Journal

J. Biol. Chem. Environ. Sci., 2018, Vol. 13(3): 197-204
http://biochemv.sci.eg

PREPARATION LOW PHENYLALANINE ACID FOODS FOR PHENYLKETONURIA PATIENTS (ARTICLE REVIEW)

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ABSTRACT

Functional foods are those foods that have a positive effect on human health, especially those suffering from certain diseases. Phenylketonuria (PKU) is one of the most widespread dysfunctions caused by an inheritable problem in the phenylalanine (Phe) metabolism.In this metabolic disease, gene mutations in phenylalanine hydroxylase (PAH) result in phenylalanine accumulation that causes varying degrees of mental retardation. According, these patients should early and regular treatment of this disease and should avoid eating all foods high content from Phe or foods which contain the industrial sweetener named aspartame because it is composed of phenylalanine and aspartic acids. This article focus spotlight on the studies conducted on the preparation foods low in their content of Phe for PKU patients .

Key words : Low phenylalanine Foods ,Phenylketonuria, Treatment.

INTRODUCTION

Protein is one of the main constituents of food protein is composed of a series of amino acids. Phenylalanine (Phe) is one of the amino acids that is needed to build protein. Because the body can not form this amino acid, it must be obtained from food. Phenylalanine ($C_9H_{11}NO_2$) classified as mono-amino-mono carboxylic neutral, aromatic and essential amino acids. In healthy people the excess normal level of phe convertes to tyrosine by phenylalanine hydroxylase. When the body is unable to produce sufficient enough

from phenylalanine hydroxglase (PAH). Phe accumulates in blood causing ketonuroia disease **(Nelson and Cox.,2000)** . Phenylalanine is an amino acid which its presence is necessary for the synthesis of protein and neurotransmitters; thus, the diet of people suffering from PKU should contain small and controlled amounts of phenylalanine to have normal development **(Van Calcar and Ney, 2012)**. Minimal requirements of phynylalanine (9.1 mg/kg/d) are needed to meet the normal growth and development. Excess phenylalanine (not required for protein anabolism) is mainly metabolized in the liver by PAH. In the United Kingdom, a system of protein exchanges is used, with approximately each 1g natural protein representing a phenylalanine load of 50 mg . Most children with PKU can tolerate less than 500 mg phenylalanine or 10 g protein exchanges in 24 hrs **(Hendriksz and Walter, 2004 and Pencharz *et al.*, 2007*)***.The aim of this work was focus spotlight on the studies conducted on the preparation foods low in their content of Phe for PKU patients .

Definition of phenylketonuria (PKU) :

The genetic disorder phenylketonuria (PKU) is the inability to metabolize phenylalanine because of a lack of the enzyme phenylalanine hydroxylase. Individuals with this disorder are known as "phenylketonurics" and must regulate their intake of phenylalanine. A (rare) "variant form" of phenylketonuria called hyperphenylalaninemia is caused by the inability to synthesize a cofactor called tetrahydrobiopterin, which can be supplemented. Pregnant women with hyperphenylalaninemia may show similar symptoms of the disorder (high levels of phenylalanine in blood) but these indicators will usually disappear at the end of gestation. Pregnant women with PKU must control their blood phenylalanine levels even if the fetus is heterozygous for the defective gene because the fetus could be adversely affected due to hepatic immaturity. Individuals who cannot metabolize phenylalanine must monitor their intake of protein to control the build up of phenylalanine as their bodies convert protein into its component amino acids **(Williams,2008)** .

The obtimal time to analyze the a blood phenylalanine (Phe) sample :

(waisbren *et al* ., 2007)

Prefere the sample taken at morning and fastin as follow :

- (< 5 years / weekly) .
- (5 – 10 years / 2 or 3 / weeks) .
- (> 11 years / monthly) .

The levels of blood phenylalanine (phe) :

(waisbren *et al* ., 2007)

- If the blood phe level from 120 to 599 µmol / L is normal .
- If the blood phe level from 600 to 1200 µmol / L is moderate .
- If the blood phe level from > 1200 µmol / L is severe .

The medical treatment of phenylketonuria (pku) :

The maturation of new born screening programs along with the prompt institution of a low-Phe diet successfully prevents intellectual disability in early treated PKU patients. Dietary compliance remains to be the main issue as patients approach adolescence and adulthood resulting in poor blood the level control and leading to suboptimal outcomes in psychosocial and cognitive assessments. Tetrahydrobiopetrin (BH_4) therapy has been successful, however only a minor proportion of PKU patients benefit from this treatment. Contrasting data has been generated from studies using large neutral amino acid (LNAA) as an alternative to dietary therapy and it has been only recommended for adult PKU patients who do not adhere to the diet. The incorporation of glycomacropeptides (GMP) into low-Phe diet has improved palatability, variety and convenience of the diet and has resulted in a better control of blood Phe levels providing a more physiological form of amino acid to be consumed by PKU patients. Although studies using GMP as an alternative to the amino acid supplement has been promising, long-term studies are needed to evaluate the safety and efficacy. Studies using gene therapy have been progressing and are still ongoing and the use of the alternative enzyme, phenylalanine ammonia-lyase (PAL) (PEGylated form) as an enzyme substitution therapy has reached phase III clinical trials, however the efficiency of the PAL reduced over time and immune reaction were elicited in some patients. The use of probiotics to

produce and deliver the PAL enzyme has gained more attention and studies are ongoing regarding the safety and efficacy of this approach **(Naz and John, 2015)**.

