3. V. P. Bond, T. M. Fliedner, and J. O. Archambeau. Mammalian Radiation Lethality, New York (1965).
4. B. J. Bryant, Exp. Cell Res., **21**, No. 3, 70 (1960).
5. K. E. Fichrelius and H. Diderholm, Acta Path. Microbiol. Scand., **52**, No. 1, 11 (1961).
6. M. Hill and V. Drasil, Exp. Cell Res., **21**, No. 3, 569 (1960).
7. H. R. Jervis, M. M. McLaughlan, and M. C. Johnson, Radiat. Res., **45**, No. 3, 613 (1971).
8. J. F. R. Kerr and J. Searle, Radiation Biology in Cancer Research, New York (1980).
9. J. F. R. Kerr, A. H. Wyllie, and A. R. Currie, Brit. J. Cancer, **26**, No. 2, 239 (1972).
10. M. Kotani, A. Yamashita, F. Rai, et al., Blood, **29**, No. 4, Part 2, 239 (1967).
11. J. P. Loutit, Lancet, **2**, 1106 (1962).
12. J. M. Martinez-Penuella, A. Domingues, and M. L. Gomez, Path. Res. Pract., **1**, 122 (1979).
13. R. G. Murray and A. Murray, The Lymphocyte in Immunology and Haemopoiesis, London (1967).
14. E. A. Smuckler and J. L. James, Pharmacol. Rev., **36**, No. 2, Suppl. 77 (1984).
15. O. A. Trowell, J. Biophys. Biochem. Cytol., **3**, No. 2, 217 (1957).

MECHANISM OF ACTION OF CHORIONIC GONADOTROPHIN ON LACTATE DEHYDROGENASE ACTIVITY

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KEY WORDS: chorionic gonadotrophin; lactate dehydrogenase

Proliferation and differentiation of all cells in the body are under the control of many different mechanisms involving the biologically active compounds of protein nature. A special place among these compounds is occupied by chorionic gonadotrophin (CG). It is considered that any nonendocrine tissue in which intensive cell proliferation takes place may be a source of CG [2]. There is some evidence that CG is involved in prostaglandin synthesis, and in intracellular protein synthesis [6]. The study of its effect on the liver has shown that this hormone is closely connected with the liver, as is shown by stimulation of regeneration and reversibility of pathological changes in the structure and function of that organ [7]. The number of normal hepatocytes increases rapidly under these circumstances, the number of degenerating cell forms decreases, normal lipid metabolism is restored, and the quantity of excessively growing connective tissue and activity of lysosomal enzymes are reduced. Meanwhile, in the liver tissue, activity of organ-specific enzymes (urokinase, frustose-1-phosphate aldolase) and of alanine aminotransferase is increased, evidence of intensification of enzyme synthesis [1, 3, 4].

Thus CG, by reducing the intensity of catabolism in the pathologically changed liver, makes hepatocyte destruction less likely and promotes acceleration of regeneration in the organ and in that way affects the activity of various intracellular enzymes. The mechanism of action of CG on enzymes has not yet been finally settled.

Our aim was to study the effect of CG on the catalytic properties of lactate dehydrogenase in vitro.

EXPERIMENTAL METHOD

Preincubation of CG in a dose of 5 mg/ml (50 U/ml) with a solution of the enzyme lactate dehydrogenase (LDH) from porcine muscle ("Reanal") was carried out in vitro for 10 min. LDH activity was then determined [5]. To

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TABLE 1. Lactate Dehydrogenase Activity (in nmoles NADH/min) Under the Influence of CG (M ± m, n = 10)

LDH activity	Intact enzyme	Preincubation of CG with LDH
Direct reaction	321,0±7,2	267,1±5,5*
Reversed reaction	148,3±5,7	253,2±9,6*

TABLE 2. Kinetic Characteristics of LDH Under the Influence of CG in Vitro

Kinetic parameters	Intact enzyme	Preincubation of CG with LDH
K_m (lactate), M	0,0196	0,0171
V_{max}, nmoles NADH/min	821,12	711,03
K_m (pyruvate), M	0,00659	0,0101
V_{max}, nmoles NADH/min	579,23	865,41

Legend. Mean values of K_m and V_{max} are given (n = 10).

determine the kinetic parameters of the enzyme reaction (Michaelis constant, K_m; maximal reaction velocity, V_{max}) LDH activity was studied by the use of four increasing concentrations of lactate and pyruvate, and with saturating concentrations of NAD and NADH.

