RHEOLOGIC PROPERTIES OF THE PROTEIN HYDROLYSATE «HYDROPROT» IN SOME HEAVY PATHOLOGICAL CONDITIONS (CHANGES IN ERYTHROCYTE FLEXIBILITY). PART ONE

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In the past few years, the rheological properties of rheodextrans have been extensively studied. Their mechanism of action is conditioned mainly by the reduction of plasma viscosity and by obviating the aggregation of high molecular weight dextrans. In this case it is a matter of a mechanical sanogenetic effect. Thereafter, the satisfactory outcome of rheology disturbances depends exclusively on the degree of metabolism normalization in the microcirculation system..

The objective of the work presented is to study the rheological properties of the protein hydrolysate Hydroprot (9) at erythrocyte level. A number of observations on the properties of the above hydrolysate to prolong the validity term of conserved blood and erythrocyite mass (4) led us to undertake the researches described, on the ground of the assumption that amino acids exert a particularly favourable effect on the functional fitness of the membrane. Three heavy pathological conditions were deliberately selected as object of study since in them it was known or supposed that a severe derangement of rheology existed.

Material and Method

I. Hemorrhagic shock observations were made in 32 dogs; the half of the series was protected with protein hydrolysate. The modified model of Wiggers was used to reproduce the shock (6). In the various stages of shock assays were performed of erythrocytes according to Teitle (10), blood pH (using the Astrup apparatus), and hematocrit values. Protein hydrolysate was administered 24 and half an hour before the experiment, at dose 5 ml/kg weight, the first time — subcutaneously, and the second — intravenously. II. Atherosclerosis was reproduced after the method of Anichkov in 41 rabbits (7), by increasing the dose of cholesterol up to 1 g/kg weight, and after the method of Ginter and co-authors (8) — in 23 guinea pigs.

Samples for erythrocytes' flexibility and hematocrit study were taken from the arterial blood after killing the animals. The rabbits were injected subcutaneously with protein hydrolysate at 5 ml/kg weight daily dose, over a 45-day period, and the guinea pigs — with 0.5 ml/100 g weight every other day, over a 130-day period. The control animals were subjected to injections with the same doses physiologic salt solution.

III. Thermal lesions were produced in 31 rabbits weighing 1900—2200g, divided up into three groups: intact, with burns and animals with burns treated with protein hydrolysate.

Burns were produced with a petrol burner, at 30 seconds exposure, on the back and both flanks, and the lesions involved nearly 20 per cent of the total body surface. Protein hydrolysate (5 ml/kg weight) was injected intraperitoneally, immediately after inflicting the burn injury. Blood samples for erythrocyte flexibility investigation were taken within 30—40 min after the burn.

Results and Discussion

I. From figure 1 it can be seen that the data concerning pH of the blood in the unprotected animals show substantially lower values than those in the animals experimented upon in the hypotensive period; at the end of the period the values in the protected group are close to those in the unprotected animals during the first hour of hypotension.

Complete blood reinfusion elevates pH with an ensuing tendency, similar to that observed in the unprotected animals, to approximate the starting values.

The changes in flexibility of erythrocytes in the various phases of shock are analogical. Here too, the lowering of values in the protected animals scarcely takes place towards the end of the hypotensive period, and the values are comparable to those in unprotected animals in the first hour of hypotension. Blood reinfusion leads to a more substantial improvement of flexibility among the protected animals.

Hematocrit in the protected animals exhibits a tendency to be reduced at the end of the hypotensive period, whereas in the unprotected animals a tendency for an increase between the second and third hour of the same period is noted. During and after reinfusion in either of the groups, values approximating the starting figures are recorded, with a tendency for elevated levels being maintained in the unprotected animals.

The data reported point to the fact that protein hydrolysate, applied protectively, improves some of the basic pathogenic aspects of the experimentally induced hemorrhagic shock. Metabolic acidosis, if judged from pH changes in the blood, manifests hardly at the end of the third hour of the hypotensive period. A parallel course is also disclosed by the curves of the flexibility values for erythrocytes and blood hematocrit (Fig. 1). The hematocrit values are considered as a convincing evidence of a lengthened dilution phase in the protected animals, a fact confirmed by the data concerning changes in the volume ratios of fluids and form elements in the blood stream and tissue spaces, established independently by one of the authors (6).

