raises the defensive potential of both immune and hemostatic reactions of the organism, as the results of our investigation show.

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HORMONAL ACTIVITY OF AN $ACTH_{4-10}$ ANALOG — A LONG-ACTING LEARNING STIMULATOR

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UDC 612.821.1/3.014.46:615.357.814.32:577.175.325

KEY WORDS: long action; adrenocorticotrophic hormone; steroidogenic activity; melanocyte-stimulating activity; corticosterone.

The ACTH fragments $ACTH_{4-7}$ and $ACTH_{4-10}$ affect learning processes in animals and man in very small doses (10-100 μg/kg) [3, 6]. An essential defect of these compounds is the short duration of their action, possibly due to rapid degradation by enzymes. To increase the metabolic resistance of these compounds the writers have synthesized a number of $ACTH_{4-10}$ analogs and have found that $ACTH_{4-7}$ Pro—Gly—Pro: methionyl-glutamyl-histidyl-phenylalanyl-prolyl-glycyl-proline (I) which, unlike the natural $ACTH_{4-10}$ fragments, acts for a much longer time in virtually the same dose [4], is the most effective analog. It was interesting to study peptide I for its ACTH-like hormonal activity. Some ACTH fragments are known to possess hormonal activity to a certain degree, and this is undesirable when these compounds are to be used as regulators of higher nervous activity.

In this investigation the steroidogenic and melanocyte-stimulating activity of peptide I was compared with that of $ACTH_{1-24}$ and $ACTH_{5-10}$. Steroidogenic activity was determined *in vitro* as the quantity of corticosterone formed after incubation of isolated fascicular cells of the adrenal cortex with different concentrations of the test substances [5]. $ACTH_{1-24}$, obtained from Ciba-Geigy AG (Switzerland), was used as the standard compound. Compound $ACTH_{5-7}$ (from Serva, West Germany) was found to have the maximal steroidogenic effect in a concentration of 10^{-5} M, producing the same increase in the corticosterone concentration

TABLE 1. Steroidogenic Activity of ACTH Fragments on Isolated Rat Adrenal Cells ($M \pm \Delta m$)

Concentration of $ACTH_{1-24}$, M	Corticosterone, μg per sample	Concentration of peptide, M	Corticosterone, μg per sample of $ACTH_{4-7}$
0	0,0016±0,003	10^{-6}	0,018±0,02
10^{-11}	0,047±0,006		
10^{-10}	0,136±0,008	10^{-5}	0,018±0,003
10^{-9}	0,460±0,007		
10^{-8}	0,490±0,003	10^{-4}	0,017±0,004

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 101, No. 3, pp. 267-268, March, 1986. Original article submitted April 4, 1985.

0007-4888/86/0003-0255$12.50

TABLE 2. Melanocyte-Stimulating Activity of ACTH Fragments on Isolated Frog-Skin (M ± Δm)

Concentration of peptide, M	Darkening of skin, %		
	$ACTH_{1-24}$	$ACTH_{5-10}$	$ACTH_{4-7}$ (Pro-Gly-Pro)
10^{-7}	11,08±1,50	—	—
$2 \cdot 10^{-7}$	18,38±2,02	—	—
10^{-6}	27,21±2,14	—	—
$2 \cdot 10^{-5}$	—	7,78±0,92	0,92±0,40
10^{-4}	—	15,00±1,99	2,08±0,77
$2 \cdot 10^{-4}$	—	20,89±2,84	3,42±1,16
10^{-3}	—	—	—

Legend. Darkening of the skin by 10% or more was taken to be significant.

in the incubation medium as $ACTH_{1-24}$ (Table 1). The melanocyte-stimulating activity of the compounds *in vitro* was determined by measuring darkening of isolated frog skin after incubation with different concentrations of the test peptides [2]. $ACTH_{1-24}$ and $ACTH_{5-10}$, obtained from Serva, were used for comparison (Table 2). The results were subjected to statistical analysis [1].

Thus in the concentrations used, $ACTH_{4-7}$ (Pro—Gly—Pro) has no hormonal effect, whereas the peptide with the natural sequence $ACTH_{5-10}$ is active even in lower concentrations. This is an undoubted advantage when this compound is to be used as a long-acting stimulator of learning.

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