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Determination of Protein Quality of Products Used in Amino Acid Metabolism Diseases with Protein Digestibility-Corrected Amino Acid Score Method: A Descriptive Cross-Sectional Research

Amino Asit Metabolizması Hastalıklarında Kullanılan Ürünlerin Protein Kalitesinin Protein Sindirilebilirliği Düzeltilmiş Amino Asit Skoru Yöntemi ile Belirlenmesi: Tanımlayıcı Kesitsel Araştırma

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ABSTRACT Objective: The aim of this study was to evaluate the protein quality of products used in the nutritional treatment of phenylketonuria (PKU) and maple syrup urine disease (MSUD). **Material and Methods:** Protein digestibility corrected amino acid score (PDCAAS) method was used to evaluate protein quality. Thirty two products including 14 PKU Specialty Products, 5 PKU-glycomacroeptide (PKU-GMP) products and 13 MSUD products were analyzed. **Results:** PDCAAS scores of PKU products were between 94-100%; PDCAAS scores of PKU-GMP products were between 35-99%. In general, the limiting amino acids were the sulfur amino acid group with 11 products. The PDCAAS score of MSUD products was between 24-49% and the limiting amino acids of these products were commonly sulfurous amino acid group. **Conclusion:** Present study revealed that the protein quality and PDCAAS value of PKU specialty products (except PKU-GMP) were generally high. PDCAAS value of PKU-GMP specialty products differed among themselves. The differences between PDCAAS value of PKU-GMP specialty products may attributed to the variability of amino acids supplemented in the products. In MSUD products, protein quality and PDCAAS value were generally lower than PKU specialty products (except PKU-GMP), which related to the limitation of valine, isoleucine, and leucine. Studies on therapeutic foods developed against congenital amino acid disorders are limited; further studies are needed.

Keywords: Phenylketonuria; maple syrup urine disease; congenital metabolic disorders; protein digestibility corrected amino acid score; protein quality

ÖZET Amaç: Bu çalışmanın amacı, fenilketonüri [Phenylketonuria (PKU)] ve akçaağaç şurubu idrar hastalığı [Maple Syrup Urine Disease (MSUD)] beslenme tedavisinde kullanılan ürünlerin protein kalitesinin değerlendirilmesidir. **Gereç ve Yöntemler:** Protein kalitesinin değerlendirilmesinde protein sindirilebilirliği düzeltilmiş amino asit skoru [Protein Digestibility Corrected Amino Acid Score (PDCAAS)] yöntemi kullanılmıştır. On dört PKU Özel Ürünü, 5 PKU-glikomakroeptit (PKU-GMP) ürünü, 13 MSUD ürünü olmak üzere 32 ürün incelenmiştir. **Bulgular:** PKU ürünlerinin PDCAAS skoru %94-100 arasında; PKU-GMP ürünlerinin PDCAAS skoru %35-99 arasında bulunmuştur. Genel olarak sınırlayıcı amino asitleri 11 ürün ile sülfürlü amino asit grubu olmuştur. MSUD ürünlerinin PDCAAS skoru %24-49 arasında bulunmuştur ve bu ürünlerin sınırlayıcı amino asitleri yaygın olarak sülfürlü amino asit grubu olmuştur. **Sonuç:** Mevcut çalışma, PKU özel ürünlerinin (PKU-GMP hariç) protein kalitesinin ve PDCAAS değerinin genel olarak yüksek olduğunu ortaya koymuştur. PKU-GMP özel ürünlerinin PDCAAS değeri kendi aralarında farklılık göstermiştir. PKU-GMP özel ürünlerinin PDCAAS değerleri arasındaki farklılıklar, ürünlere eklenen amino asitlerin değişkenliğine bağlanabilir. MSUD ürünlerinde protein kalitesi ve PDCAAS değeri, valin, izolösin ve lösin sınırlamasıyla ilişkili olarak PKU özel ürünlerinden (PKU-GMP hariç) genellikle daha düşüktür. Konjenital amino asit bozukluklarına karşı geliştirilen terapötik gıdalar üzerine çalışmalar sınırlıdır; daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Fenilketonüri; akçaağaç şurubu idrar hastalığı; doğuştan metabolizma bozuklukları; protein sindirilebilirliği düzeltilmiş amino asit skoru; protein kalitesi

