# BIOGERONTOLOGY

# Effect of the Dipeptide Vilon on Activity of Digestive Enzyme in Rats of Various Ages

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Peroral administration of Vilon (Lys-Glu) to male and female Wistar rats aging 3 and 11 months changed activity of digestive enzymes (invertase, maltase, alkaline phosphatase, and amino- and dipeptidases) in various portions of the gastrointestinal tract. The increase in enzyme activity was most pronounced in 11-month-old animals, which diminished differences between rats of various ages. Our results indicate that Vilon produces positive effects on digestive enzyme activity during aging.

**Key Words:** *aging; Vilon; peptides; digestive enzymes; gastrointestinal tract*

Studies of the mechanisms of aging are important for elaboration of methods and preparations prolonging the life span [1]. Our previous studies showed that Epithalamin and Epithalon, complex polypeptide preparations isolated from the pineal gland and thymus, possess geroprotective properties [5,8]. Other thymic peptides, including thymosin-$\alpha_1$, also have geroprotective activity [9]. Studies of the amino acid composition of Thymalin, other thymic peptides, and some cytokines allowed us to synthesize dipeptide Vilon (Lys-Glu), which increases the life span in mice and inhibits the development of spontaneous neoplasms [7]. The digestive system plays an important role during aging, since its dysfunction accelerates involution processes and provokes the development of severe age-related diseases [2,3,6].

Here we studied the effects of Vilon given perorally to rats of different ages on activity of digestive enzyme in various portions of the gastrointestinal tract.

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## MATERIALS AND METHODS

Experiments were performed on 32 Wistar rats aging 3 and 11 months, including males (180 and more than 400 g, respectively) and females (180-200 and 300 g, respectively). Control animals received standard diet for 2 weeks. Other rats were kept under similar conditions and daily received 100 μg Vilon (perorally) for 2 weeks. The animals had free access to water. Body weights were measured before and after the experiment. Activities of membrane-bound enzymes invertase (EC 3.2.1.48), maltase (EC 3.2.1.20), alkaline phosphatase (EC 3.1.3.1), and aminopeptidase M (EC 3.4.11.2) and intracellular glycyl-L-leucine dipeptidase (EC 3.4.13.2) were measured in homogenates from stomach, duodenal, jejunal, ileal, and large intestinal mucosa. Enzyme activities were measured routinely [4] and expressed in μmol hydrolysis products/g wet tissue/min. The results were analyzed by Student's *t* test.

## RESULTS

Peroral treatment with Vilon for 2 weeks did not change body weight, but decreased the weights of the ileal

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mucosa in 3-month-old females (by 60%), large intestine mucosa in 11-month-old females (by 60%), and duodenal mucosa in 3-month-old males (by 2.5 times) compared to the control.

In 3-month-old males Vilon had no effect on invertase and aminopeptidase M activities, but 2-fold decreased maltase activity in the jejunum, ileum, and large intestine (Table 1, Fig. 1, *a*) and 3.5-fold increased alkaline phosphatase activity in the jejunum and glycyl-L-leucine dipeptidase activity in the stomach compared to the control (Fig. 1, *b*, *c*).

In 3-month-old females Vilon did not change maltase and glycyl-L-leucine dipeptidase activities in various portions of the gastrointestinal tract, but decreased invertase activity in the small intestine and alkaline phosphatase and aminopeptidase M activities in the duodenum compared. The preparation 1.4- and 3-fold increased aminopeptidase M activity in the ileum and large intestine, respectively (Table 1, Fig. 1, *a*).

In 11-month-old males Vilon increased invertase activity in the duodenum and jejunum (by 2.6 and 1.5 times, respectively), maltase and aminopeptidase M activities in the duodenum (by 1.8 times, Table 1, Fig. 1, *a*), and alkaline phosphatase activity in the jejunum and duodenum (by 1.8 times, Fig. 1, *b*). The preparation decreased invertase activity in the stomach (Table 1) and glycyl-L-leucine dipeptidase activity in the jejunum (Fig. 1, *c*) by 2 and 2.1 times, respectively, compared to the control.

