CURRENT LITERATURE

The antagonism of the vascular effects of 5 Hydroxytryptamine by BOL 148 and sodium salicylate in the human subject *by W. E. Glover, R. J. arshall and R. F. Whelan, (1957):* **Brit. J. Pharmacol., 12,** *498.*

5 Hydroxytryptamine (5HT) injected intra-arterially into the fore-arm of normal human beings produced subjective sensations of tingling and a transient increase followed by a decrease in blood flow proportional to the dose. These effects were antagonised by intra-arterial and intravenous 2-bromo-(+)-lysergic acid diethylamide bitartrate (BOL 148). Sodium salicylate also antagonised them, but the intra-arterial dose needed produced a systemic blood concentration approximating that obtained by intravenous injection. Both antagonists were specific, as no changes were noted with nor-adrenalin and histamine responses, but while BOL 148 acted locally, directly on the receptors of 5HT, sodium salicylate acted through an unknown indirect mechanism which might involve hormonal, possibly adrenocortical, responses.

R. A.

A Note on the acute toxicity of hydrolysable and condensed tannins *by M. G. Armstrong, E. G. Clarke and E. Cotchin., (1957)* **: J. Pharm. Pharmacol., 9,** *98.*

The hydrolysable tannins yield sugars and gallic acid on acid hydrolysis, the condensed type yield insoluble substances called phlobaphenes. The toxicity of tannic acid, acorn myrabolon, sumac and chestnut tannins as examples of the former were compared with spruce; quelracho, mimosa, mangrove and gambier, as examples of the latter. They were given by various routes to mice. While intravenous injections of both were instantaneously fatal, by intra-peritoneal, intramuscular and subcutaneous routes, the hydrolysable type had a higher death rate the lesion being centrolobular hepatic necrosis. If the diminished toxicity of the condensed type is true also when applied to burnt areas, then the further investigation of this line of treatment is warranted.

R.A.

Pharmacology of a new hypotensive steroid : 17- ∝ Propyl-4, 5β-Dihydro-19-Nortestosterone *by F. M. Sturtevent (1957)* : **J. Pharmacol. Exper. Therap., 121**, *369.*

The antihypertensive action of 17- ∝ -propyl-4-5β-dihydro-19 nortestosterone (5c-6584) was studied in meta-corticoid, meta-renal and adrenal regeneration hypertensive rats in acute and chronic trials. The steroid caused a significant drop in blood pressure in all three types in both trials. It showed no other endocrinal activity characteristic of its structure when assayed for adrenocortical oestrogenic and androgenic effects. It had also no antiarrhythmic or anaesthetic action, but potentiated barbiturate sleeping time in mice. The possible mechanism of hypotension which appears unrelated to endocrinal effects is under investigation.

R. A.

Morphine Antagonism *by F. H. Shaw; S. Gershan and G. A. Bentley, (1957)* : **J. Pharm. Pharmacol., 9**, *666.*

While amiphenazole is used fairly satisfactorily as a partial clinical morphine antagonist it does not antagonise completely the nausea and respiratory depression; hence a better antagonist is desirable. A series of compounds were tested in dogs, among these cyclizine chloride, chlorcyclizine and avil exhibited partial antagonism, the former two were as good as amiphenozale and tetrahydroaminacrin. A mixture of the last two drugs were found effective in doses less than half the arousal dose of each. The authors conclude that basic compounds with one or more N containing rings and one or more amino side chains may display antimorphine properties.

R.A.

The assay of Acetylcholine on the superfused frog rectus muscle *by A. Ahmed and N. R. W. Taylor, (1957)* : **J. Pharm. Pharmacol., 9**, *536.*

The superfused method of assay was accurate as the bath method but more sensitive. Responses could be obtained with 1/10th to 1/20th the dose of acetylcholine needed for the latter technique.

R. A.

Metabolism of Insuline—I^{131} in the Extrahepatic Tissues *by D. R. Drury, M. A. Karasek and A. N. Wick (1958)* : **Am. J. Physiol., 192,** *501.*

Using 3 types of rabbit preparations intact, eviscerated nephrectomized, eviscerated with kidney intact the distribution and degradation of insulin I^{131} was studied. Trichloracetic acid (TCA) precipitation of plasma removed the intact molecule, leaving the degradation products in the soluble part, hence estimation of I^{131} in the plasma and the TCA soluble fraction was carried out. The biological activity of insulin was also measured in some of the eviscerated animals by estimating the rate of fall of blood glucose; the glucose space was taken as 250 ml/kg. Degradation was rapid in the intact and operated animals with intact kidney, and much slower in the eviscerated and nephrectomized animal which, therefore, was chiefly studied the kidney apparently playing a major role in degrading it.

Insulin I^{131} passed fairly rapidly into the tissue spaces and in a steady state the plasma concentration reflected its tissue activity. The biological activity, however, was highest in the second hour after injection due either to sluggish movement back into the blood or binding (Stadie) by tissue.

