RESEARCH REPORT

Table of Phenylalanine Content of Foods: Comparative Analysis of Data Compiled in Food Composition Tables

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Abstract *Background*: Knowing the phenylalanine (Phe) content of foods is essential for managing the diet of patients with phenylketonuria. Data on the Phe content of foods are scarce and sometimes vary between different Food Composition Tables (FCT). Brazil created its own table of the Phe contents of fruits and vegetables based exclusively on the chemical analysis of protein content, considering that proteins contain 3–4% Phe (TCFA/ANVISA). This study compared the protein and Phe contents of vegetables and fruits provided by the TCFA/ANVISA with those listed in international food composition tables.

Methods: The Phe content of 71 fruits and vegetables listed in TCFA/ANVISAwas classified into four subgroups, and the Wilcoxon nonparametric test compared the Phe and mean protein contents provided by the FCTs. All tests considered the

bilateral hypothesis, and the level of significance was set at 5%. The Spearman's correlation coefficient measured the statistical dependence between Phe and protein contents.

Results: The mean Phe content was $\langle 50 \rangle$ mg Phe/100 g for 15 fruits; >50 mg/100 g for 11 type-A vegetables; $<$ 50 mg/100 g for 8 type-B vegetables; \leq 50 mg/100 g for 7 type-C vegetables. The percentage of Phe in protein varied from 3.13 \pm 1.03% to 3.74 \pm 2.55% in fruits; 3.33 \pm 1.41 to 4.82 ± 1.17 in type-A vegetables; $3.46 \pm 1.25\%$ to 4.83 ± 2.46 in type-B vegetables; and $3.14\% \pm 1.49$ to $4.62\% \pm 2.26$ in type-C vegetables.

Conclusions: The Phe and protein contents provided by most FCTs were positively correlated, suggesting that it is possible to estimate the Phe content of fruits by multiplying its protein content by 3%. For type-A, -B, and -C vegetables, 4% may be used.

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d Composition Tables (FCTs) and searchable databases vide information on nutrients, but data about the amino content of foods are frequently either unavailable, ce, or outdated (Pennington [2008](#page-9-0); Nalin et al. [2010;](#page-9-0) Bonald et al. [2010;](#page-9-0) Demirkol et al. [2011\)](#page-8-0). This is one he various factors that may explain the absence of the amino acid profile of fresh fruits and vegetables in several Is (Charrondiere et al. [2013;](#page-8-0) Blau et al. [2010](#page-8-0); Feillet . [2010a](#page-8-0), [b](#page-8-0); Guimarães and Lanfer Marquez [2002](#page-8-0), [2005;](#page-8-0) enfield and Southgate [2003](#page-8-0); Osmo et al. [2008](#page-9-0)).

Phenylketonuria (PKU) is the most common inborn error mino acid metabolism with a global prevalence ranging $n \approx 1:30,000$ to 1:1,000 of live newborns, depending on ntry (Monteiro and Cândido [2006](#page-9-0); Ahring et al. [2009;](#page-8-0)

Martins et al. [2009;](#page-9-0) Blau et al. [2010\)](#page-8-0). Due to persistently high plasma Phe level, untreated PKU causes neurological impairment, intellectual disability, speech delay, convulsions, skin hypopigmentation, and eczema, among others (Brandalize and Czeresnia [2004;](#page-8-0) Feillet et al. [2010a](#page-8-0), [b;](#page-8-0) De Groot et al. [2010;](#page-8-0) Camp et al. [2012\)](#page-8-0).

Reliable information on the Phe content of foods is indispensable for patients with phenylketonuria, since they require a diet low in this essential amino acid. Fresh fruits and vegetables are poor protein sources that do not contribute significantly to protein requirement. Although no consensus has been reached, some studies suggest that patients with phenylketonuria should be allowed to consume low-Phe fruits and vegetables. No significant negative impact on short-term metabolic control has been observed, but the literature encourages more research to confirm this finding (Mac Donald et al. [2003;](#page-9-0) Weetch and MacDonald [2006](#page-9-0); MacDonald et al. [2011](#page-9-0); Rohde et al. [2012](#page-9-0); Zimmermann et al. [2012](#page-9-0)).