In 11-month-old females Vilon increased maltase activity in the duodenum, jejunum, and ileum (by 1.2, 1.5, and 1.3 times, respectively), alkaline phosphatase activity in the jejunum and ileum (by 2.2. times), and dipeptidase activity in the duodenum (by 1.8 times, Table 1, Fig. 1, *b*, *c*) compared to the control. Invertase activity 2-fold decreased only in the large intestine (Table 1). Vilon had no effect on aminopeptidase M activity.

Aging is accompanied by progressive involution of the mucosa in various portions of the digestive tract, which is probably associated with changes in the intensity of regeneration and development of degenerative and atrophic processes characterized by shortening and thickening of villi, decrease in the number of microvilli, and structural impairment of the glicocalix [2,3]. The activity of enzymes involved in final stages of disintegration of disaccharides, dipeptides, and phosphoric acid esters also changes during aging [6].

Our experiments showed that activity of digestive enzymes in young rats (particularly, in males) is higher than in old animals.

The dipeptide Vilon ( poorly hydrolyzable peptide) given perorally for 2 weeks affects activity of digestive enzymes in the gastrointestinal tract. It should be emphasized that Vilon produces age- and sex-dependent effects on digestive enzyme activities. The

**TABLE 1.** Effect of Vilon on Invertase and Maltase Activities (μmol/min/g) in the Stomach and Intestine in Rats of Various Ages (*M*±*m*)

| Organ | | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 3 months | | 11 months | | 3 months | | 11 months | |
| | | control | Vilon | control | Vilon | control | Vilon | control | Vilon |
| Stomach | invertase | 0.33±0.06 | 0.36±0.01 | 0.54±0.09 | 0.28±0.07* | 0.04±0.03 | 0.30±0.14 | 1.29±0.28 | 0.22±0.16 |
| | maltase | 2.09±0.14 | 2.92±0.13 | 2.57±0.66 | 4.01±0.55 | 3.12±0.56 | 3.67±0.48 | 3.54±0.35 | 2.42±0.53 |
| Duodenum | invertase | 5.71±0.83 | 3.16±0.56* | 4.40±1.04 | 11.60±2.16* | 8.62±1.01 | 3.19±1.16* | 6.74±1.55 | 4.65±2.11 |
| | maltase | 35.20±2.73 | 28.90±1.89 | 26.30±2.46 | 48.20±5.97* | 35.80±3.01 | 27.70±7.47 | 31.00±0.27 | 38.10±1.24* |
| Jejunum | invertase | 10.30±1.85 | 10.10±1.19 | 14.10±1.43 | 21.90±2.04* | 17.80±3.48 | 10.70±2.46 | 14.30±0.24 | 9.39±2.51 |
| | maltase | 56.20±2.83 | 30.50±1.04* | 46.40±5.78 | 48.30±2.94 | 37.70±1.50 | 44.20±2.84 | 29.80±0.41 | 44.20±3.25* |
| Ileum | invertase | 2.63±0.91 | 4.27±0.36 | 3.43±0.88 | 4.05±0.5 | 18.44±0.71 | 4.95±0.55* | 2.67±0.34 | 2.64±0.73 |
| | maltase | 30.60±0.44 | 14.50±0.31* | 23.90±1.82 | 24.10±1.67 | 18.80±0.80 | 22.40±1.48 | 15.20±0.17 | 21.80±1.60* |
| Large intestine | invertase | 1.10±0.26 | 1.99±0.55 | 2.14±0.22 | 1.20±0.49 | 0.45±0.06 | 0.42±0.09 | 0.64±0.06 | 0.34±0.06* |
| | maltase | 5.15±0.64 | 3.00±0.10* | 4.71±0.37 | 4.79±0.21 | 3.78±0.17 | 4.50±0.40 | 3.65±0.65 | 4.32±0.33 |

