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Effect of Vilon and Epithalon on Glucose and Glycine Absorption in Various Regions of Small Intestine in Aged Rats

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Vilon (Lys-Glu) and Epithalon (Ala-Glu-Asp-Gly) administered orally for 1 month improved transport characteristics of the small intestine in aged rats. Vilon enhanced passive glucose accumulation in the serous fluid in inverted sac made from the distal region of the small intestine, while Epithalon enhanced this process in the medial region. Vilon stimulated active glucose accumulation in the serous sac of the medial small intestine, Epithalon — in the proximal and distal small intestinal segments. Glycine absorption increased only in the proximal intestinal segment under the effect of Epithalon.

Key Words: *peptides; Vilon; Epithalon; aging; transport of glucose and glycine*

Aging is characterized by degenerative processes, impaired adaptive capacities, and disturbances in gene regulation resulting in abnormal protein synthesis, unstable function of various body systems, and development of age-related pathology [7]. Age-related involution of the digestive tract is associated with impairment of not only hydrolytic, but also absorption (transport) functions. This was clearly demonstrated for glucose absorption in aged humans and animals [1,2,5,12]. Impairment of digestive and transport processes in the digestive tract can accelerate aging of the organism. Detailed information on the dynamics of age-dependent changes in various organs and tissues is important for elaboration of geroprotective drugs. Taking into account the important physiological role of endogenous peptides in the regulation of aging, the search for peptides possessing geroprotective properties is of particular importance [9]. It was previously shown that oral administration of Vilon (Lys-Glu) and Epithalon (Ala-Glu-Asp-Gly) activates digestive enzymes in the small intestine of aged rats [8,10].

The aim of the present study was examination of the effect of Vilon and Epithalon on glucose and glycine absorption in various regions of small intestine in aged rats.

MATERIALS AND METHODS

The experiments were carried out on 15-month-old male rats (n=16) weighing 460-500 g. Control animals were kept on a standard diet for 1 month. Experimental rats kept under similar conditions daily received 100 μg Vilon or Epithalon (peptides were synthesized by E. I. Grigor'ev, Institute of Bioregulation and Gerontology).

Glucose and glycine transport was studied by a modified method of inverted intestinal sac [4]. Proximal, medial, and distal segments of the small intestine

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(3-cm long) were turned out and filled with 0.3 ml Ringer's solution, pH 7.4 (serous fluid). The sacs were incubated for 60 min in Ringer's solution (pH 7.4) containing 20 mM glucose or glycine in the presence of oxygen and nitrogen. Substrate absorption (per 1 g wet tissue) was evaluated by their accumulation in the serous fluid in the presence of oxygen. Passive substrate transport was evaluated by their accumulation in the serous fluid in the presence of nitrogen (anoxia). Active transport component was calculated as the difference between substrate accumulation in the serous fluid in the presence of oxygen and nitrogen. Glucose and glycine concentrations were determined by glucose oxidase method [12] and by the technique described elsewhere [6], respectively.

The results were processed statistically using Student t test and Mann—Whitney U test.

RESULTS

Oral administration of Vilon and Epithalon to aged rats for 1 month had no effect on body weight and weight and length of the small intestine compared to the corresponding parameters in untreated controls.

In control rats passive glucose transport (Fig. 1, *a, b*) was high in all examined regions of the small intestine, being higher in the medial region both for glucose and glycine compared to proximal and distal regions.

Vilon significantly (by 60%, $p<0.05$) increased passive glucose absorption only in the distal intestinal region, which manifested in its enhanced accumulation in the presence of nitrogen. Thus, maximum passive glucose transport was shifted to the distal region, whereas in thecontrol it was characteristic of the medial region.

Epithalon had no effect on glucose accumulation in the proximal portion, but increased passive glucose transport in the medial and distal segments 2.2-fold ($p<0.05$) and by 40%, respectively. The distribution of passive glucose accumulation along the small intestine was characterized by its increase in the medial region, especially in Epithalon-treated rats.

In control rats, the level of active glucose accumulation in the serous fluid of different intestinal re-

