Hyperglycaemia and insulin inhibition caused by drugs may be more common than hitherto believed, and studies both of structure-function relationships as well as mechanisms of insulin inhibition may throw light on a possible contributory cause of eventual insulin failure and the development of diabetes mellitus.

The relationship between chemical structure of a new dicarboxylic amino-acid derivative and antigastrin activity in the rat

A. L. ROVATI, *Department of Pharmacology, Rotta Research Laboratories S.p.A., Milan, Italy*

The antisecretory non-anticholinergic activity of a series of amino-acid derivatives (Rovati, Casula & Da Re, 1967a) has previously been investigated. The pharmacological properties of one of them N-benzoyl-N′,N′-di-*n*-propyl-DL-isoglutamine (CR 242*, xylamide†, Milid‡) (Rovati, Casula & Da Re, 1967b) was particularly studied.

Sixty rats were treated according to a technique modified from Lai (1964). The gastric secretion was stimulated by "Leo" gastrin tetrapeptide through continuous intravenous infusion at a dose of 25 mg/kg per hr. The infusion lasted 2 hr and secretion was collected every 10 min. An hour later, xylamide was injected intravenously at a dose of 500 mg/kg. A group of the animals was also injected with N-benzoyl glutamic acid which is xylamide less the amide group at equimolecular doses. Atropine at a dose of 30 mg/kg was also used. Histamine acid phosphate (5 mg/kg) and histamine and gastrin tetrapeptide at the doses indicated were also used as stimulating agents. The results obtained demonstrate that: (1) the stimulation induced by gastrin tetrapeptide gives a secretory response with a regression line of $y=0.096x+7.89$ ($F=29.3$) where $y=\mu$-equi H^+ and $x=$time in min; (2) xylamide produced a reduction of secretion that during the first 30 min diminished according to the regression line: $y=-0.466x+19.56$ ($F=22.90$); (3) N-benzoyl glutamic acid had no activity; (4) xylamide is also effective against histamine but ineffective against a combination of histamine and gastrin tetrapeptide. It seems important to emphasize the anti-gastrin activity of xylamide and the complete ineffectiveness of N-benzoyl glutamic acid. These compounds differ by an amide group. In the same way, gastrin lacks activity when the amide of the terminal amino-acid is missing (Gregory & Tracy, 1964).

* Laboratory denomination. † Common name. ‡ Trademark.

REFERENCES

GREGORY, R. A. & TRACY, HILDA J. (1964). The constitution and properties of two gastrins from hog antral mucosa. *Gut*, **5**, 103.

LAI, K. S. (1964). Studies on gastrin. *Gut*, **5**, 327–341.

ROVATI, A. L., CASULA, P. L. & DA RE, G. (1967a). Attività antisecretiva di alcuni nuovi composti privi di attrività anticolinergica. *Minerva Medica*, **58**, 3651–3653.

ROVATI, A. L., CASULA, P. L. & DA RE, G. (1967b). Farmacologia e tossicologia sperimentale di un nuovo prodotto non anticolinergico ad attività antisecretiva e gastroprotettiva (CR 242-Xylamide-Milid®). *Minerva Medica*, **58**, 3656–3670.

Alloxan on islet cell membrane potentials

P. M. DEAN* and E. K. MATTHEWS, *Department of Pharmacology, University of Cambridge, England*

The powerful diabetogenic action of alloxan may be explained by its ability to alter the permeability of pancreatic β-cells (Watkins, Cooperstein & Lazarow, 1964).