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INSULIN-SECRETIONAL EFFECT OF EXOGENIC AMINO ACIDS IN RABBITS

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D,L-arginine and L-lysine, introduced into the alimentary canal (IAC), caused significant secretion of insulin in rabbits, whereas D,L-methionine or L-phenylalanine evoked only a small effect. Also, intravenous (IV) injection of D,L-arginine caused dose dependent and biphasic insulin output. On the other hand, L-phenylalanine given IV decreased both basal and glucose – stimulated insulin level in blood.

Key words: *insulin secretion, arginine, lysine, methionine, phenylalanine, glucose*

INTRODUCTION

Insulin – secretional effect of amino acids has been studied many times. This phenomenon depends on the species and amino acid used (1–3). Intravenous administration of amino acids in man showed the strong insulin – secretional effect of arginine, lysine, phenylalanine and leucine (2), while in rat the most effective were arginine, leucine and valine (4). As yet, rabbits have been used very rarely in such studies for their less sensibility as herbivorous. But it was stated both in the *in vivo* and *in vitro* experiments that the main role can play leucine, lysine, arginine and isoleucine (5–7).

Considering the small amount of information about this phenomenon in rabbit and aiming to put some more light on the different action of amino acids, the authors investigated some essential amino acids with or without glucose, giving them intravenously or to the alimentary canal.

MATERIAL AND METHODS

In all experiments adult male rabbits with body weight of about 4 kg were used. The animals were kept in standard conditions and fed on the commercial fodder for rabbits (LSK, Motycz, Poland) until being fasted for 18 hours before experiments. Each group consisted of 6 rabbits.

Amino acids, dissolved in distilled water, were introduced into the alimentary canal (IAC) or intravenously (IV) in the volume of 3.33 ml/kg b.w. In the IAC experiments L-Lys, D,L-Met, D,L-Arg and L-Phe in the total amount of 0.5 mmol/kg b.w. were used. In the IV investigations animals were treated with D,L-Arg (0.2 and 0.5 mmol/kg b.w.) or L-Phe (0.5 mmol/kg b.w.).

The control group received always pure water.

In order to explain very weak or even an inhibitory effect of L-Phe, this amino acid was used both alone (0.5 mmol/kg b.w.) and with D-glucose (0.5 mmol/kg b.w.). Simultaneously, D-glucose (0.5 mmol/kg b.w.) was introduced alone as the background.

Blood samples were taken from the marginal veins of animals' right ear just before treatment (min 0) and next at min. 5, 10, 20, 30, 40 after IV administration or at min. 60 after IAC loading.

Serum insulin was determined radioimmunologically (Ins-Set Test, Świerk, Poland).

Results were analyzed statistically using the Student's t-test.

RESULTS

IAC administration of used amino acids increased the blood insulin level at min. 60 (*Fig. 1*). This secretion was significant for Arg and to the less degree for Lys, whereas Met and especially Phe caused purely slight effect.

