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HORMONES AND CHOLINERGIC AGENTS  
IN INSULIN SECRETION IN VITRO

By

DALE A. <sup>11/8/67</sup>MAYHEW

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Indiana University

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Accepted by the faculty of the Graduate School,  
Department of Pharmacology, Indiana University, in partial  
fulfillment of the requirements for the Doctor of Philoso-  
phy degree.

Peter H. Wright, M.D., Chairman

Peter H. Wright

James Ashmore, Ph.D.

James Ashmore

Alan M. Goldberg, Ph.D.

Alan Goldberg

Ward W. Moore, Ph.D.

Ward W. Moore

Robert Forney, Ph.D.

Robert B. Forney

F.W. Hughes, Ph.D.

Deceased 1968.

D.R. Challenger

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## Chapter IV

### Summary

A number of recent studies indicate that insulin release may be partially controlled through the adenylylase system in the pancreatic beta cell. Two agents, theophylline and glucagon, are known to increase the cellular level of cyclic 3'5'-AMP in islets of Langerhans. It has been postulated that the increased level of cyclic nucleotide induced by these compounds is responsible for their stimulant effect on insulin release.

The objectives of the present study were a.) to examine the effect on insulin secretion of agents and hormones which are known to act on the adenylylase system in other tissues; and b.) to study the effects of cholinergic agents on insulin release from the pancreas of the rat, rabbit, dog and man.

Theophylline and glucagon were found to stimulate insulin release from the rat pancreas. ACTH and TSH have a similar but much weaker effect. These agents have no effect on secretion in the absence or at low concentrations of glucose, but they augment the stimulant effect of a high glucose concentration. Carbachol, a cholinergic agent, has no effect on secretion induced by glucose in low concentration from the pancreas of the rat. On the other hand, at high glucose concentrations carbachol consistently depresses

the stimulant effect of glucose. The effects in rat pancreas appear to be unique for in the pancreas of the rabbit, dog, and man carbachol augments the effect of glucose especially, and most consistently, at a high glucose concentration.

Theophylline, glucagon, ACTH, and TSH increase intracellular cyclic 3'5'-AMP in other tissues, and cholinergic agents decrease activity of the adenylcyclase system in the heart. Findings in the present study suggest that insulin secretion from rat pancreas could be partially regulated by the cellular level of cyclic 3'5'-AMP. Thus, theophylline, glucagon, ACTH, and TSH could augment and carbachol could inhibit secretion by respectively increasing or decreasing the cellular level of cyclic 3'5'-AMP.