

sample provided by Dr. Fowden proved chromatographically indistinguishable from our *trans*-4-hydroxypipicolic acid, and its was similarly epimerized by hot baryta. Structural and stereochemical investigation of the *trans*-4-hydroxypipicolic acid from *Acacia* species is continuing, and details will be published elsewhere.

We thank Dr. L. Fowden for a sample of the acid from thrift and for comparing it with our imino-acid, and we are grateful to Dr. H. Plieninger and Dr. H. Vanderhaeghe respectively for samples of *cis*-3- and *cis*-4-hydroxypipicolic acids. This work was carried out during tenure of a General Motors Holden Fellowship (by P.I.M.).

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ANIMAL PHYSIOLOGY

Increase by Chlorothiazide of the Paralysing Activity of *d*-Tubocurarine Chloride

It is a well-established fact that chlorothiazide potentiates the hypotensive effects of ganglion-blocking agents¹⁻². However, the way this potentiation is brought about is not clear. It has been thought that chlorothiazide acts either by a direct hypotensive action², or by sodium depletion³, or by reduction in plasma-volume³, or as in the case of mecamilamine and possibly of pempidine, by a reduction in renal excretion⁴ of the ganglion-blocking agents. From a pharmacological view-point there is a good deal of similarity between the neuromuscular junction and the gangliarsynapsis.

We have therefore investigated whether the paralysing activity in a rabbit, treated with *d*-tubocurarine chloride, could be modified by a previous intravenous injection of chlorothiazide.

In evaluating the paralysing activity of *d*-tubocurarine we have taken into account: (a) the appearance of muscular insufficiency that allows the animal, when set in a lateral position, quickly to resume its normal stand-up position (partial paralysis); (b) the appearance of a muscular insufficiency that deprives the animal of its ability to resume its stand-up position (total paralysis); (c) the animal's death owing to a respiratory insufficiency.

We have summarized our results in Table 1.

It is evident that chlorothiazide pretreatment potentiates the neuromuscular-blocking activity of *d*-tubocurarine. Hydrochlorothiazide, on the other hand, is ineffective in 10-100 mgm./kgm. dose intravenously in increasing *d*-tubocurarine paralysis.

The mechanism of chlorothiazide action is not clear as yet.

Our results will be published elsewhere in detail.

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Are Mucosal Nerve Fibres Essential for the Peristaltic Reflex?

RECENTLY Bülbring and co-workers^{1,2} abolished the peristaltic reflex in an isolated piece of intestine by scraping off its mucous membrane and assigned an essential role in the initiation of the reflex to processes of sensory neurones which are distributed to the intestinal mucosa.

In the experiments reported here, an attempt was made to destroy the mucous membrane selectively by local administration of a protein-precipitating chemical. Silver nitrate and tannic acid were chosen as suitable chemical agents.

The method of eliciting the peristaltic reflex in an excised loop of guinea-pig ileum mounted in an organ bath³, was modified so that the output of each peristaltic wave could be directly measured; this permitted to distinguish unequivocally between peristalsis which propelled fluid in a cephalocaudal direction, and pendular activity which did not. In order to avoid formation of silver chloride, the tubings and the intestinal lumen were thoroughly flushed with distilled water before and after the administration of silver nitrate.

Among various concentrations tried, a 30 per cent silver nitrate and a 20 per cent tannic acid solution proved suitable when left in contact with the mucosal surface for about 10 and 30 sec. respectively. After such treatment peristaltic activity continued in its normal pattern of co-ordinated contractions of the longitudinal and circular muscle layers. The amount of fluid expelled was generally slightly reduced and so was the size of the longitudinal contractions and at the same time the response of the longitudinal muscle to acetylcholine, indicating that some damage had occurred to all layers of the intestinal wall. As controls revealed, part of this could be accounted for by the mechanical strain exerted on the wall by forcing the solutions and wash fluid through the lumen in a specified time. However, in two experiments, peristaltic activity was even increased after treatment with 30 per cent silver nitrate solution.

Histological investigation of these preparations, carried out by Dr. M. R. Crompton of the Department of Histology, showed that most of the mucous membrane and parts of the muscularis mucosae were destroyed.

Table 1. PARALYSING ACTIVITY OF *d*-TUBOCURARINE CHLORIDE IN RABBITS TREATED WITH CHLOROTHIAZIDE AND HYDROCHLOROTHIAZIDE

Pretreatment	mgm./kgm. i.v.	<i>d</i> -tubocurarine μgm./kgm. i.v.	Interval between the two treatments min.	Animals with partial paralysis/ treated animals	Animals with total paralysis/ treated animals	Dead animals/ treated animals
—	—	125	—	11/18	0/18	0/18
Chlorothiazide	100	125	10	7/7	7/7	2/7
"	"	125	15	2/2	2/2	0/2
"	"	125	30	3/3	0/3	0/3
Hydrochlorothiazide	100	125	1-14	7/9	1/9	0/9
"	10	125	6-18	4/6	2/6	0/6