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Inborn errors of metabolism are inherited single-gene disorders resulting from the deficiency or abnormality of an enzyme, cofactor or transporter, leading to accumulation of a substrate or deficiency of a product.[1] Genetic defects in the biosynthesis, degradation or transport of amino acids lead to various inborn errors of amino acid metabolism, including branched-chain amino acid metabolism, glycine metabolism, aromatic amino acid metabolism, sulfated amino acid metabolism and other disorders.[2] Congenital amino acid defects are a heterogeneous group that includes phenylketonuria (PKU), maple syrup urine disease (MSUD), homocystinuria, tyrosinemia Type I and II (TYR I and TYR II), organic acidemias and urea cycle disorders.[3] PKU is an inherited autosomal recessive metabolic disorder caused by a deficiency of the enzyme phenylanalanine hydroxylase (PAH), with an incidence of approximately 1 in 10,000 newborns in most Caucasian populations of Northern and Western Europe. Untreated PKU causes severe irreversible neurological and cognitive impairments within the 1st year after birth due to high phenylalanine (Phe) concentrations, which also causes low tyrosine (Tyr) levels.[4]

MSUD is an autosomal recessive disorder caused by deficient activity of the branched-chain alpha-keto acid dehydrogenase (BCKAD) complex.[5] Deficiency in the activity of the BCKAD complex causes MSUD, an inborn error of metabolism characterized by toxic accumulation of branched-chain amino acids (BCAAs) and related α-keto acids.[6] MSUD is categorized as classic (severe), moderate or intermittent phenotype, and patients affected by the classic form have episodes of ketoacidosis, apnea, seizures and coma that can lead to death.[5]

Disorders of protein and amino acid metabolism are managed with lifelong dietary restriction, and the main goal of nutritional therapy is to reduce the production of toxic substances by restricting offending nutrients in the patient's diet, to provide sufficient calories and protein for optimal growth and development, and to provide essential vitamins and minerals.[7] Dietary management includes consumption of foods that are naturally very low in protein, such as a moderate but clearly restricted allocation of natural protein, a protein substitute that does not contain the disease-causing amino acid, special low-protein products to meet the patient's energy requirements, or other protein-free energy sources.[3] To maintain body functions and growth, humans need certain minimum protein intake levels as well as adequate amounts of dietary essential amino acids that are not synthesized by the body.[8] Amino acid disorder-specific protein substitutes are an important source of protein in diet-treated amino acid disorders. These protein substitutes are available in various presentations (powders, gels, liquids). Their fat and carbohydrate content is variable and they are an important dietary supplement for protein metabolism, including protein homeostasis, growth.[3] The range of therapeutic foods in PKU and MSUD varies according to the age and metabolic requirements of the individual. In infancy, special formulas without Phe in PKU and BCAA in MSUD are used to support growth and development. In childhood, low-protein natural foods are added to the diet, while special medical foods and supplements are used to supplement the missing amino acids. During adolescence, energy and protein needs increase due to rapid growth and hormonal changes, but strict Phe and BCAA restrictions are maintained to avoid the risk of metabolic crisis. In adulthood, some individuals can tolerate a certain amount of natural protein, but therapeutic foods continue to be used for metabolic control; in special cases, such as pregnancy, the diet is more strictly regulated. In elderly, essential nutrients can be increased to prevent muscle loss and maintain general health. At all ages, a personalized therapeutic nutrition plan should be implemented that is appropriate to the individual's energy and nutrient requirements and maintains metabolic balance.[9]

