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Description

Field of the Invention

The present invention relates to a novel parenteral alimentation solution. More particularly, it relates to a parenteral alimentation solution having excellent nutritional properties and also containing a reducing sugar as a physiological energy source, an amino acid mixture as a nitrogen source and electrolytes as essential nutrients together.

Background of the Invention

Up to now, any parenteral alimentation solution which contains a reducing sugar as well as essential and non-essential amino acids and further contains electrolytes essential for the living body such as sodium, potassium, phosphorus, magnesium, chlorine and the like has not been put to practical use. For example, although an amino acid infusion solution containing electrolytes has been known, no reducing sugar is contained therein and, in an infusion solution containing both amino acids and a reducing sugar, only sodium and chlorine are present as electrolytes [Iyakuin Kenkyu, 72, (1), 91—111 (1981)]. In addition, these sodium and chlorine are not intentionally added to an infusion solution but they are inevitably derived from an amino acid component used. For example, when an amino acid is used in the form of its hydrochloride, chlorine is derived therefrom and, when an amino acid hydrochloride is neutralized, sodium is derived therefrom.

In addition to difficulty of determination of an optimum composition, a parenteral alimentation solution containing a reducing sugar, amino acids and electrolytes which are essential nutrients has not been hitherto put to practical use because it is not possible to overcome such a technical difficulty that the alimentation solution is colored in brown (so-called, browning) due to Maillard reaction of a reducing sugar, for example, glucose with an amino acid during heat sterilization or storage and that browning due to the amino acid and glucose is more accelerated and increased in the presence of electrolytes [The Journal of Nutrition, 112, 1631—1637 (1982)]. Thus, in order to prevent such browning, it has been proposed to reduce amounts of electrolytes and further to use L-tryptophan and L-proline which are said to be mainly responsible for browning [The Journal of Nutrition, 112, 1634 (1982)] in their N-acylated forms [Japanese Patent Laid Open Publication No. 115909/1976; and Shinyaku to Rinsho, 29, 305 (1980)].

However, even if it is possible to prevent browning of an infusion solution by using L-proline and L-tryptophan in their N-acylated forms, it is hard to say that N-acylated forms of L-proline and L-tryptophan are most suitable for the living body because these N-acylated amino acids per se are non-physiological amino acids. In addition, as electrolytes, only sodium and chlorine are contained in the infusion solution

prepared according to such a known method, but other electrolytes essential to the living body such as potassium, magnesium, phosphorus, etc., are not contacted therein.

In EP—A—13962, a parenteral infusion solution containing amino acids, salts and sorbite or xylite is disclosed. Furthermore, there is described in EP—A—034 034 a nutrient composition comprising amino acids, carbohydrate fat, vitamin and mineral. The known parenteral solutions do not contain glucose since the glucose is stored separately and mixed only at the moment of application.

Accordingly, up to now, in practice, an electrolyte infusion solution and an amino acid-reducing sugar infusion solution has been admixed just prior to administration or they have been separately administered. However, in case of admixing these solutions, it is necessary to control the pH and osmotic pressure of the resulting mixture suitable for a patient to be administered because they are different from those of the original solutions as prepared and, in addition, there is such a problem that the amounts of sodium and chlorine in the mixture should be calculated so as to avoid administration of excess amounts of sodium and chlorine to a patient, when the solutions contain sodium and chlorine. Further, when the solutions are admixed, possibility of contamination with various microorganisms is increased. In case of administering both solutions separately and successively, a long infusion time is required, which causes pain to a patient for a long time. Further, there is such a problem that, above all, a sufficient nutritional effect can not be expected because each electrolyte which is necessary for an amino acid metabolism is not infused at the same time of infusion of the amino acid.

Thus, in this field of the art, it has been strongly requested to develop a parenteral alimentation solution in which amino acids per se are used without any modification and a reducing sugar and electrolytes are added, in addition, browning due to Maillard reaction is prevented.

Objects and Summary of the Invention

The present inventors have intensively studied to solve the above problems. As the result, it has been found that a parenteral alimentation solution showing excellent nutritive effect and at the same time causing no substantial browning can be obtained by balancing a ratio of composition of the three components a reducing sugar, physiological amino acids and electrolytes within a specific range.

The main object of the present invention is to provide a parenteral alimentation solution which contained a reducing sugar, physiological amino acids and electrolytes and is substantially prevented from browning.

This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description.

According to the present invention, there is provided a parenteral alimentation solution which comprises a reducing sugar, physiological amino acids and electrolytes in the composition and the amount shown in Table 1.