Therefore, it is crucial to know the Phe content of fruits and vegetables and their variability in international food tables and searchable food composition databases to guarantee that fruits and vegetables indeed contribute little to Phe intake. The present study compared the Phe content of fresh fruits and vegetables listed in the Brazilian PKU table (TCFA/ANVISA), with those listed in eight international FCTs. Additionally, the possibility of using the mean Phe content of the FCTs for some fruits and vegetables was investigated.

Methods

The project was approved by the Research Ethics Committee of the School of Health Sciences of the University of Brasilia (N. 389.679/2013).

Food Composition Tables and Study Design

Table of Phenylalanine Content of Foods of the Brazilian National Sanitary Surveillance Agency (TCFA/ANVISA)

Table [1](#page-2-0) of TCFA/ANVISA lists 71 fresh fruits and vegetables, which were grouped into subgroups according to their edible parts: fruits $(n = 27)$; type-A vegetables $(n = 18)$: the edible parts of these vegetables are the leaves, flowers, buds, or stems; type-B vegetables $(n = 14)$: the edible parts of these vegetables are fruits, seeds, or parts that develop on the ground; and type-C vegetables (n) $= 12$): the edible parts of these vegetables are those that grow underground and palm trees.

The TCFA/ANVISA includes moisture, protein, and Phe contents. The protein content of all fruits and vegetables

was given by their total N content, determined by Kjeldahl's method, which was then multiplied by 5.7 to obtain the crude protein content. The Phe content was estimated by multiplying the protein content by 4% and expressed as mg Phe/100 g food. Therefore, 1 g of fruit or vegetable protein has about 40 mg of Phe. The value of 4% was taken from studies that reported that fruits and vegetables contain about 40 mg of Phe per gram of protein, which is lower than the Phe content of other types of natural proteins, such as animal proteins, which seem to have a Phe content closer to 5% (50 mg/g protein) (Ahring et al. [2009;](#page-8-0) Weetch and MacDonald [2006](#page-9-0); MacDonald et al. [2011;](#page-9-0) AGÊNCIA NACIONAL DE VIGILÂNCIA SANITÁRIA [2013](#page-9-0)). In most countries including the United States (USA), multiplying plant protein content by 5% would force patients to eat less for fear of reaching the actual daily Phe intake tolerance.

International Food Composition Tables

The protein and Phe contents of foods provided by the TCFA/ANVISA were compared with those furnished by eight international FCTs listed in the International Food Composition Tables Directory (Table [2](#page-3-0)). The directory is maintained by the International Network of Food Data Systems (INFOODS) ([www.fao.org/infoods\)](http://www.fao.org/infoods). In addition to the FCTs listed by INFOODS, the Low Protein Food List for PKU (LPFL-PKU) was also included, due to its relevance for patients with phenylketonuria (Schuett [2010](#page-9-0)).

The international tables were selected based on the following criteria: free internet access; available in electronic format: such as Excel, Access, or PDF files, or online database; available in English, Portuguese, or Spanish; and containing the Phe content of fruits and vegetables with a protein content of 5% or less. The exclusion criteria were: restricted access; information not available in English or Spanish; Phe content not available for some or all items, or available only for fresh vegetables and fruits that do not have similar counterparts in the TCFA/ANVISA Table.

Moisture, protein, and Phe contents provided by the eight international FCTs were determined by different analytical techniques used specifically to construct the FCTs. Sometimes data were also obtained from analytical data published in the literature or compiled from other databases and FCTs (Table [2\)](#page-3-0).

Fresh vegetables listed in the TCFA/ANVISA Table were compared with their counterparts in the international FCTs and identified by their popular and scientific names, by the edible parts, and also by their taxonomic description, including genus, species, and variety. Different varieties of fruits and vegetables of the same species, and fruits and vegetables without variety information were grouped, and

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b The edible part of the vegetables consists of fruits, seeds, or parts that develop on the ground

cConsists of the parts that grow underground and palm trees

Table 2 Food composition tables included in the study

the mean Phe content was calculated. However, some fruits and vegetables, which are commonly found in Brazil, were not found in the international FCTs. Hence, they were maintained in the TCFA/ANVISA Table (Table [1](#page-2-0)), but were not compared.