The effects of proteins on body functions such as immunity, host defense, growth, mental development and learning capacity are related not only to protein quantity but also to protein quality.[9] Protein quality measures bioavailability, more broadly the proportion of amino acids that can be absorbed from the diet and utilized in the body.[10] A relative measure to determine the capacity of protein sources and diets to meet the body's demand for amino acids and nitrogen.[11] Since the approval of protein digestibility corrected amino acid score (PDCAAS) by the Committee on Plant Proteins of the Codex Alimentarius

Commission and the United Nations Food and Agriculture Organization (FAO)/World Health Organization (WHO) Expert Consultation on Protein Quality Assessment, PDCAAS has been widely adopted as the standard method for determining the quality of dietary protein.[12]

The amino acid and protein contents of special products used in the treatment of patients with congenital disorders of amino acid metabolism have been investigated, but it is important to evaluate the protein quality as well as the protein quantity of these products. For that purpose, the present study aims to evaluate the protein quality of specialty products (SP) consumed by PKU and MSUD patients who have been on a diet restricted from natural protein throughout their lives.

MATERIAL AND METHODS

ETHICAL APPROVAL

This study did not require ethical approval, informed consent, or adherence to the Declaration of Helsinki as it did not involve human participants or identifiable personal data.

RESEARCH TYPE

This study is designed as a descriptive cross-sectional study investigating the determination of protein quality in PKU and MSUD specialty products. It theoretically evaluates the protein quality of PKU-specific products using the PDCAAS method based on existing nutrient composition data.

SELECTION OF DATA

Within the scope of the study, 19 PKU [14 PKU specialty products, 5 glycomacroeptide (GMP) specialty products] and 13 MSUD SP were analyzed to determine protein quality according to PDCAAS method. The ingredients of PKU and MSUD products were taken from the product label information of the relevant companies.

CALCULATION OF AMINO ACID SCORES OF PRODUCTS

When calculating the amino acid score, 11 amino acids were evaluated, including histidine (His), isoleucine (Ile), leucine (Leu), lysine (Lys), methionine, cysteine, Phe, Tyr, threonine (Thr), tryptophan (Trp) and valine (Val). The calculation consists of 9 separate categories. For the sulfurous amino acid group (SAA), methionine and cysteine were summed. Likewise, Phe and Tyr were collected for the aromatic amino acid group (AAA). The above-mentioned 11 amino acids found in SP and diets were identified and the amount of these amino acids in 1 gram of protein was calculated. It was then divided by the amino acid reference values found in FAO (Table 1).[10] When determining reference values, the age groups for which specific products are used were considered. The lowest value among the calculated results was determined as the limiting amino acid.

CALCULATING THE PROTEIN QUALITY OF PRODUCTS

In this study, the PDCAAS method recommended by FAO and WHO was used to determine the protein quality of the special products given for PKU and MSUD patients and the diets selected for PKU patients.[13] In the 1st step of the calculation, the limiting amino acid of the products and diets was found by calculating the amino acid scores of the products and diets. In the 2nd step, the products and diets were mul-

TABLE 1: Reference scoring model for amino acid requirements by age groups (mg/g protein).[10]

Age	His	Ile	Leu	Lys	SAA	AAA	Thr	Trp	Val
0.5	20	32	66	57	27	52	31	8.5	43
1-2	18	31	63	52	25	46	27	7	41
3-10	16	30	61	48	23	41	25	6.6	40
11-14	16	30	61	48	23	41	25	6.6	40
15-18	16	30	60	47	23	40	24	6.3	40
>18	15	30	59	45	22	38	23	6.0	39

His: Histidin; Ile: Isoleucine; Leu: Leucine; Lys: Lysine; SAA: Sulfurous amino acid group; AAA: Amino acid group; Thr: Threonine; Tyr: Tyrosine; Trp: Tryptophan; Val: Valine

tiplied by the protein digestibility factor, which is the actual fecal digestibility determined. Thus, the PDCAAS value of the products and diets was calculated. The PDCAAS value is scored between 0-100 and values above 100 points are cut to 100 points. Values close to 100 indicate that the protein quality of products and diets is high, while values far from 100 indicate that the protein quality is low.[11]

Special products produced for MSUD do not contain Leu, Ile, Val. During the PDCAAS calculation, the amino acids not present in the special product were averaged with the least abundant amino acid. This amino acid was chosen as the limiting amino acid. PDCAAS calculation of PKU special products was made according to the reference calculation.

