Pre-clinical testing of Acizol: An efficacy in experimental cardiology

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1. Introduction: Acizol was developed by pharmaceutical association "Makiz-pharma" (Moscow). Acizol as antidote to carbon oxide belonging to series of zinc organic compound is effective antioxidant. Experimental studies showed that Acizol is effective antidote, providing necessary level of organism resistance to carbon oxide intoxication in wide range of the poison concentration and time of poisoning. The mechanism of Acizol action is influence on cooperative hemoglobin interaction, which can improve oxygen properties of blood and decrease relative affinity of hemoglobin to carbon dioxide. Activation of the central nervous system, improvement of vegetomotor and psychomotor autoregulation, increase in physical endurance and working capacity of experimental animals were demonstrated. Adaptation, antiradical and reparation properties of Acizol were registered.
We studied Acizol specific pharmacology activity at intragastric introduction on cardiac ischemia. Two experimental models were used (cardiac infarction and calcium arrhythmia).

2. MATERIALS AND METHODS. The Study was done on unbred white rats. Rats were obtained at the Rappolovo animal farm (Saint-Petersburg). Rat age - 2.5-3 months, weight - 150–160 g. Quarantine (acclimatization period) for all animals lasted 14 days.
Cardiac infarction modeling was done by the left coronary artery dressing [G.I. Djachuk, G. A. Lapkina, 1992].

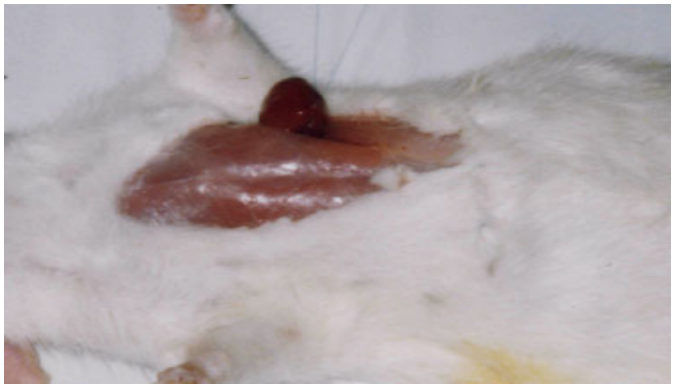


Fig. 1.The left coronary artery dressing

Five Study animal groups were formed

1. Intact animals
2. Animals with cardiac infarction (no treatment);
3. Animals with cardiac infarction – Enalapril 1 mg/kg);
4. Animals with cardiac infarction - Streptokinase (22 000 IU/kg);
5. Animals with cardiac infarction - Acizol (60mg/kg);

Survival rate, electrocardiography and histology indices were registered.

