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A NEW PREPARATION FOR PARENTERAL NUTRITION -- AMINOPHOSPHOLIPID

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From the Plant of Medicinal Preparations of the Leningrad Order of Labor Red Banner Meat Combine imeni S. M. Kirov.

During the past 15 years many various preparations have been suggested for the parenteral nutrition of patients in a number of countries, including the Soviet Union. The hydrolysates of protein occupy among them a special place. They are distinguished by their physiological value (E. Abderhalden, 1934; Rose, Haines, Johnson, 1942; Elman, 1948, etc.), as well as by the fact that, if they contain over 45 percent of amino nitrogen and are properly purified, they are completely devoid of anaphylactic and pyrogenotoxic properties (Z. A. Chaplygina, 1954; T. I. Golubev, 1957; Ramasarma, 1951, etc.). This renders the use of protein hydrolysates in medicine more promising in comparison to other similar preparations.

However, with all their positive qualities, the hydrolysates possess very low caloric value, 15 to 20 calories per 100 ml. Therefore, to raise the nutritive value of hydrolysates, five percent glucose and four to five percent alcohol are often added to them (I. I. Deryabin, A. P. Aleskovskiy, A. V. Yevdokimov, 1956; Rice, Orr, Enquist, 1950, etc.). The caloric value of hydrolysate is thus raised to 70 to 80 calories per 100 ml. However, the energy expenditure of a patient during a 24-hour period may vary, according to Verner (1949), within the range of 1200 to 1800 calories; therefore, to compensate, the patient must receive over two liters of hydrolysate containing glucose and alcohol.

If we take into account that protein hydrolysates can be administered parenterally only by the drip method,

it becomes obvious that this is not an easy task.

To raise caloricity and thus reduce the volume of the administered hydrolysate, studies have been conducted lately, especially in the United States, on obtaining fat emulsions suitable for parenteral nutrition (Gorens, Geyer, Stare, 1949; Shafirov, Mucholland, 1949; Geyer, Stare, 1951; Stare, Geyer, 1951).

As the liquid phase of these emulsions, the hydrolysates of protein containing glucose and other components are being tried out. It is possible, thus, to obtain a considerable rise in the caloricity of the hydrolysate and at the same time reduce the dosage essential to the maintenance of the patient's nitrogen balance in parenteral nutrition.

The value of fats to the organism consists not only of their high caloricity. It is known that many fats, especially vegetable fats, contain physiologically essential fatty acids. They are the highly unsaturated fatty acids, such as linoleic, linolenic, and arachidonic acid acids. According to the data of Thomasson (1953), Deuel, Reiser (1955), etc., the highly unsaturated fatty acids are needed in a number of functions of an animal organism.

Of the highly unsaturated fatty acids, the most active is linoleic acid which is transformed into arachidonic acid in the organism. According to the data of Schweigart (1956), the requirement of linoleic acid by an adult human fluctuates between seven to ten grams per day.

The substantial defect of fatty emulsions obtained by foreign authors lies in the fact that in their preparation cocoanut oil or cocoanut fat are used which, as is known, are completely deprived of highly unsaturated fatty acids.

In our studies we set ourselves the task of obtaining such a preparation for parenteral nutrition which would possess high caloric value and contain all nutritive substances and vitamins essential to the life of an organism.

This goal, it seems to us, has been achieved in the development of the preparation aminophospholipid.

The method of obtaining aminophospholipid is as follows: following an appropriate thermal processing, the whole blood of killed animals is subjected to digestion by proteolytic enzymes (a minced and activated pancreas of a hog)(1). The protein hydrolysate thus obtained after an appropriate purification has the following chemical composition (in gram-percentages per 100 ml of the solution):

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(1) This part of the work was done with the participation of the co-workers of the Leningrad Meat Combine imeni S. M. Kirov.

Total nitrogen	0.85
Amino nitrogen	0.67
Tryptophan	0.210
Methionine	0.199
Calcium	Traces
Phosphorus (total)	0.010
Iron	0.0015
Solid residue	5.79

Depth of hydrolysis $\left(\frac{N\ --\ NH2}{N\ total}\right)$ in percentages = 79; pH of solution = 6.8

Judging by the degree of splitting (79 percent), the hydrolysate consists almost entirely of amino acids. This has important significance in the quality of the preparation because, according to numerous data by foreign authors (G. Borsuk, 1957), peptides or partial hydrolysates of protein proved to be less effective in animal nutrition than amino-acids or whole hydrolysates.

Our attention is attracted also by the high percentage of the content of most important aminoacids -- tryptophan and methionine. However, it turned out at the same time that the hydrolysate is very poor in salts of calcium, phosphorus, and iron. The salt composition of the hydrolysate was improved by the addition of 0.5 percent of Na_2HPO_4, 0.1 percent of $CaCl_2$, and 0.005 percent of $FeCl_3$.

