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"Transformation of pancreatic secretion with intraduodenal administration of trypsin and amylase with nonspecific substrates for them."

Abduraxmanov Avazbek Xoshimovich – Associate Professor at the Department of Normal Physiology, Andijan State Medical Institute, Andijan, Uzbekistan.

Abstract: The results of the study on the effects of enter sorbents allowed us to draw a fundamental conclusion, in our view, that the inhibitory influence on the secretion of pancreatic enzymes is exerted by only the solubilized enzymes in the duodenum contents. Immobilized enzymes bound to enter sorbents lose or significantly reduce this ability to inhibit pancreatic secretion.

The de-blocking effects are also induced by nutrients introduced intraduodenally. In our laboratory, it has been demonstrated (Korotko G.F., Baybekova G.D.) that starch as a substrate for amylase removes its selective inhibitory effect on the secretion of pancreatic amylase; the selective inhibition of pancreatic protein secretion is reduced by intraduodenal administration of protein, and emulsified fat eliminates inhibitory effects on pancreatic secretion of lipase. The fundamental similarity of effects between sorbents and nutrients, considering the latter as factors immobilizing enzymes, allows us to observe some external analogy between the comparable effects.

However, it is evident that in the earlier conducted research in our laboratory, a certain idealized situation of removing the specific inhibitory effect of an enzyme with its specific substrate was analyzed. Naturally, in the duodenal chyme, there are polyenzymatic and polysubstrate processes. Therefore, it seemed interesting and important to study the influence on the pancreatic secretion of the intraduodenal introduction of an enzyme, and subsequently, of this enzyme combined with a substrate non-specific to it. It is precisely the effects of such an intraduodenal situation that are being analyzed in this present work.

The research objective.

In the duodenal chyme, there are polyenzymatic and polysubstrate processes occurring. Therefore, it was deemed interesting and important to study the influence on the pancreatic secretion of the intraduodenal introduction of an enzyme, and subsequently, of this enzyme combined with a substrate non-specific to it. It is precisely the effects of such an intraduodenal situation that are being analyzed in this present work.

Materials and methods of the study

To address the outlined tasks, we conducted a series of experiments using acute methodology. In most experiment series, pancreatic juice, blood, and urine were collected hourly. The initial two hours of all experiments served as baseline periods with no additional stimulation or interventions apart from the initial setup. The contents of the subsequent hours of the experiments are described separately for each series below. Stimulation of pancreatic secretion was carried out throughout the entire experiment. In most experiment series, it was accomplished by intraduodenal administration of acid-hydrolyzed histidine.

In experiment series (6) involving 3 dogs, the influence of intraduodenal administration of pancreatic amylase (0.15 mcg/kg/h) without and with fat (vegetable oil, 4 ml/h) on the secretion of pancreatic enzymes, their activity in blood plasma, and excretion in urine was studied.

In experiment series (8) involving 5 dogs, the impact of intraduodenal administration of pancreatic amylase (0.15 mcg/kg/h) without and with egg white (65.4 ml/h) on the secretion of pancreatic enzymes, their activity in blood plasma, and excretion in urine was investigated.

In experiment series (6) involving 3 dogs, the effects of intraduodenal administration of trypsin (0.1 mg/kg/h) without and with fat (vegetable oil, 4 ml/h) on the secretion of pancreatic enzymes, their activity in blood plasma, and excretion in urine were examined.

In experiment series (6) involving 3 dogs, the impact of intraduodenal administration of trypsin (0.1 mg/kg/h) without and with starch (10% 4 ml/h) on the secretion of pancreatic enzymes, their activity in blood plasma, and excretion in urine were studied

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The results of the study and their discussion

The results of acute experiments on dogs showed (Figure 1A) that intraduodenal administration of trypsin inhibited the stimulated hydro lysin-induced secretion of the pancreas: the secretion volume decreased, as did the secretion rate of amylase and proteinases. However, intraduodenal administration of the same amount of trypsin with fat (purified emulsified cottonseed salad oil, 4 ml/hour) did not inhibit pancreatic secretion. In other words, fat eliminated the inhibitory effects of trypsin. Administration of trypsin with a second substrate non-specific to it—starch, one hour after their introduction—restored the volume of pancreatic secretion, and the rate of amylase and proteinase secretion, but led to a decrease in lipase secretion rate. This not only relieved the inhibitory effect of trypsin but also modified its influence— in the presence of starch, it inhibited the secretion of pancreatic lipase. An hour after the introduction of trypsin and starch into the duodenum, there was an even greater reduction in lipase and proteinase secretion.