TABLE 1

Components	Amount
<i>Sugar</i>	<i>g/l</i>
Reducing sugar	30— 150
<i>Physiological amino acids</i>	<i>mg/l</i>
L-Isoleucine	2100—2810
L-Leucine	3340—4460
L-Valine	2220—2970
L-Methionine	960—1290
L-Cysteine	0—1000
L-Cystine	0— 200
L-Phenylalanine	1900—2540
L-Tyrosine	0—1000
L-Tryptophan	390— 530
L-Lysine	1980—2640
L-Threonine	1180—1580
L-Arginine	2740—3660
L-Histidine	1160—1550
L-Alanine	2120—2840
L-Aspartic acid	120— 220
L-Glutamic acid	0— 170
Glycine	1360—1820
L-Proline	1580—2110
L-Serine	1030—1390
<i>Electrolytes</i>	<i>mmol/l</i>
Sodium	25— 60
Chlorine	35— 65
Potassium	10— 40
Magnesium	0— 5
Phosphorus	0— 10

(Provided that all or a part of cyteine and/or cytine may be replaced by methionine, and all or a part of tyrosine may be replaced by phenylalanine.)

The parenteral alimentation solution of the present invention is prepared by admixing the above components in distilled water for infusion, filtering the resulting mixture and sterilizing the mixture.

Detailed Description of the Invention

The parenteral alimentation solution of the present invention which has the above composition and contains the above component in the amount as shown in Table 1 can be administered to a human patient by various routes (e.g. peripheral intravenous administration, central intravenous administration) according to a desired purpose. Particularly, the parenteral alimentation solution of the present invention has a composition suitable for peripheral intravenous administration. Additionally, the parenteral alimentation solution shows excellent nutritional effect because it has such novel characteristics that it contains all three essential components, i.e., a reducing sugar which is a physiological energy source, a well-balanced amino acid mixture which is a physiological nitrogen source and electrolytes essential for the living body in a stable state. For example, a reducing sugar is most readily metabolized as an energy source and effectively utilized and it makes utilization of the other component, amino acids, in a protein synthesis possible. Further, the parenteral alimentation solution of the present invention has such characteristics that, in view of the feature of amino acid metabolism in nutrition via a vein, the amino acid composition has such a high branched-chain amino acid content as 29—33% (w/w) based on the weight of the total amino acids with maintaining balance of amino acid composition such as the ratio of total amino acids and essential amino acids, the ratio of essential amino acids and non-essential amino acids or the like and that the solution contains sufficient other nutritive amino acids. In addition, with regard to the electrolyte composition, the parenteral alimentation solution of the present invention has such characteristics that it contains electrolytes in an amount just enough to maintain nutrition. As a preferred aspect of the composition of the parenteral alimentation solution of the present invention having the above characteristics, there can be exemplified the solution having the following composition of a reducing sugar, amino acids and electrolytes.

<i>Sugar</i>	<i>g/l</i>
Reducing sugar	30— 150
<i>Physiological amino acids</i>	<i>mg/l</i>
L-Isoleucine	2100—2810

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<i>Physiological amino acids</i>	<i>mg/l</i>
L-Leucine	3340—4460
L-Valine	2220—2970
L-Methionine	960—1290
L-Cysteine	0—1000
L-Cystine	0—200
L-Phenylalanine	1900—2540
L-Tyrosine	0—1000
L-Tryptophan	390—530
L-Lysine	1980—2640
L-Threonine	1180—1580
L-Arginine	2740—3660
L-Histidine	1160—1550
L-Alanine	2120—2840
L-Aspartic acid	120—170
L-Glutamic acid	120—170
Glycine	1360—1820
L-Proline	1580—2110
L-Serine	1030—1390
<i>Electrolytes</i>	<i>mmol/l</i>
Sodium	25—60
Chlorine	35—65
Potassium	10—40
Magnesium	0—5
Phosphorus	0—10

(Provided that all or a part of cyteine and/or cytine may be replaced by methionine, and all or a part of tyrosine may be replaced by phenylalanine.)

As another preferred aspect of the composition of the parenteral alimentation solution of the present invention having the above characteristics, there can be exemplified the solution having the following composition of a reducing sugar, amino acids and electrolytes.

<i>Reducing sugar</i>	<i>g/l</i>
glucose	71—79
<i>Amino acids</i>	<i>mg/l</i>
L-Isoleucine	2220—2460
L-Leucine	3520—3900
L-Valine	2350—2600
L-Methionine	1010—1420
L-Phenylalanine	2010—2230
L-Tyrosine	130—150
L-Tryptophan	410—470
L-Lysine	2090—2310
L-Threonine	1250—1390
L-Arginine	2890—3210
L-Histidine	1220—1360
L-Alanine	2240—2490
L-Aspartic acid	130—170
L-Glutamic acid	0—150
Glycine	1430—1590
L-Proline	1670—1850
L-Serine	1090—1220
<i>Electrolytes</i>	<i>mmol/l</i>
Sodium	25—35
Chlorine	45—55
Potassium	20—30
Magnesium	1.5—2.5
Phosphorus	1.5—2.5

(Provided that, if necessary, L-cysteine and/or L-cystine may be further added to the above composition in an amount of 260—290 mg/l.)

In the parenteral alimentation solution of the present invention, the reducing sugar used is not limited to a specific one so far as it can be metabolized and utilized as an energy source in the living body. However, glucose and maltose

are preferable and they may be used alone or in a combination thereof.

