EFFECT OF THE POLYVALENT PROTEINASE INHIBITOR TRASYLOL ON ANTIBODY FORMATION UNDER NORMAL CONDITIONS AND IN EXPERIMENTAL ATHEROSCLEROSIS

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Antibody formation against sheep's red cells and human serum albumin took place with the same intensity in rabbits with alimentary atherosclerosis as in normal animals. Trasylol did not affect antibody formation in healthy animals but sharply inhibited the formation of specific immunoglobulins (especially 7S) in rabbits with experimental atherosclerosis. This suggests that trasylol acts not by directly inhibiting the function of lymphoid tissue cells, but by inhibiting an immunostimulant factor that circulates in the blood stream in experimental atherosclerosis.

KEY WORDS: Atherosclerosis; trasylol; antibody formation.

The sera of rabbits with experimental atherosclerosis, if injected together with antigen, stimulate antibody formation in intact animals [2]. The immunostimulant effect disappears completely after treatment of the sera with the polyvalent proteinase inhibitor trasylol.

The ability of trasylol to inhibit antibody formation in animals with experimental atherosclerosis was investigated.

EXPERIMENTAL METHOD

Experiments were carried out on 24 male rabbits weighing 2.3-2.5 kg, divided into four groups with six rabbits in each group. The rabbits of groups 1 and 2 were kept on the usual diet, but those of groups 3 and 4 received added cholesterol in a dose of 0.5 g/kg body weight daily for 13 weeks before immunization. The rabbits of groups 1 and 3 were immunized intravenously with sheep's red cells (1 ml of a 20% suspension/kg body weight) and crystalline human serum albumin (40 mg/kg body weight). The animals of groups 2 and 4 received trasylol in a dose of 5000 K.I.U. (kallikrein inhibitor units) per injection by intravenous drip simultaneously with the antigen and 24 h later. The titer of antibodies against sheep's red cells in the blood serum were determined by the active hemagglutination test and the titer against human serum albumin by the passive hemagglutination test. The content of 7S antibodies against both antigens was determined after degradation of the 19S immunoglobulins by 2-mercaptoethanol at pH 7.2 [3].

EXPERIMENTAL RESULTS

The experiments showed that antibody formation against both antigens was indistinguishable in rabbits with alimentary atherosclerosis and in control animals (Table 1).

Trasylol did not affect the formation of antierythrocytic and antialbumin antibodies in healthy animals, but it sharply inhibited the formation of specific immunoglobulins (especially 7S) in rabbits with experimental atherosclerosis. This suggests that trasylol acts not by directly inhibiting the function of lymphoid

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TABLE 1. Effect of Trasylol on Formation of Antibodies against Sheep's Red Cells under Normal Conditions and in Experimental Atherosclerosis

Antibodies	Group of animals	Before immunization		After immunization			
				5th day		10th day	
		titer of antibodies	P	titer of antibodies	P	titer of antibodies	P
Before treatment with 2-mercaptoethanol	1	1,67 (1—3)	—	3,00 (2—4)	—	5,50 (4—7)	—
	2	1,83 (1—3)	>0,05	3,17 (2—4)	>0,05	6,00 (4—8)	>0,05
	3	1,83 (1—2)	>0,05	2,83 (2—4)	>0,05	5,67 (4—8)	>0,05
	4	1,83 (1—3)	>0,05	2,17 (1—3)	>0,05	3,17 (2—4)	<0,05
After treatment with 2-mercaptoethanol	1	—		—		2,17 (1—3)	
	2	—		—		2,33 (1—3)	>0,05
	3	—		—		2,67 (1—5)	>0,05
	4	—		—		0	

Antibodies	Group of animals	After immunication					
		15th day		20th day		25th day	
		titer of antibodies	P	titer of antibodies	P	titer of antibodies	P
Before treatment with 2-mercaptoethanol	1	4,67 (4—6)	—	3,17 (2—4)	—	2,50 (2—3)	—
	2	4,83 (3—7)	>0,05	3,33 (2—4)	>0,05	2,33 (2—3)	>0,05
	3	5,17 (3—8)	>0,05	3,50 (2—5)	>0,05	2,50 (2—3)	>0,05
	4	3,00 (2—4)	<0,05	2,17 (1—3)	>0,05	1,83 (1—3)	>0,05
After treatment with 2-mercaptoethanol	1	3,67 (3—5)	—	3,17 (2—4)	—	2,50 (2—3)	—
	2	3,83 (3—5)	>0,05	3,17 (2—4)	>0,05	2,33 (2—3)	>0,05
	3	3,50 (3—5)	>0,05	3,50 (2—5)	>0,05	2,50 (2—3)	>0,05
	4	0		0		0	

Legend: Arithmetic mean values of $\log_2$ of antibody titers and limits of their variation (in parentheses) are shown; P calculated by Wilcoxon—Mann-Whitney criterion [1].

tissue cells, but by inhibiting the immunostimulant factor that circulates in the blood serum in experimental atherosclerosis.

It can be postulated on the basis of these results that some form of equilibrium arises in rabbits with experimental atherosclerosis between the immunodepressant effects of cholesterol or its metabolic products and the immunostimulant action of a serum factor, which is probably a proteolytic enzyme or its activator. Trasylol disturbs its equilibrium and thus causes inhibition of antibody biosynthesis in animals with experimental atherosclerosis.

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