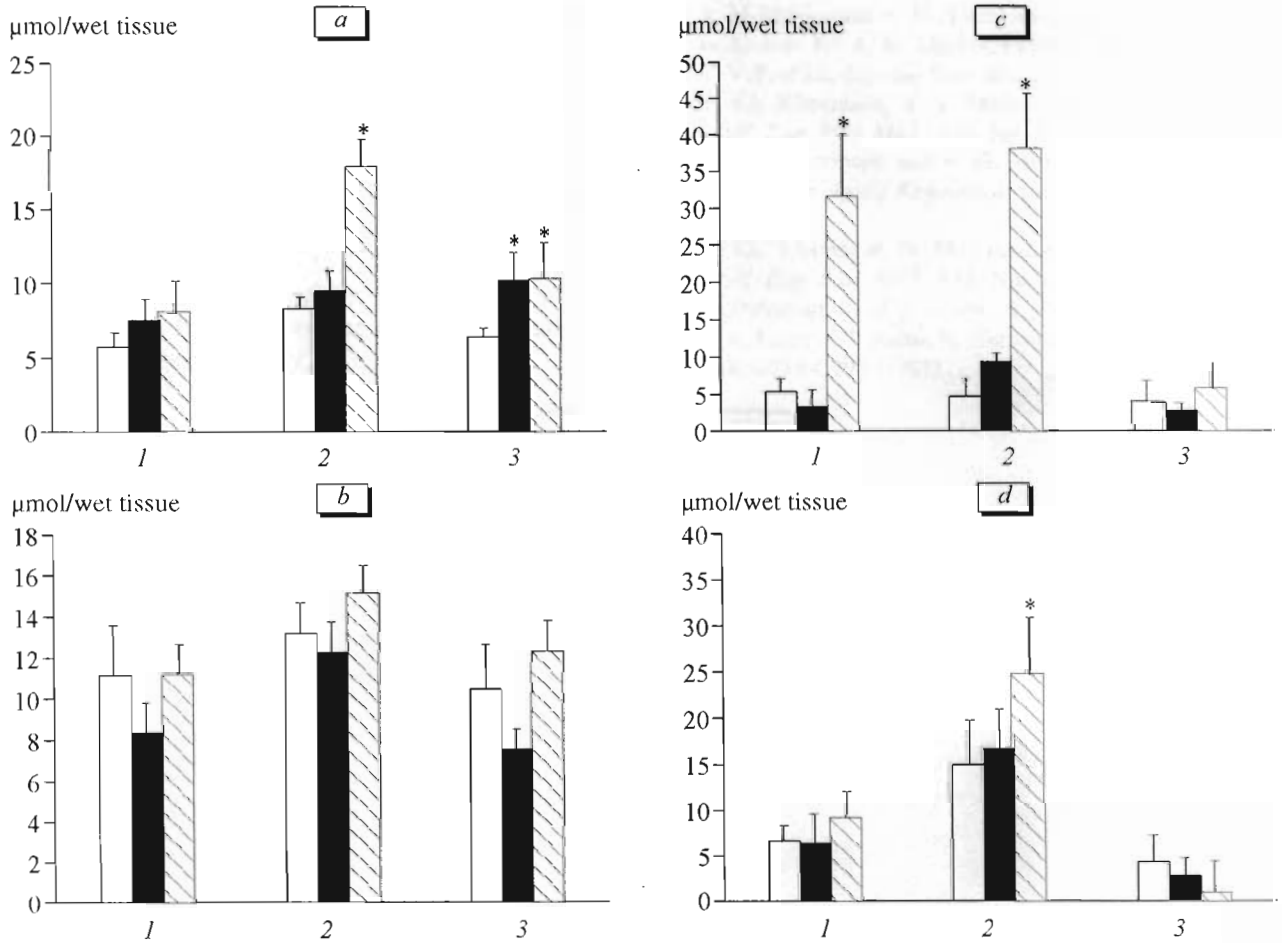

Fig. 1. Passive (*a, b*) and active (*c, d*) transport of glucose (*a, c*) and glycine (*b, d*) in the proximal (*1*), medial (*2*), and distal (*3*) regions of small intestine. Dark bars: Vilon, hatched bars: Epithalon. *$p<0.05$ compared to the control (open bars).

gions was relatively low and varied from 3.91±2.74 to 5.38±1.65 μmol/g wet tissue (Fig. 1, *c*). In Vilon-treated group this parameter was low in the proximal and distal regions, but increased in the medial region, which changed the proximodistal gradient of active transport in experimental rats compared to controls.

Epithalon significantly increased active glucose accumulation in the proximal and medial regions of the small intestine (6- and 8-fold, respectively), but had no effect on the distal region.

In control rats, the rate of active accumulation of glycine surpassed that of glucose, especially in the medial region (Fig. 1, *d*). Epithalon 2-fold increased active glycine accumulation in the proximal and medial intestinal regions compared to the control ($p<0.05$), while in the distal region this process was inhibited (or even absent). The proximodistal gradient of active glycine transport along the small intestine was similar in both groups.

Thus, we demonstrated positive effect of Vilon and Epithalon (low hydrolysable peptides) on absorption of nutrients, in particular glucose and glycine. The mechanisms of glucose and glycine transport were previously examined in detail [3]. It should be noted that test preparations produced the most pronounced effects on passive and active glucose transport. Vilon 1.6-fold increased passive glucose accumulation in the serous fluid of inverted distal intestine, while Epithalon 2.2-fold increased this process in the medial intestine. Vilon and Epithalon significantly increased active glucose absorption. Vilon 2-fold enhanced glucose accumulation in the serous fluid of inverted sac from the medial intestine, while Epithalon 6- and 8-fold increased in this component in the proximal and medial regions, respectively.

Peptides produced no significant effects on passive glycine absorbtion. However, Epithalon increased active glycine absorption in the proximal and medial small intestine.

Our previous results on the effects of Vilon and Epithalon on activity of digestive enzymes and present data on glucose and glycine absorbtion in the small intestine of aged rats show that the examined peptides improve enzyme activity and transport in the intestine, stimulate food assimilation, and normalize digestive functions during aging.

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