Patented Nov. 28, 1944 2,364,008

UNITED STATES PATENT OFFICE

2,364,008

PROCESS OF MAKING A NUTRIENT MATERIAL

Elmer H. Stuart, Indianapolis, Ind., assignor to Eli Lilly and Company, Indianapolis, Ind., a corporation of Indiana

No Drawing. Application September 23, 1940, Serial No. 358,037

1 Claim. (Cl. 99—14)

This invention relates to nutrient substances and more particularly to nutrient materials suitable for oral, rectal, and intravenous administration.

An object of this invention is to provide a material which supplies the necessary nitrogenous materials required for the sustenance of life, which is readily assimilated, which is non-toxic, and which is economical to prepare.

It has been well established that approximately nine or ten amino acids in the presence of other amino acids comprise the necessary nitrogenous materials required for the maintenance of life. (The Chemistry of the Amino Acids and Proteins, by Carl L. A. Schmidt, published by Charles C. Thomas, 1938, page 986.) These amino acids are usually derived from proteins, and ordinarily the human or animal would be adequately supplied with these essential amino acids from foods which are customarily consumed. However, when situations arise which interfere with normal digestion, it is necessary to supply the required elements for sustenance by parenteral administration. For this purpose mixtures of amino acids have heretofore been proposed. A review of the literature reveals the unanimous belief that the digestion of the protein must be such that the protein is broken down into free amino acids. In conformity with this belief, the nutrient material for the supply of nitrogenous material required for the sustenance of life heretofore used intravenously contained essentially free amino acids obtained by the complete digestion of a protein material. (Journal of the American Medical Assn., vol. 112, No. 9, pp. 796–802.) These mixtures of free amino acids, however, have been found to be relatively unsatisfactory.

In accordance with this invention, a nutrient material is provided which supplies all of the nitrogenous materials required for the maintenance of life and which is markedly less toxic than the mixtures of amino acids heretofore employed. This nutrient material is suitable for oral, rectal, and parenteral administration and more particularly for intravenous administration. A group of rabbits was given two grams each of the nutrient material of this invention daily and a similar group was supplied with an equal quantity of mixtures of free amino acids prepared by the complete digestion of proteins with pancreatic enzymes. Both compositions were administered intravenously and the rabbits received no further nutrient material other than glucose and water. The daily loss of weight in the rabbits treated with the nutrient material of this invention was about one half of that of rabbits supplied with the mixture of free amino acids. For a 14-day period, in many cases those treated with the free amino acids died, while in the vast majority of cases the rabbits supplied with the nutrient material of this invention survived.

The nutrient material of this invention comprises polypeptides which are suitable for oral, rectal, and parenteral administration. These polypeptides are water-soluble, are not precipitated by chloracetic acid, and give a positive biuret reaction. Amino acids give a negative biuret reaction. The color obtained in the biuret test with the polypeptides is somewhat different from that obtained from the proteins from which the polypeptides are derived in that the polypeptides yield a characteristic pink color, whereas the original proteins give a blue violet colored biuret reaction. The polypeptides contain chemically-combined amino acids, can be obtained most economically from natural proteins, and are markedly less toxic and more readily soluble in water than are the free amino acids which are chemically combined in the polypeptides. The polypeptides of this invention are soluble in water having a hydrogen ion concentration of pH 6.

The polypeptides of this invention are prepared by digesting a protein in a medium having a pH between 4 and 5 with a proteolytic enzyme, such as papain, or those occurring in liver, kidney, and other animal tissue. However, it is preferred to employ papain. The protein is desirably a natural protein, such as casein, the protein from soy bean, or certain animal tissues. Preferably, the protein or plurality of proteins employed for preparing the polypeptides contains all of the amino acids required for the supply of the necessary nitrogenous materials for the sustenance of life. The rate at which the digestion proceeds is dependent upon the temperature. Most proteolytic enzymes operate most satisfactorily at about 37° C. Temperatures below 37° C. require a much longer period of digestion. In the case of papain, the rate of digestion may be markedly increased by using temperatures as high as 70° C. This digestion is continued desirably until the amount of free carboxyl groups in one gram of the dried digested material is equivalent to between 0.075 and 0.2 gram of sodium hydroxide. The free carboxylic group is determined by the method described in Allen's Commercial Organic Analysis, fifth edition, published by P. Blakiston's Son & Co., Inc., 1930, pp. 727–729, in