Nutritional requirements for phenylketonuria (PKU) treatment :

Nutritional requirements for PKU treatment may be supplied in 1 of 3 ways: (1) consumption of food based on its protein and phenylalanine content such that less than 10 g intact protein is provided on a daily basis; (2) free intake of foods naturally very low in protein; and (3) production of foods with proteins or peptides that either lack of phenylalanine or contain all L-AAs except phenylalanine, trace minerals, and vitamins **(MacDonald *et al*., 2011a).**

Important warnings :

Some foods contain artificial sweetener aspartame. This sweetener composed of phe and aspartic acid. Under the trade named Nutrasweet (E951) or (condril). Accordingly, all products contain aspartame must be labeled with warning to aid individuals who have been diagnosed with PKU, so that they can be avoid such foods. As well as avoiding the drugs and treatments which PKU Patients having it and may be contain Phe **(Filer and Steginк,1988)**.

The challenges which face production of low phenylalanine (Phe) foods :

Elimination of phe from food presents major technological sensory evaluation (texture, color, shelf – life and taste), nutritional value (lack of protein, mineral and vitamins) costs of production of PKU foods are big challenge encountrered in order to production these foods. These challenges could be taken into account considered **(Giovannini *et al.*,2007)**

Food planning :

Functional or dietetic foods prepared to meet the particular nutritional needs of people whose assimilation and metabolism of foods are modified or for whom a particular effect is obtained by a controlled intake of foods or individual nutrients. They may be formulated for people suffering from physiological disorders or for healthy people with additional needs **(Patel,2015)**.

Nutritional therapy :

Nowadays, dietitian exert great efforts for prepare foods named functional foods for people who suffer from certain dieases such as diabetes, anemia, osteoporosis, cardiovascular and PKU side by side with/or alternative treatment and drug **(Smith, 1994; and Lara *et al.*, *2005)***Therefore the Preparation low phenylalanine foods for Phenylketonuria patients have been reviewed as shown in **Table (1)** .

Table (1) Preparation low phenylalanine acid foods for Phenylketonuria patients

Food	Method	Phe removal	Reference
Fish protein concentrate (FPC)	Using pepsin and pronase enzymes with the Sephadex G-15 as adsorbent activity for (FPC) and (SPI)	99.95 % (FPC)	**Yamashita *et al.*, (1976)**
Soybean protein isolate (SPI)		99.77 % (SPI)	
Rice protein	Using corolase PP enzyme with activated carbon (AC) as adsorbent support	0.39-68.34 mg/100g^{-1}	**Bizzotto *et al.*, (2006)**
Whey protein	Using pancreatin enzyme with activated carbon (AC) as adsorbent support	75% to 99% (2.3 – 38.2 mg Phe/100g)	**Fernanda *et al.*, (2006)**
Corn flour	Using pancreatin enzyme with activated carbon (AC) as adsorbent support	97.55% (149.27mg/100g)	**Capobiango *et al.*, (2007)**
Rice grain	Using pancreatin enzyme with activated carbon (AC) as adsorbent support	72 to 100% (0.28-95 mg/100g)	**Lopes *et al.*, (2008)**
Wheat flour	Using alkaline protease enzyme from *Bacillus licheniformis* , pancreatin enzyme, and crude enzymatic extract from pineapple peel with activated carbon (AC) as adsorbent support	66.28% (522.44 mg/100g/ k^{-1})	**Carreira *et al.*, (2009)**
Beans	Using protease enzyme from papay carica with activated carbon (AC) as adsorbent support	25.4 to 87.9% (433.7 – 2679.8 mg phe/ 100g^{-1})	**Marialice *et al.*,(2011)**
Milk	Using proteas enzyme from *Bacillus subtilis* with (AC) as adsorbent support	16.28 - 58.26%	**Marialice *et al.*, (2012)**
Lentil flour (LF)	Using pepsin enzyme from porcine gastric mucosa , proteas enzyme from *Aspergillus oryzae* and proteas enzyme type XIV from *Streptomyces griseus* followed by filtration through activated charcoal column for (LF) and (AF)	1.5 – 45 mg Phe / dL (LF)	**Elevina *et al* ., (2013)**
Amaranth flour (AF)		5 – 45 mg Phe / dL (AF)	

It can be concluded from this review that the food system is the cornerstone or backbone for treating PKU patients. So, parents should apply nutritional and medical guide lines to their children. With early diagnosis (via blood analysis), early treatment and regular treatment.

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إعداد أغذية منخفضة المحتوى من حمض الفينيل ألانين لمرضى الفينيل كيتونوريا

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الأغذية الوظيفية هى تلك الأغذية التى لها تأثير إيجابى على صحة الإنسان وخاصة الذين يعانون من أمراض معينة ومن هؤلاء مرضى الفينيل كيتونوريا وهو مرض ناتج عن نقص إنزيم الفينيل ألانين هيدروكسيليز فى الأطفال بسبب خلل وراثى فى الجين المسؤول عنه وهذا الإنزيم مسؤول عن التمثيل الغذائى لحمض الفينيل ألانين ونقص الإنزيم يؤدى إلى ارتفاع مستوى الحمض فى الدم ويؤدى التأخير فى تشخيص وعلاج هذا المرض إلى التخلف العقلى الدائم وبناءً على ذلك يجب على هؤلاء المرضى العلاج المبكر والمنتظم لهذا المرض وتجنب تناول كل الأغذية ذات المحتوى العالى من ذلك الحمض أو التى تحتوى على المحلى الاصطناعى الأسبرتام لأنه يتكون من حمضى الفينيل ألانين والأسبارتيك، وهذه المقالة تركز بؤرة الضوء على الدراسات التى تمت على إعداد أغذية منخفضة فى محتواها من حمض الفينيل ألانين لمرضى الفينيل كيتونوريا.