3. Results and discussions.

3.1. **Experimental cardiac infarction**

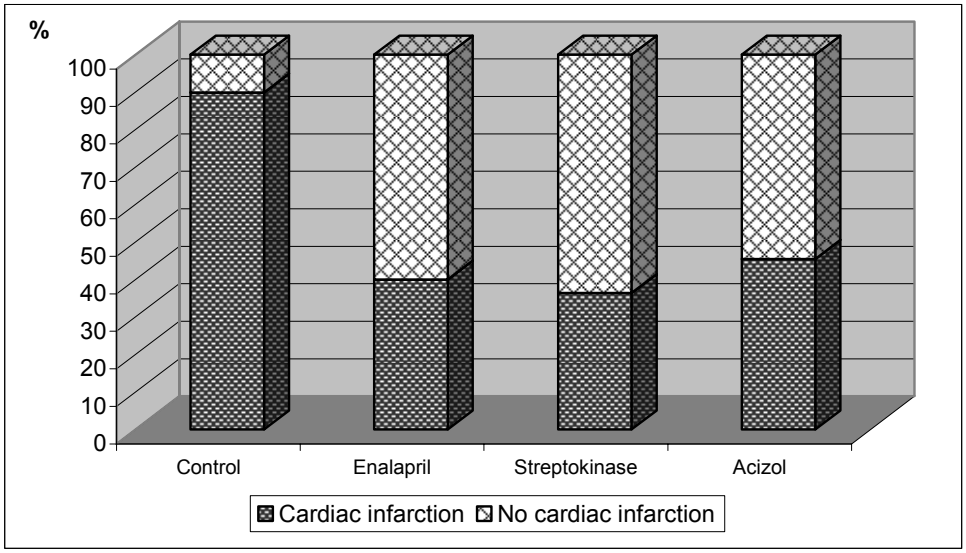


Fig. 2. Cardiac infarction rate in experimental groups

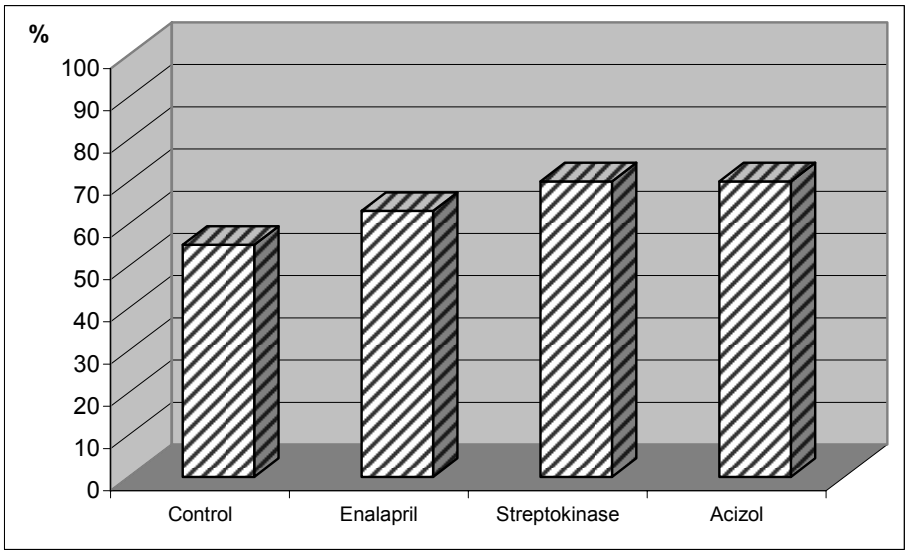


Fig. 3.Survival rate in experimental group

Table 1

Segment ST in experimental animals 1 hour after cardiac infarction, M ± m

Parameters	**Group**			
	Control	Enalapril	Streptokinase	Acizol
ST mm (+)	2.04±0.22	0.78±0.13 *	0.77±0.10*	0.66±0.14*

*) — significant differences from the control ($p<0.05$)

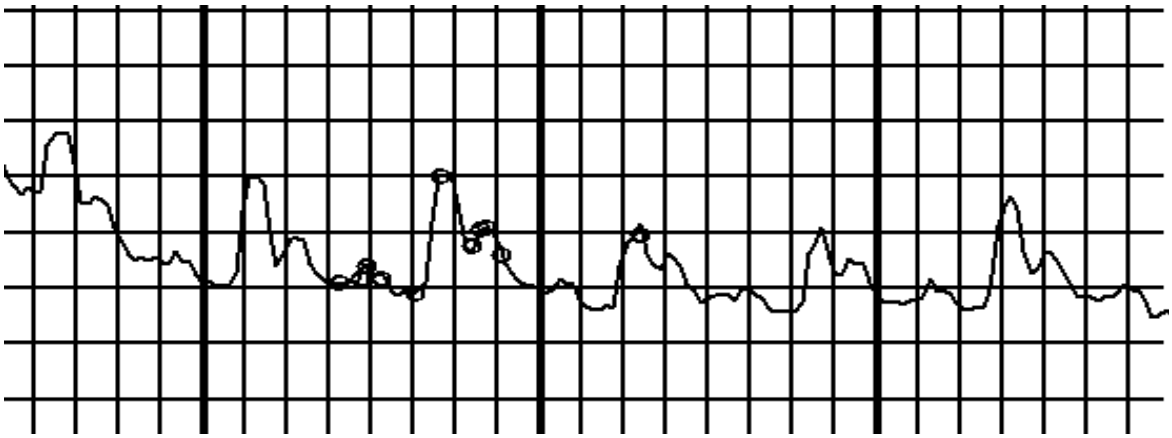


Fig. 4. Rat ECG (Group Control) 1 hour after cardiac infarction

Table 2

Segment ST in experimental animals 7 days after cardiac infarction, M ± m

Показатели	**Экспериментальная группа**			
	Control	Enalapril	Streptokinase	Acizol
ST mm (-)	1.11±0.13	0.44±0.11 *	0.29±0.13*	0.24±0.12*

