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Redefining the PKU Diet: Novel Functional Foods with Low Phenylalanine and High Nutritional Value

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Abstract

Phenylketonuria (PKU) is an inherited metabolic disorder that is defined as the deficiency of phenylalanine hydroxylase, which requires lifelong dietary management to avoid neurotoxicity and metabolic imbalances. PKU diet is semi-synthetic with managed consumption of natural low-protein foods, and phenylalanine-free protein replacement options and specialized dietetic products.

The aim of this study is to identify potential new sources of low-phenylalanine (low-Phe) products, that are rich in copper, providing an optimized and sustainable PKU diet and supply all the essential nutrients. The nutritional analysis of selected foods showed optimal amino acid content and a high content of essential micronutrients such as copper, folate, C, E, and K. Expanding the range of low - phenylalanine foods through reliable data on amino-acids composition will improve the accuracy of dietary calculations and allow more flexible and culturally sensitive dietary intervention. Further, chronic deficiencies in calcium, iron, zinc, and vitamin B12 require tailoring supplementation.

Keywords: phenylketonuria (PKU); functional nutrition; optimization; innovation; metabolic disorders

1. Introduction

The study aims to answer one main question: what plant-based food products could correct or prevent copper and cobalamin deficit in individuals suffering from phenylketonuria (PKU)?

Phenylketonuria is an inherited rare metabolic disorder resulting from the mutation in the phenylalanine hydroxylase gene. Amino acid metabolism is disrupted as a result of these genetic defects impairing the enzymatic conversion of phenylalanine (Phe) into tyrosine (Tyr). As a consequence, excess phenylalanine builds up in the blood and tissues, particularly the brain, in which it has neurotoxic effects [1]. These are associated with both the toxic accumulation
of phenylalanine as well as a lack of tyrosine, which decreases the synthesis of crucial neurotransmitters such as dopamine and noradrenaline [1,2]. PKU treatment's main focus is to balance phenylalanine and tyrosine levels between safe limit and optimal protein for growth and development. The cornerstone of care remains lifelong low-protein diet with phenylalanine-free amino acids. These synthetic mixtures also provide essential amino acids, such as tyrosine, needed vitamins and minerals. A targeted low-Phe diet is personalized, mixing specific amounts of natural products with specially-developed low-protein ingredients, and Phe-free protein substitutes that are essential for the nutrition needs while maintaining metabolic stability [3, 4].

Phenylalanine (Phe) is an essential amino acid

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that occurs naturally in dietary proteins of plant and animal origin. Phenylalanine content in foods can be estimated using nutrition labels because one gram of natural protein typically contains around 50 mg Phe. In individuals with classical PKU, daily tolerance typically ranges between 220 and 240 mg of Phe, equivalent to an intake of approximately 4–5 grams of natural protein per day [1].

Although current recommendations suggest that tyrosine should account for 80% of total aromatic amino acids, this proportion may exceed actual requirements. A more appropriate level, similar to that of healthy individuals, is estimated at around 45%. In children with classical PKU, mean tyrosine needs were determined to be 19.2 $mg \cdot kg^{-1} \cdot day^{-1}$ using the $F^{13}CO_2$ technique and 16.3 $mg \cdot kg^{-1} \cdot day^{-1}$ based on oxidation response data [5].

To explore alternative therapeutic strategies for adults with phenylketonuria (PKU) and improve adherence to dietary treatment, Burlina AP et al. (2019) [6] conducted a study on 12 patients (5 females and 7 males), aged 19–38 years, all exhibiting suboptimal phenylalanine control. The intervention evaluated the effects of a new slow-release large neutral amino acid (LNAA) formulation on blood phenylalanine and tyrosine levels, the latter commonly reduced in PKU.

After a period of 12 months in which patients followed a low phenylalanine diet supplemented by large neutral amino acids (LNAA), stable plasma phenylalanine levels and a substantial increase in tyrosine levels were observed, resulting in improved metabolic balance The LNAA preparation provided ~80% of total daily protein needs, including protein-required amino acids such as arginine, aspartate, and tyrosine, was delivered with sodium alginate as a carrier.

The nutritional quality of LNAA was noted for high protein (around 70.8 g/100 g) and insignificant phenylalanine content, therefore supporting protein synthesis without an increase in blood Phe. These findings suggest that long-term LNAA supplementation contributes to better metabolic outcomes in adults with PKU while maintaining phenylalanine control [7].

Strict adherence to dietary recommendations plays a central role in ensuring adequate intake of essential nutrients, trace elements, and micronutrients, which are vital for optimal development and for reducing long-term complications, and consists of a carefully controlled selection of foods that limit phenylalanine intake while ensuring adequate nutrition [8].

Among naturally occurring low-protein options, certain *starches* — including cassava flour, arrowroot, sago, tapioca, and corn starch — contain a phenylalanine content of 25mg/100g, and can therefore be consumed freely on a low-phenylalanine diet [9, 10].

