EFFECT OF RUTIN ON CHOLESTEROL CONCENTRATION IN CANINE LYMPH, BLOOD, AND TISSUES

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The relative constancy of the composition and properties of the internal medium of organs, tissues, and cells is maintained, on the one hand, by assimilation of the necessary substances from the blood and, on the other hand, by removal of their metabolic products. To maintain this constancy of the internal medium of each organ and of the body as a whole, the drainage and transport functions of the lymphatic system play an important role.

To study the functions of the blood-lymphatic barriers, a particularly important aspect is investigation of permeability for substances participating in the formation and maintenance of the internal medium. These substances include cholesterol, which is concerned in some of the most important biochemical and physical processes.

An important role in the regulation of vaso-tissue permeability is ascribed to the mucolytic system, whose properties correlate to some degree with the presence of hormones and vitamins in the medium. It has been shown [1, 3, 5, 7, 9] that vitamin P affects vaso-tissue permeability. In medical practice vitamin P or its analog rutin is used to lower permeability and to reduce fragility of capillaries and also for the prevention of hemorrhages in hypertension. However, participation of the lymphatic system in the transport, distribution and also, perhaps, the structural reorganization of lipid complexes and, in particular, of cholesterol, under the influence of vitamin P has not yet been studied.

The object of this investigation was to study the character of changes in the concentration of total, esterified, and free cholesterol and in the lymph flow in dogs under the influence of rutin.

EXPERIMENTAL METHOD

Experiments were carried out on nine dogs anesthetized with morphine and hexobarbital. The animals were kept on an ordinary diet. Biochemical analyses were undertaken not earlier than 12-14 h after taking food. Samples of lymph from the thoracic duct and of blood from the femoral vein and artery were taken before injection of rutin and at 15-min intervals for 45 min after injection. A solution of rutin was injected into the animal's femoral vein in a dose of 3 mg/kg body weight. The concentration of total cholesterol in the blood serum and lymph was determined by the method in [10] and in the tissues as in [8], esterified cholesterol was determined by the digitonin method [4]. The lymph flow and systemic arterial pressure were recorded by means of an eight-channel automatic writer of potentiometric type. The numerical results were subjected to statistical analysis and significance was determined from Student's table.

EXPERIMENTAL RESULTS

The study of the effect of rutin on the character of changes in the concentration of total, esterified, and free cholesterol in the biological fluids and tissues showed (Table 1) that the concentration of total and free cholesterol in serum from venous blood was higher ($P < 0.05$) than in serum from arterial blood. The concentrations of total and esterified cholesterol in lymph from the thoracic duct were significantly lower ($P < 0.001$) than in serum from venous arterial blood.

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TABLE 1. Concentrations of Total (I), Esterified (II), and Free (III) Cholesterol (in mg%) in Biological Fluids and Tissues under the Influence of Rutin (M ± m)

Experimental conditions	Duration of action of preparation, min	Arterial blood			Venous blood			Lymph from thoracic duct			Total tissue cholesterol		
		I	II	III	I	II	III	I	II	III	I	II	III
Normal	—	160,8±13,0	136,5±17,8	24,3±7,0	199,9±31,5	129,7±21,2	70,2±9,3	71,3±5,9	45,1±10,0	26,2±4,0	195,0±14,0	47,9±3,4	199,8±39,9
Injection of rutin	15	140,7±30,8	106,7±27,6	34,1±12,7	161,2±36,6	111,7±18,3	49,5±10,2	76,0±9,3	53,9±14,4	22,1±5,0	—	—	—
	30	149,3±39,0	101,4±20,3	47,9±5,0*	168,0±40,7	115,3±24,6	53,0±10,1	72,0±13,8	31,8±9,0	40,2±5,8	—	—	—
	45	139,3±33,2	85,6±11,2	53,7±10,8*	160,8±28,6	116,1±26,8*	44,7±12,1*	87,6±13,1	57,5±13,4	30,1±8,2	97,2±2,8*	19,1±0,9*	95,7±16,9*

*$P < 0.05$.

The concentrations of total and esterified cholesterol in arterial blood 30 and 45 min after injection of rutin were lower, but not significantly ($P > 0.05$), by 7.2 and 13.4% and 25.8 and 37.3%, respectively, whereas the free cholesterol concentration was higher by 97.1% and 120.9%, respectively, ($P < 0.001$). At this same time the total cholesterol level in venous blood was reduced ($P > 0.05$) by 16.0 and 19.6%, that of esterified cholesterol by 11.2 and 10.5% ($P > 0.05$), and the free cholesterol level by 25.5 and 36.5% ($P < 0.005$), respectively. The concentrations of total, esterified, and free cholesterol in lymph from the thoracic duct was higher than in the control ($P < 0.05$). The concentration of total cholesterol in the popliteal lymph node, gastrocnemius muscle, and liver was significantly reduced by the action of rutin ($P < 0.001$). Free cholesterol from arterial blood passes into the interstitial space, where it undergoes esterification. The results obtained on esterification of cholesterol in the interstitial space confirmed the data of Glomset et al. [11], who showed that esterification cannot be adequately carried out in human plasma; they postulated the presence of a high potential capacity for cholesterol esterification in the interstitial space. Stokke et al. [12] also found that cholesterol undergoes esterification in cardiac lymph and in the interstitial space in dogs. Bavina [2] considers that cholesterol is esterified by different mechanisms in blood and tissues.

The venous and lymphatic systems take part in the removal of esterified cholesterol from the interstitial space.

The present experiments showed that after injection of rutin in a dose of 3 mg/kg the arterial pressure of the dogs remained unchanged throughout the experiment but the lymph flow was increased by 32.1, 100.1, 119.8, 95.3, and 145.5% after 2, 5, 15, 45, and 75 min, respectively. The increase in lymph flow after injection of rutin was accompanied by an increase in cholesterol resorption from the interstitial space by the roots of the lymphatic system, i.e., lymph plays an essential role in the process of cholesterol transport in the body. Under the influence of rutin, besides an increase in cholesterol removal by the lymphatic system from the interstitial space, a fall in its level in the tissues also was observed. It has been shown [13] that vitamin P acts on the pituitary-adrenal system, conserving adrenalin, and the latter, which stimulates pituitary function, leads to an increase in secretion of adrenocortical hormones. We know that cholesterol can be converted into steroid hormones and cholic acids.

The activating role of rutin in oxidation-reduction processes in the body during disturbances of vaso-tissue permeability (atherosclerosis) was demonstrated previously [3, 6]. It can accordingly be postulated that under the present experimental conditions cholesterol conversion took place, with the result that its level in the tissues fell.

The lymphatic system in animals thus plays an important role in the transport of cholesterol formed as a result of metabolism under the influence of rutin from the interstitial spaces.

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