EXPERIMENTAL RESULTS

The investigations showed that preincubation of LDH with CG in vitro led to conformational changes in the enzyme molecule, and these were reflected in its catalytic activity. As a result there was a significant decrease in activity of the direct lactate dehydrogenase reaction by 18% and an increase in activity of the reversed LDH reaction by 42% compared with the control (Table 1). The results indicate a direct action of the glycoprotein CG on the enzyme, leading to inhibition of the aerobic form of LDH and activation of its anaerobic form.

The aerobic form of lactate dehydrogenase, incidentally, is characteristic of embryonic liver tissue, but in the adult, on the contrary, activity of the anaerobic form of the enzyme predominates [8]. Thus in vitro there is a direct nonspecific action of CG on activity of the direct and reversed lactate-dehydrogenase reaction.

To study the mechanism of action of CG on the enzyme we investigated the kinetics of the direct and reversed LDH reactions. The kinetic characteristics of the enzyme are given in Table 2. Plotting data for dependence of the initial velocity (V_0) of the lactate dehydrogenase reaction during a change in substrate (lactate) concentration between Lineweaver–Burk coordinates showed that under the influence of CG the value of K_m (for lactate) and V_{max} of the enzyme reaction was reduced. Meanwhile the K_m/V_{max} ratio showed virtually no change relative to the control. These kinetic changes in the enzyme reaction characterize a noncompetitive type of inhibition of LDH activity.

For the reversed lactate dehydrogenase reaction dependence of V_0 on the substrate (pyruvate) between Lineweaver–Burk coordinates was opposite in character, for in that case the value of K_m (for pyruvate) and V_{max} increased by the same amount compared with the control. The changes in kinetics of LDH obtained under the influence of CG can be regarded as the noncompetitive type of activation of the enzyme.

One possible explanation of these results may be that any inhibitor or activator which prevents (or accelerates) breakdown of the enzyme–substrate complex (ES) into products, if it binds with one of the intermediates to form a "dead end" complex or if it causes reversal of one stage in accordance with the law of mass action, it ought to

depress (or raise) the value of V_{max}. With this type of action of the inhibitor (activator) the relative amounts of the free enzyme and the ES complex as a rule will be reduced, and this also leads to a change in the value of K_m.

When using the complete Botts–Morales system it is convenient to examine inhibition and activation of the direct and reversed lactate dehydrogenase reactions by CG together. Since differences between them are quantitative rather than qualitative in character, the same algebraic relationships are valid for both cases.

It can be concluded that CG has a direct action on LDH in vitro. This suggests that this glycoprotein may take on the role in the cell of a nonspecific regulator of the lactate dehydrogenase reaction. Moreover, the character of the effect of CG on the enzyme is that of a noncompetitive mechanism of action.

REFERENCES

1. T. V. Blinova, A. A. Kosykh, and I. M. Solopaeva, Vopr. Med. Khim., No. 3, 410 (1980).
2. V. B. Vinnitskii, M. D. Mosienko, and G. V. Glinskii, Biology of Markers of Cancer and Pregnancy [in Russian], Kiev (1990).
3. N. L. Ivanova and G. V. Malyugin, Pharmacologic Regulation of Regeneration under Experimental and Clinical Conditions [in Russian], Ioshkar-Ola (1979), p. 139.
4. A. A. Kosykh, Regeneration of the Liver: Regeneration Therapy of Liver Diseases [in Russian], Gor'kii (1985), p. 18.
5. G. A. Kochetov, Textbook of Practical Enzymology [in Russian], Moscow (1980).
6. I. M. Solopaeva, N. M. Roshchina, and N. L. Ivanova, Byull. Éksp. Biol. Med., No. 12, 40 (1983).
7. I. M. Solopaeva, Regeneration, Adaptation, and Homeostasis [in Russian], Gor'kii (1991), p. 14.
8. I. A. Khodosova, Enzymes of Tumor Cells [in Russian], Leningrad (1988).

NEW APPROACHES TO AN UNDERSTANDING OF THE HEMODYNAMIC NORM

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The norm is nowadays widely regarded as the zone of optimal function of an organism. Normal values of both morphologic and functional parameters are drawn up on the basis of calculation of their mean values in man, assuming homogeneity of the groups. Yet recent investigations have shown that an intrinsic heterogeneity exists for many parameters in healthy individuals. Numerous studies of the state of the cardiovascular system of the healthy human population have shown that maximal and minimal values of many hemodynamic parameters, studied under conditions close to those of basal metabolism, differ from one another by as much as 2-4 times. Facts such as these have been explained, not by certain particular features of the values under consideration, but by technical errors in data collection [10, 11]. It was Savitskii (1974) who first drew attention to typologic differences in the central hemodynamics of patients with essential hypertension. Using the cardiac index (CI) as his basis, he distinguished

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