Common *foods that are naturally very low in protein* — such as vegan cheese made from oils and starch (phenylalanine ≤25 mg/100 g), butter, margarine, vegetable oils, sugar, jam, honey, and sweets meeting the same phenylalanine criteria — may also be freely incorporated into the diet. Assortments of specifically manufactured starch-based *low-protein foods* (e.g., bread, flour, pasta, and biscuits) are commercially existing, though access to these products differs among European countries [9, 10].

Additionally, *herbs, spices, and flavoring agents* can be used without restriction, as the quantities typically used in cooking contribute negligible amounts of phenylalanine. Acceptable *beverages* include water, fruit juices, lemonade, cola, squash, black or green tea, coffee, tonic water, and soda water, provided they are aspartame-free. Finally, *low-protein milk substitutes* that contribute ≤25 mg of phenylalanine over 24 hours may be used without restriction, while those exceeding this threshold should be measured and included within the total daily phenylalanine allowance [9, 10].

Fruits and vegetables are an essential part of the PKU diet as they have relatively low protein content, 1–1.5% in fruits, and 3–8% in vegetables [11]. The majority contain 20–40 mg phenylalanine per gram of protein, or <75 mg phenylalanine per 100 g, so they can be consumed flexibly. However, some varieties - such as spinach, peas, kale, and sweetcorn - have a higher amount of phenylalanine, which needs moderation of portions [10] [12]. Including them provides dietary diversity and increases the presence of essential vitamins, minerals, fiber, and phytochemicals. These bioactive substances also promote a favorable gut microbiota and are correlated with less risk of cardiovascular diseases, cancer, and cognitive dysfunction [1].

Despite the immense achievements in nutritional treatment, malnutrition and obesity are persistent problems for children and adults with PKU [13]. The Phe-restricted diet commonly results in increased carbohydrate intake [14], along with a build-up of visceral fat, which increase cardiovascular risk and type 2 diabetes [15]. As a result, dietary management should adhere to balancing elements of metabolic safety with global nutritional adequacy whilst also adapting to cultural and individual differences [16].

Vitamin B12 status represents a key indicator of nutritional adequacy in children with phenylketonuria (PKU). Studies have stated a high prevalence of vitamin B12 deficiency with adult PKU patients who adhered to less restrictive protein diets. Most folate concentrations were normal, although a small proportion showed mild biochemical characteristics of vitamin B12 deficiency, indicative of deficiencies following lower vitamin B12 and B6 intake. An association between reduced vitamin B12 intakes and reduced serum cobalamin concentrations was found, supporting the idea that nutritional intake and supplementation needs to be monitored as well to avoid such deficiencies [2].

Patients with phenylketonuria (PKU) often exhibit increased insulin resistance as they possess a higher HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) index than healthy controls. This change in glucose homeostasis can most likely be ascribed to the long-term maintenance of carbohydrate-rich diets currently recommended in the treatment of PKU, especially in the context of an intake of calories exceeding energy requirements [17].

Furthermore, serum triglycerides and a greater atherogenic lipoprotein profile in PKU adults has also been reported elsewhere, which may suggest synergy with lipid metabolism combined with the level and intake of carbohydrates [18]. However, overall lipid intake by this group is considered within the RDA.

In addition, elevated phenylalanine level was associated with changes in cholesterol synthesis. This effect is thought to occur via an important mechanism of altered regulation of 3-hydroxy-3-methylglutaryl-CoA reductase as well as inhibition of mevalonate 5-pyrophosphate decarboxylase. Furthermore, increased utilization of acetyl-CoA in phenylacetylglutamine biosynthesis might further explain the hypocholesterolemia frequently observed in patients with PKU [19].

Glycomacropeptide (GMP) is a natural protein derived from cheese whey that holds particular value in the dietary management of pheny-lketonuria (PKU), as it is the only known natural dietary protein that contains only trace levels of Phe, tyrosine (Tyr), and tryptophan [20].

Moreover, GMP is naturally rich in several non-toxic large neutral amino acids (LNAA), such as isoleucine, threonine, and valine. In order for GMP to serve as a complete protein source for PKU patients, supplementation with five limiting amino acids: arginine, histidine, leucine, tryptophan, and tyrosine, is needed. Experimental studies from the PKU mouse model confirmed that GMP enriched with these amino acids can maintain normal growth and improve metabolic function by greatly reducing phenylalanine concentrations in plasma and brain, compared with a conventional amino acid-based diet. In contrast to synthetic AA mixtures, GMP has functional properties - namely, good thermal stability and solubility at low pH - ideal for PKU-suitable food development [21].

GMP-based food could serve a few significant health purposes. It would first and foremost facilitate a dietary switch from a high-carbohydrate, high-calorie diet to one rich in protein and lower in calories, thus helping to prevent obesity and type 2 diabetes. Secondly, GMP has enriched branched-chain amino acids (BCAAs) and essential amino acids (EAAs) compared with a theoretical average protein, which also provides a much higher nutritional value [22]. Third, GMP exhibits many bioactive profiles, the most noteworthy ones being antimicrobial and antiviral action, endotoxin neutralization, stimulation of Bifidobacterium growth, and immune-homeostatic modulation [23].