*) — significant differences from the control ($p<0.05$)

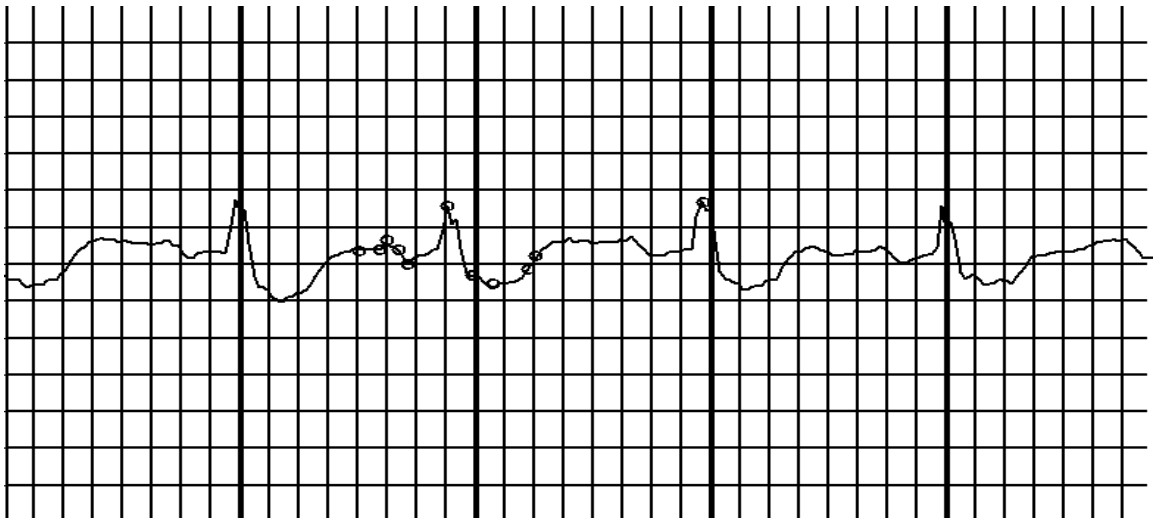


Fig. 5. Rat ECG (Group Control) 7 days after cardiac infarction

Table 3

ECG in experimental animals on cardiac infarction model, % of Norm

Parameters	HR	**P**	**R**	**S**	**T**	**PQ**	**QT**
Control							
1 hour	76,42•	63,38•	259,55•	256,95•	177,58•	141,66•	158,43•
7 days	114,41*	75,41•	169,32*•	173,52*•	122,86*	138,27•	166,22•
Enalapril							
1 hour	59,09•	38,35•	155,84•	47.94•	125.61•	99,9	109,95
7 days	62,64•	36,21•	142,36•	75.22*•	109.42*	96,42	99,47
Streptokinase							
1 hour	103,88	93,58	267,98•	187,96•	125,72•	96,26	93,29
7 days	109,46	108,85	258,88•	164,27•	106,72*	89,67	93,94
Acizol							
1 hour	96,76	94,13	187,75•	110,93	174,32•	87,52•	88,43•
7 days	91,37	101,83	192,83•	85,73•*	167,48•	108,32*	104,32*

*) — significant differences from the control ($p<0.05$)

•) — significant differences from the intact animals ($p<0.05$)