The protein contents in the international FCTs were calculated using a conversion factor of 6.25 to transform total N into protein by considering that the protein fraction has a mean nitrogen content of 16%. However, all data from the TCFA/ANVISA Table used a conversion factor of 5.75, which seems to be closest to the actual protein content (Greenfield and Southgate [2003](#page-8-0)). Therefore, the protein level contents provided by the different tables could only be compared after recalculating all the data using the conversion factor of 5.75.

In addition to absolute Phe content, we calculated the percent contribution of Phe in the protein of each food to verify whether Phe content was relatively constant for each type of vegetable, therefore, possibly genetically determined. Then the percentage of Phe present in the proteins of the fruits and vegetables listed in the international FCTs were compared with the Phe content of 4% in vegetable proteins used by the TCFA/ANVISA Table.

Statistical Analysis

The Wilcoxon nonparametric test compared the protein and Phe contents provided by the TCFA/ANVISA Table and each of the eight international FCTs. All tests considered bilateral hypotheses and used a significance level of 5%. The correlation between Phe and protein contents was given by Spearman's correlation coefficient (Conover and Conover [1980\)](#page-8-0).

Results

From the total number of fruits listed in the TCFA/ ANVISA, 11 could not be compared because they were either not present in the majority of the other tables, or the Phe content was not provided. Some of these fruits are tropical, so analytical information is not easily available. The excluded fruits are: acai, cashew, Indian cherry, soursop, jackfruit, sweet passion fruit, pequi, sugar apple, Surinam cherry, pomegranate, and tamarind. Four type-A vegetables (butter green bean, Dutch string bean, endive, and string bean), two type-B vegetables (scarlet eggplant and bur cucumber), and two type-C vegetables (palm heart and pupunha palm heart) also were not compared because they were not listed in the other tables.

Figure [1a](#page-5-0)–d shows the Phe content of fruits and vegetables listed in the nine FCTs, including the TCFA/ ANVISA Table. Fruits have the lowest protein content and, as expected, the lowest Phe content. In Fig. [1a,](#page-5-0) 15 out of the 16 fruits had a mean Phe content smaller than 50 mg/ 100 g fruit, ranging from 8 to 49 mg/100 g. The only exception was avocado, which varied considerably, from 45 to 150 mg/100 g. The median Phe content of avocado, considering the eight FCTs and the TCFA/ANVISA Table, was 93 mg/100 g, which might be the most accurate Phe content of this fruit. In the TCFA/ANVISA Table, the Phe content of avocado is 45 mg/100 g, so this value should be reexamined to confirm the discrepancy in relation to the other FCTs.

In the international FCTs, the proportion of Phe in protein varied from $3.13 \pm 1.03\%$ to $3.74 \pm 2.55\%$ and was always lower than 4%, with significant differences between five international FCTs and the TCFA/ANVISA Table, which varied from $3.13\% \pm 1.03$ to $3.28\% \pm 0.93$ (Table [3a\)](#page-7-0). Therefore, the results suggest that it is possible to estimate the Phe content of fruits by multiplying their protein content by 3%.

Vegetables have also very low Phe content, but in general and with some overlapping, they seem to have more Phe than fruits. Figure [1b](#page-5-0) shows the Phe content furnished by the FCTs for 15 study vegetables. On average, 11 out of the 15 type-A vegetables had a mean Phe content higher than 50 mg/100 g, ranging from 53 to 179 mg/100 g. The Phe content of proteins in these foods provided by the international FCTs ranged from $3.33 \pm 1.41\%$ to $4.82\% \pm 1.17$, with no significant differences between the eight FCTs and the TCFA/ANVISA Table (Table [3a\)](#page-7-0).

Not all 14 type-B vegetables listed in the TCFA/ ANVISA Table were listed in the international FCTs, which resulted in a variable number of samples. Figure [1c](#page-5-0) shows the Phe content of 12 type-B vegetables. Of these, eight have a mean Phe content lower than 50 mg/100 g, ranging from 20 to 47 mg/100 g. The Phe content of peapods was variable and higher than 200 mg/100 g. Peapod is a legume with high protein content associated with degree of ripeness, as protein is synthesized in advanced maturation stages.