This method marks a transition away from completely synthetic amino acid products to a more physiologically balanced natural dietary approach in the management of PKU [21].

2. Materials and method

The current study has been conducted using a detailed literature review, including a critical review of over 100 peer-reviewed scientific

publications, technical databases and internet-based information in food chemistry, nutrition, horticulture and metabolic medicine. The aim was to identify plant-based foods that were naturally low in Phe content (<75 mg/100 g), which could potentially provide additional nutritional value for individuals with PKU.

Table 1. Nutritional value, Phenylalanine and Copper content of plant – based foods for PKU, based on database and literature data for 100 g F.W

Food	**Avocado (raw)**	**Pomegranate (raw)**	**Ginger (raw root)**	**Asparagus (raw)**
Phenylalanine (mg)	45 [12]	21 [12]	46 [31]	75 [32]
Energy (kcal)	223 [24]	83 [30]	80 [31]	28 [32]
Carbohydrates (g)	8.32 [24]	18.7 [30]	17.8 [31]	5.1 [32]
Protein (g)	1.81 [24]	1.67 [30]	1.82 [31]	1.44 [32]
Fat (g)	20.3 [24]	1.17 [30]	0.75 [31]	0.22 [32]
Copper (mg)	0.285 [24]	0.158 [30]	0.23 [31]	0.189 [32]
Potassium (mg)	567 [24]	236 [30]	415 [31]	202 [32]
Magnesium (mg)	32.8 [24]	12 [30]	43 [31]	14[32]
Vitamin B5 (mg)	1.4 [25]	0.377 [30]	0.203 [31]	0.274 [32]
Vit. E (mg)	2.1 [25]	0.6 [30]	0.26 [31]	1.13 [32]
Folate (µg)	129 [24]	38 [30]	11 [31]	182 [32]
Fiber (g)	6.8 [26]	4 [30]	2 [31]	2.1 [32]
Vit. C (mg)	<4 [24]	10.2 [30]	5 [31]	45.5 [32]
Vit. K (µg)	15.7–27.0 [27]	16.4 [30]	0.1 [31]	41.6 [33]
Vit. B6 (mg)	0.167 [24]	0.075 [30]	0.16 [31]	0.091 [32]
Iron (mg)	0.40 - 0.60 [28]	0.3 [30]	0.6 [31]	0.44 [32]
Calcium (mg)	9 - 9.8 [28]	10 [30]	16 [31]	24 [32]
Beta-caroten (mg)	0.063 [29]	0 [30]	0 [31]	0.449 [32]
Food	**Beet greens (raw)**	**Black Olives (canned)**	**Physalis (raw)**	**Green kiwi (raw)**
Phenylalanine (mg)	58 [34]	0 [35]	39.1 [36]	44 [12]
Energy (kcal)	22 [34]	116 [35]	53 [37]	65 [44]
Carbohydrates (g)	4.33 [34]	6.04 [35]	11.2 [37]	13.8 [44]
Protein (g)	2.2 [34]	0.84 [35]	1.9 [37]	1.01 [44]
Fat (g)	0.13 [34]	10.9 [35]	0.7 [37]	0.64 [44]
Copper (mg)	0.191 [34]	0.251 [35]	0.28 [38]	0.128 [44]
Potassium (mg)	762 [34]	8 [35]	253 [39]	302 [44]
Magnesium (mg)	70 [34]	4 [35]	20 [39]	14.8 [44]
Vitamin B5 (mg)	0.25 [34]	0 [35]	0.286 [40]	0.183 [45]
Vit. E (mg)	1.5 [34]	1.65 [35]	2.34 [39]	1.46 [45]
Folate (µg)	15 [34]	0 [35]	0 [37]	33 [44]
Fiber (g)	3.7 [34]	1.6 [35]	5.16 [39]	2.1 [44]
Vit. C (mg)	30 [34]	0.9 [35]	11 [37]	58.8 [44]
Vit. K (µg)	400 [34]	1.4 [35]	20 [41]	30.3 [45]
Vit. B6 (mg)	0.106 [34]	0.009 [35]	4.59 [42]	0.063 [45]
Iron (mg)	2.57 [34]	6.28 [35]	1 [37]	0.04 [44]
Calcium (mg)	117 [34]	88 [35]	9 [37]	24 [44]
Beta-caroten (mg)	3.79 [34]	0.198 [35]	1.12-1.73 [43]	0.052 [45]

Articles were selected according to amino acid profiling importance and micronutrient composition. Significant attention has been paid to foods rich in essential vitamins such as vitamin C, E, K, folic acid, minerals such as copper, iron, zinc, potassium and bioactive compounds with antioxidant activity and metabolic benefits. Data were analyzed from a variety of sources (e.g., USDA FoodData Central, PubMed, and leading nutrition journals) to standardize and confirm the quality of the study. In order to address the main research question, a comprehensive table was developed using data extracted from the reviewed scientific literature and relevant nutrition databases. The graphical fingerprint of data was created using MVSP program, version 3.22.