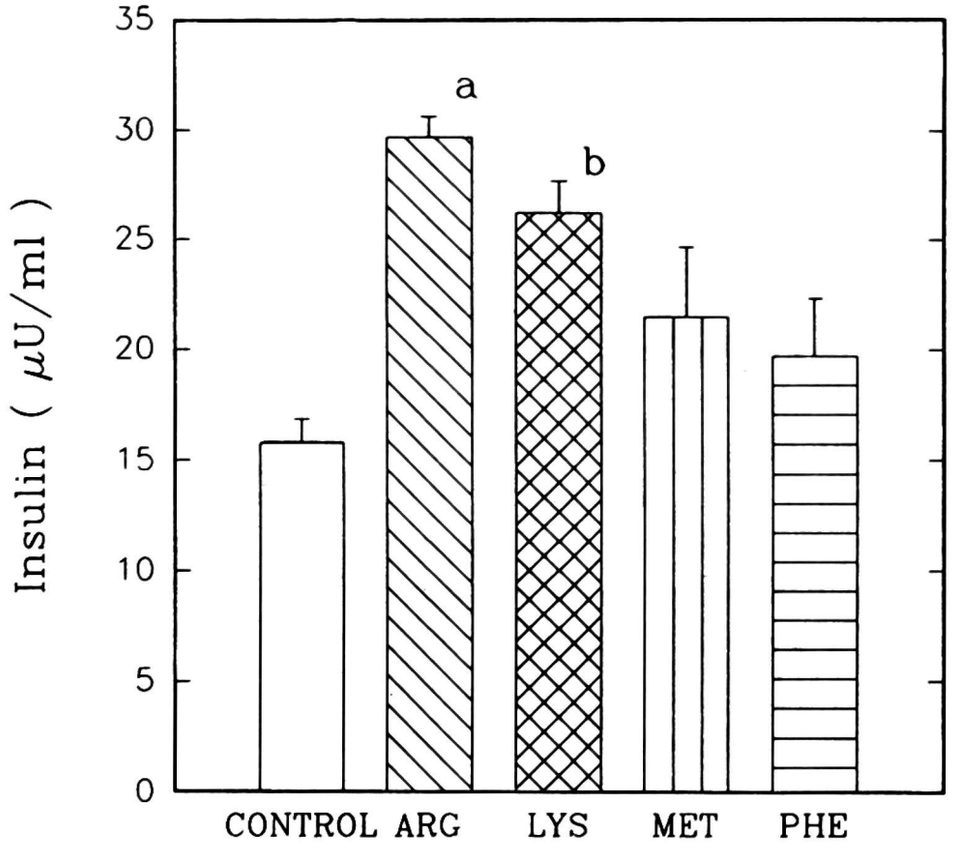

Fig. 1. Effect of amino acids (0.5 mmol/kg b.w.) on insulin concentration in blood (mean ± SEM, n = 6) at min 60 after loading into alimentary canal (IAC). Statistically significant differences in comparison to Control are expressed: a – $p<0.01$, b – $p<0.02$.

In IV investigations (*Fig. 2*) Arg stimulated insulin output at both used doses. The higher concentration of amino acid, however, evoked stronger and markedly biphasic secretion (maximum at min. 5 and 30). In these manners Phe showed rather inihibiting properties. In order to confirm this focus,