The mean Phe content in the protein fraction of type-B vegetables provided by the TCFA/ANVISA Table did not differ significantly from those provided by three of the eight international FCTs (FAO-AA, FCNT/Germany, and NUTTAB/Australia), whose percentages varied from $3.46 \pm 1.25\%$ (FAO-AA) to $4.07 \pm 1.64\%$ (FCNT/Germany). In the other FCTs, the mean percentages were significantly higher, varying from $4.28 \pm 0.96\%$ (LPFL-PKU/USA) to $4.83 \pm 2.46\%$ (HCNT/Canada) (Table [3a\)](#page-7-0). However, the percentages of 27% Phe in the protein fraction of pumpkin provided by DTU FOOD (Denmark) and of roughly 11% in green pepper provided by HCNT (Canada) and USDA-SR (USA) may be incorrect because they differ greatly the percentages provided by the literature (3–5%) and do need confirmation (Greenfield and Southgate [2003;](#page-8-0) de Menezes et al. [2003](#page-8-0)).

Figure [1d](#page-5-0) shows the Phe content of 12 type-C vegetables even though not all of them were listed in the international FCTs, resulting in the comparison of a variable number of samples. On average, seven of these foods had a Phe content of 50 mg/100 g or less, ranging from 22 to 50 mg/ 100 g. The mean Phe content of the other four type-C vegetables varied from 73 to 88 mg/100 g, except for garlic, which had a mean Phe content of 190 mg/100 g. The Phe content in the protein of 50% of these foods varied significantly, from 3.14 \pm 1.49% to 4.62 \pm 2.26% in the international FCTs, but the contents were not significantly different from those provided by the TCFA/ANVISA Table (Table [3a\)](#page-7-0).

Phe and protein contents were positively correlated in all FCTs (Table [3b](#page-7-0)). The correlation for fruits was statistically significant in all eight international FCTs, and the Spearman's correlation coefficient varied from $\rho = 0.692$ to 0.972 ($p < 0.05$). For type-C vegetables the correlation was significant in seven of the eight FCTs ($\rho = 0.664$ to 0.995; $p < 0.05$). The correlation for type-A vegetables was significant in six FCTs (Spearman, $\rho = 0.879$ to 1.000; $p < 0.05$). The correlation for type-B vegetables was significant in three FCTs ($\rho = 0.900$ to 1.000; $p < 0.05$).

Discussion

The present study compared the Phe content of fresh fruits and vegetables listed in nine food composition tables. The Brazilian table (TCFA/ANVISA) was used as reference for the number of samples compared. The possibility of using a mean Phe content for each food group was also investigated.

Based on our results about 70% of the fresh fruits and vegetables listed in the FCTs have similar Phe content: apple, artichoke, arugula, aubergine, banana, cassava, cauliflower, chayote, chicory, cucumber, endive, fig, grape, kiwi, leek, lettuce, mandarin, mango, melon, okra, onion, papaya, peach, pear, persimmon, pineapple, plum, squash summer, strawberry, taro, turnip, yellow pepper, radish, red pepper, white and red cabbage, and tomato.

Fig. 1 Phenylalanine content (mg/100 g) of fruits (a) and type-A, -B, and -C vegetables (b, c, d) provided by TCFA/ANVISA (gray dots) and eight international food composition tables (black dots): DTU

FOOD/Denmark, FAO-AA, FCNT/Germany, HCNT/Canada, LPFL-PKU/USA, NUTTAB/Australia, NZFC/New Zealand, USDA-SR/ USA. Legend for fruits: Grape, several varieties (Thompson, White,

The Phe content of about 30% of the study fresh fruits and vegetables differ considerably between the nine FCTs: avocado, beet root, carrot, celery seed, coriander, garlic, green pepper, kale, onion spring or scallion, parsley, pea, potato, pumpkin, kent pumpkin, spinach, swiss chard, watercress, sweet potato, and yam.