3. Results and discussion

The estimated phenylalanine requirement for healthy adults is approximately 38 mg/ kg/day, with the condition of no tyrosine intake [46]. In patients with classical PKU, however, tolerance is often between 220-240 mg/day, and around 4-5 g/day of natural protein is typically consumed [1].

The diet-related study on the plant-based food compositions for phenylalanine (Phe) indicated significant differences in concentrations, macronutrient distribution and compositions of micronutrients among the studied plants, and confirmed their value in the therapeutic diet of phenylketonuria (PKU).

Figure 1 helps to identify the main foods able to contribute with higher contend of copper and/or other nutritional components in order to answer the main question regarding the deficit of copper and cobalamin in individuals suffering from phenylketonuria (PKU). Based on this data fingerprint we can advise the use of diets based on avocado, pomegranate, physalis and green kiwi added to any quantity of black olives for low Phe, while avocado, black olives and physalis are also able to supply the required quantities of copper.

Phenylalanine content was found to be ~ 0 mg/100 g in canned black olives and 75 mg/100 g in raw asparagus. Among these, the minimum levels of Phe were found in black olives (0 mg/100 g) and pomegranate (21 mg/100 g), whilst, raw asparagus (75 mg/100 g) and beet greens (58 mg/100 g) were observed to have the highest Phe values. Phe content ≤ 75 mg per 100 g was present in all samples as determined from a guideline for the unrestricted (or moderate) amounts of Phe in PKU diets.

Energy values varied widely from 22 kcal/100 g in beet greens to 223 kcal/100 g in avocado: indicative of different fat and carbohydrate content. Avocado (20.3 g/100 g) shows the highest caloric value, while leafy vegetables, like beet greens and asparagus were showing the least measured energy-rich foods.

There were moderately low macronutrient-based protein levels overall: canned black olives provided ~0.84 g/100 g and beet greens were 2.20 g/100 g, signifying these foods are appropriate for use in low-phenylalanine meal planning. The carbohydrate composition distribution was even more varied on which pomegranate (18.7 g/100 g) and ginger root (17.8 g/100 g) were the two richest products, providing the majority of the energy consumption with the help of natural sugars. There was also an increased lipid content found in avocado and olives, with high mono-unsaturated fatty acids for cardiovascular health support [47].

In particular avocado was abundant in potassium (576 mg), magnesium (32.8 mg), vitamin B5 (1.4 mg), vitamin E (2.1 mg) and folate (129 µg), which are associated with electrolytes, antioxidants and nervous system homeostasis [48]. Pomegranate contained high quantities of vitamin K (16.4 µg), vitamin C (10.2 mg) and dietary fiber (4 g), which are important in vascular health and immunity [48].

The beneficial properties of ginger were potassium, magnesium (43 mg), vitamin B6 (0.16 mg), and vitamin C (5 mg) in terms of anti-inflammatory and antioxidant activity [49]. Asparagus contained iron (0.44 mg), vitamin K (45.5 µg), and folate (182 µg), which play crucial roles in the formation of red blood cells and cell division [48, 50].