DETERMINATION OF PROTEIN DIGESTIBILITY FACTORS OF PRODUCTS AND DIETS

In the last step of the PDCAAS calculation, the limiting amino acid found in the amino acid score is multiplied by the protein digestibility factor, which is the actual fecal digestibility value. Table 2 shows the digestibility factors of the products selected in the current study.

In a study conducted by Pellegrino et al. the actual fecal digestibility of whey protein was compared and protein digestibility was found to be 98% for whey protein, 100% for whey protein concentrate and 99% for hydrolyzed whey protein.[15] Since the products used in the present study were hydrolyzed and elemental products, the digestibility factor of whey protein was taken as 99%. Hydrolyzed/elemental formulas are formulas designed to reduce/eliminate protein allergenicity, prevent or treat allergic disorders. Formulas are broadly divided into intensely hydrolyzed (peptide-based) and amino acid-based formulas. Intensely hydrolyzed formulas contain peptide bases, which are casein or whey hydrolysates. These formulas have virtually no protein residue and are completely broken down to amino acids. Depending on the source of the proteins, these formulas can be derived from bovine casein, bovine whey protein, a mixture of casein and whey proteins or a mixture of soy proteins and ox collagen.[19] Studies conclude that hydrolysates of whey and casein proteins, whether partially hydrolyzed or highly hydrolyzed, have the same effects on nitrogen intake, weight gain, protein digestibility and serum protein concentration as their natural counterparts. Furthermore, hydrolyzed proteins are completely digested in the small intestine, while nonhydrolyzed proteins (caseins, α-lactalbumin, β-lactoglobulin, conglutinin, glycine) are only partially digested in the simulated gastrointestinal tract.[16] In the light of the literature research, in the present study, the digestibility factor of hydrolyzed/elemental products was taken as 97%, which is the highest value of the digestibility factor of cow's milk-based foods in the range of 87-97%.

TABLE 2: Digestibility factors of selected products

Product	Digestibility factor
Cow milk based products	92%[14]
Soy based products	93%[14]
Whey protein	99%[15]
Hydrolyzed/elemental formula/product	97%[14,16-18]

RESULTS

The amino acid content of PKU products including PKU-SP and PKU-GMP in 1 g protein is shown in Table 3.

As seen in Table 3, the Phe content of PKU-SP is 0 mg. However, PKU-GMP products contain Phe amino acid, albeit in low amounts.

The amino acid content of MSUD SP in 1 g protein is given in Table 4.

As seen in Table 4, the leucine, isoleucine and valine contents of MSUD-Specialty Products are 0 mg.

Protein content, PDCAAS value and limiting amino acids of PKU-Special Products and PKU-GMP products were presented in Table 5.

As seen in Table 5, the protein and PDCAAS values of PKU special products and the amino acid acids with the lowest amino acid scores are listed. The protein values of the products vary considerably. The product with the lowest protein content is PKU-SP-11 with 12 g, while the lowest PKU-GMP product is PKU-GMP-4 with 4 g. The product with the highest protein content is PKU-SP-7 and PKU-SP-14

TABLE 3: Amino acid content of PKU special products in 1 g protein (mg)