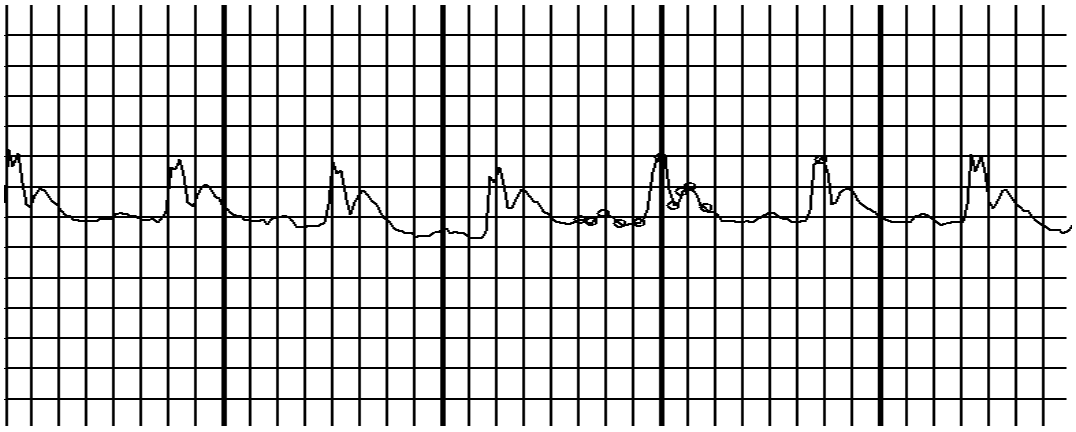


Fig 6. Rat ECG (Group Enalapril) 1 hour after cardiac infarction

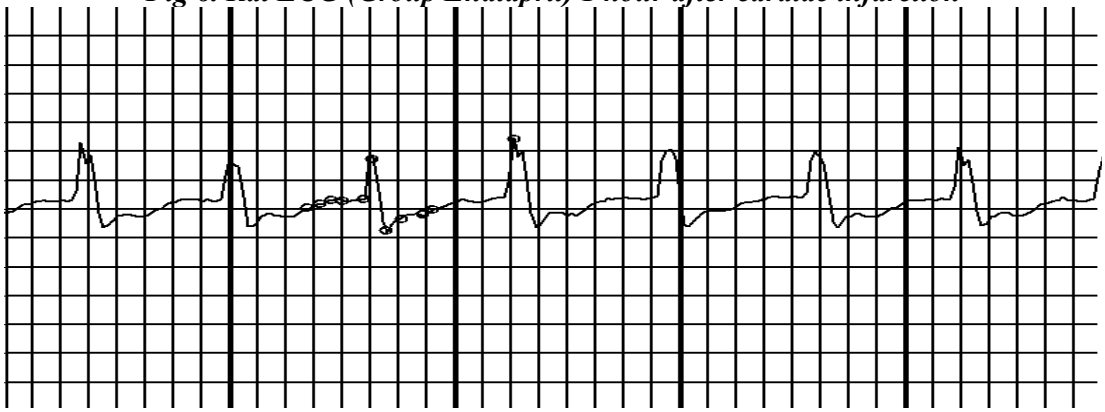


Fig 7. Rat ECG (Group Enalapril) 7 days after cardiac infarction