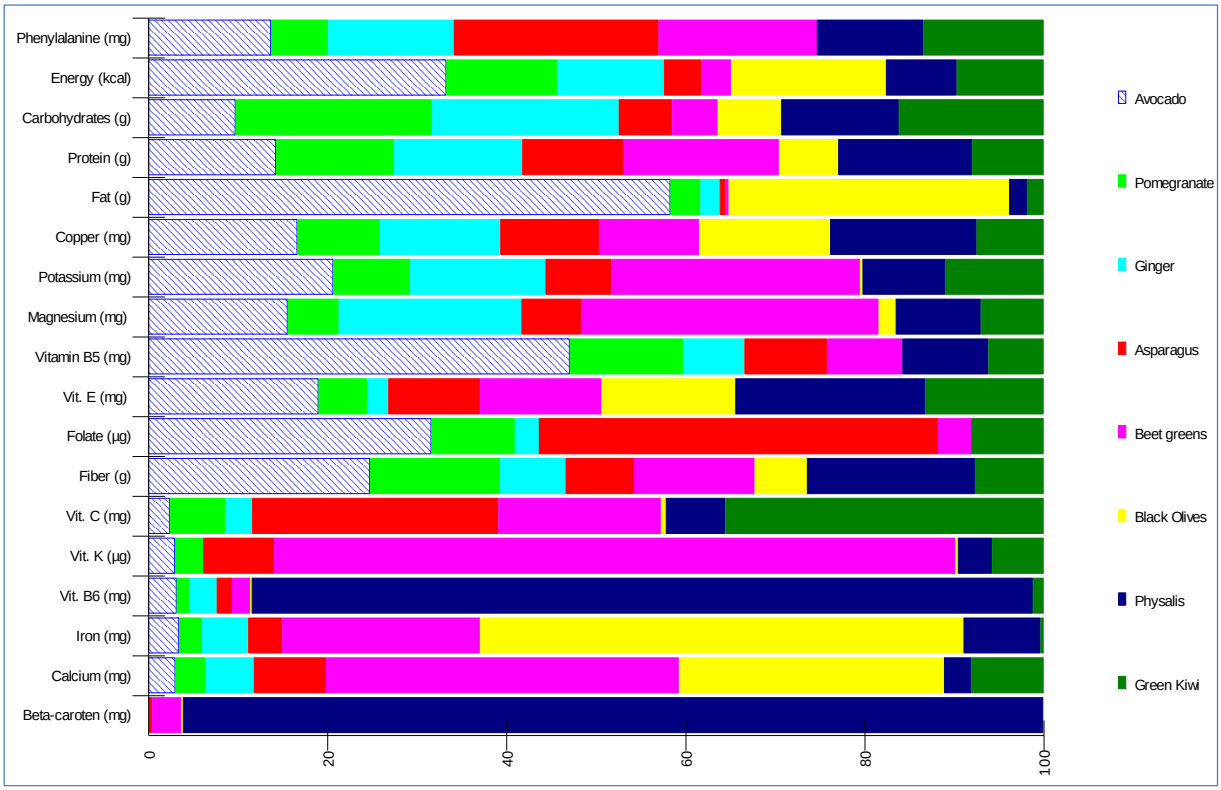

Figure 1. Graphical fingerprint of normalized standardized data

Overall, beet greens have the highest nutrient content, as they are rich in calcium (117 mg), magnesium (70 mg), potassium (762 mg) and fiber (3.7 g) which supports cardiovascular and digestive health [48, 51]. Black olives were rich in vitamin E (1.65 mg), iron (6.28 mg), and calcium (88 mg), proving a good antioxidant power and uptake of minerals [48].

Physalis possess high contents of vitamin C(11mg), beta-carotene (1.12–1.73 mg), and 34 different withanolide derivatives, exhibiting antioxidant and anti-inflammatory activities [52]. Green kiwi provided the highest content of vitamin C (58.8 mg) in the tested extracts, potassium (302 mg), fiber (2.1 g), and vitamin K (40.3 µg), further justifying the immune and metabolic benefits [48, 51].

Copper was identified as the most important micronutrient in this study, and the highest contents were reported for avocado and black olives. For a significant dietary source of copper with comparatively lower lipid content, physalis and ginger represent suitable plant-based options. This trace element is known to contribute in a number of enzymatic systems responsible for oxidative defense, iron metabolism, and neurological function [48]. As a result, its adequate intake is important for maintaining metabolic homeostasis, especially in phenylketonuria (PKU) patients.

Although copper and vitamin B12 act through separate metabolic pathways, both are essential for red blood cell formation and neurological function [53,54]. Maintaining appropriate copper intake can enhance enzymatic activity in response to nutritional imbalances that arise from decreased cobalamin concentration [48].

In addition, multiple of the evaluated foods, such as avocado, beet greens, asparagus, and physalis also contain essential micronutrients, including vitamins C and K, folate, magnesium, and fiber. Such substances can contribute to antioxidant defense, gut microbiota balance, vascular protection and also provide further nutrient supplementation to patients on a low-protein, phenylalanine-restricted diet.

4. Conclusions

This study highlights the potential of nutritional optimization and innovation to improve for the better management of phenylketonuria (PKU). The identification of low-phenylalanine plant-based foods (< 75 mg/100 g), such as black olives, avocado, beet greens, asparagus, pomegranate, physalis, and

green kiwi, expands safe natural options for individuals with PKU while providing essential micronutrients and bioactive compounds that support metabolic control and antioxidant defense. Based on the analysis, avocado and black olives could be considered the most valuable plant-based sources of copper, providing the highest concentrations among the analyzed foods. If a lower lipid intake is required, physalis and ginger represent useful alternatives with significant contents of copper. Due to their low phenylalanine content, these foods can be safely incorporated into the diet of individuals with phenylketonuria (PKU) without imposing additional dietary restrictions.

Based on multiple research studies (Table 1) by combining these foods with fortified medical substitutes can ensure both metabolic stability and nutritional adequacy, reducing common deficiencies and supporting gut and cardiovascular health. Accordingly, dietary innovation based on amino acid profiling fostering flexibility, cultural relevance and adherence to treatment will be more effective. Further studies on amino acid composition, bioavailability, and fortification should remain on board to maximize PKU dietary therapy.

Conflicts of interest / Competing interests: No conflict of interest

Ethics approval: No ethic situation.

Availability of data and material: The data have been reviewed depending on the literature.