Besides, the following ingredients were added to the hydrolysate: glucose 5 percent, redistilled alcohol 5 percent (in volume), and vitamins (B_1 three mg/liter, B_2 mg/liter, B_6 2.5 mg/liter, B_{12} 30 gamma/liter, PP 10 mg/liter, C 100 mg/liter, and pantothenate of calcium 10 mg/liter).

The protein hydrolysate enriched with glucose, alcohol, mineral substances, and vitamins, served as a base (liquid phase) for obtaining a fat emulsion -- the aminophospholipid preparation.

As a source of fat in the manufacture of this preparation, fresh sunflower oil (non-purified) was used; it contains, according to the data by Duel (1954), 68 percent of linoleic acid.

As fat emulsifier we employed, in contradistinction to foreign authors who had used synthetic emulsifiers for this purpose, natural substances -- soybean phosphatides. Phosphatides possess high emulsifying properties (K. S. Popov and L. A. Grauerman, 1958) and constitute very import-

ant compounds in the organism, entering into the composition of all tissues and cells of our body (O. K. Palladina, 1958).

At the present our native industry is manufacturing soybean and other vegetable phosphatides in large quantities for use in the food trade.

The Chemical Composition and Caloricity of Aminophospholipid

Name of component	In percentages per 100 ml of the preparation	Caloricity
Protein substances (non-replaceable and replaceable aminoacids.....	5.5	23.65
Carbohydrates (mainly glucose).....	5.12	22.02
Fats (non-purified sunflower oil, etc.).....	5.50	51.15
Phosphatides (soybean, etc.).	1.10	9.30
Alcohol redistilled.....	5.00	46.50
Potassium.....	0.20	--
Sodium	0.39	--
Calcium	0.073	--
Phosphorus (total)	0.171	--
Iron.....	0.005	--
Chlorine	0.204	--
Vitamins (B_1, B_2, B_6, B_{12}, PP, C and Pantothenate of calcium [1].....		
pH.....	6.85	
Total calories		152.62

[1] These vitamins, added to the hydrolysate, were not determined in the aminophospholipid.

The chemical composition of phosphatides may vary depending on the nature of the fat or oil from which they had been obtained. Phosphatide obtained from soybean oil has the following chemical composition in percentages (data by Markley, 1951): lecithin -- 21, cephalin -- 19, phosphoinositide -- 20, soybean oil -- 35 to 40, sterols, tocopherol (Vitamin E) -- 2, carbohydrates (free) -- 5.

The following glycerides are contained in soybean oil (in percentages): olein -- 25 to 36, of linoleic acid -- 52 to 65, and of linolenic acid -- 2.0 to 3.0.

In the preparation of the fat emulsion, the vegetable oil was mixed with the phosphatide, heated, and the mixture in the amount of six percent was added (in small portions) to the hydrolysate and stirred thoroughly. The stirring was done with a laboratory apparatus, a homogenizer (see illustration) which made 8000 revolutions per minute.

The emulsion thus obtained (aminophospholipid) had fat drops of one micron size, and upon prolonged preservation proved to be sufficiently stable.

Our subsequent observations showed that the liquid phase of aminophospholipid (the hydrolysate of protein with glucose, salts, and vitamins dissolved in it) can be dried, and the vegetable oil with phosphatide can be placed in ampoules. This processing preserves the aminophospholipid very markedly, and the transportation and storage of the preparation are thereby considerably facilitated.

The method of preparing aminophospholipid from a dry protein hydrolysate is simple. It consists of dissolving the hydrolysate in sterile distilled water, adding vegetable oil containing phosphatides and alcohol, and the proper stirring of the mixture with a homogenizer.

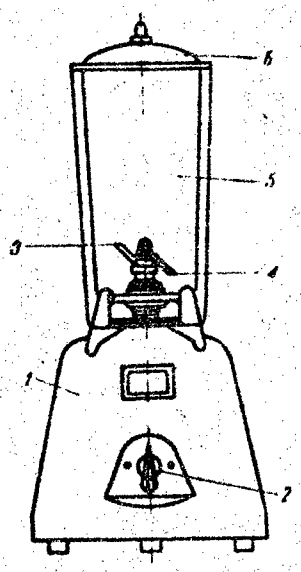
The chemical composition and caloricity of aminophospholipid is cited in the table.

Aminophospholipid has been tested on animals (dogs, rabbits, guinea pigs, and mice). It proved to be free of toxic properties, caused no embolisms, produced no pyrogenic reaction, possessed no anaphylactic properties, and proved to be fully suitable for parenteral administration (intravenous, subcutaneous, and intramuscular).

In studying the biological value of aminophospholipids, we established that from the very first day following injection, it can maintain a positive nitrogen balance in animals (dogs) on a high level.

It is possible that aminophospholipid will find its use as a blood substitute in acute hemorrhages.

This problem requires special study.



Homogenizer "EMIB"

1 body of the device with the electric motors;

2 switch for changing the number of revolutions;

3, 4 -- two knives, the cutting (3) and the mixing knife (4);

5 glass jar;

6 jar cover.

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