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NUTRITIONAL CONTENTS OF LOW PHENYLALANINE DIETS: A MINI REVIEW

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KEY WORDS:
phenylketonuria, phenylalanine, patients, aspartame, diet

ABSTRACT

Increased interest in the utilization of nutrition management of patients with phenylketonuria is clear. Applications include a small measured amount of phenylalanine given in the form of exchange food, phenylalanine-free protein substitute and low phenylalanine foods. In this article, the essential nutritional contents of low phenylalanine diets and the latest techniques and procedures used for creating several types of low phenylalanine diets from different food sources for persons with phenylketonuria are reviewed. The principles of these methods are described. Most of the techniques and procedures employed to remove Phe from the protein hydrolysate are based on the liberation of the amino acid using enzymatic hydrolysis. Free Phe is then removed via adsorption. Therefore, knowing the phenylalanine (Phe) content of foods as well as principles of procedures and techniques used for creating low Phe diets is very important for managing the diet of patients with phenylketonuria. Allowed foods and foods that should be avoided by persons with phenylketonuria are mentioned. Low Phe cereal based foods (i. e. toast bread, pasta, shamy bread, pan bread and rice) and dairy based foods are also considered. The US FDA regulation of aspartame labeling is also stated.

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ПИЩЕВАЯ ЦЕННОСТЬ ДИЕТ С НИЗКИМ СОДЕРЖАНИЕМ ФЕНИЛАЛАНИНА: МИНИ-ОБЗОР

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КЛЮЧЕВЫЕ СЛОВА:
фенилкетонурия, фенилаланин, пациенты, аспартам, диета

АННОТАЦИЯ

Повышенный интерес к применению управления питанием пациентов с фенилкетонурией очевиден. Примеры использования включают небольшие определенные количества фенилаланина, поступающего в виде «обменных» пищевых продуктов, не содержащую фенилаланин белковую замену и пищевые продукты с низким содержанием фенилаланина. В данной статье сделан обзор содержания важных компонентов диет с низким содержанием фенилаланина и самых современных методов и процедур, используемых для создания нескольких видов диет с низким содержанием фенилаланина из различных пищевых источников для лиц с фенилкетонурией. Описаны принципы этих методов. Большинство методов и процедур, применяемых для удаления Phe из белкового гидролизата, основано на высвобождении аминокислоты, используя ферментативный гидролиз. Свободный Phe затем удаляется путем адсорбции. Таким образом, знание содержания фенилаланина в пищевых продуктах, а также принципов методов и процедур, применяемых для создания диет с низким содержанием фенилаланина, очень важно для управления диетой для пациентов с фенилкетонурией. Перечислены разрешенные пищевые продукты и продукты, употребления которых следует избегать пациентам с фенилкетонурией. Также рассмотрены пищевые продукты на основе зерновых (т. е. хлеб для тостов, макаронные изделия, пита, формовой хлеб и рис) и молочные продукты. Также сообщается о регулировании US FDA маркировки аспартама.

1. Introduction

Phenylketonuria (PKU) disorder is caused by deficiency of phenylalanine hydroxylase (PAH, EC1.14.16.1) enzyme required to break down an amino acid called phenylalanine (Phe) and consequently leads to accumulation of Phe (Figure 1) in organs and blood of patients [1,2,3]. The prevalence of PKU in the world is 1:10,000 [1], while the incidence rate of PKU is 1:125,000 in Japan [4], 1:7,500 in Egypt [5,6], 1:116,006 in Philippines [7], 1:223,735 in Thailand [8], 1:83,333 in Singapore [9], 1:15,924 in China [10] and 1:4,500 in Ireland and Western Scotland [11]. Van Calcar and Ney [12] described the PKU symptoms as follows: an off-odor, nervous system problems, intellectual disability, delayed development, social and mental problems. For seven decades, the world has depended on the healing power of medical foods (i. e. food formulations intended for dietary management of PKU patients). The nutritional, biochemical and clinical follow-up of persons with PKU requires inspection of the body mass index, nutrient deficiency signs, intake of nutrients and biomarkers [13]. Zaky et al. [14] reported that early diagnosis of phenylketonuria and the use of a Phe-restricted diet lead to avoiding growth problems. A Phe-restricted diet is a phenylalanine-free amino acid containing formula enriched with minerals, vitamins, fatty acids and tyrosine [15].

The nutritional treatment for PKU depends on decreasing protein ingestion and reducing Phe supply to cover the minimum dietary intakes of PKU persons [16]. Children with PKU can tolerate up to 500 mg Phe per day [1, 17]. PKU persons who eat diets that contain protein or aspartame (an artificial sweetener composed of phenylalanine and aspartic acid) may have health problems. Therefore, these persons need to follow free or low Phe diets. Yaseen and Shouk [18] stated that diets low in Phe contain one of the following three parts: a small measured amount of phenylalanine given in the form of exchange food, protein substitute that includes all non-phenylalanine amino acids (i. e. amino acids powder, liquid, tablets, bars and capsules) and low phenylalanine foods (Figure 2) that can be eaten without restriction (i. e. jams, jellies, honey, sugar, vegetable oil, butter, spices, starches and aspartame free drinks). On the other hand, foods containing a high percentage of Phe must be avoided. Such foods include meat and meat products, milk and milk products, legumes and legume products, cereals and cereal products. MacDonald et al. [19] suggested that fruits and vegetables containing 51–75 mg Phe/100 g cause no problem for persons with PKU. Guimarães and Lanfer-Marquez [20] found some dried soups low in Phe that can potentially be used as food choice for persons with phenylketonuria.