The amino acid used in the parenteral alimentation solution of the present invention may be either in the free acid form or in the form of a salt thereof with a metal such as potassium or sodium, a mineral acid such as sulfuric acid or hydrochloric acid, or an organic acid such as acetic acid or malic acid. Further, the amino acid may be in the form of a salt with another amino acid, a peptide and the like. In the amino acid composition of the alimentation solution of the present invention, all or a part of L-cysteine and/or L-cystine can be replaced by L-methionine because, as a sulfur containing amino acid, L-cysteine and L-cystine are nutritionally equivalent to L-methionine. Likewise, all or a part of tyrosine which is an aromatic amino acid can be replaced by L-phenylalanine.

Further, as the electrolytes used in the alimentation solution fluid of the present invention, there can be used as a sodium source a commonly used sodium compound such as sodium hydroxide, sodium chloride, a sodium salt of an organic acid, a sodium salt of an amino acid, etc., as a chlorine source hydrochloric acid, sodium chloride, potassium chloride, a hydrochloride of an amino acid, etc.; as a potassium source potassium hydroxide, potassium chloride, a potassium salt of an organic acid, a potassium salt of an amino acid, etc.; and as magnesium source magnesium chloride, magnesium sulfate, a magnesium salt of an organic acid, a magnesium salt of an amino acid, etc. As a source for phosphorus, sodium and potassium, there can be also used disodium monohydrogen phosphate, sodium dihydrogen phosphate, potassium monohydrogen phosphate, dipotassium dihydrogen phosphate, etc. The concentrations of the above reducing sugar, amino acids and electrolytes in the alimentation solution can be appropriately varied within the range shown in Table 1 according to conditions and age of a patient to be treated, diseases to be treated, etc. The preferred concentration range for the reducing sugar is about 5—9 w/v%, particularly, 6—8 w/v% and, for the amino acids, preferably, the total amino acid concentration range is about 2.5—3.5 w/v%. For the electrolytes, it is preferable that the concentration of sodium ion is 25—35 mmol/l, the concentration of potassium ion is 20—30 mmol/l, the concentration of chlorine ion is 45—55 mmol/l, the concentration of magnesium ion is 1.5—2.5 mmol/l and the concentration of phosphorus ion is 1.5—2.5 mmol/l. In addition, in view of stabilization of the alimentation solution, it is preferable to adjust each concentration of the reducing sugar and the amino acids so that the product of the concentration (w/v%) of the reducing sugar (as glucose) by that of the total amino acids is 7—25, preferably 12—24, most preferably 17—23 because an excellent stabilization effect can be obtained.

It is preferable to adjust the pH of the parenteral alimentation solution of the present invention to

4.0—6.0. The alimentation solution can further contain other ingredients commonly used in the preparation of an infusion fluid such as a stabilizing agent, an agent for adjusting pH, etc.

The parenteral alimentation solution of the present invention can be prepared according to a conventional technique for the preparation of a conventional infusion solution or injectable preparation by admixing the above components in distilled water for infusion, filtering the resulting mixture and sterilizing the mixture. Filtration can be effected by using a microporous membrane filter such as Millipore filter. The parenteral alimentation solution of the present invention can be subjected to heat sterilization.

The parenteral alimentation solution of the present invention thus obtained contains all three components of the reducing sugar, the amino acids and the electrolytes and has excellent nutritional properties. Further, in the parenteral alimentation solution of the present invention, although all the amino acids used are physiological amino acids, browning can be prevented without using any non-physiological amino acid such as N-acetyl-tryptophan. In addition, there is no need to use other infusion solution in combination with the parenteral alimentation solution of the present invention because the latter solution contains substantially all the components considered to be required for a peripheral intravenous infusion solution and, thereby, problems accompanying with using the other infusion solution (e.g. variation of nature of the resulting mixture, contamination with microorganisms or foreign materials) can be avoided. However, if necessary, a suitable infusion solution may be mixed into the solution of this invention.

The following examples further illustrate the present invention in detail but are not to be construed to limit the scope thereof.

Example 1

Formulation	
Components	Amount
Glucose	75 g
L-Isoleucine	2.34 g
L-Leucine	3.71 g
L-Valine	2.48 g
L-Methionine	1.07 g
L-Phenylalanine	2.12 g
L-Tyrosine	0.14 g
L-Threonine	1.32 g
L-Alanine	2.37 g

Formulation	
Components	Amount
L-Proline	1.76 g
L-Serine	1.16 g
Glycine	1.51 g
L-Aspartic acid	0.14 g
L-Glutamic acid	0.14 g
L-Arginine	0.78 g
L-Arginine hydrochloride	2.74 g
L-Histidine	1.29 g
L-Lysine hydrochloride	2.75 g
L-Cysteine hydrochloride	0.36 g
L-Tryptophan	0.44 g
Sodium lactate	3.36 g
Potassium chloride	1.27 g
Dipotassium monohydrogen phosphate	0.26 g
Magnesium chloride hexahydrate	0.30 g
Sodium hydrogen sulfite	0.50 g

The above components were dissolved in 750 ml of distilled water for injection and to the solution was added additional distilled water to bring the total volume of the solution to 1 liter. The solution was filtered through Millipore filter and distributed in an amount of 200 ml per vial. The vials were sealed and sterilized with heating to obtain the desired parenteral alimentation solution.