References

1. Rondanelli M., Porta F, Gasparri C., Barrile G.C., Alessandro Cavioni, Francesca Mansueto, Giuseppe Mazzola, Zaira Patelli, Gabriella Peroni, Martina Pirola, Claudia Razza, Alice Tartara, Simone Perna, A food pyramid for adult patients with phenylketonuria and a systematic review on the current evidences regarding the optimal dietary treatment of adult patients with PKU, *Clinical Nutrition*, Volume 42, Issue 5, **2023**, Pages 732-763, ISSN 0261-5614, https://doi.org/10.1016/j.clnu.2023.03.007.
2. Anton-Păduraru, D.-T.; Trofin, F.; Chis, A.; Sur, L.M.; Streangă, V.; Mîndru, D.E.; Dorneanu, O.S.; Păduraru, D.; Nastase, E.V.; Vulturar, R. Current Insights into Nutritional Management of Phenylketonuria: An Update for Children and Adolescents. *Children* **2025**, 12, 199. https://doi.org/10.3390/children 12020199
3. Cazzorla C., Bensi G., Biasucci G., Leuzzi V., Manti F., Musumeci A., Papadia F., Stoppioni V., Tummolo A., Vendemiale M., Polo G., Burlina A., Living with phenylketonuria in adulthood: The PKU Attitude study, *Molecular Genetics and Metabolism Reports*, Volume 16, **2018**, 39-45, https://doi.org/10.1016/j.ymgmr.2018.06.007.
4. Rodrigues C, Pinto A, Faria A, Teixeira D, van Wegberg AMJ, Ahring K, Feillet F, Calhau C, MacDonald A, Moreira-Rosário A, et al. Is the Phenylalanine-Restricted Diet a Risk Factor for Overweight or Obesity in Patients with Phenylketonuria (PKU)? A Systematic Review and Meta-Analysis. *Nutrients*. **2021;** 13(10): 3443. https://doi.org/10.3390/nu13103443
5. Bross R., Ball R.O., Clarke J.T.R., Pencharz P.B., Tyrosine requirements in children with classical PKU determined by indicator amino acid oxidation. *American Journal of Physiology-Endocrinology and Metabolism* **2000,** 278:2, E195-E201 https://journals.physiology.org/doi/abs/10.1152/ajpendo.2000.278.2.E195
6. Burlina AP, Cazzorla C, Massa P, Polo G, Loro C, Gueraldi D, Burlina AB. Large Neutral Amino Acid Therapy Increases Tyrosine Levels in Adult Patients with Phenylketonuria: A Long-Term Study. *Nutrients.* **2019**; 11(10):2541. https://doi.org/10.3390/nu11102541
7. Burlina AP, Cazzorla C, Massa P, Loro C, Gueraldi D, Burlina AB. The Impact of a Slow-Release Large Neutral Amino Acids Supplement on Treatment Adherence in Adult Patients with Phenylketonuria. *Nutrients*. **2020**; 12(7):2078. https://doi.org/10.3390/nu12072078
8. Montoya Parra, G.A., Singh, R.H., Cetinyurek-Yavuz, A. et al. Status of nutrients important in brain function in phenylketonuria: a systematic review and meta-analysis. *Orphanet J Rare Dis* 13, 101 **2018**. https://doi.org/10.1186/s13023-018-0839-x
9. Evans S, Ford S, Adam S, Adams S, Ash J, Ashmore C, Caine G, Carruthers R, Cawtherley S, Chahal S, Clark A, Cochrane B, Daly A, Dines K, Dixon M, Dunlop C, Ellerton C, French M, Gaff L, Gingell C, Green D, Gribben J, Grimsley A, Hallam P, Hendroff U, Hill M, Hoban R, Howe S, Hunjan I, Kaalund K, Kelleher E, Khan F, Kitchen S, Lang K, Lowry S, Males J, Martin

G, McStravick N, Micciche A, Newby C, Nicol C, Pereira R, Robertson L, Ross K, Simpson E, Singleton K, Skeath R, Stafford J, Terry A, Thom R, Tooke A, vanWyk K, White F, White L, MacDonald A. Development of national consensus statements on food labelling interpretation and protein allocation in a low phenylalanine diet for PKU. *Orphanet J Rare Dis.* **2019** Jan 3;14(1):2. doi: 10.1186/s13023-018-0950-z.