There is sufficient reason to accept that protein hydrolysate, after modifying the state of metabolic acidosis, improves the membranous properties of erythrocytes, rendering them more flexible and, on the other hand, interferes with their aggregation. All factors referred to improve the rheology

of blood, and maintain steady metabolic processes in the microcirculation system, which, in turn, exerts effect on dilutional processes, and once again, on the compensatory mechanisms of the organism. It is no mere chance

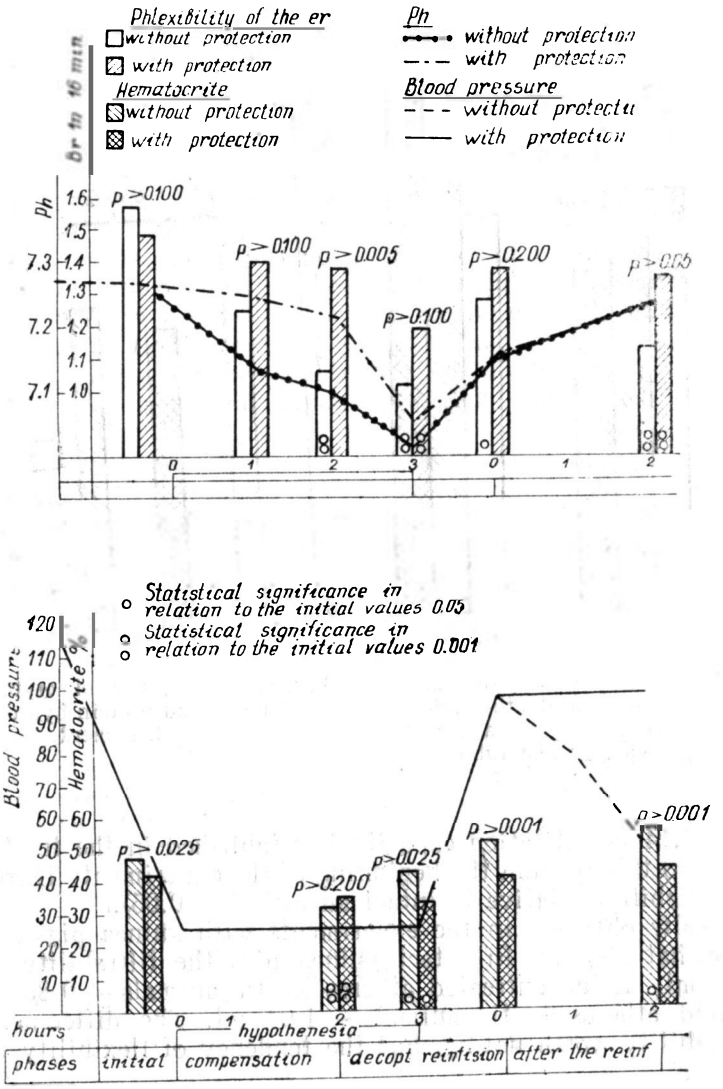

Fig. 1. Changes in pH, flexibility and hematocrit in experimental hemorrhagic shock and protein hydrolysate treatment.

that the outcome of hemorrhagic shock (5) among the protected animals shows about 20 per cent lethality, against 80 per cent among the unprotected ones.

II. It is evident from figure 2 that erythrocyte flexibility in experimentally induced atherosclerosis deteriorates compared with that in intact animals (0.97 against 1.35, $P<0.001$). Protein hydrolysate treatment manifests itself through a tendency of the flexibility of erythrocytes to im-

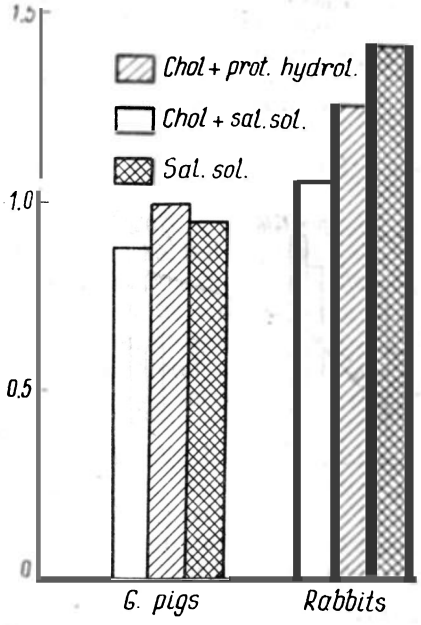

Fig. 2. Changes in the flexibility of erythrocytes in experimental atherosclerosis and after protein hydrolysate administration in guinea pigs and rabbits.

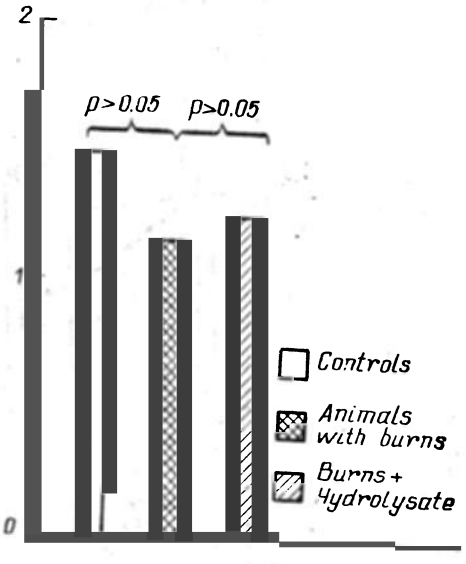

Fig. 3. Flexibility of erythrocytes in burns and protein hydrolysate treatment.

prove. A 1.14 ml filtration capacity is established in the treated animals about the 45 th day from the beginning of the experiment. There is no statistical reliability relative to intact animals ($P>0.05$).

