ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Benadryl and Pyribenzamine Hydrochlorides, Identification and Differentiation of. T. J. Haley. (*J. Amer. pharm. Ass., Sci. Ed.*, 1948, **37**, 294.) The reactions of 12 precipitants and 16 colorimetric reagents with benadryl hydrochloride (diphenhydramine hydrochloride) and with pyribenzamine hydrochloride (tripelennamine hydrochloride) are described. Only chloroplatinic acid, 5 per cent., could be used by precipitation for identigfication and differentiation between these two. Benadryl gives a granular orange precipitate of leaf-like crystals in crosses with some cigar-shaped crystals. Pyribenzamine gives a granular orange precipitate of rosettes and sheaves of flat plates on drying. The colour reactions are distinctive; with concentrated sulphuric acid, benadryl gives an orange colour and pyribenzamine a greenish yellow colour; complete destruction of the organic compounds by the strong acid results in a dark brown to black solution unsuitable for qualitative analysis. With potassium dichromate and concentrated sulphuric acid, benadryl forms a yellow solution and pyribenzamine a brown solution. Resorcinol and concentrated sulphuric acid gives an orange and then reddish orange colour with benadryl, which becomes wine-coloured when diluted with water; the same reagent gives a yellowish green and then deep green colour with pyribenzamine which becomes olive-green on dilution with water. Furfurol 1 per cent. overlay sulphuric acid gives an orange-brown colour changing to yellow-green on shaking with benadryl, and a black colour which does not alter on shaking with pyribenzamine. Mandelin's reagent gives a red colour with oily red globules with benadryl, and a chocolate-brown colour with pyribenzamine; Marquis' reagent, yields a colour change with benadryl from canary-yellow to reddish-orange to chocolate-brown, and from red to deep reddish-brown with pyribenzamine; Mecke's reagent, gives a canary-yellow then reddish-yellow colour with benadryl, and a nut-brown colour with pyribenzamine; and Fröhde's reagent gives a canary-yellow colour followed by orange and then red with benadryl, but with pyribenzamine yields a pale pink followed by a deep rust colour.

L. H. P.

Progesterone, Photometric Determination of. E. Diding. (*Svensk. Farm. Tidskr.*, 1949, **53**, 269.) The method is based on the formation of a red dinitrophenylhydrazone, soluble in chloroform. The colour is stable for at least 24 hours. Details are as follows: 5 ml. of an alcoholic solution, containing 0·25 to 1·25 mg. of progesterone is treated with 3·0 ml. of a freshly-prepared 0·25 per cent solution of 2·4-dinitrophenylhydrazine in 2M hydrochloric acid. The mixture, in a covered beaker, is heated on the water-bath for 15 minutes, then treated with 10 ml. of 2M hydrochloric acid, and heated for a further 30 minutes to remove the alcohol. The precipitate is transferred to a sintered glass filter, washed with hydrochloric acid, and then with water. After drying *in vacuo*, the dinitrophenylhydrazone is dissolved in chloroform to 100 ml., and the extinction is determined at 440 mμ. For solutions in oil, 5 ml. of the solution is dissolved in 10 ml. of hexane and extracted with 4 quantities, each of 5 ml., of alcohol

(90 per cent.). The alcoholic extracts are washed with 20 ml. of hexane, which is then washed with 2 quantities, each of 5 ml., of alcohol. The alcoholic solutions are filtered and evaporated to dryness, and the residue is dissolved in alcohol and treated as before. G. M.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

***nor*-Adrenaline in Adrenal Medulla, Evidence for Occurrence of.** M. Goldenberg, M. Faber, E. J. Alston and E. C. Chargaff. (*Science*, 1949, **109**, 534.) By paper chromatography using phenol saturated with water as eluent in an atmosphere of hydrogen chloride it has been found that samples of U.S.P. Reference Standard Epinephrine contained 12 to 18 per cent. of *nor*-adrenaline and that one sample contained as much as 36 per cent. The adrenaline fractions from three chromaffin tissue tumours were found to contain 50 to 90 per cent of *nor*-adrenaline. It is pointed out that adrenaline and *nor*-adrenaline differ significantly in their pharmacological actions both as regards effect on cardiac output and on carbohydrate metabolism. If it is assumed that natural adrenaline as secreted by the adrenal gland maintains a constant content of *nor*-adrenaline, present concepts of adrenal secretion remain valid. If, however, under varying physiological conditions the *nor*-adrenaline content of the secreted natural adrenaline varies then it is considered that current views of the physiology of the adrenal medulla may have to be modified. Under pathological conditions such as in pheochromacytoma, hæmodyamic effects and the influence on carbohydrate metabolism are profoundly altered by the high content of *nor*-adrenaline in the secreted medullary hormone. The biological assay of tumour extracts is discussed. F. H.