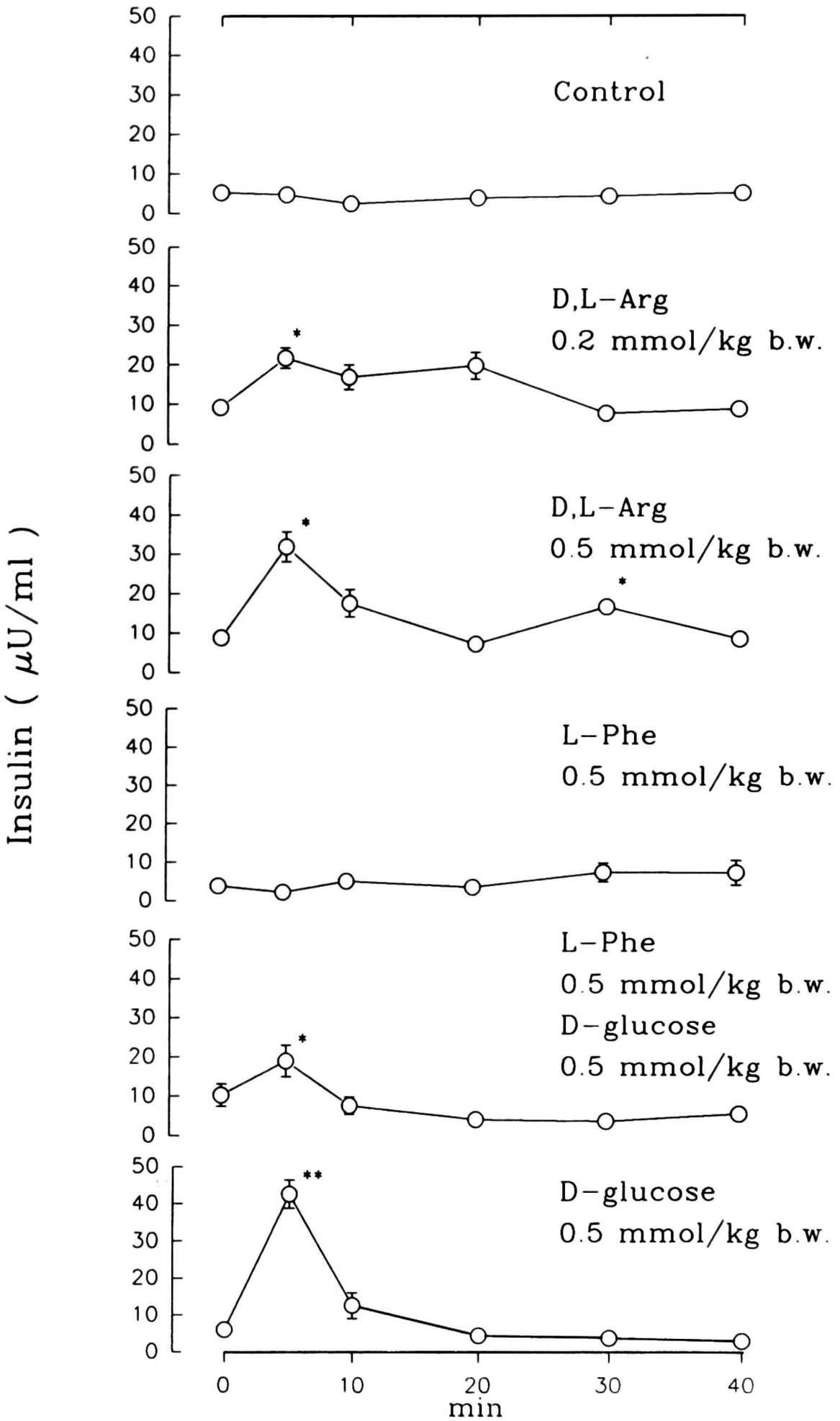

Fig. 2. Effect of intravenous (IV) administration of amino acids and/or glucose on insulin concentration in blood (mean ± SEM, n = 6) Statistically significant differences in comparison to Control are expressed: * – $p < 0.05$, ** – $p < 0.001$.

glucose – induced insulin output was compared to that caused by glucose in the presene of L-Phe (0.5 mmol/kg b. w. each). In this experiment Phe supplement reduced glucose – induced insulin secretion for over 50% (*Fig. 2*).

DISCUSSION

The obtained results indicate that both IAC and IV administration of exogenic amino acids modify insulin secretion pattern. However this process involves not only stimulation (Arg, Lys) but also inhibition of the hormone secretion.

The most potent compounds in the case of IAC administration (*Fig. 1*) were D,L-Arg and L-Lys, whereas D,L-Met and L-Phe caused only small enhancement of insulin concentration. This secretional potency can have its source of course in the direct action of amino acids on islets of Langerhans, but – on the other hand – these agents can stimulate other hormones that change insulin secretion (8–10). Arginine was very potent not only in IAC but also in IV experiments (*Fig. 2*). Simultaneously, the reaction of pancreas on this amino acid seems to be dose – dependent in rabbit, because higher concentration of Arg (0.5 mmol/kg b. w.) reflected in higher maximum level of blood insulin. At the same time, the insulin secretion is biphasic and that focus is especially strongly marked for mentioned above higher dose of the amino acid and it is in good agreement with data obtained in the *in vivo* investigations in man (11) and *in vitro* experiments in rat (12).

Very interesting is lack of effect or even an inhibitory action of L-Phe on insulin secretion while giving this agent alone. It is quite the contrary to facts that this amino acid stimulates insulin secretion *in vivo* in man (2) and dog (13) and *in vitro* by the perfused rat pancreas (14, 15). In addition, to confirm this inhibitory properties in rabbit the authors introduced L-Phe together with glucose and compared the insulin secretion pattern to that obtained in the case of using glucose alone (*Fig. 2*). And the results indicate clearly, that this amino acid diminishes glucose – induced hormone output for over 50%. However, it is very difficult to explain mechanisms of that kind of action in rabbit, taking into consideration stimulating properties of L-Phe in man, dog and rat (2, 13–15).

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