**Note**. *$p<0.05$ compared to the control.

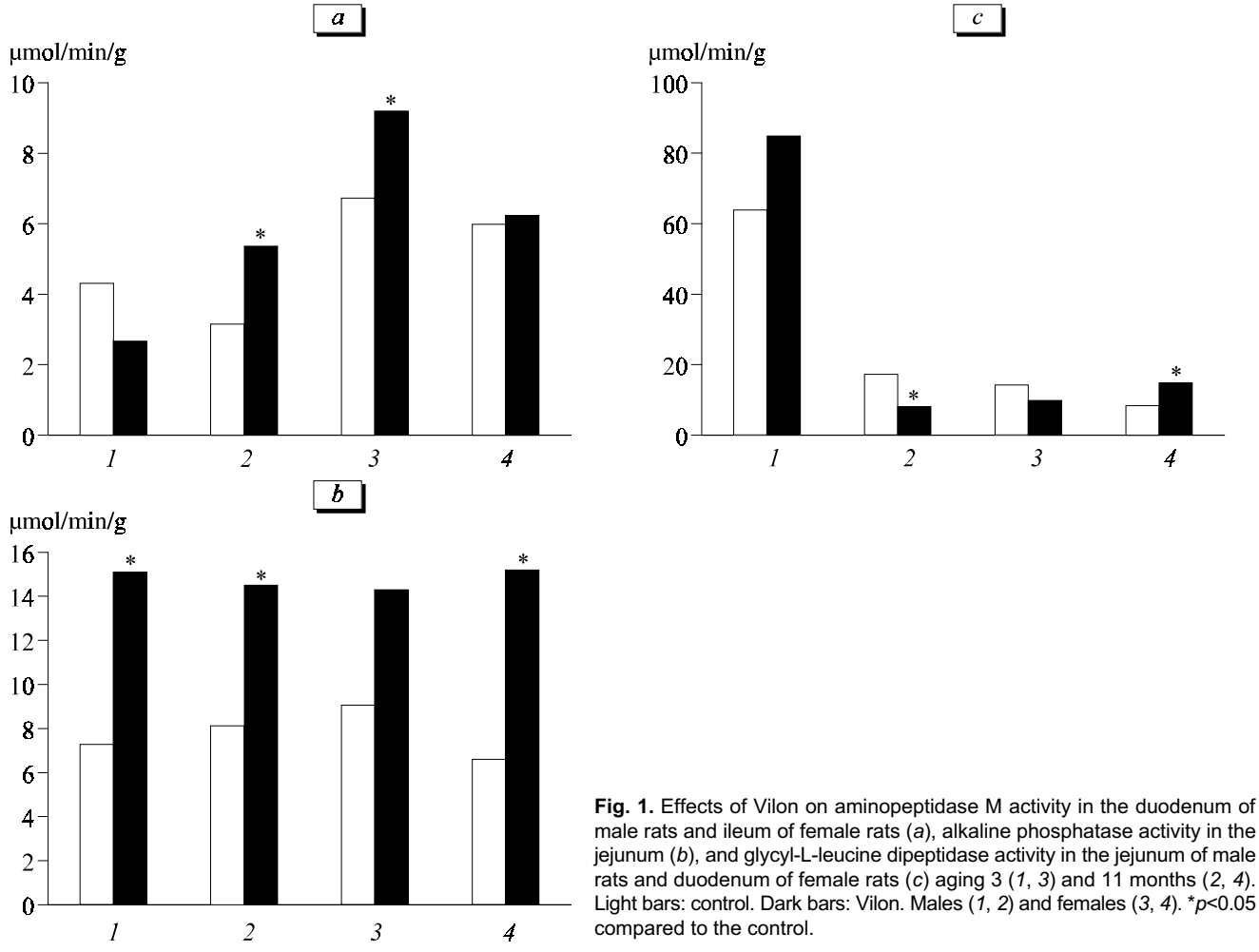


**Fig. 1.** Effects of Vilon on aminopeptidase M activity in the duodenum of male rats and ileum of female rats (*a*), alkaline phosphatase activity in the jejunum (*b*), and glycyl-L-leucine dipeptidase activity in the jejunum of male rats and duodenum of female rats (*c*) aging 3 (*1*, *3*) and 11 months (*2*, *4*). Light bars: control. Dark bars: Vilon. Males (*1*, *2*) and females (*3*, *4*). *$p<0.05$ compared to the control.

increase in digestive enzyme activity caused by Vilon is more pronounced in old animals. After treatment with Vilon the activity of digestive enzymes in the gastrointestinal tract of 11-month-old males and females did not differ from that in 3-month-old rats. It can be assumed that Vilon resistant to hydrolysis by intestinal peptidases and absorbed in unchanged form, is involved in the intermediate metabolism and modulates activity of digestive enzymes. This is probably accompanied by changes in the synthesis and degradation of these enzymes, as well as in the ratio between these processes.

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