10. MacDonald, A., van Wegberg, A.M.J., Ahring, K. et al. PKU dietary handbook to accompany PKU guidelines. *Orphanet J Rare Dis* 15, 171 (**2020**). https://doi.org/10.1186/s13023-020-01391-y
11. Ford S, Ilgaz F, Hawker S, Cochrane B, Hill M, Ellerton C, MacDonald A. Amino Acid Analyses of Plant Foods Used in the Dietary Management of Inherited Amino Acid Disorders. *Nutrients*. **2023**; 15(10):2387. https://doi.org/10.3390/nu15102387
12. Araújo ACMF, Araújo WMC, Marquez UML, Akutsu R, Nakano EY. Table of Phenylalanine Content of Foods: Comparative Analysis of Data Compiled in Food Composition Tables. *JIMD* Rep. **2017**; 34:87-96. doi: 10.1007/8904_2016_12. Epub 2016 Oct 8. PMID: 27718212; PMCID: PMC5509543.
13. Rocha JC, MacDonald A. Dietary intervention in the management of phenylketonuria: current perspectives. *Pediatric Health Med Ther*. **2016** Dec 1; 7:155-163. doi: 10.2147/ PHMT.S49329. PMID: 29388626; PMCID: PMC5683291.
14. Lubina O, Daly A, Auzenbaha M, Gailite L, Laktina S, Macdonald A. Nutritional profiling of foods for Phenylketonuria. *Sci Rep*. **2025** Jul 2;15(1):22538. doi: 10.1038/s41598-025-06633-2.
15. Weerd JCV, Wegberg AMJV, Boer TS, Engelke UFH, Coene KLM, Wevers RA, Bakker SJL, Blaauw P, Groen J, Spronsen FJV, Heiner-Fokkema MR. Impact of Phenylketonuria on the Serum Metabolome and Plasma Lipidome: A Study in Early-Treated Patients. *Metabolites*. **2024** Aug 30;14(9):479. doi: 10.3390/metabo14090479. PMID: 39330486; PMCID: PMC11434371.
16. Tankeu AT, Pavlidou DC, Superti-Furga A, Gariani K, Tran C. Overweight and obesity in adult patients with phenylketonuria: a systematic review. *Orphanet J Rare Dis*. **2023** Feb 22;18(1):37. doi: 10.1186/s13023-023-02636-2. PMID: 36814307; PMCID: PMC9945382.
17. Couce, M.L., Sánchez-Pintos, P., Vitoria, I. et al. Carbohydrate status in patients with phenylketonuria. *Orphanet J Rare Dis* 13, 103 **2018**. https://doi.org/10.1186/s13023-018-0847-x
18. Azabdaftari A, van der Giet M, Schuchardt M, Hennermann JB, Plöckinger U, Querfeld U. The cardiovascular phenotype of adult patients with phenylketonuria. *Orphanet J Rare Dis.* **2019** Sep 6;14(1):213. doi: 10.1186/s13023-019-1188-0. PMID: 31492166; PMCID: PMC6731621.
19. Mezzomo TR, Dias MRMG, Santos T, Pereira RM. Dietary intake in individuals with phenylketonuria: an integrative review. *Nutr Hosp.* **2024** Feb 15;41(1):212-223. English. doi: 10.20960/nh.04579. PMID: 37705455.
20. Pena MJ, Pinto A, Daly A, MacDonald A, Azevedo L, Rocha JC, Borges N. The Use of Glycomacropeptide in Patients with Phenylketonuria: A Systematic Review and Meta-Analysis. *Nutrients*. **2018**; 10(11):1794. https://doi.org/10.3390/nu10111794
21. Macleod EL, Ney DM. Nutritional Management of Phenylketonuria. *Ann Nestle Eng.* **2010** Jun;68(2):58-69. doi: 10.1159/000312813. PMID: 22475869; PMCID: PMC2901905.
22. Etzel M.R., Manufacture and Use of Dairy Protein Fractions, *The Journal of Nutrition*, Volume 134, Issue 4, **2004**, Pages 996S-1002S, ISSN 0022-3166, https://doi.org/10.1093/jn/134.4.996S.
23. Brody EP. Biological activities of bovine glycomacropeptide. *British Journal of Nutritio*n. **2000**; 84(S1):39-46. doi:10.1017/S0007114500002233
24. https://fdc.nal.usda.gov/food-details/ 2710824/nutrients, (Accessed in 14.10.2025)
25. https://redcliffelabs.com/myhealth/food-and-nutrition/calories-in-an-avocado-nutrients-and-health-benefits/, (Accessed in 14.10.2025)
26. Nuray Z. U., Torsten Bohn, Clinton S. K., Schwartz S. J., Carotenoid Absorption from Salad and Salsa by Humans Is Enhanced by the Addition of Avocado or Avocado Oil12, *The Journal of Nutrition*, Volume 135, Issue 3, **2005**, 431-436, https: //doi.org/10.1093/jn/135.3.431.
27. Halder M, Petsophonsakul P, Akbulut AC, Pavlic A, Bohan F, Anderson E, Maresz K, Kramann R, Schurgers L. Vitamin K: Double Bonds beyond Coagulation Insights into Differences between Vitamin K1 and K2 in Health and Disease. *Int J Mol Sci*. **2019,** Feb 19;20(4):896. doi: 10.3390/ijms20040896.
28. Nair, S. S., & Chandran, A. Nutrient composition of avocado fruits of selected cultivars grown in Kerala. *Int J Food Sci Nutr*, **2018**. 3(3), 65-67.
29. Dreher ML, Davenport AJ. Hass avocado composition and potential health effects. *Crit*