Even after sterilization, the alimentation solution thus obtained was colorless and clear and no browning was observed.

Example 2

Formulation	
Components	Amount
Glucose	700 g
L-Isoleucine	25.5 g
L-Leucine	40.4 g
L-Valine	27.0 g
L-Methionine	11.7 g
L-Phenylalanine	23.1 g
L-Tyrosine	1.5 g
L-Threonine	14.4 g
L-Alanine	25.8 g
L-Proline	19.2 g
L-Serine	12.6 g
Glycine	16.5 g
L-Aspartic acid	1.5 g
L-Glutamic acid	1.5 g
L-Arginine	33.3 g
L-Histidine	14.1 g
L-Lysine hydrochloride	30.0 g
L-Cysteine hydrochloride	1.3 g
L-Tryptophan	4.8 g
Sodium chloride	17.5 g
Potassium chloride	12.7 g
Dipotassium monohydrogen phosphate	2.6 g
Magnesium chloride hexahydrate	3.0 g
Sodium hydrogen sulfite	5.0 g

The above components were dissolved in 7 liters of distilled water for injection and to the solution was added additional distilled water to bring the total volume of the solution to 10 liters. The solution was filtered through Millipore filter and distributed in an amount of 500 ml per vial. The vials were sealed and sterilized with heating to obtain the desired parenteral alimentation solution.

Even after sterilization, the alimentation solution thus obtained was colorless and clear and no browning was observed.

Example 3

Components	Formulation	Amount
Glucose		750 g
L-Isoleucine		23.4 g
L-Leucine		37.1 g
L-Valine		24.8 g
L-Methionine		12.8 g
L-Phenylalanine		21.2 g
L-Tyrosine		1.4 g
L-Threonine		13.2 g
L-Alanine		23.7 g
L-Proline		17.6 g
L-Serine		11.6 g
Glycine		15.1 g
L-Aspartic acid		1.4 g
L-Glutamic acid		1.4 g
L-Arginine		29.3 g
L-Arginine hydrochloride		1.5 g
L-Histidine hydrochloride monohydrate		17.4 g
L-Lysine hydrochloride		27.5 g
L-Cysteine		1.0 g
L-Tryptophan		4.8 g
Sodium lactate		33.6 g
Potassium chloride		12.7 g
Dipotassium monohydrogen phosphate		2.6 g

Components	Formulation	Amount
Magnesium chloride hexahydrate		3.0 g
Sodium hydrogen sulfite		5.0 g

The above components were dissolved in 7 liters of distilled water for injection and to the solution was added additional distilled water to bring the total volume of the solution to 10 liters. The solution was filtered through Millipore filter and distributed in an amount of 1000 ml per bag made of a soft plastic (crosslinked EVA). The bags were sealed and sterilized with heating to obtain the desired parenteral alimentation solution.

Even after sterilization, the alimentation solution thus obtained was colorless and clear and no browning was observed.

Example 4

Components	Formulation	Amount
Maltose		1000 g
L-Isoleucine		25.5 g
L-Leucine		40.4 g
L-Valine		27.0 g
L-Methionine		11.7 g
L-Phenylalanine		23.1 g
L-Tyrosine		1.5 g
L-Threonine		14.4 g
L-Alanine		25.8 g
L-Proline		19.2 g
L-Serine		12.6 g
Glycine		16.5 g
L-Aspartic acid		1.5 g
L-Glutamic acid		1.5 g
L-Arginine		8.5 g
L-Arginine hydrochloride		30.0 g
L-Histidine		14.1 g
L-Lysine hydrochloride		30.0 g

Formulation Components	Amount
L-Cysteine hydrochloride	4.0 g
L-Tryptophan	4.8 g
Sodium lactate	33.6 g
Potassium chloride	12.7 g
Dipotassium monohydrogen phosphate	2.6 g
Magnesium chloride hexahydrate	3.0 g
Sodium hydrogen sulfite	5.0 g

The above components were dissolved in 7.5 liters of distilled water for injection and to the solution was added additional distilled water to bring the total volume of the solution to 10 liters. The solution was filtered through Millipore filter and distributed in an amount of 1000 ml per bag made of a soft plastic (crosslinked EVA). The bags were sealed and sterilized with heating to obtain the desired parenteral alimentation solution.

Even after sterilization, the alimentation solution thus obtained was colorless and clear and no browning was observed.

