditions reduced sensitivity. On a micro scale, about 0·03μl. of reagent is added to 0·1 μl. of a 0·1 per cent morphine hydrochloride solution. A picture of the crystalline complex is given together with the ultra-violet and infra-red absorption spectra, the X-ray defraction pattern, optical rotation and the solubility behaviour. D. B. C.

Nerve Gases, Detection and Estimation of, by a Fluorescence Reaction. B. Gehauf and J. Goldsen. (*Analyt. Chem.*, 1957, **29**, 276.) The reaction depends upon the oxidation of indole to the highly fluorescent indoxyl and indigo white by alkaline peroxide in the presence of nerve gases such as sarin, soman and tabun. These have the structure either of the type R(R′O)(PO)F or $R_2N(R'O)(PO)CN$. The final stage of the reaction is indigo which is non-fluorescent, but a reaction based upon indigo formation is far less sensitive than one based upon the intermediate transient fluorescent products. The sensitivity of the fluorescent reaction is claimed to be at least 50 times greater than that of the best available colour reaction. Under the conditions used it

was possible to determine 0·05 μg. of sarin, $CH_3(C_3H_7O)(PO)F$, in 10 ml. of solution, and refinements in the technique might decrease this figure to 0·001 μg. The difficulty of the method arises from the short duration, 30 to 60 seconds, of the fluorescence, but methods for stabilising this fluorescent stage are suggested. A complete study of interference has not yet been made.

D. B. C.

Poppy Capsules, Isolation of Alkaloids in, with Ion Exchangers. J. Böswart and A. Jindra. (*Českoslov. Farm.*, 1957, **6**, 82.) The extraction of morphine from poppy capsules is studied, a number of different solvents being used under various conditions. Hot aqueous or methanolic alkaline (containing sodium carbonate or ammonia) solutions give the best results. Pure methanol extracts only 50 per cent of the morphine. Morphine is absorbed from methanolic extracts by the strong anion exchangers Lewatit MN and Amberlite IRA-400, from which it is eluted by N hydrochloric or 0·5N acetic acid. The cation exchanger Wofatit F absorbs morphine from aqueous extracts and it is eluted by a 5 per cent aqueous or methanolic solution of ammonia. For the analytical separation of morphine, the total opium alkaloids are first separated on Wofatit F. The solution of alkaloids is then passed through a column of Lewatit MN and the column is eluted with a 5 per cent solution of ammonia; the morphine, which is retained while the other alkaloids pass through, is finally eluted with N hydrochloric acid and determined polarographically by the method of Holubek (*Pharm. Zentralh.*, 1955, **94**, 347). E. H.

Solanaceous Alkaloids, Purity of. J. Büchi and H. Schumacher. (*Pharm. Acta Helvet.*, 1957, **32**, 75.) The aim of this investigation was the separation and quantitative determination of small amounts of subsidiary alkaloids in commercial alkaloidal products. To this end three paper chromatographic procedures were designed, (A) employing an organic solvent as mobile phase, (B) employing water as mobile phase and (C) employing an optically active acid (di-*p*-toluyl-l-tartaric acid) and an organic solvent as the mobile phase. These enabled a complete separation of the solanaceous alkaloids to be made including hyoscyamine and atropine. By means of procedures B and C, the optical isomers (+)- and (−)-hyoscyamine were separated for the first time. The best reagent for the determination of the alkaloids proved to be Dragendorff's reagent which revealed the presence of 5 μg. of atropine, hyoscyamine, scopolamine and apoatropine and 3 μg. of tropine. It was possible to chromatograph comparatively large amounts of alkaloids e.g., 500 μg., and to separate therefrom the amounts indicated above. It is suggested that these assays for accompanying alkaloids are more sensitive than those officially prescribed and could be used to supplement them. D. B. C.

Sulphadiazine, Sulphathiazole and Sulphadimidine in Tablets, Identification of. F. Abaffy and S. Kveder. (*Acta pharm. Jug.*, 1956, **6**, 200.) Samples of sulphadiazine, sulphathiazole, sulphadimidine, sulphaguanidine, sulphamerazine, sulphanilamide and phthalylsulphathiazole were submitted to partition chromatography on Whatman No. 1 paper using the descending technique, with a 2:1 mixture of butanol and water as the developing solvent. R_F values are given for the three buffer solutions used as the stationary phase. Tablets containing sulphadiazine, sulphathiazole and sulphadimidine were extracted with pyridine and the extract examined by paper chromatography, using the circular, ascending and descending techniques. The sulphonamides were

separated by using paper impregnated with McIlvaine's buffer solution pH 8. The position of the sulphonamide spots was detected by applying a 1 per cent ethanolic solution of *p*-dimethylaminobenzaldehyde, drying and exposing the paper to the vapour of hydrochloric acid. G. B.