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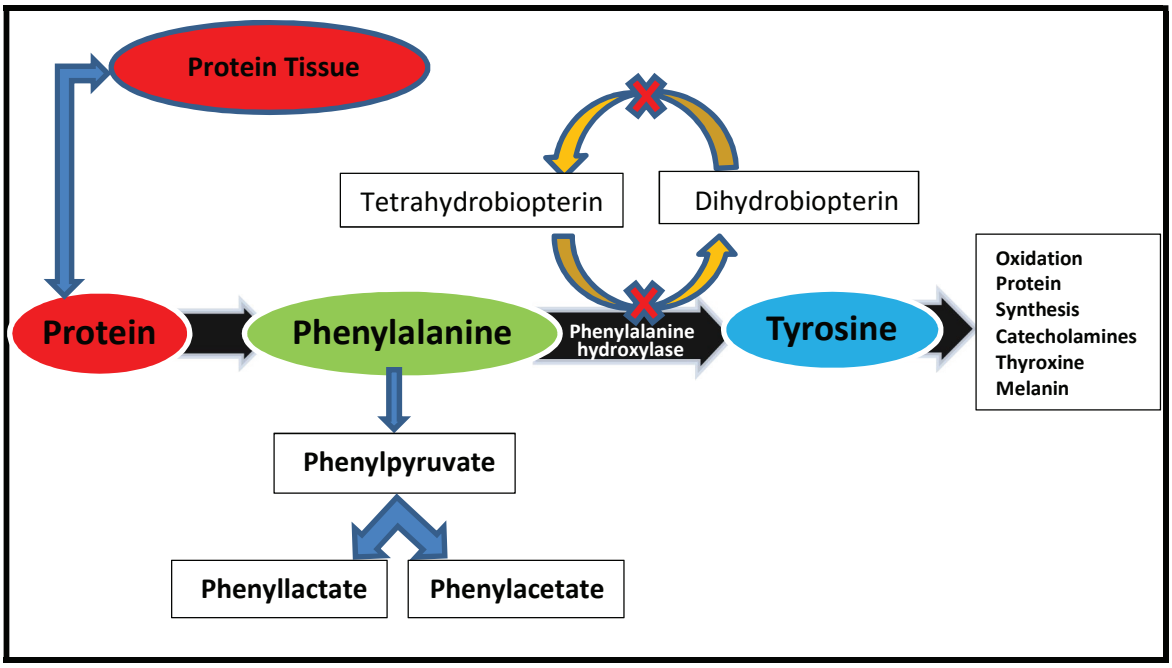

Figure 1. **Metabolism of phenylalanine in phenylketonuria patients**
Рисунок 1. **Метаболизм фенилаланина у пациентов с фенилкетонурией**

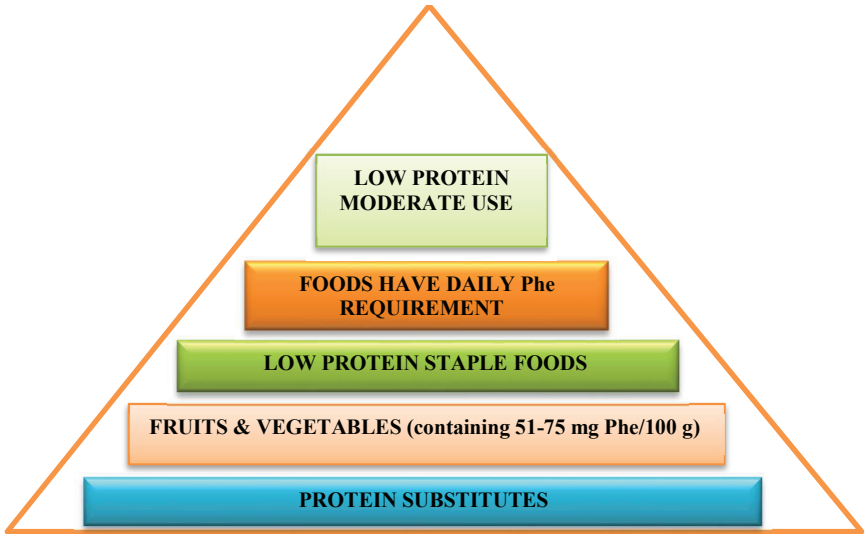

Figure 2. **Food hierarchy for PKU patients**
Рисунок 2. **Иерархия пищевых продуктов у пациентов с фенилкетонурией**

Many researchers have designed a lot of low phenylalanine diets by selecting different ingredients low in protein, i. e. gums, starch, cellulose derivatives. Ozboy [21] used corn starch, emulsifier, xanthan and carrageenan for preparing low phenylalanine corn starch-gum bread for PKU persons. On the other hand, these diets may be of low sensory quality, expensive, deficient in some important nutrients and have short shelf life [22]. Based on the above-mentioned considerations, this article briefly reviews the nutritional contents of PKU diets from either cereal or dairy based foods, and procedures and techniques used for creating low Phe diets.

