of 30 various drugs were studied earlier by using the gasping model. The most effective drugs, such as high-dose amitriptiline, pentobarbital, diazepam, etc. (those which decrease locomotor activity [7]) increased gasping time only by 36-74% (8-16 sec.) [7,11,12]. The evidence suggests that adenosine and its analogs can be regarded as most promising cerebroprotective drugs in brain ischemia.

The effect of adenosine is probably to be attributed to a decrease of neuron activity due to reduced O_2 consumption and body temperature drop [3] and/or due to the inhibited release of excitatory amino acids [8] and other neurohormones, such as catecholamines.

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Protective Effect of 2,3-Butanedione Monoxime on the Myocardial Ischemia in Rats

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The recovery of heart pump function after cardioplegic arrest depends considerably on the degree of preservation of high-energy phosphates in the myocardial tissue. One of the ways to protect the ischemized myocardium consists in the reduction of cell ATPase activity. In this respect 2,3-butanedione monoxime (BDM) may be of the great value due to its ability to reduce the sensitivity of contractile proteins to Ca-ions as well as its direct inhibitory effect on the myosin-actin interaction [1,2,6,7]. BDM has been shown to be able to slow considerably the reduction of the content of high-energy phosphates in the rat heart under conditions of hypoxia [10].

Table 1. ATPase Activity of Myocytes (μmole P_i/min·μg protein) Isolated from Myocardial Bioptates in Control and in Experiments with BDM (M±m)

Conditions	before cardioplegia		after reperfusion	
	Ca, Mg-ATPase	Mg-ATPase	Ca, Mg-ATPase	Mg-ATPase
control n=6	0,11±0,01	0,05±0,00	0,12±0,03	0,06±0,01
BDM n=4	0,12±0,01	0,05±0,00	0,12±0,00	0,05±0,00

The purpose of the present work was to determine whether BDM possesses

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a protective effect under conditions of ischemia and reperfusion after the cardioplegic arrest of the isolated heart.

MATERIAL AND METHODS

Rats weighting 300-400 g were used in the experiments. The animals were anesthesized by urethane intraperitoneal injection (1.6 g/kg). The pump function [8,9] of isolated hearts was studied in the experiments. The left auricle was filled with the perfusion solution under the pressure created by the height of the level of liquid above the heart and the LV (left ventricle) filling pressure for a diastole was measured. During systole the solution from the ventricle leaked out through the aorta, aortal cannula and air-reservoir.

The resistance to cardiac output was created using a needle 1 mm in diameter and 40 mm in length near the outlet of the system.

Krebs-Henseleit solution for the perfusion contained (in mM) 118 NaCl, 4.7 KCl, 3 $CaCl_2$, 1.2 $MgSO_4$, 25 $NaHCO_3$, 0.5 Na-EDTA, 11 glucose. The solution was saturated with carbogen (95% O_2 and 5% CO_2) (pH 7.36 at 37°C). The mean aortic pressure and the heart rate were monitored with a Gould Statham P23Db electromanometer hooked up to a Gould Brush 2400 monitor. The aortic output and coronary flow were measured. From the data obtained the minute volume and external cardiac output were calculated.

After the registration of the initial parameters, the cardioplegic solution was delivered to the aorta for 5 min, after which heart perfusion was discontinued. The period of ischemia lasted for 30 min. Reperfusion was performed with Krebs-Henseleit solution for 45 min. Two runs of experiments were carried out. In the first run, serving as the control, the cardioplegic solution contained (in mM): 118 NaCl, 18.8 KCl, 1.8 $CaCl_2$, 1.2 $MgSO_4$, 1.2 KH_2PO_4, 25 $NaHCO_3$, 0.5 Na-EDTA, and 20 mannitol. In the second run the cardioplegic solution contained BDM instead of mannitol and the Ca^{2+}-concentration was increased to 2.7 mM to compensate for the part of the Ca^{2+} bound with BDM according to its BDM-binding constant [3].

In several experiments of both runs a heart biopsy was carried out. Pieces of the epicardium of the left ventricle (LV) wall weighting 3-10 g were taken. Biopsy was performed before the cardioplegical heart arrest and at the end of the reperfusion period. Isolated myocytes separated by collagenase from the bioptates obtained were suspended in 1% Triton X-100 solution. ATPase activity of the myocytes was measured in a medium containing (in mM) 25 imidazole, 100 NaCl, 10 KCl, 8 $MgCl_2$, 5 ATP, 0.5 dithiothreitol, 1.5 oubaine, 1 phosphoenolpyruvate, 0.15 NaDH, as well as 2 IU/ml pyruvate kinase and lactate dehydrogenase, pH 7.1. The NaDH disintegration rate was registered according to changes in the optical