Vitamin D and Related Compounds, Determination of. W. H. C. Shaw and J. P. Jefferies. (*Analyst*, 1957, **82**, 8.) A method is described for the assay of the individual components of the mixture of compounds formed during irradiation of the provitamins D (ergosterol or 7-dehydrocholesterol) involving preliminary precipitation of the unchanged provitamins with digitonin, and then the chromatographic separation of the other constituents into two bands. The first band contained the precalciferols 2 and 3 and the lumisterols 2 and 3, the second contained calciferol, the tachysterols 2 and 3 and vitamin D_3. Formulae are given for calculating the percentage of the constituents of each band from ultra-violet absorbtion data. As a check a further colorimetric assay was done on each band using antimony trichloride in chloroform which gave the percentage of precalciferol in the first band and the sum of the vitamin D and tachysterol in the second. The solvent used was 6 per cent v/v of acetone in light petroleum, boiling range 40 to 60°. The size of the sample used was about 30 mg., and experiments were done on known irradiation compounds to ensure that recovery was good. In most cases it exceeded 95 per cent, and was never below 80 per cent. The method was also applicable to the determination of the precalciferols and vitamins D in preparations of the pure vitamins D, but in its present form is unsuitable for materials of low potency or those containing vitamin A. Products obtained under different conditions of irradiation were examined, and the results discussed in relation to the structural changes taking place during, and subsequent to irradiation, and in relation to the results of biological assays. D. B. C.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Phenylalanine Inhibition of Tyrosine Metabolism in Liver. I. J. Bickis, J. P. Kennedy and J. H. Quastel. (*Nature Lond.*, 1957, **179**, 1124.) Studying the factors which influence tyrosine breakdown to acetoacetate in isolated liver tissue, results have been obtained which indicate that (–)-phenylalanine exercises a considerable inhibitory action on tyrosine metabolism in liver slices. Experiments were carried out with freshly cut rat liver slices incubated in the presence of solutions of (–)-tyrosine, potassium α-ketoglutarate and sodium ascorbate at 37° in the conventional Warburg manometric apparatus. The acetoacetate formed was measured by addition of aniline at the end of the incubation period, the citrate salt being used. The carbon dioxide thus liberated was a measure of the acetoacetate produced. It was found that both (–)-tyrosine and (–)-glycyl-tyrosine yield substantial increases of the rates of acetoacetate formation. The addition of (–)-phenylalanine brings about a negligible rise in acetoacetate formation. When (–)-phenylalanine was mixed with (–)-tyrosine or (–)-glycyl-tyrosine the rate of acetoacetate formation from the latter amino acids was decreased almost to the level found with (–)-phenylalanine alone. This inhibitory effect of phenylalanine is unlikely to be due to competition for the α-ketoglutarate which brings about the preliminary transamination before oxidation takes place.

It may be due to competition with tyrosine for transport into the liver cell but it may also be due to the formation of phenylpyruvate produced either by oxidation of (–)-phenylalanine in the liver or by transamination. Results from experiments with radioactive (–)-tyrosine and (–)-phenylalanine lead to the conclusion that phenylalanine exercises an inhibition of tyrosine metabolism in the liver, the inhibition being effected by phenylpyruvate produced in the tissue from the phenylalanine either by oxidation or by transamination. The inhibition by phenylpyruvate is not due to isotopic dilution by hydroxyphenylpyruvate as there is no evidence that this substance is formed in the rat liver; nor does phenylpyruvate give rise to significant quantities of acetoacetate. The results do not rule out the possibility that phenylalanine may itself exert an inhibitory effect on tyrosine breakdown; but if so, the inhibition takes place only with intact cells, for no such effect is observed in the rat liver extract. The uptake of free tyrosine by rat liver slices amounts approximately to that calculated for passive diffusion of the amino acid into the tissue, and the uptake is not adversely affected by the presence of phenylalanine or phenylpyruvate. Incorporation of tyrosine into proteins of the liver slices is, however, definitely affected by phenylalanine and phenylpyruvate. Whether the inhibitory effect of (–)-phenylalanine on tyrosine incorporation is due to competition for incorporation or competition for activation preliminary to incorporation, is a matter for further investigation. These results have a bearing on the interpretation of the metabolic findings in phenylketonuria. In this disorder, which is characterised by mental defect, the conversion of phenylalanine to tyrosine is reduced or arrested. Thus the blood phenylalanine concentration is increased many times over the normal value. Phenylpyruvate is excreted in large amounts. An interference by phenylalanine or by phenylpyruvate with hormone production may throw some light on the problem of the connection between phenylketonuria and mental defect.

