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Evaluation of hydrolyzed collagen supplement labels for human consumption

Avaliação de rotulagem de suplementos de colágeno hidrolisado para consumo humano

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Highlights

Hydrolyzed collagen supplements showed variable collagen contents.
Only one supplement presented all the requirements established by current legislation.
Increased regulatory inspection is needed to ensure the quality of supplements.

Abstract

Hydrolyzed collagen is a dietary supplement marketed for promoting health in aging-related conditions. This study aimed to evaluate the labeling of seven commercial hydrolyzed collagen supplements and analyze their collagen, total protein, and vitamin C contents, comparing them to the label declarations. The supplements were identified by letters A through G, and their labels were assessed in accordance with the technical requirements of the Brazilian Health Regulatory Agency (ANVISA). Additionally, the total protein, total collagen, and vitamin C contents were quantified. Only brand D met all regulatory requirements among the seven supplements. Three supplements (E, F, and G) showed lower protein contents than declared, while three others (A, B, and C) had values similar to those on the label. The collagen content in two supplements (B and D) matched label declarations, while one (F) contained 35.97% less collagen than stated. Moreover, two brands (A and C) had higher vitamin C contents than declared, while two others (D and E) matched the label claims. A wide variation was found in the commercial offerings of hydrolyzed collagen supplements with missing mandatory labeling information and discrepancies between declared and actual protein, collagen, and vitamin C contents. These findings highlight the need for greater quality control by manufacturers, stricter regulatory inspections, and increased consumer awareness.

Key words: Protein. Quality. Supplementation. Collagen. Vitamin C.

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Resumo

Os hidrolisados de colágeno são suplementos alimentares comercializados para promoção da saúde em doenças do envelhecimento. O objetivo deste trabalho foi avaliar a rotulagem de sete suplementos hidrolisados de colágeno comerciais e analisar os conteúdos de colágeno, de proteína total e de vitamina C comparando-os com os declarados no rótulo. Os suplementos foram identificados por letras de A a G e seus rótulos analisados quanto às exigências dos regulamentos técnicos da Agência Nacional de Vigilância Sanitária (ANVISA), além disso, foram quantificados o teor de proteína total, colágeno total e vitamina C. Dos 7 suplementos avaliados, a marca D foi a única que apresentou todos os requisitos exigidos. Em relação ao teor de proteína, três suplementos (E, F, G) apresentaram valor inferior ao declarado e três (A, B, C) resultados similares ao rótulo. O teor do colágeno de dois suplementos (B, D) foram semelhantes ao declarado no rótulo e um (F) apresentou 35,97% menos colágeno. Quanto a vitamina C, duas marcas (A e C) apresentaram maior teor, enquanto outras duas (D e E) apresentaram valores semelhantes ao rótulo. Há diversidade na oferta de suplementos hidrolisados de colágeno com ausência de informações exigidas pela legislação e com quantidades declaradas nos rótulos de proteína, colágeno e vitamina C que não correspondem à realidade, evidenciando a necessidade de maior controle de qualidade pelos fabricantes, inspeções mais rigorosas, e maiores cuidados dos consumidores.

Palavras-chave: Proteína. Qualidade. Suplementação. Colágeno. Vitamina C.

Introduction

Dietary supplements are defined as orally ingested products presented in various pharmaceutical forms intended to supplement the diet of healthy individuals with nutrients, bioactive substances, enzymes, or probiotics, either isolated or combined, according to Resolution RDC No. 243, July 26, 2018 (Resolução No 243 - Ministério da Saúde, 2018).

Collagen is the most abundant extracellular matrix protein in animals, accounting for approximately 30% of the total body protein mass, and is primarily found in fibrous tissues such as skin, bones, blood vessels, tendons, muscles, cornea, ligaments, and dentin (Tang et al., 2022). Collagen is a fibrous protein composed of a triple-helix structure formed by three alpha-helical polypeptide chains, with a repetitive amino acid sequence rich in glycine (33%), proline, and hydroxyproline (22%) (Pearson et al., 1985; Lawrie, 2005; Ricard-Blum, 2011; Musayeva et al., 2022). Ascorbic acid (vitamin C) plays an essential role in collagen synthesis, acting as a cofactor in the hydroxylation reactions of proline and lysine. In its absence, cells are unable to hydroxylate the Y-position proline in the tripeptide unit, leading to collagen instability and connective tissue disorders, as observed in scurvy (Gonçalves & Campos, 2006).