The differences may stem from several factors, such as accuracy of protein and Phe estimates, origin of the food, genetic variability, climate, degree of maturation, time of harvest, and even a transcription error of raw data, which cannot be omitted. Therefore, an adequate number of samples of these vegetables should be reanalyzed to obtain more accurate Phe and protein estimates, and consequently explain or correct the different protein and Phe contents provided by the FCTs. Result dispersion may be minimized by analyzing a representative number of samples of the species and varieties of fruits and vegetables cultivated and consumed in a country, taking into account factors that may affect nutrient composition (de Menezes et al. [2003](#page-8-0)). The sampling design, analytical method, expression of the results, and data treatment should also be considered.

According to the nine FTCs, 58 and 84% of the 55 fresh study fruits and vegetables had a mean Phe content of 50 mg/100 g or less, and 100 mg/100 g or less, respectively. Since clinical trials suggest that fruits and vegetables with Phe content of 50 mg to 100 mg/100 g are safe for patients with phenylketonuria, these fruits and vegetables could be classified as unrestricted for these individuals (Mac Donald et al. [2003;](#page-9-0) Weetch and MacDonald [2006](#page-9-0); MacDonald et al. [2011;](#page-9-0) Rohde et al. [2012](#page-9-0); Zimmermann et al. [2012\)](#page-9-0).

We understand that the data in the FCTs, some based on chemical analyses and some on the literature, and the small number of analyzed samples are study limitations. Therefore, caution is advised when using the Phe contents provided by the FCTs, since many factors contribute to different or incorrect results.

Although chemical analyses are recommended to obtain more accurate Phe content data, the positive correlation

⁄-Fig. 1 (continued) Niagara) (Vitis sp.); Peach, Brazilian and international (Prunus persica); Pear, Williams (Pyrus communis L.); Strawberry (Fragaria vesca L.); Mandarin, Mungote and Ponkan (Citrus reticulata "Murgote"); Melon (Cucumis melo); Mango (Mangifera indica L.); Papaya (Carica papaya L.), Apple (Pyrus malus); Kiwi fruit (Actinidia chinensis Plack.); Fig (Ficus carica L.); Persimmon (Diospyros kaki L.); Banana (several varieties) (Musa sp.); Plum (Prunus salicina Lindl.); Pineapple (Ananas comosus); Avocado (Persea americana mil.). Legend for type-A vegetables: Parsley (Petroselinum sativum), Spices, celery seed (Apium graveolens L.), Arugula (Erucata sativa), Cabbage, white and red (Brassica oleracea L.), Spinach (Tetragonia expansa Murr.), Cauliflower (Brassica oleracea L.), Kale (Brassica oleracea L.), Coriander (Coriandrum sativum L.), Chicory greens (Cichorium intybus L.), Onions spring or scallions (Allium fistulosum L.), Chicory (Chicorium endivia), Lettuce (Lactuca sativa L.), Artichokes, globe (Cynara scolimus L.), Water-

found between the protein and Phe contents of the study fruits and vegetables indicates that Phe content can be reliably estimated from protein content.

Pimentel et al. ([2014](#page-9-0)) made a similar attempt by analyzing the protein and amino acid contents of 16 vegetable and fruit preparations usually included in the diet of Portuguese patients with phenylketonuria. The Phe and protein contents of these preparations were highly correlated. Lanfer Marquez et al. [\(1997](#page-9-0)) studied the chemical composition of cereal flakes and found a linear correlation between the samples' total nitrogen and Phe contents.

Hence, given the scarcity of analytical Phe data and the present comparative analysis, the Phe content of fresh fruits and vegetables can be estimated from their protein content, despite the limitations associated with result accuracy. Comparative analyses indicated that 3% seems to be the most appropriate multiplier to calculate the Phe content in the fruit protein contents provided by most FCTs.

For type-A, type-B, and type-C vegetables, the results support the possibility of estimating the Phe content of leaf vegetables by multiplying their protein content by 4%, as performed by the TCFA/ANVISA Table (Brazil) and most FCTs. These results confirm the literature reports that Phe contributes with 3–5% of the total amino acid content of these foods (Weetch and MacDonald [2006;](#page-9-0) Bremer et al. [1996](#page-8-0)). However, when the percentage of 3 or 4% is used for estimating Phe content, the result is lower than 50 mg/g of protein. When the percentage of 5% is used, the result exceeds 50 mg/g of protein.