M. M.

BIOCHEMICAL ANALYSIS

Ammonia, Determination of, in Blood. D. G. Nathan and F. L. Rodkey. (*J. Lab. clin. Med.*, 1957, **49**, 779.) A colorimetric microdiffusion technique is described for the analysis of ammonia in blood. Pipette 3 ml. of 20 per cent trichloroacetic acid into a centrifuge tube. Cool in ice and add 3 ml. of freshly drawn blood. Shake and store in ice. To assay, shake, centrifuge and record the total volume in the tube and the volume of the precipitate. Decant the clear supernatant fluid. Transfer 1 ml. aliquots of the supernatant to separate 25 ml. penicillin bottles. Moisten a glass rod, previously placed in the rubber stopper, with one drop of 1M citric acid. Distribute the acid in a thin film covering the rod to within 5 mm. of the stopper (acidified rod). Add 1 ml. of saturated potassium carbonate solution. Avoid mixing the two solutions. Insert the acidified rod and stopper tightly. Take care to avoid contact of the acidified rod with either the bottle or its contents. Prepare blank and standard samples with 1 ml. of ammonia free water, or 1 ml. of ammonium sulphate solution containing 1 μg. of NH_3-N, in place of the filtrate. Rotate all the samples for 30 minutes on a rotator. Remove the stoppers and acidified rods from the bottles and place in Pyrex Klett tubes. Wash each rod with 2 ml. of a mixture of equal parts of ninhydrin solution and pH 5 citrate buffer. Cap the tubes and place in a boiling water bath for 30 minutes. Remove from the bath and cool. Add 50 per cent ethanol to make a total volume of 10 ml. in each tube, cover with parafilm and mix by inversion. Clean the outside of the tubes and read in a Klett colorimeter with a No. 56 filter. Subtract the reading of the

blank from the readings of the unknown and standard solutions. The concentration of blood ammonia nitrogen is calculated from the NH_3-N in 1 ml. of the filtrate by the following formula.

$$(NH_3\text{-}N)_{B1} = \frac{(NH_3-N)_F\,(V_t-0{\cdot}10V_p)}{(V_t-V_{tca})}$$

V_t = total volume in centrifuge tube (supernatant plus precipitate).

V_p = total volume of precipitate.

V_{tca} = volume of trichloroacetic acid added to centrifuge tube.

$(NH_3\text{-}N)_F$ = concentration of ammonia in the supernatant fluid expressed as μg. of NH_3-N per ml. of fluid.

$(NH_3\text{-}N)_{B1}$ = concentration of ammonia in blood as μg. of NH_3-N per ml. of blood.

The venous blood ammonia concentration of normal fasting human subjects was found to be $0{\cdot}77 \pm 0{\cdot}28$ μg. NH_3-N per ml. G. F. S.

Glucose and Fructose, Simultaneous Measurement of. W. L. Brown, M. K. Young and L. G. Seraile. (*J. Lab. clin. Med.*, 1957, **49**, 630.) A method is described for the simultaneous determination of glucose and fructose in biological materials, based on the development of colour with an anthrone reagent at 75° and 100°. A good precision is obtained. For estimation in blood, pipette 0·25 ml. of plasma into 5 ml. of water in a test-tube, add 1 ml. of 10 per cent zinc sulphate and allow to stand for five minutes. Now add 1·0 ml. of 0·5 N sodium hydroxide, cap the tube with parafilm, shake vigorously and centrifuge. Place two 1 ml. aliquots in cuvettes, immerse in a beaker of cold water and shake during the addition of 10 ml. of 0·2 per cent anthrone reagent (prepared by dissolving 2 g. of anthrone in 250 ml. of concentrated sulphuric acid and adding 500 ml. of concentrated sulphuric acid previously diluted by adding to 250 ml. of water and cooling). One of the cuvettes is then placed in a water bath at 75° and the other in a water bath at 100°. Heat for seven minutes and cool for ten minutes. Read the optical densities of both solutions in a spectrophotometer at 630 mμ and compare with reagent blanks and duplicate standards of glucose and fructose treated in the same way. The standards contain 60 μg./ml. and are prepared daily from stock solutions containing 100 mg. of glucose or fructose in 0·25 per cent benzoic acid solution. The concentrations of glucose and fructose are calculated by substitution in the following equations.

$$\text{Glucose conc./ml.} = \frac{(\text{O.D.U.}_{100} \times KF_{75})-(\text{O.D.U.}_{75} \times KF_{100})}{(KF_{75} \times KG_{100})-(KF_{100} \times KG_{75})}$$

$$\text{Fructose conc./ml.} = \frac{(\text{O.D.U.}_{75} \times KG_{100})-(\text{O.D.U.}_{100} \times KG_{75})}{(KF_{75} \times KG_{100})-(KF_{100} \times KG_{75})}$$

when O.D.G. = optical density of glucose standard

O.D.F. = optical density of fructose standard

O.D.U. = optical density of unknown mixture.