Example 5

Formulation Components	Amount
Glucose	750 g
L-Isoleucine	24.1 g
L-Leucine	38.6 g
L-Valine	25.0 g
L-Methionine	13.7 g
L-Phenylalanine	21.1 g
L-Tyrosine	1.4 g
L-Threonine	13.2 g
L-Alanine	23.7 g
L-Proline	17.0 g
L-Serine	10.3 g
Glycine	15.1 g
L-Aspartic acid	1.4 g

Formulation Components	Amount
L-Glutamic acid	1.4 g
L-Arginine	29.8 g
L-Histidine hydrochloride monohydrate	17.4 g
L-Lysine hydrochloride	27.5 g
L-Tryptophan	4.4 g
Sodium chloride	0.9 g
Potassium chloride	15.8 g
Dipotassium monohydrogen phosphate	2.6 g
Magnesium chloride hexahydrate	3.0 g
Sodium lactate	28.5 g
Lactic acid	2.25 g

The above components were dissolved in 7.5 liters of distilled water for injection and to the solution was added additional distilled water to bring the total volume of the solution to 10 liters. The solution was filtered through Millipore filter and distributed in an amount of 500 ml per vial. The vials were sealed and sterilized with heating to obtain the desired parenteral alimentation solution.

Even after sterilization, the alimentation solution thus obtained was colorless and clear and no browning was observed.

Claims

1. A parenteral alimentation solution which comprises a reducing sugar, physiological amino acids and electrolytes in the composition and the amount as shown in Table 1:

TABLE 1

Components	Amount
<i>Sugar</i>	<i>g/l</i>
Reducing sugar	30—150
<i>Physiological amino acids</i>	<i>mg/l</i>
L-Isoleucine	2100—2810
L-Leucine	3340—4460

Formulation Components	Amount
L-Cysteine hydrochloride	4.0 g
L-Tryptophan	4.8 g
Sodium lactate	33.6 g
Potassium chloride	12.7 g
Dipotassium monohydrogen phosphate	2.6 g
Magnesium chloride hexahydrate	3.0 g
Sodium hydrogen sulfite	5.0 g

The above components were dissolved in 7.5 liters of distilled water for injection and to the solution was added additional distilled water to bring the total volume of the solution to 10 liters. The solution was filtered through Millipore filter and distributed in an amount of 1000 ml per bag made of a soft plastic (crosslinked EVA). The bags were sealed and sterilized with heating to obtain the desired parenteral alimentation solution.

Even after sterilization, the alimentation solution thus obtained was colorless and clear and no browning was observed.

Example 5

Formulation Components	Amount
Glucose	750 g
L-Isoleucine	24.1 g
L-Leucine	38.6 g
L-Valine	25.0 g
L-Methionine	13.7 g
L-Phenylalanine	21.1 g
L-Tyrosine	1.4 g
L-Threonine	13.2 g
L-Alanine	23.7 g
L-Proline	17.0 g
L-Serine	10.3 g
Glycine	15.1 g
L-Aspartic acid	1.4 g

Formulation Components	Amount
L-Glutamic acid	1.4 g
L-Arginine	29.8 g
L-Histidine hydrochloride monohydrate	17.4 g
L-Lysine hydrochloride	27.5 g
L-Tryptophan	4.4 g
Sodium chloride	0.9 g
Potassium chloride	15.8 g
Dipotassium monohydrogen phosphate	2.6 g
Magnesium chloride hexahydrate	3.0 g
Sodium lactate	28.5 g
Lactic acid	2.25 g

The above components were dissolved in 7.5 liters of distilled water for injection and to the solution was added additional distilled water to bring the total volume of the solution to 10 liters. The solution was filtered through Millipore filter and distributed in an amount of 500 ml per vial. The vials were sealed and sterilized with heating to obtain the desired parenteral alimentation solution.

Even after sterilization, the alimentation solution thus obtained was colorless and clear and no browning was observed.

Claims

1. A parenteral alimentation solution which comprises a reducing sugar, physiological amino acids and electrolytes in the composition and the amount as shown in Table 1:

TABLE 1

Components	Amount
<i>Sugar</i>	<i>g/l</i>
Reducing sugar	30— 150
<i>Physiological amino acids</i>	<i>mg/l</i>
L-Isoleucine	2100—2810
L-Leucine	3340—4460



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TABLE 1 (continued)

Components	Amount
<i>Physiological amino acids</i>	<i>mg/l</i>
L-Valine	2220—2970
L-Methionine	960—1290
L-Cysteine	0—1000
L-Cystine	0—200
L-Phenylalanine	1900—2540
L-Tyrosine	0—1000
L-Tryptophan	390—530
L-Lysine	1980—2640
L-Threonine	1180—1580
L-Arginine	2740—3660
L-Histidine	1160—1550
L-Alanine	2120—2840
L-Aspartic acid	120—220
L-Glutamic acid	0—170
Glycine	1360—1820
L-Proline	1580—2110
L-Serine	1030—1390
<i>Electrolytes</i>	<i>mmol/l</i>
Sodium	25—60
Chlorine	35—65
Potassium	10—40
Magnesium	0—5
Phosphorus	0—10

Provided that all or a part of cysteine and/or cystine may be replaced by methionine, and all or a part of tyrosine may be replaced by phenylalanine.