Processed plant-based foods, such as fruit and vegetable juices, and jams, should also be studied to determine whether the correlation between the Phe and protein contents of fresh vegetables and fruits also applies to these products. If so, the concentrations of 3–5% Phe in proteins could be used to estimate the Phe content of these products. Vegetable and fruit preparations should also be chemically analyzed because processing may change the Phe content of the food (Weetch and MacDonald [2006;](#page-9-0) Pimentel et al.

cress (Nasturtium officinale L.), Chard, Swiss (Beta vulgaris L. var. cicla). Legend for type-B vegetables: Tomatoes, several varieties (Solanum lycopersicon Mill., Lycopersicon sp.), Okra (Hibiscus esculentus), Pepper, sweet, red (Capsicum annuum), Pepper, sweet, green (Capsicum annuum), Pepper, sweet, yellow (Capsicum annuum), Cucumber (Cucumis sativus L.), Peas, green (Pisum sativum L.), Chayote (Sechium edule), Aubergine (Solanum melogena L.), Kent pumpkin (Cucurbita maxima), Butter, squash, (Cucurbita pepo), Pumpkin (Cucurbita spp.). Legend for type-C vegetables: Radish (Raphanus sativus), Turnip (Brassica rapa L.), Cassava (Manihot esculenta Crantz Manihot utilissima), Yam (Colocasia esculenta), Carrot (Daucus carota L.), Onion (Allium cepa L.), Taro (Dioscorea spp.), Beet root (Beta vulgaris), Sweet potato (Ipomoea batatas L.), Potato (Solanum tuberosum), Garlic (Allium sativum L.), Leek (Allium porrum L.)

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Table 3 Mean, standard deviation, and comparative analysis of the percentage of phenylalanine in the protein portion of foods (a) and association between the Phe and protein contents

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 Mean Phe content±standard deviation in the protein fraction provided by international FCTs Mean Phe content±standard deviation in the protein fraction provided by TCFA/ANVISA [2014\)](#page-9-0). Weetch and MacDonald ([2006\)](#page-9-0) found that the Phe content of different potato varieties prepared in different ways resulted in a mean Phe content of 28 mg/g of protein. For cooked potatoes, the Phe content varied from 44 mg to 109 mg/100 g. The vegetable preparations analyzed by Pimentel et al. [\(2014](#page-9-0)) had Phe contents of 12 mg to 33 mg/ g of protein, and Phe and protein contents were highly correlated.

Conclusion

For fruits, 3% seems to be the best multiplier. For type-A, - B, and -C vegetables, 4% may be used. Analysis of the Phe and protein contents of the 55 fruits and vegetables listed in the nine FCTs indicated that it is possible to calculate mean Phe content from the amounts of Phe and protein provided by the various FCTs. In the absence of analytical Phe data, it is possible to estimate the Phe content of fresh fruits and vegetables from their protein content, despite the limitations associated with the accuracy of this method.

These findings may be useful for updating FCTs for patients with phenylketonuria, assisting dietitians in their practice and patients in estimating the Phe content of their diet. This information may increase the number of dietary options that best fit patients with phenylketonuria's daily routine.

It is important to create national FCTs with Phe data in the local language, accessible to the population, and to include in local FCTs regional fruits, vegetables, and preparations that would not normally be found in international FCTs.

Knowing Phe content variability in fruits and vegetables may help to reduce uncertainty, provide more reliable Phe contents, and expand the dietary guidelines of foods for patients with phenylketonuria.

Take-Home Message

The Phe content of most fresh fruits and vegetables listed in Brazilian PKU table is similar to those listed in other food composition tables.

Compliance with Ethics Guidelines

Ana Claudia Marquim Araújo, Wilma M. C. Araújo, Ursula M. Lanfer Marquez, Rita Akutsu, and Eduardo Y. Nakano declare that they have no conflict of interest.

This chapter does not contain any studies with human or animal subjects performed by any of the authors.

Authors' Contributions

A.C.M.A. designed and conducted the research, analyzed samples, performed the statistical analyses, and wrote the paper; W.M.C.A. designed the research and wrote the paper; U.M.L.M. designed the research and reviewed the manuscript; R.A. reviewed the manuscript; E.Y.N. performed the statistical analyses.

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