2. Low phenylalanine cereal based products preparation

Gluten accounts for 85% of wheat proteins and is composed of gliadin and glutenin fractions. Gliadin fraction is rich in phenylalanine. The separation of gliadin from wheat flour leads to reduction of the Phe content by 43.2% in the final product compared to the control [23]. Gliadin was separated (de-gliadin) using propanol to reduce the phenylalanine content in bread and pasta [11]. Table 1 summarizes formulas of low phenylalanine cereal based products such as pan bread, toast bread, Egyptian shamy bread, pasta and low Phe rice.

Table 1. **Formulas of low phenylalanine cereal based products**
Таблица 1. **Рецептуры продуктов на основе зерновых с низким содержанием фенилаланина**

Ingredients	Food products	References
Wheat flour (72%), corn starch, pectin, carboxymethyl cellulose (CMC), yeast, NaCl and water	Pan bread	[24]
Wheat flour (72%), corn starch, pectin, CMC and water	Pasta	[25]
Low protein flour (1st break wheat flour), corn starch, pectin, CMC, yeast, NaCl and water	Egyptian shamy bread	[18]
Gliadin-free wheat flour, pectin, Arabic gum or CMC, yeast, NaCl and water	Toast bread	[23]
De-gliadin wheat flour, pectin, CMC, Arabic gum and water	Pasta	[11]
Rice	Low Phe rice	[26]

3. Low phenylalanine dairy based products preparation

Also, many researchers have prepared low phenylalanine dairy products for PKU people as shown in Table 2. Silva et al. [16] employed an immobilization technique using papain and pancreatin enzymes on activated carbon and alumina to produce low Phe whey for PKU patients. Hassanpour et al. [27] produced low Phe milk formula that imitates human milk for phenylketonuria infants. The produced milk formula contained suitable amounts of essential amino acids and vitamins.

Table 2. **Low phenylalanine dairy products**

Таблица 2. **Молочные продукты с низким содержанием фенилаланина**

Ingredients	Dairy products	References
Whey hydrolysate	Low Phe whey	[16, 28]
Whey protein glycomacropeptide (GMP)	Low Phe whey	[12, 29]
Milk formula	Low Phe milk	[27]
Skim milk hydrolysate	Low Phe skim milk	[30]

4. Procedures and techniques used for creating low phenylalanine diets and foods

Several techniques and procedures were used by many researchers to create different types of PKU diets. Most of the procedures employed to remove Phe from protein hydrolysate are based on the liberation of the amino acid via enzymatic hydrolysis. Liberated Phe is then removed using activated carbon or resin (adsorption) or by gel filtration. The procedures and techniques are presented in Table 3.

5. Regulations

The incidence of PKU varies across the world and PKU management differs widely from country to country. In addition, the nutritional status of patients is different depending on the severity of PKU and treatment type [13,32]. The same authors suggested that European guidelines based on the Appraisal of Guidelines for Research and Evaluation (AGREE) and Scottish Intercollegiate Guidelines Network (SIGN) procedures must be used as PKU management in all European Union countries. In the USA, the US FDA [33] is involved in the regulation of aspartame (composed of phenylalanine and aspartic acid). Aspartame is used as a sweet tasting substance, which is 180 times as sweet as sucrose. The package labeling and other labeling must contain precautions statement for phenylketonurics: Contains Phenylalanine.

6. Conclusion

The above findings may be useful for nutritionists, dietitians and physicians in knowing, preparing, designing and nutrition management of patients with phenylketonuria. This review offers various food choices for persons with phenylketonuria and several procedures and techniques for creating diets low in Phe. In the coming decade, efforts and studies must be continued to find more food choices and procedures to prepare foods for phenylketonurics.

Table 3. **Procedures and techniques used for creating low phenylalanine diets and foods**

Таблица 3. **Процедуры и методы, используемые для создания рационов и пищевых продуктов с низким содержанием фенилаланина**

Food or food ingredients	Procedure	References
De-gliadin wheat flour	Extraction of gliadin using 55% (v/v) 1-propanol at room temperature	[23]
Low protein flour	1st break flour using flour mills	[25]
Low Phe whey hydrolysate	Enzymatic hydrolysis and resin adsorbent	[28]
Low Phe whey hydrolysate	Enzyme immobilization technology and activated carbon	[16]
Low Phe whey protein	Whey protein glycomacropeptide (GMP)	[12]
Low Phe milk	Formulation (human milk analogue)	[27]
Low Phe beans	A protease and activated carbon as Phe adsorbent	[31]
Low Phe rice	Papain and activated carbon	[26]
Low Phe skim milk	Papain and pepsin, and activated carbon	[30]

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The author has the sole responsibility for writing the manuscript and is responsible for plagiarism.	Автор имеет единоличное отношение к написанию рукописи и несет ответственность за плагиат
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