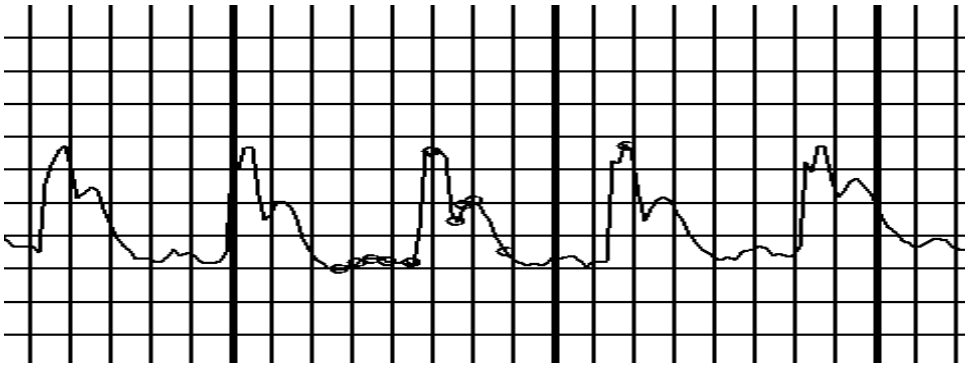


Fig8. Rat ECG (Group Acizol) 1 hour after cardiac infarction

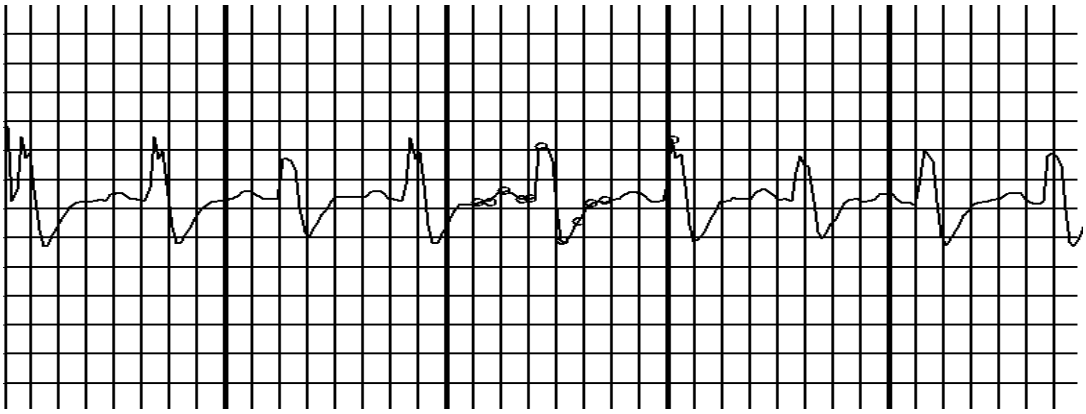
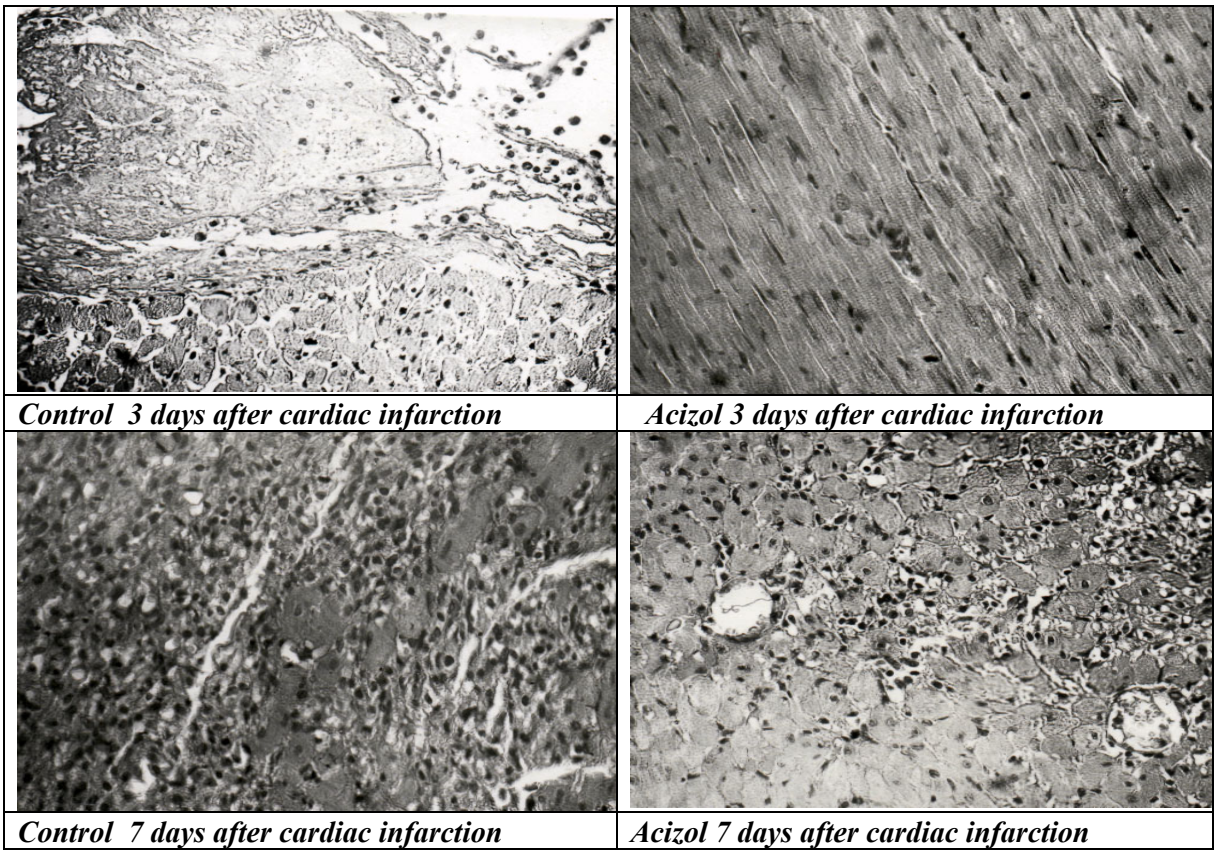