2. A parenteral alimentation solution according to claim 1, wherein the solution has the following composition:

<i>Sugar</i>	<i>g/l</i>
Reducing sugar	30—150
<i>Physiological amino acids</i>	<i>mg/l</i>
L-Isoleucine	2100—2810
L-Leucine	3340—4460
L-Valine	2220—2970
L-Methionine	960—1290
L-Cysteine	0—1000
L-Cystine	0—200
L-Phenylalanine	1900—2540
L-Tyrosine	0—1000
L-Tryptophan	390—530
L-Lysine	1980—2640
L-Threonine	1180—1580
L-Arginine	2740—3660
L-Histidine	1160—1550
L-Alanine	2120—2840
L-Aspartic acid	120—170
L-Glutamic acid	120—170
Glycine	1360—1820
L-Proline	1580—2110
L-Serine	1030—1390
<i>Electrolytes</i>	<i>mmol/l</i>
Sodium	25—60
Chlorine	35—65
Potassium	10—40
Magnesium	0—5
Phosphorus	0—10

Provided that all or a part of cysteine and/or cystine may be replaced by methionine, and all or a part of tyrosine may be replaced by phenylalanine.



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3. A parenteral alimentation solution according to claim 1, wherein the concentration of the reducing sugar is about 5—9 w/v%.

4. A parenteral alimentation solution according to claim 3, wherein the concentration of the reducing sugar is 6—8 w/v%.

5. A parenteral alimentation solution according to claim 1, wherein the total amino acid concentration is about 2.5—3.5 w/v%.

6. A parenteral alimentation solution according to claim 1, wherein the concentration of the electrolytes are as follows:

Sodium	25—35 mmol/l
Potassium	20—30 mmol/l
Chlorine	45—55 mmol/l
Magnesium	1.5—2.5 mmol/l
Phosphorus	1.5—2.5 mmol/l

7. A parenteral alimentation solution according to claim 1, wherein the product of the concentration of the reducing sugar (as glucose) by that of the total amino acids (w/v%) is 7—25.

8. A parenteral alimentation solution according to claim 7, wherein the product is 12—24.

9. A parenteral alimentation solution according to claim 7, wherein the product is 17—23.

10. A parenteral alimentation solution according to claim 1, wherein pH of the fluid is 4.0—6.0.

11. A parenteral alimentation solution according to claim 1, wherein the reducing sugar is glucose and/or maltose.

12. A parenteral alimentation solution according to claim 11 wherein the fluid has the following composition:

Reducing sugar	g/l
Glucose	71— 79
Amino acids	mg/l
L-Isoleucine	2220—2460
L-Leucine	3520—3900
L-Valine	2350—2600
L-Methionine	1010—1420
L-Phenylalanine	2010—2230
L-Tyrosine	130— 150
L-Tryptophan	410— 470
L-Lysine	2090—2310
L-Threonine	1250—1390
L-Arginine	2890—3210

Amino acids	mg/l
L-Histidine	1220—1360
L-Alanine	2240—2490
L-Aspartic acid	130— 170
L-Glutamic acid	0— 150
Glycine	1430—1590
L-Proline	1670—1850
L-Serine	1090—1220
Electrolytes	mmol/l
Sodium	25— 35
Chlorine	45— 55
Potassium	20— 30
Magnesium	1.5— 2.5
Phosphorus	1.5— 2.5

Provided that, L-cysteine and/or L-cystine may be further added to the above composition in an amount of 260—290 mg/l.

Patentansprüche

1. Parenterale Ernährungslösung, die einen reduzierenden Zucker, physiologische Aminosäuren und Elektrolyte in einer Zusammensetzung und in einer Menge gemäss der Tabelle 1 enthält:

TABELLE 1

KOMPONENTEN	MENGE
<i>Zucker:</i>	<i>g/l</i>
reduzierender Zucker	30— 150
<i>physiologische Aminosäuren: mg/l</i>	
L-Isoleucin	2100—2810
L-Leucin	3340—4460
L-Valin	2220—2970
L-Methionin	960—1290
L-Cystein	0—1000
L-Cystin	0— 200
L-Phenylalanin	1900—2540



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TABELLE 1 (cont.)

KOMPONENTEN	MENGE
<i>physiologische Aminosäuren: mg/l</i>	
L-Tyrosin	0—1000
L-Tryptophan	390— 530
L-Lysin	1980—2640
L-Threonin	1180—1580
L-Arginin	2740—3660
L-Histidin	1160—1550
L-Alanin	2120—2840
L-Asparaginsäure	120— 220
L-Glutaminsäure	0— 170
Glycin	1360—1820
L-Prolin	1580—2110
L-Serin	1030—1390
<i>Elektrolyte: mMol/l</i>	
Natrium	25— 60
Chlor	35— 65
Kalium	10— 40
Magnesium	0— 5
Phosphor	0— 10

wobei alles oder ein Teil des Cysteins und/oder Cystins durch Methionin ersetzt sein kann und alles oder ein Teil des Tyrosins durch Phenylalanin ersetzt sein kann.