The results obtained in the experiments with guinea pigs at 130 days are somewhat similar. In intact guinea pigs the filtrability established was 0.96 ml, in the untreated atherosclerotic animals — 0.86 ml, and in the treated atherosclerotic animals — 1.04 ml. The difference does not show reliability worth noting, but the tendency of flexibility to improve is present.

The data reported by one of the authors (1), concerning changes in lipid metabolism, blood supply of the internal organs and aortic wall (studied after Sapirstein — 2), methionine distribution and macroscopic changes in the intima of the aorta and internal organs (3) are in support of this tendency for rheological properties of the erythrocytes to improve in animals treated with protein hydrolysate.

III. The results in the experiments with burns are analogical (Fig. 3). While in intact animals the filtrability value amounts to 1.49 ml, in those with burns it is 1.15 ml, and in those treated with protein hydrolysate — 1.24 ml. The difference in values, although unreliable, displays the same regularity as in the animals with hemorrhagic shock and atherosclerosis. The study on rheological changes in burns under the effect of protein hydrolysate is still in its initial phase.

Concluston

The results submitted concerning the changes in flexibility of erythrocytes in experimentally induced hemorrhagic shock, experimental atherosclerosis and in burns point to a positive effect of protein hydrolysate on the rheology of erythrocytes. In the experimentally induced hemorrhagic shock, the changes in flexibility, as well as those in pH and hematocrit are reliable relative to changes in the control animals. The modified data in the animals with experimental atherosclerosis and burns, although unreliable relative to untreated animals, reveal a pronounced tendency for flexibility properties to improve.

The assumption is warranted that protein hydrolysate amino acids, after modifying the electric potentials on the surface of erythrocytes, account for their flexibility properties improvement. An effect is produced similar to the «rejuvenation» of erythrocytes, provided we base our arguments on the fact, established by Usami and co-authors (11), that young erythrocytes have lower viscosity than «adult» ones.

REFERENCES

1. Демирева, К., И. Попдимитров. V научна сесия на Мед. ф-тет Варна, 1973 (под печат). — 2. Демирева, К., И. Попдимитров. III нац. конф. по радиология и радиобиология, Пловдив, 1973. Резюмета на докладите — стр. 57. — 3. Попдимитров, И., К. Демирева. III нац. конф. по радиология и радиобиология, Пловдив, 1973. Резюмета на докладите — стр. 58. — 4. Попдимитров, И., В. Торрес, А. Пакман и Н. Родригес. *Пер Бюл. хем. кръвопр.,* 4, 1970, 11—15. — 5. Томова, И., И. Попдимитров Х. Гетов и К. Гекова. *Въпр. хемат. кръвопр.,* 1970, XIII, 199. — 6. Томова, И. дисертация: Експериментални проучвания върху патогенезата на необратимия хеморагичен шок, София, 1973. — 7. Anitschkow, N. *Beitr. path. Anat.* 1913, 56, 739 (cited by I. Balo, in Atherosclerosis, Moscow, 1961, 98). — 8. Ginter, E., J. Babala, P. Bobek, Z. Dumbalova. *Cor vasa,* 1968, 10 (2) 121—129. — 9. Popdimitrov, I., A. Rodrigues, A. Pakman. *Rev Cub. Med.,* 5, 1966, 409. — 10. Teitle, T. *Nouv. Rev. Franc. d'hemat.,* 1967, 7 195. — 11. Usami, S., S. Chien, M. J. Gregersen. *Theoret.* Clin. Hemorheol., Proc. II Int. Conf., 1969, 266.

РЕОЛОГИЧЕСКИЕ СВОЙСТВА ГИДРОЛИЗАТА БЕЛКА «ГИДРОПРОТ» ПРИ НЕКОТОРЫХ ТЯЖЕЛЫХ ПАТОЛОГИЧЕСКИХ СОСТОЯНИЯХ

(I. сообщение)

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РЕЗЮМЕ

Исследования проведены в 3 постановках на экспериментальных моделях: 1) геморрагический шок по Wiggers (модифицированный) — на 22 собаках; 2) атеросклероз путем подкармливания холестерином — на 22 кроликах; 3) Ожог — на 20 кроликах. Использован гидролизат белка «Гидропрот» из говяжей крови.

Во все трех постановках устанавливается укорочение времени фильтрации эритроцитов (по Teitle) у протектированных или третированных гидролизатом белка животных, в отношении к контрольным. Гематокрит, исследованный у животных с геморрагическим шоком, показывает также достоверно более низкие цифры, что указывает на улучшенную гемодилюцию в течение гипотенсивного периода.

Делается предположение, что аминокислоты гидролизата белка, взаимодействуя с электрическими потенциалами на поверхности эритроцитной мембраны, придают ей свойство лучшей фильтруемости. Улучшенная реология эритроцитов является вероятно одним из важных саногенезных механизмов, которые благоприятствуют исходу из этих тяжелых патологических состояний при протекции или терапии гидролизатом белка.