Fig 9. Rat ECG (Group Acizol) 7 days after cardiac infarction



Control 3 days after cardiac infarction	*Acizol 3 days after cardiac infarction*
Control 7 days after cardiac infarction	*Acizol 7 days after cardiac infarction*

Fig.10. Acizol impact on histological changes in experimental rats

3.2. Calcium arrhythmia

Table 4

Calcium arrhythmia in control rats

№	Latent period, sec	Fibrillation time, sec	Life time, sec
1	7	18	42
2	5	12	48
3	10	20	59
4	8	16	42
5	12	13	60
6	6	19	51
M	**8.00**	**16.33**	**50.33**
m	**1.06**	**1.33**	**3.23**

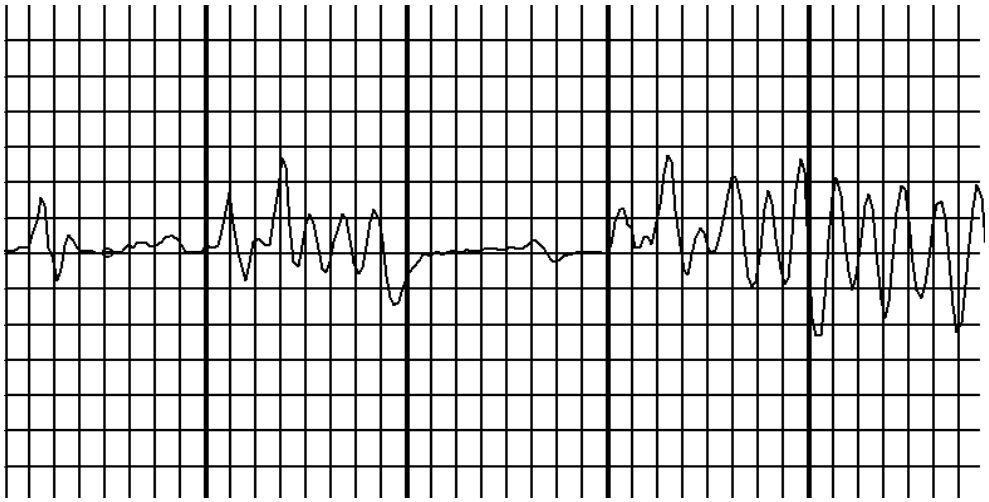


Fig 11. ЭКГ Rat ECG on Calcium arrhythmia (Group Control), 5 sec

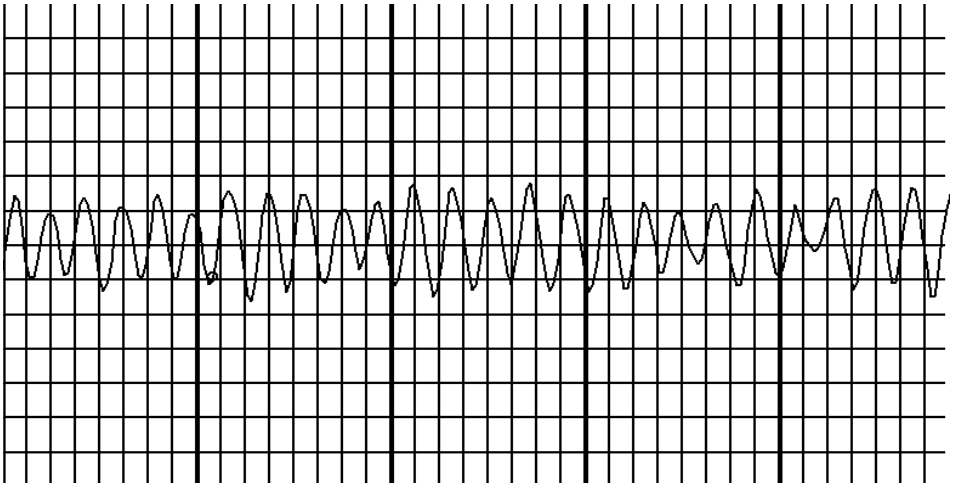


Fig 12. ЭКГ Rat ECG on Calcium arrhythmia (Group Control), 12 sec

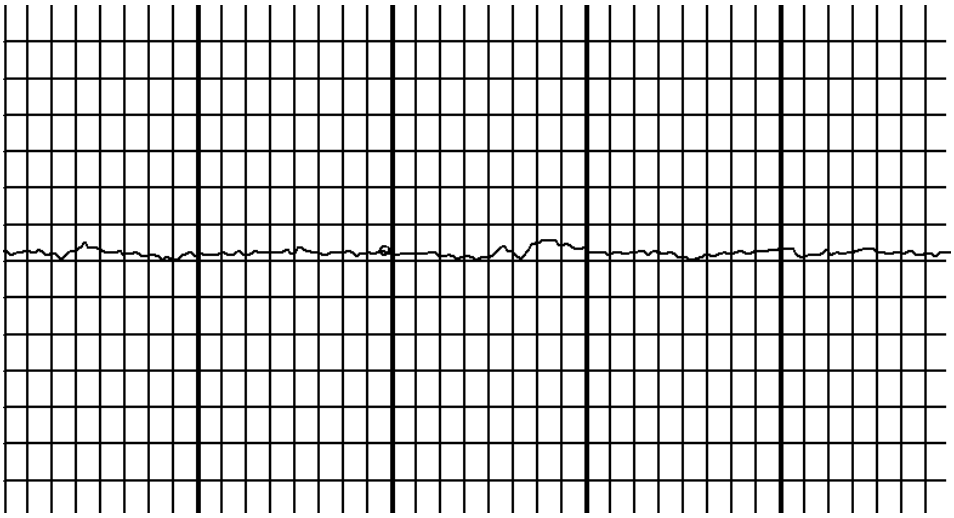


Fig. 13. ЭКГ Rat ECG on Calcium arrhythmia (Group Control), 48 sec

Table 5

Acizol impact on Calcium arrhythmia in rats

№	Latent period, sec	Fibrillation time, sec	Life time, sec
1	11	22	78
2	16	26	54
3	12	35	78
4	18	24	69
5	13	28	65
6	19	31	73
M	**18.83***	**27.67***	**69.50***
m	**1.35**	**1.94**	**3.73**

*) — significant differences from the control ($p<0.05$)