Hydrolyzed collagen is commercially obtained from the skin or bones of slaughtered animals (bovine, porcine, poultry, and fish) and has water solubility and a high protein content (Harris et al., 2021; Musayeva et al., 2022). It is widely used in the food industry due to its structural, biological, physical,

and chemical characteristics (Tang et al., 2022). More recently, it has been marketed as a dietary supplement for promoting health and supporting the maintenance and regeneration of skin, bones, cartilage tissues, and the extracellular matrix, especially in aging-related processes.

The human body gradually reduces its natural collagen production with advancing age due to the activity of collagenase and elastase enzymes, which degrade collagen and elastin fibers, initiating the aging process (Harris et al., 2021). Collagen hydrolysates are rapidly digested and absorbed into the bloodstream due to their low molecular weight (Musayeva et al., 2022).

Supplementation with hydrolyzed collagen has been associated with improvements in conditions such as skin aging, bone regeneration, osteoporosis, osteoarthritis, and rheumatoid arthritis (Lopes et al., 2019; Harris et al., 2021; Leite et al., 2023). Collagen hydrolysates have also been investigated for potential benefits in cognitive impairment, including Alzheimer's disease and dementia (Harris et al., 2021).

In Brazil, hydrolyzed collagen supplements are freely marketed without the need for a prescription or registration with the Brazilian Health Regulatory Agency (ANVISA) (Resolução No 843 - ANVISA, 2024). Normative Instruction No. 28 of July 2018 (Instrução Normativa nº 28- ANVISA, 2018) and Normative Instruction No. 102 of October 15, 2021 (Instrução Normativa No 102 - ANVISA, 2021) are currently in force to regulate their use limits, claims, and labeling requirements.

Therefore, these products must be marketed in compliance with current regulations and feature appropriate labeling to ensure public well-being and the delivery of high-quality products. This study aimed to evaluate the labeling of seven commercial hydrolyzed collagen supplements and analyze their collagen, total protein, and vitamin C contents, comparing them with the amounts declared on the product labels.

Material and Methods

Raw material

Samples were randomly selected from the local market, without prior selection based on specifications, brand, formulation, or presentation. Capsule samples were disintegrated to obtain their internal powdered content for analysis. Tablet samples were ground using a mortar and pestle until fine and homogeneous granules were obtained. Powdered samples required no pre-treatment. The samples from different brands were coded with the letters A through G to preserve the anonymity of the manufacturers.

Labeling

Samples from different brands were evaluated for compliance with the requirements established by the following resolutions that were in effect at the time of product commercialization: RDC No. 243 of July 26, 2018 (Resolução No 243 - Ministério da Saúde, 2018), RDC No. 429 of October 8, 2020 (Resolução No 429 - Ministério da Saúde, 2020), IN No. 28 of July 26, 2018 (Instrução Normativa No 28 - ANVISA, 2018), and IN No. 102 of October

15, 2021 (Instrução Normativa No 102 - ANVISA, 2021). The assessed requirements included: batch number and expiration date, manufacturer information, allergen declaration, individual names of nutrients, bioactive substances and enzymes, serving size, storage instructions (including post-opening), and net content, as required by RDC No. 243 of July 26, 2018 (Resolução No 243 - Ministério da Saúde, 2018). The findings were recorded as Declared (D) or Not Declared (ND). The declared quantities of collagen, protein, and vitamin C per serving were also recorded for comparison with laboratory results, following RDC No. 429 of October 8, 2020 (Resolução No 429 - Ministério da Saúde, 2020), Article 33, item II, which states that the contents of protein, amino acids, dietary fiber, monounsaturated fats, polyunsaturated fats, vitamins, minerals, and bioactive compounds must not be less than 20% below the declared value.

Protein determination

Protein content was determined in triplicate using the micro-Kjeldahl method (Association of Official Analytical Chemists [AOAC], 2012), which is based on nitrogen quantification through digestion, distillation, and titration, with conversion to protein using a nitrogen-to-protein conversion factor of 6.25.