	PKU-SP-1	PKU-SP-2	PKU-SP-3	PKU-SP-4	PKU-SP-5	PKU-SP-6	PKU-SP-7	PKU-SP-8	PKU-SP-9	PKU-SP-10	PKU SP-11	PKU-SP-12	PKU-SP-13	PKU-SP-14	PKU-GMP-1	PKU-GMP-2	PKU-GMP-3	PKU-GMP-4	PKU-GMP-5
His (mg)	25.30	46.6	41.9	31.5	26	22.7	25	25	42.8	39.5	40.8	45.8	43.16	42.5	22.6	24.16	29.24	40	35.8
Ile (mg)	70.98	71.1	72.7	76.84	65.8	71	65	50	68.5	62	72.5	71.7	74.3	74.5	51.8	47.5	67.2	72.5	72.5
Leu (mg)	129.6	122.2	114.6	126.31	108.4	131.8	110	80	114.2	106.5	113.3	122.7	112.7	117	103.6	180	197.8	152.5	153.9
Lys (mg)	80.24	82.2	75.5	86.3	76.8	80	78.3	66	88.5	81.5	74.16	93.7	76.7	77.3	87.8	70	38.9	42.5	48.57
Methionine (mg)	22.2	19.25	20.27	29.4	26	21.8	25	26	18.2	17	20	19.6	21.5	20.6	11.8	8	9.74	12.5	14.28
Cysteine (mg)	14.8	15.18	13.63	14.7	13.3	15	12.5	33.9	13.7	12.75	13.3	15	14.38	13.9	0.5	0.45	0	15	6.16
Phe (mg)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1	1	2.3	1.75	1.78
Tyr (mg)	98.7	106.6	107.6	95.7	64.4	100	65	95	100	94	106.6	108.27	110.3	109.8	77.10	93.3	83.82	100	114.8
Thr (mg)	46.2	60	74.12	60	51.6	45.9	51.6	90	54.2	52	73.3	60	76.7	75.6	81.05	74.1	107.2	112.5	116.96
Trp (mg)	17.9	22.9	23	24.2	19.2	18.18	21.6	15	22.2	20.5	22.5	24.13	23.9	23.3	25	14	10.7	25	20.53
Val (mg)	77	77.7	84.6	81	76	76.8	78.3	60	71.4	69	83.3	78.62	86.3	86.16	44.4	40.83	57.5	87.5	58.39

PKU-SP: Phenylketonuria-specialty products; PKU-GMP: Phenylketonuria-glycomacroeptide; His: Histidin; Ile: Isoleucine; Leu: Leucine; Lys: Lysine; Phe: Phenylalanine; Tyr: Tyrosine; Thr: Threonine; Trp: Tryptophan; Val: Valine

TABLE 4: Amino acid content of MSUD SP in 1 g protein (mg)

	MSUD-SP-1	MSUD-SP-2	MSUD-SP-3	MSUD-SP-4	MSUD-SP-5	MSUD-SP-6	MSUD-SP-7	MSUD -SP-8	MSUD-SP-9	MSUD-SP-10	MSUD-SP-11	MSUD-SP-12	MSUD-SP-13
His (mg)	61	31.8	33.95	59.2	40	31.6	37	57.5	71.6	71.1	49.4	43.16	41.7
Ile (mg)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Leu (mg)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Lys (mg)	110	94.8	109.2	107.4	71	95	120.8	105	90.8	90.3	123.4	90.33	87.5
Metiyonin (mg)	25.9	31.8	29	25.1	17	31.6	32	24.75	29.6	29.3	19.7	25.8	25.1
Sistein (mg)	19.8	15.9	20.98	19.25	24	15.8	22.9	20	11.2	11.1	4.9	17.9	17.3
Phe (mg)	71.7	56.4	56.79	69.6	47	56.6	62	70	88	87.4	86.3	67.5	65.4
Tyr (mg)	71.7	69.2	56.79	69.6	80	70	62	70	88	87.4	86.3	71.8	69.5
Thr (mg)	80.15	64.4	49.91	77.7	52	65	50.8	77.5	72.4	71.9	76.3	64.6	62.5
Trp (mg)	32.06	25.2	25.3	31.1	21	25	27	32.5	53.2	52.8	49.4	35.8	34.7
Val (mg)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0