$$KG_{75} = \frac{\text{O.D.G. at 75°}}{\text{conc. glucose/ml.}} \qquad KG_{100} = \frac{\text{O.D.G. at 100°}}{\text{conc. glucose/ml.}}$$

$$KF_{75} = \frac{\text{O.D.F. at 75°}}{\text{conc. fructose/ml.}} \qquad KF_{100} = \frac{\text{O.D.F. at 100°}}{\text{conc. fructose/ml.}}$$

G. F. S.

Salicylic Acid, Determination of, in Plasma. S. P. Chiang and S. Freeman. (*J. Lab. clin. Med.*, 1957, **49**, 481.) A micromethod is described for the separation of salicylates from plasma proteins and for their estimation. Twenty μl. of plasma is applied to a strip of 3 MM Whatman filter paper, previously extracted with ethanol and dried. Dry at room temperature and add 20 μl. of 6N hydrochloric acid on the same spot as the plasma. Allow to dry. Carry out ascending paper chromatography in test tubes containing 1 ml. of ethanol until the solvent front has travelled to a marked 50 mm. line. Dry in air and repeat this procedure three more times. Cut from the paper strip an area 3 mm. above and 7 mm. below the solvent line. Place in a test tube, add 500 μl. of water and 20 μl. of a 1 per cent solution of ferric nitrate in 0·07N nitric acid. Mix frequently over 30 minutes. Place in a microcell and read the optical density at 540 mμ in a spectrophotometer. Compare with standards prepared by adding 20 μl. of standard solutions of salicylic acid containing 100, 200 and 400 μg./l. added to strips of filter paper on which 20 μl. of salicylate free plasma has been dried. The standards are treated the same way as the test. The results are calculated from the difference in optical density obtained with the patients plasma before and after treatment with salicylates by reference to the standard curve. G. F. S.

Salicylsulphonic Acid Test for Protein in Urine. D. N. Baron. (*Brit. med. J.*, 1957, **1**, 628.) The use of a proprietary tablet, containing salicylsulphonic acid, effervescing agents and a trace of bromcresol green (Altest), is described for the detection of protein in urine. Place about 4 ml. of the filtered urine in a test-tube and add one test tablet. When the tablet is dissolved shake the tube and examine the fluid, which should be yellow. If green the fluid is still alkaline and another one or two tablets are added until yellow. Protein is present when the mixture is cloudy or shows a white precipitate. The test can detect 0·005 g. of protein per 100 ml. of urine, which is comparable with the salicylsulphonic acid solution test, but slightly less sensitive than the boiling test. G. F. S.

CHEMOTHERAPY

Phenazines with high Antituberculosis Activity. V. C. Barry, J. G. Belton, M. L. Conalty, J. M. Denneny, D. W. Edward, J. F. O'Sullivan, D. Twomey and F. Winder. (*Nature, Lond.*, 1957, **179**, 1013.) These riminocompounds are obtained by condensing *o*-phenylenediamine derivatives with diarylamino-*o*-quinones. This paper is concerned with the biological properties of one of these derivatives, B.663. The methods used in screening for antituberculosis activity in mice were as follows: groups of 8 to 10 mice were infected intravenously with the isoniazid-sensitive Ravenel Rv bovine strain of *M. tuberculosis* or with an isoniazid-resistant variant of that strain. Drugs were administered in the diet (*a*) for 14 days commencing on the day of infection, that is, "protective screening", (*b*) for 14 days commencing on the sixth day after infection, that is, "established disease screening" and (*c*) as in (*a*) but using the isoniazid-resistant variant. Median survival times of the control groups (both isoniazid-sensitive and -resistant were about sixteen days. It was found that B.663 is more active than isoniazid on a weight for weight basis and considerably more active on a molar basis. The activity is greater than that observed with other antituberculosis substances such as *p*-aminosalicylate, streptomycin or the thiosemicarbazones. B.663 showed a striking effect in established tuberculosis of guinea pigs. It was also found to accumulate in the tissues of mice and

guinea pigs. Prophylactic experiments showed that 10 mg./kg./day for 14 days, terminated as long as 4 weeks before infection, confers protection. Part of the action of these rimino-compounds may be due to their withdrawal of hydrogen from the respiratory chain and part due to their peroxide formation. M. M.