2. Parenterale Ernährungslösung gemäss Anspruch 1, in welcher die Lösung die folgende Zusammensetzung hat:

<i>Zucker:</i>	<i>g/l</i>
reduzierender Zucker	30— 150
<i>physiologische Aminosäuren: mg/l</i>	
L-Isoleucin	2100—2810
L-Leucin	3340—4460
L-Valin	2220—2970
L-Methionin	960—1290
L-Cystein	0—1000

physiologische Aminosäuren: mg/l

L-Cystin	0— 200
L-Phenylalanin	1900—2540
L-Tyrosin	0—1000
L-Tryptophan	390— 530
L-Lysin	1980—2640
L-Threonin	1180—1580
L-Arginin	2740—3660
L-Histidin	1160—1550
L-Alanin	2120—2840
L-Asparaginsäure	120— 170
L-Glutaminsäure	120— 170
Glycin	1360—1820
L-Prolin	1580—2110
L-Serin	1030—1390
<i>Elektrolyte: mMol/l</i>	
Natrium	25— 60
Chlor	35— 65
Kalium	10— 40
Magnesium	0— 5
Phosphor	0— 10

wobei alles oder ein Teil des Cysteins und/oder Cystins durch Methionin ersetzt sein kann und alles oder ein Teil des Tyrosins durch Phenylalanin ersetzt sein kann.

3. Parenterale Ernährungslösung gemäss Anspruch 1, in welcher die Konzentration an reduzierendem Zucker etwa 5 bis 9 G/V-% beträgt.

4. Parenterale Ernährungslösung gemäss Anspruch 3, in welcher die Konzentration des reduzierenden Zuckers 6 bis 8 G/V-% beträgt.

5. Parenterale Ernährungslösung gemäss Anspruch 1, in welcher die Gesamt-Aminosäurekonzentration etwa 2,5 bis 3,5 G/V-% beträgt.

6. Parenterale Ernährungslösung gemäss Anspruch 1, in welcher die Konzentration der Elektrolyten die folgende ist:

	<i>mMol/l</i>
Natrium	25—35
Kalium	20—30



	<i>mMol/l</i>	
Chlor	45—55	
Magnesium	1,5—2,5	5
Phosphor	1,5—2,5	

7. Parenterale Ernährungslösung gemäss Anspruch 1, in welcher das Produkt aus der Konzentration des reduzierenden Zuckers (als Glucose) mit dem der gesamten Aminosäuren (G/V-%) 7 bis 25 beträgt.

8. Parenterale Ernährungslösung gemäss Anspruch 7, in welcher das Produkt 12 bis 24 beträgt.

9. Parenterale Ernährungslösung gemäss Anspruch 7, in welcher das Produkt 17 bis 23 beträgt.

10. Parenterale Ernährungslösung gemäss Anspruch 1, in welcher der pH-Wert der Flüssigkeit 4,0 bis 6,0 beträgt.

11. Parenterale Ernährungslösung gemäss Anspruch 1, in welcher der reduzierende Zucker Glucose und/oder Maltose ist.

12. Parenterale Ernährungslösung gemäss Anspruch 11, in welcher die Flüssigkeit folgende Zusammensetzung hat:

<i>reduzierender Zucker:</i>	<i>g/l</i>	
Glucose	71— 79	
<i>Aminosäuren</i>	<i>mg/l</i>	
L-Isoleucin	2220—2460	35
L-Leucin	3520—3900	
L-Valin	2350—2600	40
L-Methionin	1010—1420	
L-Phenylalanin	2010—2230	45
L-Tyrosin	130— 150	
L-Tryptophan	410— 470	
L-Lysin	2090—2310	50
L-Threonin	1250—1390	
L-Arginin	2890—3210	55
L-Histidin	1220—1360	
L-Alanin	2240—2490	
L-Asparaginsäure	130— 170	60
L-Glutaminsäure	0— 150	
Glycin	1430—1590	65

<i>Aminosäuren</i>	<i>mg/l</i>
L-Prolin	1670—1850
L-Serin	1090—1220
<i>Elektrolyte:</i>	<i>mMol/l</i>
Natrium	25— 35
Chlor	45— 55
Kalium	20— 30
Magnesium	1,5— 2,5
Phosphor	1,5— 2,5

wobei L-Cystein und/oder L-Cystin zu der obigen Zusammensetzung noch in einer Menge von 260 bis 290 mg/l zugegeben werden können.

Revendications

1. Solution alimentaire parentérale, caractérisée en ce qu'elle comprend un sucre réducteur, des électrolytes et des acides aminés, physiologiques, en la composition et les proportions présentées dans le Tableau 1 qui suit:

TABLEAU 1

<i>Composants</i>	<i>Quantité</i>
<i>Sucre</i>	<i>g/l</i>
Sucre réducteur	30— 150
<i>Acides aminés physiologiques</i>	<i>mg/l</i>
L-Isoleucine	2100—2810
L-Léucine	3340—4460
L-Valine	2220—2970
L-Méthionine	960—1290
L-Cystéine	0—1000
L-Cystine	0— 200
L-Phénylalanine	1900—2540
L-Tyrosine	0—1000
L-Tryptophane	390— 530
L-Lysine	1980—2640
L-Thréonine	1180—1580
L-Arginine	2740—3660



TABLEAU 1 (cont.)