In another series of experiments, amylase was introduced into the duodenum (Figure 1B), which reduced the volume of pancreatic secretion, the amylolytic activity of the juice, and consequently, the amylase secretion rate by approximately 50% of the initial level. In these experiments, a characteristic selective effect was noted, reducing the amylolytic activity of the juice and the secretion rate of amylase, confirming previously obtained data (Korotko G.F., Baybekova G.D.). The introduced fat with amylase relieved its inhibitory effects on the secretion of pancreatic amylase. Amylase with egg white led to a sharp decrease in secretion volume and consequently, a reduction in lipase and proteinase secretion rates, but the selective inhibitory effect of amylase with egg white was eliminated.

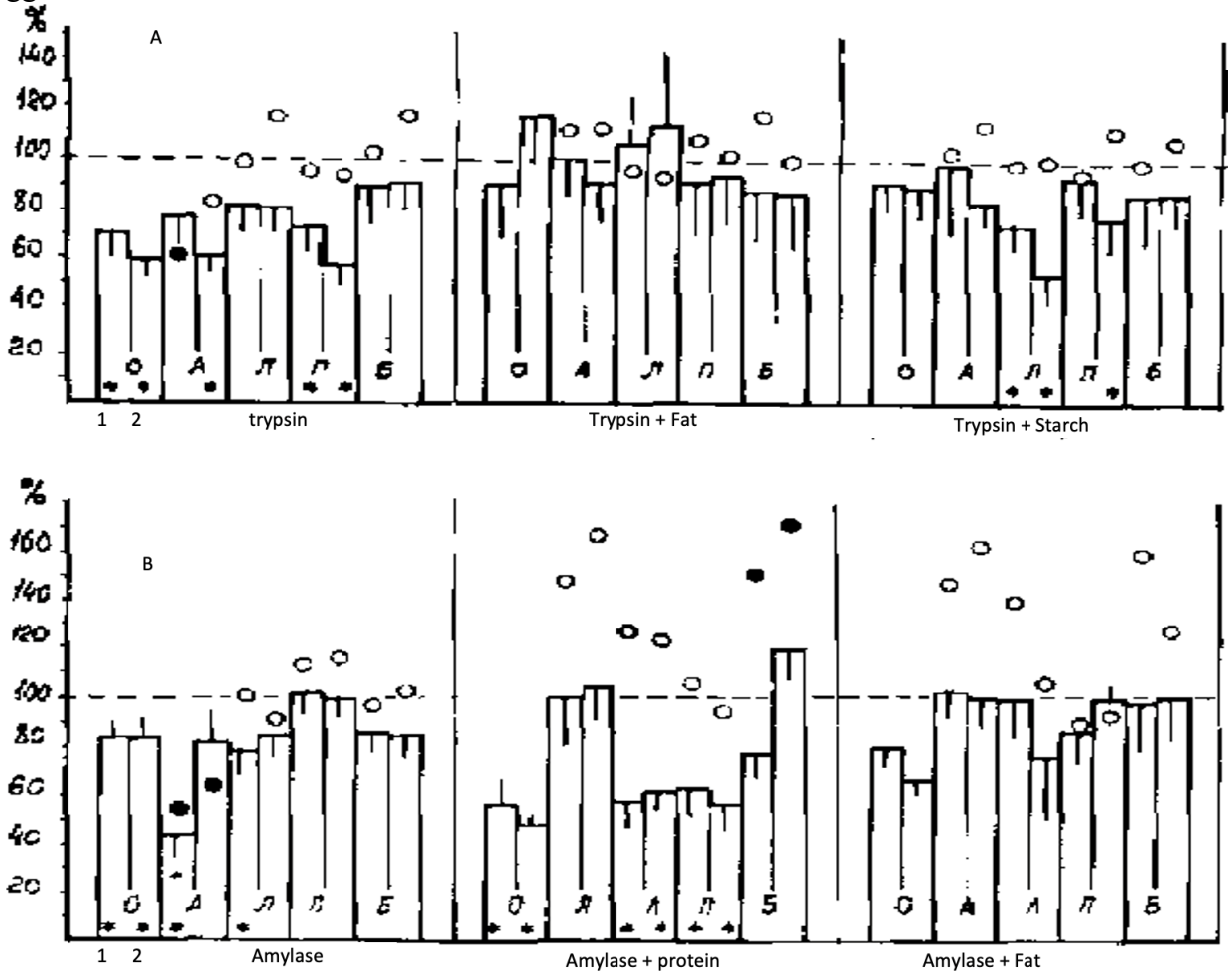

Fig. 1. Influence on the inhibitory effects of pancreatic secretion by trypsin (A) and amylase (B) of substrates non-specific to them (in percentages to the parameters before the introduction of enzymes).

Abbreviations: 0 - juice volume, A - amylase, L - lipase, P - proteases, B - total protein, circles - enzyme activity, bars - their hourly rate, ● and * - significant deviation from control (background), 1 - hour of the introduction of the substances under investigation, 2 - subsequent hour.

The presented material allows us to conclude that not only does the enzyme's connection with a substrate-

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specific to it alleviate the inhibitory effects of the enzyme on its secretion by the pancreas, but also non-specific substances for this enzyme either alleviate, as happened under the influence of fat, or modify, as happened under the influence of starch and protein, its regulatory properties.

Thus, our experiments have revealed that non-specific substrates alter the regulatory effects of pancreatic enzymes. This can be explained not only by the adsorption of enzymes by substrates but also by the modification of enzyme properties, as the effect of enzyme adsorption is evident in the relief of their selective inhibitory influences on the secretion of corresponding enzymes by the pancreas. This can be observed in the results where the fat emulsion influenced the removal of trypsin and amylase effects. Regarding the effects of starch and protein, it's noteworthy not only for the removal of specific inhibitory influences of these enzymes but also for the modification of the inhibition effects on the secretion of other pancreatic hydrolases.