Threo-β-Phenylserine, the Antiviral Action of. L. Dickinson and M. J. Thompson, with an appendix by J. S. Nicholson, (*Brit. J. Pharmacol.*, 1957, **12**, 66.) L-*Threo*-phenylserine and esters of *threo*-phenylserine were the most active of a series of compounds tested against influenza A virus in tissue culture. Substitution of the β-OH or α-NH_2 group abolished activity. The activity of phenylserine was reversed competitively by phenylalanine. Phenylserine had no action on free virus or on the adsorption of virus to host cells. It prevented virus growth if added during the first half of the latent period. Phenylalanine appears to be necessary for virus synthesis and could be supplied by glycylphenylalanine, phenylalanylglycine or phenylalanine ethyl ester, but not by *N*-acetylphenylalanine. Phenylserine had no significant action against ectromelia infections in mice, even when the amino acid content had been depleted by starvation. *Threo*-β-phenylserine was relatively non-toxic to the host cells investigated, compared with *p*-fluorophenylalanine which has been reported to be active against poliomyelitis virus at 0·04 to 0·1 mg./ml., but cytostatic at 0·1 mg./ml. G. P.

PHARMACY

Albomycin and Grisein, Similarity of. E. O. Stapley and R. E. Ormond. *Science*, 1957, **125**, 587.) Albomycin, isolated from *Actinomyces subtropicus* by Soviet workers and grisein, isolated from *Streptomyces griseus* by Waksman and colleagues are red-coloured substances containing amino acids and iron, having similar activity against a number of species of bacteria. Samples of the two substances were compared to establish whether or not they are identical. Paper and column chromatography and counter-current distribution analysis showed that both antibiotics consist of four active substances, of which a highly active one (A) and a weakly active one (D) are stable, while a less stable component (C) was found to break down during purification, with the formation of more (A). Cross-resistance between the antibiotics was demonstrated in 12 antibiotic-resistant strains of *Escherichia coli*. Cross-resistance also developed to viomycin, but not to 12 other antibiotics produced by actinomycetes. It is concluded that the two antibiotics are closely similar chemically, and identical in their antimicrobial activity. G. B.

PHARMACOLOGY AND THERAPEUTICS

Chlorhexidine for Local Treatment of Burns and Scalds. J. C. Grant and J. C. Findlay. (*Lancet*, 1957, **1**, 862.) A method is described for the treatment of burns using a 0·5 per cent solution of chlorhexidine. The patient after admission to hospital is sedated, and, if necessary, given intravenous fluid. The burn is cleaned with 1 per cent cetrimide, rinsed with normal saline and covered with gauze soaked in 0·5 per cent chlorhexidine solution, using aseptic precautions. The gauze dressings are resoaked with the chlorhexidine solution twice daily, and twice a week are removed to allow inspection of the lesion and removal of separating sloughs. The areas are not left exposed until epithelial cover is complete. In 108 treated patients results have been excellent and

infection rare. Superficial burns heal rapidly by regeneration of the surviving epithelium, and in the deep burns, after separation or removal of the sloughs, a clean granulating surface presents, which is eminently suitable for grafting. The practical advantages of the method over aseptic and antibiotic methods are discussed. G. F. S.

Diamorphine and Pholcodine, Comparison of, as Cough Suppressants. E. S. Snell and P. Armitage. (*Lancet*, 1957, **1**, 860.) A controlled clinical trial is reported of a comparison of the relative effectiveness as cough suppressants of heroin linctus B.P.C., a pholcodine preparation and a placebo in 45 patients with chronic coughs. The mixtures were numbered 1, 2 and 3 and the patients instructed to take 120 minims at night using each mixture for two nights. They were asked to state their preference, which was recorded. It became clear that patients were rarely able to state their preferences since they usually gave a tie for first or last place, so for statistical analysis a new type of "restricted sequential procedure" was adopted, which is described. At the 5 per cent level of significance there was no evidence of a difference between the heroin and pholcodine preparations, but both were more effective than the placebo. G. F. S.

Dipipanone Hydrochloride, Analgesic Activity of. D. A. Cahal. (*Brit. J. Pharmacol.*, 1957, **12**, 97.) The analgesic activity of dipipanone hydrochloride was assessed against ischaemic muscular pain in healthy human volunteers. The drug was administered by subcutaneous injection, 0·5N-saline being used as a control since pain caused by the drug indicated its use rather than normal saline. Observations of pain threshold were made at ten minute intervals during the first hour of the action of the drug, and thereafter at hourly intervals. Peak effects were registered about two hours after administration at all dose levels of the drug. The lowest dose causing a significant rise in pain threshold was 10·0 mg. The effects of increase in dose showed a linear function between log dose and response. The most common side effects observed were drowsiness, euphoria, nausea and vertigo. Two of the twenty-six subjects were hypersensitive to the drug. The drug appears to be a histamine liberator, indicated by the generalised pruritus in some subjects and weal and flare production on intradermal injection, together with incidence of epigastric discomfort and headache. Injection of the drug in all subjects was painful and often the pain was very persistent. Many subjects had tenderness and induration at the sites of subcutaneous injection for many weeks. After intradermal injection, slight ulceration often occurred, the ulcers healing only slowly and leaving pigmented scars. G. P.