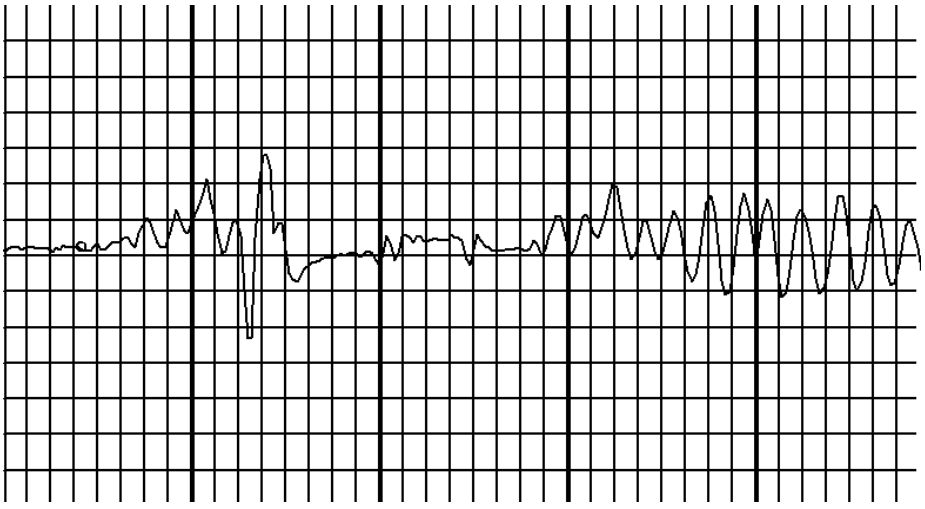


Fig. 14. ЭКГ Rat ECG on Calcium arrhythmia (Group Acizol), 18 sec

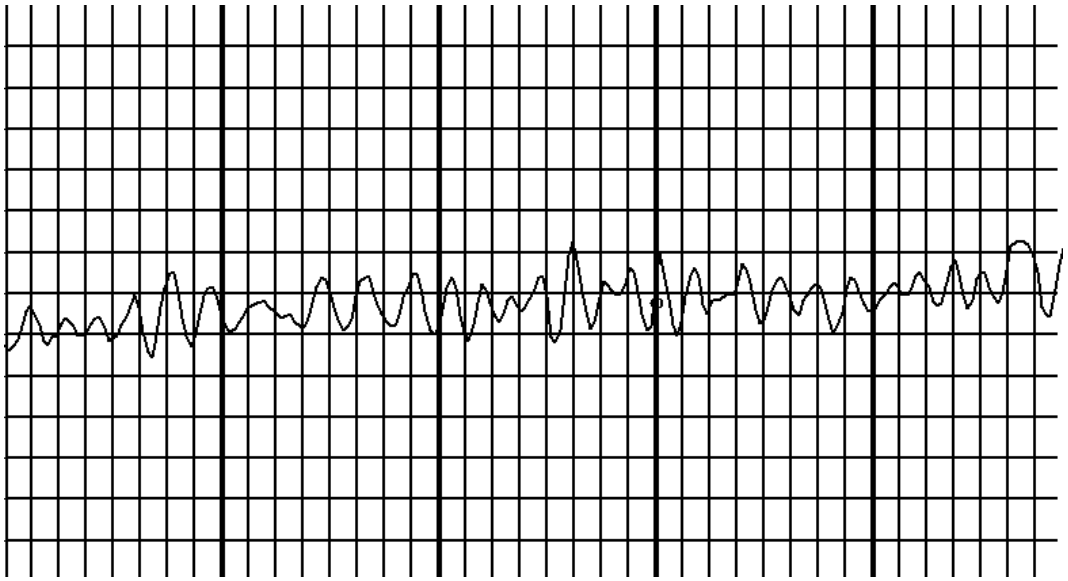


Fig. 15. ЭКГ Rat ECG on Calcium arrhythmia (Group Acizol), 24 sec

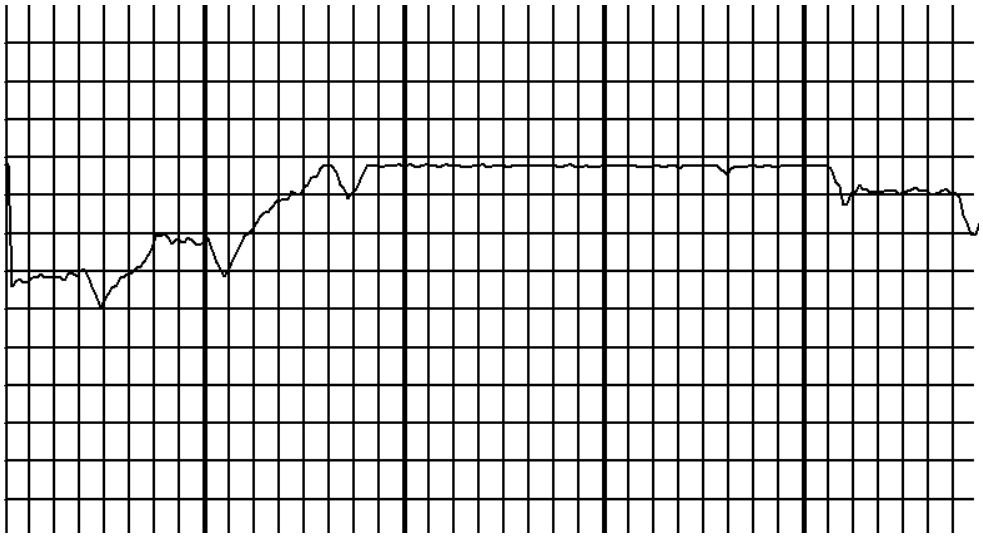


Fig. 16. ЭКГ Rat ECG on Calcium arrhythmia (Group Acizol), 69 sec

4. CONCLUSION:

1. **Experimental studies showed that Acizol has antiichemic properties, like as Enalapril and Streptokinase:** Acizol can increase an experimental animals survival rate on 20%, decrease a heart attack frequency approximately in 2 times, increase a cardiac tonus in 2 times, accelerate atrioventricular conductivity on 25% in comparison with the control.
2. **Acizol has antiarrhythmic properties**: lengthening of the latent period on 70% and lengthening of the fibrillation time on 80%. Increasing time of a life of experimental animals on 40% in comparison with the control was registered.

Acizol is perspective drug for prophylaxis and cardiac ischemia treatment.