Hence, the solubilized pancreatic enzymes present in duodenal contents have the property of inhibiting pancreatic secretion, whereas enzymes immobilized by substrates and adsorbents either do not possess this property or possess it to a lesser extent. This might be a result of complex transformations of enzyme properties, which encompass not only catalytic but also regulatory centers. Simpler substrate-enzyme interactions are not excluded. For instance, the fat emulsion acted as an adsorbent on the effects of trypsin and amylase, alleviating the inhibition of pancreatic enzyme secretion observed in experiments with intraduodenal administration of trypsin and amylase. This can be explained by the adsorption of enzymes at the emulsion phase boundary.

The influence of starch on the trypsin effect was more complex, not only alleviating the inhibitory effect on proteinase and amylase secretion but also inhibiting lipase secretion. Even more complex were the effects of egg white in the pancreas reaction to intraduodenal amylase introduction. The protein itself has multiple components in its influence—the proton linkage in acid-hydrolyzed histidine, hence the increase in gastric content pH, and nonspecific enzyme linkage. It's noteworthy that the decrease in lipase and proteinase secretion was due to a reduction in secretion volume. Thus, here, the inhibition of secretin releases due to decreased duodenal content acidity played a role. However, the secretion of total protein in the juice following the introduction of amylase and egg white into the intestine was increased.

Conclusions

The material presented in this study allows for the following summary conclusions:

1. Secretion of pancreatic enzymes is selectively inhibited by pancreatic enzymes present in the contents of the duodenum.
2. De-blocking effects are induced not only by specific but also by non-specific substrates introduced into the duodenum along with enzymes. Additionally, there might be a modifying influence of the introduced substrate on the enzyme spectrum of pancreatic juice.
3. The transformation of effects from intraduodenal enzyme introduction with non-specific substrates involves different mechanisms.
4. Not only the physicochemical sorption of pancreatic enzymes in the duodenal content eliminates their inhibitory effects on the secretion of pancreatic enzymes, but also the interaction of their catalytic center with the substrate. There is also a possibility of modification by non-specific substrates in the regulatory properties of enzymes concerning their influence on the enzyme spectrum of pancreatic juice in the duodenum.

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