MSUD-SP: Maple syrup urine disease-specialty products; His: Histidin; Ile: Isoleucine; Leu: Leucine; Lys: Lysine; Phe: Phenylalanine; Tyr: Tyrosine; Thr: Threonine; Trp: Tryptophan; Val: Valine

TABLE 5: Protein content, PDCAAS value and limited amino acids of PKU specialty products

	PKU-SP-1	PKU-SP-2	PKU-SP-3	PKU-SP-4	PKU-SP-5	PKU-SP-6	PKU-SP-7	PKU-SP-8	PKU-SP-9	PKU-SP-10	PKU-SP-11	PKU-SP-12	PKU-SP-13	PKU-GMP-1	PKU-GMP-2	PKU-GMP-3	PKU-GMP-4	PKU-GMP-5
Protein (g/100g)	16.2	13.5	14.3	9.5	50	22	60	28	35	20	12	29	41.7	60	38	6	19	4	56
PDCAAS	1	1	1	1	1	1	0.94	1	1	1	1	1	1	1	0.52	0.35	0.41	0.87	0.99
Limited amino acid	His	SAA	SAA	Lys	AAA	His	His	Leu	SAA	SAA	SAA	SAA	SAA	SAA	SAA	SAA	SAA	Lys	Lys

PKU-SP: Phenylketonuria-specialty products; PKU-GMP: Phenylketonuria-glycomacropeptide; PDCAAS: Protein digestibility corrected amino acid score; His: Histidin; SAA: Sulfurous amino acid group; Lys: Lysine; AAA: Amino acid group; Leu: Leucine

TABLE 6: Protein content, PDCAAS value and limited amino acids of MSUD-SP

	MSUD-SP-1	MSUD-SP-2	MSUD-SP-3	MSUD-SP-4	MSUD-SP-5	MSUD-SP-6	MSUD-SP-7	MSUD-SP-8	MSUD-SP-9	MSUD-SP-10	MSUD-SP-11	MSUD-SP-12	MSUD-SP-13
Protein (g/100g)	13.1	50	16.2	13.5	10	60	24	40	25	81	38	60	41.7
PDCAAS	0.38	0.4	0.42	0.37	0.32	0.29	0.49	0.44	0.43	0.42	0.24	0.41	0.39
Limited amino acid	SAA	His	Thr	SAA	Lys	His	Thr	SAA	SAA	SAA	SAA	Lys	His

MSUD-SP: Maple syrup urine disease- specialty products; SAA: Sulfurous amino acid group; His: Histidin; Thr: Threonine; Lys: Lysine; PDCAAS: Protein digestibility corrected amino acid score

with 60 g. The PKU-GMP product with the highest protein content is PKU-GMP-5 with 56 g. PDCAAS values of the products, the score was cut to 1 because the PDCAAS value of all PKU-SP was above 1, except for PKU-SP-7, which had a PDCAAS score of 94%. In PKU-GMP products, the PDCAAS score was more varied. The PKU-GMP product with the lowest PDCAAS score is PKU-GMP-2 with 35%. The highest PDCAAS score was PKU-GMP-5 with 99%. In general, the limiting AAA is the sulfur amino acid group. The PDCAAS score of PKU-GMP-4 product with the lowest protein content of 4 g protein was 87%, while the PDCAAS score of PKU-GMP-2 product with 6 g protein content was 35%.

Protein, PDCAAS values and limited amino acid values of products specially prepared for MSUD patients are listed in Table 6.

Table 6 lists the protein and PDCAAS values of MSUD SP and the amino acid acids with the lowest amino acid score. As in PKU products, the protein values of MSUD products are quite different. The lowest protein value is MSUD Special Product-5 with 10 g and the highest protein value is MSUD Special Product-10 with 81 g. PDCAAS values of the products were calculated. As it is known, PDCAAS values vary between 0-1 (0-100%). Values closer to 1 have higher protein quality. When we look at the products, PDCAAS scores are closer to 0. The lowest PDCAAS value is MSUD-SP-11 with 0.24 (24%) and the highest PDCAAS value is MSUD-SP-7 with 0.49 (49%). Since there are no leucine, Ile and Val values in MSUD specific products, they are considered as limiting amino acids in all products. The amino acids with the lowest amino acid score following these 3 amino acids. In this context, SAA group was the limiting amino acid in 6 products. In 3 products, the limiting amino acid was His.