Rev Food Sci Nutr. **2013**; 53(7):738-50. doi: 10.1080/10408398.2011.556759.
30. https://fdc.nal.usda.gov/food-details/169134/nutrients, (Accessed in 14.10.2025)
31. https://fdc.nal.usda.gov/food-details/169231/nutrients (Accessed in 14.10.2025)
32. https://fdc.nal.usda.gov/food-details/168389/nutrients (Accessed in 14.10.2025)
33. https://www.verywellfit.com/asparagus-nutrition-facts-calories-and-their-health-benefits-4118017(Accessed in 14.10.2025)
34. https://fdc.nal.usda.gov/food-details/170375/nutrients, (Accessed in 14.10.2025)
35. https://fdc.nal.usda.gov/food-details/2710090/nutrients, (Accessed in 14.10.2025)
36. Güleşci, N., Yücebilgic, G., Bilgin, R.. Review on Evaluation of Physalis peruviana L.'s Antioxidant, Antimicrobial and Biochemical Activities. *Asian Journal of Research in Biochemistry*. **2021**, 30-39. 10.9734/ajrb/2021/v9i230198.
37. https://fdc.nal.usda.gov/food-details/173043/nutrients, (Accessed in 14.10.2025)
38. Eken, A. Antioxidant Capacity and Metal Content of *Physalis Peruviana L*. Fruit Sold in Markets. *Journal of Clinical and Analytical Medicine*. **2016**, 7.10.4328/JCAM.2709.
39. Añibarro-Ortega M, Dias MI, Petrović J, Mandim F, Núñez S, Soković M, López V, Barros L, Pinela J. Nutrients, Phytochemicals, and In Vitro Biological Activities of Goldenberry (Physalis peruviana L.) Fruit and Calyx. *Plants*. **2025**; 14(3):327. https://doi.org/10.3390/plants14030327
40. https://m.andrafarm.com/_andra.php?_i=0-tanaman (Accessed in 14.10.2025)
41. https://world.openfoodfacts.org/product/7706899000062/physalis-comexa, (Accessed in 14.10.2025)
42. El-Beltagi, Hossam M., Safwat H., Gehan G., Basma M., Basma M. Chemical Composition and Biological Activity of Physalis peruviana L. Schlüsselwörter Physalis peruviana · Phenole· Flavonoide · DPPH · Antikanzerogene Aktivität. *Gesunde Pflanzen*. **2019**. 71. 1-10. 10.1007/s10343-019-00456-8.
43. Obregón-La Rosa AJ, Contreras-López E, Flores Juárez E, Gonzales Barrón Ú, Muñoz AM, Ramos-Escudero F. Nutritional and antioxidant profile of the Physalis fruit grown in three Andean regions of Peru. *Rocz Panstw Zakl Hig*. **2023**;74(1):49-57. doi: 10.32394/rpzh.2023.0247. PMID: 37010381.
44. https://fdc.nal.usda.gov/food-details/2710831/nutrients, (Accessed in 14.10.2025)
45. Richardson DP, Ansell J, Drummond LN. The nutritional and health attributes of kiwifruit: a review. *Eur J Nutr*. **2018** Dec;57(8):2659-2676. doi: 10.1007/s00394-018-1627-z. Epub 2018 Feb 22.
46. Kurpad A.V., Regan M.M., Raj T.D.S., Rao V.N., Gnanou J., Young V.R., The daily phenylalanine requirement of healthy Indian adults23, *The American Journal of Clinical Nutrition*,Volume 83, Issue 6, **2006**, Pages 1331-1336,ISSN 0002-9165, https://doi.org/10.1093/ajcn/83.6.1331.
47. López-Miranda J., Pérez-Martinez P., Pérez-Jiménez F., Health benefits of mono-unsaturated fatty acids, Editor(s): Christine Williams, Judith Buttriss, *In Woodhead Publishing Series in Food Science, Technology and Nutrition*, Improving the Fat Content of Foods, *Woodhead Publishing*, **2006**, pp. 71-106, ISBN 9781855739659, https://doi.org/10.1533/9781845691073.1.71.
48. Sanjeevi, Pandarinathan. Chapter: 12 *Vitamins and Minerals in Clinical Health and Disease.* **2025**. Chapter 12, https://www.researchgate.net/publication/396464590
49. Carr AC, Maggini S. Vitamin C and Immune Function. *Nutrients*. **2017** Nov 3;9(11):1211. doi: 10.3390/nu9111211.
50. Li J, Duan H, Ramaswamy H, Wang C. A Comprehensive Review of Fortification, Bioavailability, and Health Benefits of Folate. *International Journal of Molecular Sciences*. **2025**; 26(16):7703. https://doi.org/10.3390/ijms26167703
51. Alahmari LA. Dietary fiber influence on overall health, with an emphasis on CVD, diabetes, obesity, colon cancer, and inflammation. *Front Nutr*. **2024** Dec 13; 11:1510564. doi: 10.3389/fnut.2024.1510564. PMID: 39734671; PMCID: PMC11671356.
52. Huang, M., He, J.-X., Hu, H.-X., Zhang, K., Wang, X.-N., Zhao, B.-B., Lou, H.-X., Ren, D.-M., Shen, T. **2020**, Withanolides from the genus *Physalis*: a review on their phytochemical and pharmacological aspects. *J Pharm Pharmacol*, 72: 649-669. https://doi.org/10.1111/jphp.13209
53. Benjamin M. Bohrer, Review: Nutrient density and nutritional value of meat products and non-meat foods high in protein, *Trends in Food Science & Technology*, Volume 65, **2017**, 103-112, ISSN 0924-2244, https://doi.org/10.1016/j.tifs.2017.04.016.
54. National Academy of Sciences (US) and National Research Council (US) Division of Medical Sciences. *Conference on Hemoglobin*: 2–3 May 1957. Washington (DC): National Academies Press (US); **1958**. The role of copper in erythropoiesis. https://www.ncbi.nlm.nih.gov/books/NBK224294/