

plus theophylline, $1 \times 10^{-3} M$, was somewhat puzzling. There was a small increase in enzyme output, a moderate increase in volume, and a small decrease in enzyme concentration over that observed when only DcAMP was added. Synergistic stimulation of enzyme concentration and output by theophylline in combination with DcAMP may be masked by a separate antagonistic secretin-like effect of theophylline.

Cyclic AMP is known to serve a regulatory role related to a number of enzyme activities and hormonal systems. DcAMP addition produced increased enzyme output with little secretory volume change. This may reflect an absent role for cAMP in the regulation of secretin activity in the in vitro rabbit pancreas preparation or a concentration of DcAMP insufficient to stimulate secretin activity. Theophylline enhances enzyme output in the in vitro rabbit pancreas preparation, most probably on the basis of phosphodiesterase inhibition. Secondly, it appears theophylline has a second secretin-like effect on pancreatic secretion which may be unrelated to cAMP^{23,24}.

Zusammenfassung. Nachweis, dass die Zufuhr von dibutyryl-zyklischem AMP (DcAMP) in vitro die Enzym-

produktion erhöht und zwar mit nur geringer Gewichtsveränderung des Kaninchenpankreas. Die Enzymproduktion wird ebenso durch Theophyllin vermehrt und es wird vermutet, das DcAMP der Vermittler der pankreozytären Wirkung im Kaninchen ist.

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Failure of the D-Analog of Angiotensin II-Amide [D-asp (NH₂)-D-arg-D-val-D-tyr-D-val-D-his-D-prol-D-phe (OH)] to Influence Water Diuresis in the Rat¹

An analog of val⁵-angiotensin II-amide composed of the D-amino acids instead of the L-amino acids has been synthesized by VOGLER et al.² and proved biologically inactive on the guinea-pig ileum (which contracts under the influence of val⁵-angiotensin II-amide) and on the cat's blood pressure.

Val⁵-angiotensin II-amide possesses a natriuretic and diuretic effect in the rat (PETERS³, BONJOUR et al.^{4,5}) which, in animals in water diuresis, results in a large increase in the osmolar clearance without a notable change or with a slight increase in the clearance of free water. The present experiments were undertaken in order to check whether the D-analog shared this somewhat peculiar effect of L-val⁵-angiotensin II-amide.

Water diuresis was induced in a group of 10 rats by infusing a hypotonic solution of glucose and fructose containing minimal amounts of NaCl (BONJOUR et al.⁵). After equilibration and a few control periods, the D-analog of angiotensin II-amide (kindly supplied by Dr. R. O. STUDER, Hoffmann-La Roche Ltd., Basel) was added to the infusion fluid at a rate of 0.25 µg/animal/min. No change occurred in urine flow. The same experiment was repeated in a second group of animals, increasing the dose of the D-analog of angiotensin II to 2.5 µg/animal/min. This higher dose also proved completely ineffective (Table).

Zusammenfassung. Während L-val⁵-Angiotensin II bei Ratten einen ausgesprochenen diuretischen Effekt zeigt, fehlt diese Wirkung bei dem D-Analogen.

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	Urine flow	Cosm (ml/kg/min)	CH ₂ O (ml/kg/min)
Control periods	0.59 ± 0.05	0.28 ± 0.03	0.30 ± 0.02
D-angiotensin (2.5 µg/min)			
1-15 min	0.62 ± 0.05	0.32 ± 0.02	0.30 ± 0.03
16-30 min	0.57 ± 0.05	0.31 ± 0.03	0.26 ± 0.03
Control periods	0.60 ± 0.04	0.33 ± 0.02	0.27 ± 0.02

Urine flow, osmolar clearance (Cosm) and clearance of free water (CH₂O) in a group of 10 rats in water diuresis, as influenced by D-angiotensin. Values are means ± standard error (S.E.).

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