DISCUSSION

In infants and young children with PKU, more than 80% of energy and 90% of protein needs are met with Phe-free amino acid formula.[20] Protein substitutes meet protein requirements for cellular function and growth.[21] Considering the low protein intake and the fact that 90% of the protein requirement of the diet is met by protein substitutes, protein intake in the diets

of PKU patients is a very important issue, but it is also very important to consider the protein quality of these products. Therefore, in this study, the protein quality of protein substitutes and diets developed for PKU and MSUD patients were evaluated according to PDCAAS method and limiting amino acids were determined.

In a study evaluating the protein quality of follow-on formulas and ready-to-use therapeutic foods, it was reported that if the PDCAAS values of formulas or therapeutic foods were greater than 100% or 90%, the protein quality of these therapeutic foods was high. Shivakumar et al. reported that the amount of protein should be increased for products with PDCAAS values less than 90% to meet the essential amino acid requirement.[22] In the present study, all of the PKU specialty products, except for the products with GMP content, had a PDCAAS value above 95% with the desired protein quality. However, the protein quality of special products prepared for MSUD patients was found to be low with a PDCAAS score between 24-44%.

According to the calculations made in the FAO 2017 report, the PDCAAS value of peanut-containing therapeutic food containing 50% milk protein was 88% (limited to lysine), while the PDCAAS value of peanut-containing therapeutic food containing 20% milk protein was 76% (limited to lysine). In the same study, PDCAAS values were 84% (Thr-limited) for soy-corn-sorghum-amino acid therapeutic food and 91% (His-limited) for whey protein concentrate therapeutic food.[23] In the present study, the PDCAAS value of 5 PKU-SP containing soy was calculated as 1. The restricted amino acid of one of them was Leu, while the restricted amino acid of the other four was SAA group. The PDCAAS values of 3 MSUD-SP containing soy were 32%, 44% and 41%. The limiting amino acids were 2 Lys and one sulfur amino acid group. However, when the whole products are evaluated, it can be said that the SAA is concentrated as the limiting amino acid.

GMP is a commercial product used as a nutritional ingredient, suitable for supplementing diets with whey protein and for use in whey-based infant formulas. Isolation of GMP from whey results in contamination from other whey proteins such as β-lactoglobulin and α-lactalbumin, which contain Phe, and therefore, commercially available GMP contains 2.0 to 5.0 mg Phe per gram of protein, also contains a adequate amount of Thr and Ile.[20] Trp, Tyr, Phe and cysteine are absent in the pure GMP form. GMP contains insufficient amounts of the 5 essential amino acids His, Leu, methionine, Trp and Tyr, and fortification of commercial GMP products with these amino acids would allow GMP products to be used as an alternative to L-Amino Acids.[21] Among the 5 PKU-GMP products evaluated in the present study, 3 products had low PDCAAS values (0.52, 0.35, 0.41). In 3 of them, the limiting amino acid was sulfur amino acid (methionine+cysteine) group. 2 PKU-GMP products had high PDCAAS values (87%, 99%). Compared to the PDCAAS score stated in the FAO 2017 report, GMP products with low PDCAAS values were limited to methionine and cysteine amino acids, and the reason for the low PDCAAS score and protein quality was thought to be insufficient amino acid supplementation.[23]