Ethylcrotonyl Carbamide, a New Sedative. T. Canbäck, N. Diding and C. G. Lindblad. (*Svensk farm. Tidskr.*, 1957, **9**, 221.) This compound (Ektylcarbamide) may be obtained by dehydrobromination of carbromal. It shows *cis-trans-* isomerisation, and two stable forms may be obtained, melting at 198° and 158° respectively. It has been reported that, with rats, a sedative effect is obtained with oral administration of 1 per cent of the LD50, while 48 per cent had no permanent effect: 90 per cent is required for full hypnotic action. The wide margin between sedative and hypnotic action indicates that the compound should be more reliable than other sedatives. The present authors have partially confirmed this, in that they have found the minimum lethal dose (LD50) for mice to be 1 g./kg. G. M.

Histamine Release Inhibition *In Vitro* and Antianaphylactic Effects *In Vivo* of some Chemical Compounds. F. C. McIntire, R. K. Richards and L. W. Roth. (*Brit. J. Pharmacol.*, 1957, **12**, 39.) Some 2,500 compounds were tested for inhibitory activity on the anaphylactic reaction *in vitro* on the "platelet fraction" of blood from a rabbit sensitised to egg white, and *in vivo* in guinea pigs similarly sensitized. Antihistamine activity was also measured *in vivo* on guinea pigs against histamine aerosols. Several compounds were effective inhibitors of the reaction *in vitro*, but proved very toxic *in vivo* and in maximum tolerated doses none of these gave significant protection in sensitised animals when the antigen was given intravenously. When the antigen was administered as an aerosol three of the substances afforded some protection, but none of these showed any promise of being useful clinically. A number of other drugs, among them aspirin and sodium salicylate, reported to alleviate allergic symptoms or prevent anaphylactic shock, failed to inhibit histamine release *in vitro*, although in rabbits the antianaphylactic action of aspirin was confirmed *in vivo*. The histamine release by antigen from the blood of rabbits which had been treated with sufficient aspirin to protect them against anaphylaxis was not inhibited when the blood was tested *in vitro*. These results are inconsistent with the view that aspirin protects against anaphylactic shock by interfering with the antigen-antibody reaction. Substitution of a carbomethoxy group for a carbamide group in the β-position of certain quaternary pyridinium compounds changed an antianaphylactic action to one of histamine release, suggesting the possibility of a common basic mechanism of histamine release and of prevention of release, probably at the cell membrane. None of the substances active against antigen aerosols had any effect on the actions of histamine aerosols.

G. P.

5-Hydroxytryptamine, Role of, in the Inflammatory Process. B. Gözsy and L. Kátó. (*Science*, 1957, **125**, 934.) Experiments in rats have shown that while histamine and 5-hydroxytryptamine are liberated from mast cells on injury, the two substances show a different behaviour in the defence processes. 5-HT. was found to be more potent than histamine in inducing an accumulation of Indian ink or trypan blue at the site where they were administered percutaneously. The phagocytic activity of the monocytes *in vitro* was influenced by histamine, but not by 5-HT. These two substances therefore play a different role on the defence mechanisms. G. F. S.

Iron Preparations, Intramuscular, Local Effects and Mechanism of Absorption of. C. R. Beresford, L. Golberg, and J. P. Smith, (*Brit. J. Pharmacol.*, 1957, **12**, 107.) The retention in muscle of four iron-polysaccharide complexes after intramuscular injection deep into the gluteals of the rabbit was not closely related to diffusibility of the complexes in agar. There was also considerable variation among the compounds in the extent of the retention. The major part of the absorption of the iron occurred during the first 72 hours after injection. An acute inflammatory reaction was induced by the drug at the site of injection, and this appeared to govern, by increased lymphatic transport of the iron complex, the absorption after injection. The local inflammatory response in rats was accompanied by degenerative changes in the muscles, but regeneration was rapid, tissue repair being complete in less than one month, leaving no residual damage to the muscles, nerves or neighbouring tissues. Rapid fixation by tissue macrophages impeded absorption and, with some complexes, this factor may make much of the injection inaccessible. G. P.