BIOCHEMICAL ANALYSIS

Barbiturates in Tissue; Determination by Ultraviolet Absorption Spectrophotometry. G. V. R. Born. (*Biochem. J.*, 1949, **44**, 501.) A procedure based on ultraviolet spectrophotometry is described for the quantitative determination of very small amounts of barbiturates in tissues and blood. The tissue is homogenised and proteins precipitated by ethyl alcohol. The barbiturate in the acidified protein-free filtrate is extracted with ether and passed into alkali. To two samples of this alkaline solution are added phosphate or borate solutions which bring the *p*H to different known values. The extinctions at 23 mμ of the resulting solutions are measured and from these the concentration of barbiturate in the tissue can be determined by calculation. Complete elimination of contaminants is not attemped. The difficulty due to the simultaneous extraction of barbiturate and impurities absorbing in the same region of the ultraviolet is overcome by the use of differential spectrophotometry, depending on extinction-*p*H relationships. The procedure is rapid, accurate and sensitive, permitting the extinction of concentrations of barbiturates as low as 1 to 2 μg./ml. in pure solution.
S. L. W.

Nicotinamide in Biological Materials, Fluorimetric Estimation of. D. K. Chaudhuri and E. Kodicek. (*Biochem. J.*, 1949, **44**, 343.) The material under examination (5g.) is cut finely, ground with sand and 0·1N hydrochloric acid (1 to 2 ml.), transferred with 40 ml. of water to a 100-ml. beaker on a boiling water-bath and heated for 30 minutes. After

cooling, hydrochloric acid is added to *p*H 2, the mixture is centrifuged, the residue washed with 10 ml. of 0·1N hydrochloric acid and again centrifuged. The combined liquids are adjusted to a known volume (usually 40 ml.) with 0·1N hydrochloric acid, 6 ml. of a freshly prepared 25 per cent. solution of metaphosphoric acid is added and the liquid centrifuged after standing for 5 to 10 minutes. The clear solution is adjusted to *p*H 9·4 to 9·6, heated on a boiling water-bath for 30 minutes, cooled, adjusted to *p*H 7·2 and made up to 50 ml.; after filtration (Whatman No. 5) it is then treated with cyanogen bromide solution. Three determinations are made—a blank, the unknown filtrate (containing 5 to 25 μg. of nicotinamide), and the unknown to which is added an internal standard (25 μg. nicotinamide). After mixing, the three solutions are heated in a water-bath for 4 minutes at 56° to 58°C., cooled and made up to 15 ml. with water. 5N sodium hydroxide (8 ml.) is added, the volume made up to 30 ml. with water and the fluorescence read after 45 minutes at room temperature in the dark. Details of the calculation and of the reproducibility of the results are given; the method estimates the total nicotinamide content, including the free and bound forms. Specific and reproducible results were obtained for biological materials and for cereals, and the results agreed well with the reported micro-biological values. Practically all the vitamin in rat organs and muscles seemed to be present in the form of the amide, bound or free. In bran, no nicotinamide was detected before or after digestion. The breakdown product of the "precursor" of nicotinic acid present in bran appeared to be the free acid and not the amide. Yeast and wheat germ contained about 50 per cent. of the vitamin present in the amide form, bound or free.