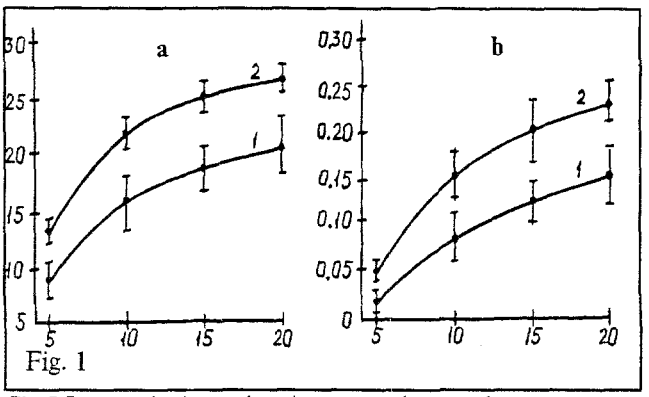

Fig. 1

Fig.1 Functional indexes of cardiac output after reperfusion.
Abscissa: LV filling pressure (mm H_2O; ordinate: a) minute volume (ml/min·g); b) external cardiac output ($J10^{-4}$min·g). 1 - control; 2 - experiments with BDM.

density of the myocyte suspension by a Shimadzu 210 LN spectrophotometer at 30°C and 340 nm. ATPase activity was also measured in myocytes from the hearts of a separate group of rats placed in a solution containing 20 mM BDM. Protein concentration was measured in accordance with the modified Lowry method [5].

RESULTS

BDM in the solution containing isolated myocytes of rat hearts was shown to reduce Mg^{2+}-ATPase activity from 0.057 to 0.040 μmole P_i/min·mg protein as well as $Ca^{2+}Mg^{2+}$ - ATPase activity from 0.206 to 0.149 μmole P_i/min·mg protein, that is, by 28 and 30%, respectively. In contrast, BDM addition to the cardioplegic solution had no discernible effect on the ATP of the myocardial bioptates taken after the reperfusion (see Table 1). The lack of BDM effect after the reperfusion may be associated with the reversibility of its influence following its removal from cardiac myocytes.

Table 2. Functional Indexes of Cardiac Output in Control and in Experiments with BDM (M±m)

Condition	before cardioplegicarrest					after reperfusion				
	MV	CF	MAP	HR	ECO	MV	CF	MAP	HR	ECO
control n=8	28,6±0,8	9,3±0,4	73±4	174±12	0,28±0,02	16±2,2	4,1±0,7	37±6	149±22	0,09±0,02
BDM n=9	30,0±0,06	9,2±0,4	74±5	191±7	0,30±0,02	22,4±1,1*	6,3±0,5*	51±4	182±8	0,15±0,02

Note: MV - minute volume, CF - coronary flow, MAP- mean artic pressure, HR - heart rate, ECO - external cardiac output. Asterisk: $p<0,05$, n - the number experiments.

In Table 2 the functional parameters of cardiac output at a moderate LV filling pressure of 10 cm H_2O are presented. Coronary flow and cardiac output were estimated to reach 44 and 55% of the pre-ischemia level, respectively, in 45 min after the reperfusion. Mean aortic pressure was shown to recover to 51%, while experimental cardiac output reached only 33% of the initial level.

The functional parameters of the hearts subjected to ischemia in BDM-containing cardioplegic solution were higher as compared to the controls. The restoration of minute volume as well as of external cardiac output increased by 19%. Mean aortic pressure and coronary flow exceeded the control level by 18 and 25%. Better restoration of minute volume and external cardiac output was detected in the entire range of volume loadings (see Fig.1)

Cardioplegic solution is known to arrest contractile function before ischemia and, therefore, to reduce the outlay of energy significantly. Nevertheless, BDM addition has an additional protective effect possibly due to its ability to inhibit ATPase activity. At least the degree of the reduction of ATPase activity of the normal heart under the influence on BDM (29%) is similar to the degree of the enhancement of pump heart function (19%).

Based on these facts, the addition of BDM to cardioplegic solution seems to reduce the disintegration rate of adenine nucleotides during ischemia.

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Solcoseryl: Ulcerostatic Effect and Its Possible Mechanisms

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Currently solcoseryl, a Swiss-Yugoslav preparation, has become a widespread agent to treat wounds of various origin. However, the mechanism of its action remains obscure.

It has been established that ulcer progression is determined by the state of the connective tissue and its components [2, 3, 7]. The balance of the latter at various stages of ulcer formation and during treatment with therapeutic agents characterizes intimate aspects of ulcerogenesis and the mechanisms of action of ulcerostatic preparations. The aim of the present study was to elucidate the dynamics of the connective tissue components in the formation of stomach ulcer and to analyze the effect of solcoseryl under experimental conditions.

MATERIAL AND METHODS

All experiments were carried out on albino laboratory rats of body weight 150-180 g. Stomach ulcer was induced by the acetate method [8]. Starting from the first day of the experiment the animals received solcoseryl intraperitoneally (2 mg/kg x 24 h). Euthanasia of the groups (n=10) was performed after 7, 14, and 28 days. The stomach was excised and the ulcer area was measures. The ulcerated tissue

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