Poliomyelitis Vaccine, British, Assessment of. Report to the Medical Research Council by the Poliomyelitis Vaccines Committee. (*Brit. med. J.*, 1957, **1**, 1271.) The report describes an investigation of the protective effect against clinical poliomyelitis in children of the vaccinations carried out in Great Britain under the auspices of the Ministry of Health and the Department of Health for Scotland in May and June, 1956. The vaccine used was a formolized vaccine containing MEF-1 type II and Saukett type III strains as used in American trials but with Brunenders type I strain instead of the more virulent Mahoney type I strain used in America. 178,161 children received two injections, each of 1 ml., at intervals of at least 3 weeks. In a sample 1 per cent, visited the day after receiving the first injection, local reactions were found to the extent of 2 to 3 per cent but were always mild. Only 6 children developed illness possibly related to the inoculation and in none of them was there a definite clinical or laboratory relation. Controls were children registered with a local authority for vaccination. During 6 months following the vaccinations poliomyelitis was reported in 512 registered children, vaccinated and unvaccinated. Among 74,660 vaccinated children aged 5½ to 9½ years, there was 1 case of paralytic poliomyelitis, corresponding to an attack rate of 1·3 per 100,000. The corresponding figure for unvaccinated children was 8·2 per 100,000. Among 74,024 children aged 1½ to 5½ years the corresponding figures were 4·1 and 20·1 per 100,000 respectively. The incidence of non-paralytic poliomyelitis was not influenced by the vaccination. 32,379 children received a single injection only and there was insufficient evidence on which to judge the effect. Although the protection conferred by the vaccine was not complete, the incidence of paralytic disease in the vaccinated children was only about one-fifth of the incidence in the unvaccinated. The degree of protection was probably quite substantial over the ages 1½ to 9½ years and although the number of observations was small it appeared that the Brunenders strain conferred protection against the prevailing type I infection. H. T. B.

Reserpine, Antileukaemic Action of. A. Goldin, R. M. Burton, S. R. Humphreys and J. M. Venditti. (*Science*, 1957, **125**, 156.) The antileukaemic action of reserpine was studied in mice inoculated with a suspension of leukaemic cells and left until the local tumour had reached an approximate diameter of 12 mm. and the systemic disease had developed. These mice were then randomised and the designated groups were treated with a single injection of reserpine. A single treatment produced an almost threefold increase in the remaining lifetime of mice with advanced leukaemia. Inhibition of the growth of the local tumour was observed consistently in the reserpine-treated mice. Reserpine also appeared to retard the usual terminal leucocytosis in the peripheral blood. A regime of daily treatment with small doses of reserpine may be superior to a large single dose. Several derivatives of reserpine also possessed some antileukaemic activity, e.g., rescinnamine, deserpedine and *iso*reserpine. The mechanism by which reserpine exerts its antileukaemic action is not known and whether the action is direct or mediated through the host is not clear. 5-Hydroxytryptamine administration alone did not influence the course of the leukaemia. Both leukaemic and non-leukaemic animals suffered severe depression at the higher dose levels of reserpine employed. This was overcome with (+)-amphetamine which did not affect the course of the experiment in any way. G. P.

Tranquillising Drugs; Allergic Reactions to. C. Bernstein and S. D. Klotz. (*J. Amer. med. Ass.*, 1957, **163**, 930.) Meprobamate gave rise to allergic reactions in 8 patients observed by the authors and in 7 other patients reported to them. The reactions included urticaria, fever, arthralgia, purpura and, in a woman being treated for lupus erythematosus, a flare-up of new skin lesions. Several of the patients with these reactions had previously used mephenesin, and there is a possibility that mephenesin may pre-sensitise patients to meprobamate. Reserpine and chlorpromazine have also caused side-effects essentially different and more variable in type. Bearing in mind the enormous quantities of these tranquillising drugs which are now being used, the incidence of allergic reactions has been extremely low, but the hazard must be kept in mind as some of the symptoms, especially the fever, may confuse the issue in the clinical course of a patient under treatment. S. L. W.

***Veratrum album*, Pharmacological Study of a New Acetone Fraction of Alkaloids of.** V. Trčka and M. Vaněček. (*Českoslov. Farm.*, 1957, **6**, 68.) Results of pharmacological tests on an acetone fraction prepared from the roots of *Veratrum album* are reported. Hypotensive studies were carried out on rabbits, cats and dogs. In comparison with Puroverin (proveratrines A and B), the preparation, termed "VER V", had one-tenth to one-fifth of the hypotensive activity in dogs, but its toxicity in mice was only one-thirtieth of that of Puroverin. Its emetic effect on dogs was also less marked. E. H.