R. E. S.

CHEMOTHERAPY

Analgesic Compounds, Potential, Preparation of. D. J. Brown, A. H. Cook and I. M. Heilbron. (*J. chem. Soc.*, 1949, Supp. 1, S.106, S 111 and S 113.) In a search for more potent analgesics than amidone analogues have been prepared and examined. Attempts to introduce thiazolyl groups into 1-diethylamino-3-phenylpentan-4-one were unsuccessful. 4-Methyl-2-(3′-diethylamino-1′-phenylpropyl) thiazole and related componds were prepared from the corresponding γ-dialkylamino-α-phenylthiobutyramide but it was not found possible to introduce ester or ketone groupings on the *tert*-carbon atom. 5-Carbethoxy-4-methyl-2-(3′-diethylamino-1′-phenylpropyl) thiazole and 4-methyl-2-(4′-diethylamino-2′-acetyl-2′-phenylbutyl)thiazole, obtained as viscous oils, were without significant analgesic action. Introduction of basic groups into 4-phenyl- and 4-methyl-2-α-carbethoxybenzyl thiazole failed to yield analgesic properties. Direct carbethoxylation or propionylation of 2-benzylthiophen followed by introduction of a basic side chain yielded products having analgesic properties. Thus 2-(3′-diethylamino-1′-carbethoxy-1′phenylpropyl)thiophen had an activity approximately one-third that of pethidine while 2-(3′-morpholino-1′-carbethoxy-1′-phenylpropyl)thiophen appeared to be four times as effective as pethidine. Other compounds prepared, such as 2-phenyl-2-diethylaminoethyl cyclohexanone were inactive.

F. H.

PHARMACOGNOSY

Cascara sagrada, Frangula and Oak Barks, Distinction between the Powders. G. G. du Chatelier. (*Ann. pharm. franc.*, 1948, **6**, 507.) The powders of these three barks can be distinguished not only by the

presence or absence of stone cells but by the characters of the crystals in the sheaths surrounding the fibres. *Oak bark*, has prismatic crystals with numerous truncations with poorly defined edges, so that the crystals appear rounded. They are elongated with the long axis at right angles to the fibres. Monoclinic crystals (rhombs) very rare. *Cascara sagrada:* crystals generally square and smaller than those of oak bark. Truncations rare, or if present, sharply defined so that the crystals are more regular in shape than those of oak bark. Monoclinic crystals frequent and mostly square. *Frangula bark:* crystal forms intermediate betwen those of the other two powders. If the crystals in oak bark are slowly dissolved in hydrochloric acid, a detached lignified envelope can be seen within the pecto-cellulose compartment of the crystal sheath; this detached envelope cannot be seen in the other two barks when treated in like manner. J. W. F.

PHARMACOLOGY AND THERAPEUTICS

Antabuse and Alcohol, Effect of on Respiration and Circulation. E. Asmussen, J. Hald, E. Jacobsen and G. Jorgenson. (*Acta Pharmacol. Toxicol.*, 1948, **4**, 297.) Alcohol does not produce circulatory or respiratory symptoms in normal human beings in a dose equivalent to 20 g. of absolute alcohol but when experimental subjects were treated with antabuse 12 hours before the intake of alcohol there was a marked increase in ventilation, a decrease in alveolar carbon dioxide, an increased pulse rate, and a slight increase in cardiac output and oxygen consumption. Antabuse-prepared individuals under the influence of alcohol must form a substance that directly or indirectly increases the irritability of the respiratory centre, and the feeling of dyspnœa is due not to a bronchoconstriction but to this increased irritability. The comparatively slight increase in cardiac output shows that there is no serious risk of too heavy a load on the heart after clinical application of antabuse, even though patients complain of serious palpitation and subjective dyspnœa. S. L. W.

Antabuse and Alcohol, Formation of Acetaldehyde after Ingestion of. J. Hald and E. Jacobsen. (*Acta Pharmacol. Toxicol.*, 1948, **4**, 305.) After intake of alcohol, human subjects treated with antabuse show a much higher concentration of acetaldehyde in blood than do untreated individuals. The authors discuss the possibility that the symptoms observed after antabuse treatment may be explained as the result of this increased formation of acetaldehyde. S. L. W.

Iodophthalein, Excretion from the Human Organism. H. O. Bang and J. Georg. (*Acta Pharmacol. Toxicol.*, 1948, **4**, 87.) A quantitative method for the determination of amounts as small as 1 μg. of iodophthalein in fæces and organic fluids is described. Injections of iodophthalein, 500 mg. intravenously, were given to normal persons, and the concentrations in plasma and urine determined. After the injection a concentration of 10 to 20 mg. per cent. is obtained. This concentration falls steadily, reaching 2 or 3 mg. per cent. 24 hours after the injection. During the next few days iodophthalein is still demonstrable in the plasma and the concentration reaches zero by about the fifth day. Only small amounts of the substance are excreted in the urine. The great bulk of the substance is excreted in the fæces, the

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