R. A.

The effect of calcium and pH on the anaphylactic reaction *by J. L. ongar and H. O. Schild (1958)*: **J. Physiol , 140,** *272.*

Chopped lungs of ginnea-pigs sensitized to egg albumin, placed in antigen containing tyrode solution released histamine. By noting the effect of removal and addition of calcium, magnesium, potassium and sodium and also adding the calcium chelating agent–versene–the authors found that calcium was needed for the anaphylactic reaction but not for histamine releases by histamine liberators–octylamine and 48/80. The pH was also vital the optimum being 7.8 and minimum 6.2, calcium and pH were interdependent, inhibition by absence of one factor was compensated by the other. The suggestion is made that calcium is needed for the activation of an enzyme system involved in the anaphylactic reaction, the pH influencing the dissociation of calcium.

R. A.

The effect of intraluminal application of 5 - Hydroxytryptamine and 5 - Hydroxytryptophan on peristalsis, the local production of 5 - HT and its release in relation to intraluminal pressure and propulsive activity *by Edith Bulbring and R. C. Y. Lin (1958)*: **J. Physiol., 140,** *381.*

An improvement of the various modifications of the Trendelenburg method of recording peristalsis has been devised, where-in drugs could be used either in the bath-outside the isolated intestinal strip-or inside the lumen, and the peristaltic reflex elicited by a constant automatic slow inflow rate causing a gradual pressure rise. The pressure change, peristaltic, propulsive activities, and outflow volume are recorded.

The effects of 5HT, lysergicacid diethylamide (LSD), 2 brom-D-Lysergic acid diethylamide (BOL), marsilid, pyridoxal, acetylcholine (ACh), histamine, hexamethonium, procaine, 5 hydroxytryptophan (5HTP) and phenyl diguanide applied both inside and outside were studied.

The strip effluent contained 5HT, the amount related to the volume and intraluminal pressure. Reduction after several hours of peristalsis was prevented by marsilid, while 5HTP and pyridoxal in the inflow greatly increased its output.

The data on all the other drugs lead the authors to conclude that peristalsis is set up by stimulation of pressure receptors in the mucosa; 5HT which is produced and stored locally, lowering the threshold for the stimulus.

Intraluminal 5HT stimulated activity, while LSD and BOL inhibited it but they, as well as 5HT, behaved alike applied outside, all inhibiting in low and abolishing it in high concentration. ACh and histamine used the same way, stimulated in low and prevented peristalsis in high concentrations due to spastic contraction. In the lumen the former had similar effects, but histamine was inactive. Procaine abolished action both inside and outside and hexamethonium on application outside, but in both these cases 5HT could be recovered from the strip effluent.

R. A.

Blood ammonia elevation and toxicity from intravenous L-amino acid administration to dogs: the Protective role of L-Arginine *by Fahey, Perry and McCoy, (1958)*: **Am. J. Physol., 192,** *311.*

The effect on blood and urine urea, ammonia and α-amino nitrogen of intravenous infusion of essential amino acid mixtures into dogs under pento-

barbital anaesthesia was studied, with and without the addition of ∝-arginine, and with prior administration of it. ∝-citrulline HCl and ∝-ornithine HCl were studied in the same way as arginine. The blood ammonia level was undisturbed with simultaneous administration of arginine and amino acids as against a marked rise with toxic manifestations and even fatality when given without it. On the basis of blood ammonia levels with ammonium chloride it was estimated that toxic fatal results occurred with levels of or above 30μg. ml. ammonia nitrogen. Prior arginine administration protected upto 3 hours and was less efficient at 6 hours. Urea formation in two hours was much higher with than without it. ∝-ornithine was as effective as ∝-arginine while ∝-citrulline was less effective. The results are an in vivo confirmation of the Krebs Hensellit cycle and stress the importance of this group of non-essential amino acids in the prevention of the toxicity of intravenous administration of the essential ones reported some times in literature.

R. A.

Effects of carbonic anhydrase inhibition on brain excitability *by Alan Koch and Dixon M. Woodbury (1958)* : **J. Pharmacol. Exper. Therap., 122,** *335.*

Experiments were carried out in rats and mice to show that acetozolamide and carbon dioxide raised the electroshock seizures threshold and abolished the extension phase of maximum electroshock seizures in a similar pattern. Tolerance to acetozolamide action was demonstrated with simultaneous cross tolerance for carbon dioxide. The nitrate ion also showed similar anticonvulsant action and tolerance, while the chloride ion had no such action. Since acetazolamide and the nitrate ions are carbonic anhydrase inhibitors and lead to increase in the total carbon dioxide in the brain cells and since carbon dioxide itself produces a similar effect, the anticonvulsant action of carbonic anhydrase inhibitors is attributed to their local action on the brain rather than to systemic acidosis.

R. A.

The action of dopamine on the arterial blood pressure of the guineapig *by O. Hornykiewicz. (1958)*: **Brit. J. Pharmacol., 13,** *91.*

Tbe vasodepressor action in guineapigs of dopamine (hydroxy tyramine, β-3 : 4-dihydroxyphenylethylamine) which is found as a precursor of nor-