APPLIED BACTERIOLOGY

Bacteria, Viable Count of, a New Technique. A. Guha. (*Nature, Lond.*, 1957, **179**, 1360.) The author describes a method by which viable cells may be identified in a culture of viable and non-viable bacteria when counted microscopically. Cultures of *E. coli* were prepared in a medium containing 1 per cent 2:3:5-triphenyltetrazolium hydrochloride. Counts of the culture were made by the haemocytometer method, using 4 per cent formalin as the dilution liquid. Bacteria which were living before the formalin treatment were distinguished by a reddish tinge, the colour being due to red formazan bodies which are produced by reduction of the tetrazolium salt by the mitochondria. Dead bacteria in the culture appeared completely transparent, so that both a total and viable cell count could be obtained. It was shown that the stained cells, not treated with formalin, were capable of growth. Unstained cells did not grow. The tetrazolium salt was apparently devoid of toxic effects to the bacteria used in these experiments. B. A. W.

***Mycobacterium tuberculosis*, Cultivation of, on Semi-solid Agar Media for Rapid Drug Sensitivity Tests.** R. Knox and R. Woodroffe. (*J. gen. Microbiol.*, 1957, **16**, 647.) This paper reports results supporting previous descriptions by the same authors of the use of semi-solid media for rapid cultivation of *M. tuberculosis* in the performance of drug sensitivity tests. Media used were those of Kirchner (without penicillin), Dubos and Fisher, all being used as semi-solid media (0·125 per cent agar) and as liquid media. Sensitivity of *M. tuberculosis* to isoniazid, streptomycin and aminosalicylic acid were determined. The organisms used were *M. tuberculosis* H37Rv strain, variants of this strain made resistant to isoniazid and streptomycin, and aminosalicylic acid resistant strains of *M. tuberculosis*. Using semi-solid media and heavy inocula, results could be read in 2 days with a hand lens and in 3 to 5 days with unaided vision. With liquid media results were less easy to read and interpret, the

(ABSTRACTS *continued on page* 704.)

the imported drugs sold in the Indian bazaars. The plants are arranged in alphabetical order of genera (the plant family being given in parenthesis). Many of the common alternative botanical names are quoted, with cross references to the accepted names: important vernacular names commonly used in different regions of India are also recorded and indexed. The various parts of the plant which comprise the drugs are then named together with a condensed list of medicinal uses. The active principles of the drugs are briefly named, together with references to published work thereon up to 1953, and an index of chemical constituents is provided. Finally, the distribution of the plants in different regions of India is stated but no descriptions of the drugs nor of the plants are given.

The volume is well produced, it is a valuable addition to our references on vegetable drugs and its compilation is the result of a very large amount of useful work. By its very nature, however, it must leave more questions unsolved than answered; thus the reader has no means of identifying an unknown drug or of confirming the characters of a named specimen by means of this volume, nor of tracing such a description in the literature; for the references quoted are almost entirely on chemical composition. These are by no means exhaustive and are (one imagines, purposely) uncritical: thus three separate sets of references are quoted to show that the principal alkaloid of *Datura metel* is atropine, is hyoscyamine, is scopolamine, respectively. Space could have been saved by a more critical appraisal of such contradictory information and might well have been used in giving references to publications on drug morphology and anatomy where known (and much does exist in widely scattered publications). An indication of toxicity or dosage might also have been given, for some relatively harmless materials are recorded along with other highly toxic drugs, e.g., *Illicium verum* and *I. religiosum* are both described as "stomach, carmin." These criticisms should not belittle the valuable nature of this book, and it is to be hoped that the detailed investigation of the rich field of Indian medicinal plants will be continued actively and critically.

J. M. ROWSON.

(ABSTRACTS *continued from page* 701.)

end point defining the initial minimal inhibitory concentration being much sharper in semi-solid media. Moreover, only in semi-solid media could be distinguished the later growth of colonies which gave a measure of the variability of resistance within a culture. These presumptive resistant colonies appeared most often with Kirchner semi-solid medium containing isoniazid and less frequently with the other 2 drugs, but the retesting of cultures from the colonies of the isoniazid medium showed that drug resistance did not always occur. If, however, the drug was not added to the inoculated medium until the 2nd or 3rd day (by this time minute colonies had appeared) a few large colonies containing truly resistant organisms later developed. Differing rates of decay of isoniazid in the different media were observed. The end points obtained with all 3 drugs in the semi-solid media were sharp and consistent. With aminosalicylic acid, the inhibitory concentration varied greatly with the inoculum size and with different strains and was attributed in part to the antagonism of *p*-aminobenzoic acid. The agar concentration used appeared to be optimal: discrete colonies developed and yet the culture was sufficiently fluid to be sucked up in a dropping pipette when picking out single colonies for subculture. The authors conclude that for all 3 drugs the Fisher semi-solid agar gave the most satisfactory results. B. A. W.