Composants	Quantité
<i>Acides aminés physiologiques mg/l</i>	
L-Histidine	1160—1550
L-Alanine	2120—2840
Acide L-aspartique	120— 220
Acide L-glutamique	0— 170
Glycine	1360—1820
L-Proline	1580—2110
L-Sérine	1030—1390
<i>Electrolytes mmoles/l</i>	
Sodium	25— 60
Chlore	35— 65
Potassium	10— 40
Magnésium	0— 5
Phosphore	0— 10

pour autant que la totalité ou une partie de la cystéine et/ou de la cystine puisse être remplacée par de la méthionine, et que la totalité ou une partie de la tyrosine puisse être remplacée par de la phénylalanine.

2. Solution alimentaire parentérale suivant la revendication 1, caractérisée en ce qu'elle possède la composition suivante:

<i>Sucre</i>	<i>g/l</i>
Sucre réducteur	30— 150
<i>Acides aminés physiologiques mg/l</i>	
L-Isoleucine	2100—2810
L-Leucine	3340—4460
L-Valine	2220—2970
L-Méthionine	960—1290
L-Cystéine	0—1000
L-Cystine	0— 200
L-Phénylalanine	1900—2540
L-Tyrosine	0—1000
L-Tryptophane	390— 530

Acides aminés physiologiques mg/l

5	L-Lysine	1980—2640
	L-Thréonine	1180—1580
	L-Arginine	2740—3660
10	L-Histidine	1160—1550
	L-Alanine	2120—2840
	Acide L-aspartique	120— 170
15	Acide L-glutamique	120— 170
	Glycine	1360—1820
20	L-Proline	1580—2110
	L-Sérine	1030—1390
	<i>Electrolytes mmoles/l</i>	
25	Sodium	25— 60
	Chlore	35— 65
30	Potassium	10— 40
	Magnésium	0— 5
	Phosphore	0— 10

avec la condition que la totalité ou une partie de la cystéine et/ou de la cystine puisse être remplacée par de la méthionine, et que la totalité ou une partie de la tyrosine puisse être remplacée par de la phénylalanine.

3. Solution alimentaire parentérale suivant la revendication 1, caractérisée en ce que la concentration du sucre réducteur varie d'environ 5 à 9% p/v.

4. Solution alimentaire parentérale suivant la revendication 3, caractérisée en ce que la concentration du sucre réducteur varie de 6 à 8% p/v.

5. Solution alimentaire parentérale suivant la revendication 1, caractérisée en ce que la concentration en acides aminés totaux varie d'environ 2,5 à 3,5% p/v.

6. Solution alimentaire parentérale suivant la revendication 1, caractérisée en ce que la concentration en électrolytes est la suivante:

25—35 mmoles/l	Sodium
20—30 mmoles/l	Potassium
45—55 mmoles/l	Chlore
1,5—2,5 mmoles/l	Magnésium
1,5—2,5 mmoles/l	Phosphore



7. Solution alimentaire parentérale suivant la revendication 1, caractérisée en ce que le produit de la concentration en sucre réducteur (comme le glucose) par celle des acides aminés totaux varie de 7 à 25% p/v.

8. Solution alimentaire parentérale suivant la revendication 7, caractérisée en ce que le produit varie de 12 à 24.

9. Solution alimentaire parentérale suivant la revendication 7, caractérisée en ce que le produit varie de 17 à 23.

10. Solution alimentaire parentérale suivant la revendication 1, caractérisée en ce que le pH du liquide varie de 4,0 à 6,0.

11. Solution alimentaire parentérale suivant la revendication 1, caractérisée en ce que le sucre réducteur est le glucose et/ou le maltose.

12. Solution alimentaire parentérale suivant la revendication 11, caractérisée en ce que le liquide possède la composition suivante:

<i>Sucre réducteur</i>	<i>g/l</i>
Glucose	71— 79
<i>Acides aminés</i>	<i>mg/l</i>
L-Isoleucine	2220—2460
L-Leucine	3520—3900
L-Valine	2350—2600
L-Méthionine	1010—1420
L-Phénylalanine	2010—2230
L-Tyrosine	130— 150
L-Tryptophane	410— 470

<i>Acides aminés</i>	<i>mg/l</i>
L-Lysine	2090—2310
L-Thréonine	1250—1390
L-Arginine	2890—3210
L-Histidine	1220—1360
L-Alanine	2240—2490
Acide L-aspartique	130— 170
Acide L-glutamique	0— 150
Glycine	1430—1590
L-Proline	1670—1850
L-Sérine	1090—1220

<i>Electrolytes</i>	<i>mmoles/l</i>
Sodium	25— 35
Chlor	45— 55
Potassium	20— 30
Magnésium	1,5— 2,5
Phosphore	1,5— 2,5

avec la condition que de la L-cystéine et/ou de la L-cystine puissent encore être ajoutées à la composition précitée en une proportion de 260 à 290 mg/l.



* C L N S *