PKU is an autosomal recessive disorder caused by deficiency or absence of PAH, the enzyme that converts the amino acid Phe to Tyr.[24] Tyr is an essential amino acid in the diet of people with PKU due to the inability to hydroxylate Phe to Tyr.[20] The therapeutic nutrients used are supplemented with Tyr.[25] When the PKU products in the current study were analyzed, PDCAAS values were found to be between 0.95-1 except for 4 GMP products. Although the Phe value of the content of the products was zero (except GMP), since Phe+Tyr (AAA) were evaluated together in the PDCAAS calculation, it is thought that Tyr supplementation to the products increased the protein quality. In MSUD special products, the fact that Leu, Ile and Val contents were zero and included separately in the PDCAAS calculation affected the protein quality value. The protein quality of the products was found to be lower than PKU products. The aim of nutrition in diseases of amino acid metabolism is to reduce the production of toxic substances by restricting offending nutrients in the patient's diet and to provide adequate calories, protein, vitamins and minerals required for optimal growth and development. Growth parameters in these patients can often

be compromised by dietary restriction.[7] However, protein intake early in life is essential for infant development.[26] However, the majority of these patients receive limited natural protein and disease-specific amino acid supplements/substitutes.[7,27] Disorder-specific amino acid supplementation is an important source of protein in diet-treated amino acid disorders, but it is also an essential nutritional supplement for protein homeostasis and protein metabolism, including growth.[3] Although the amount of protein in a given food source is primarily determined as a function of its actual nitrogen content, this crude protein content is not considered a reliable indicator of a dietary protein's ability to meet the metabolic needs of the host.[13] The protein quality of foods is an important criterion for ensuring adequate nutrition and maintaining good health.[8] The quality of dietary proteins is often defined by the extent to which the constituent amino acids match the consumer's amino acid needs.[13]

This study evaluated the protein quality of protein substitutes and diets developed for PKU and MSUD patients by PDCAAS to identify limiting amino acids. The findings revealed that PKU-SP have high protein quality, however some GMP-containing products and MSUD-SP may have inadequate protein quality due to low PDCAAS scores. Lack of methionine and cysteine in GMP-based products and leucine, Ile and Val MSUD products were found to reduce protein quality. This study also has some limitations. The theoretical nature of the study was insufficient to investigate how factors such as storage temperature, pH may cause Maillard reaction of proteins and carbohydrates in the content of therapeutic products, which may affect the bioavailability of some amino acids and affect protein quality. It is thought that evaluations are incomplete in a society where the food industry has developed to this extent and plant-based products have increased in addition to dairy-based products.

CONCLUSION

Protein substitutes, which are one of the main sources of nutritional therapy for inborn errors of amino acid metabolism and should be consumed from the moment of birth until the end of life, are very important for individuals with these diseases. PKU and MSUD patients are also included in this group. According to the results of the PDCAAS score, the protein quality of PKU SP was found to be high. However, the protein quality of MSUD SP was found to be low. Although PKU-SP had zero Phe content, supplementation with Tyr positively affected the PDCAAS score and protein quality. On the other hand, the lack of isoleucine, Leu and Val MSUD-SP negatively affected the PDCAAS score and protein quality. The protein quality of PKU-GMP products showed a wide range. The reason for this variable result is the variability of the amino acids supplemented in PKU-GMP products. Again, when we look at the balance between protein content and protein quality in PKU-GMP products, it is concluded that the protein quality of the product may be independent of the amount of protein and that the important thing is the amino acid pattern. As a result of the literature research, studies on therapeutic nutrients developed against congenital amino acid disorders are very limited, further studies focused on protein quality are definitely needed.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Özge Akgündoğdu, Elif Ede Çintesun;* ***Design:*** *Özge Akgündoğdu, Elif Ede Çintesun;* ***Control/Supervision:*** *Elif Ede Çintesun;* ***Data Collection and/or Processing:*** *Özge Akgündoğdu;* ***Analysis and/or Interpretation:*** *Özge Akgündoğdu, Elif Ede Çintesun;* ***Literature Review:*** *Özge Akgündoğdu;* ***Writing the Article:*** *Özge Akgündoğdu, Elif Ede Çintesun;* ***Critical Review:*** *Elif Ede Çintesun;* ***References and Fundings:*** *Özge Akgündoğdu;* ***Materials:*** *Özge Akgündoğdu.*

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