Collagen determination

Total collagen content was determined in triplicate by spectrophotometric quantification of hydroxyproline (Lutz, 2008). Approximately 4.0 g of each sample was weighed in duplicate, followed by the addition of 30 mL of 6 mol·L^{-1} HCl and a few glass beads. The samples underwent acid hydrolysis at 105 °C for 15 hours and filtration, and the hydrolysate was transferred to a 500-mL volumetric flask and brought to volume with distilled water. From the final dilution, 2 mL of each sample was pipetted, followed by the addition of 1 mL of chloramine T oxidizing solution, mixed, and then 1 mL of color reagent (4-dimethylaminobenzaldehyde) was added and mixed again. The tubes were immediately incubated in a water bath at 60 °C for 15 minutes. After cooling, the absorbance was measured against a blank at 558 ± 2 nm. The calculation was performed using Equation (1).

$$\left[\frac{A-b}{a.p}\right] = hydroxyproline(H) em\ g.100g^{-1} \quad (1)$$

In Equation (1), A represents the absorbance of the diluted sample filtrate, b is the linear coefficient of the calibration curve, absorptivity, the angular coefficient of the calibration curve, and p is the sample weight (g). A standard curve was prepared using hydroxyproline concentrations ranging from 0.3 to 3.6 µg·mL^{-1}. The hydroxyproline (H) result was multiplied by 8.0 to obtain the collagen content, which was expressed in grams per serving for comparison with the values declared on product labels.

Vitamin C determination

Vitamin C content was determined in duplicate using the Tillmans titrimetric method, which allows for quantification of samples with low vitamin C content (Lutz, 2008). For this analysis, approximately 1 g of each sample was weighed and transferred

into a 50 mL volumetric flask, with the volume brought to mark using 1% oxalic acid. Subsequently, 10 mL of the diluted sample was titrated with 2,6-dichlorophenolindophenol solution. A standard solution of 0.1 $mg \cdot mL^{-1}$ ascorbic acid in 1% oxalic acid was used, and 10 mL of this solution was titrated with 2,6-dichlorophenolindophenol to calculate the Tillmans factor. The vitamin C concentration in the samples was calculated using the volume of 2,6-dichlorophenolindophenol solution consumed and the Tillmans factor, and the result was expressed in mg of vitamin per serving for comparison with the label-declared values.

Results and Discussion

Table 1 shows that the collagen hydrolysates were available in different pharmaceutical forms, with powdered formulations being the most prevalent (n = 4), followed by tablets (n = 2), and only one in capsule form. Only one (D) of the seven evaluated products complied with all required items established by ANVISA for dietary supplement labeling. Two supplements (B and F) failed to meet a single criterion, specifically the specification for usage. Supplements A, C, E, and G did not include the target population for which the product is recommended. Notably, one supplement (G) failed to meet five labeling requirements and was the only one that did not list its ingredients or preparation instructions.

Only two products (C and G) failed to provide the identification of the collagen source on the label. The remaining products showed the collagen source, originating from bovine, porcine, or poultry sources.

All supplements presented batch and expiration dates, manufacturer information, allergen identification, individual names of nutrients, bioactive substances or enzymes, storage instructions (including after opening), declared serving size, and net contents.

The results indicate that many manufacturers place products on the market that do not fully comply with regulatory requirements, particularly RDC No. 243 of July 26, 2018, which establishes health requirements for dietary supplements (Resolução No 243 - Ministério da Saúde, 2018). In a study evaluating collagen-based products before and after ANVISA's new regulations, Abe-Matsumoto et al. (2021) observed that all analyzed samples (n = 16) had between one and four discrepancies with current legislation, the most common being the use of unauthorized expressions or images that may mislead consumers. Similarly, Molin et al. (2019) investigated 44 commercial dietary supplements and found that the most prevalent claims were those related to muscle building or physical performance (n = 17). Among the samples evaluated in the present study, only one supplement (brand D) featured misleading imagery suggesting performance-enhancing benefits.

Table 1
Evaluation of hydrolyzed collagen supplement in accordance with the technical requirements of the Brazilian Health Regulatory Agency (ANVISA)

Requirements Pharmaceutical forms	Brands of hydrolyzed collagen supplement						
	A Power	B Power	C Power	D Tablet	E Tablet	F Capsule	G Power
Batch number and Expiration date	D	D	D	D	D	D	D
Manufacturer information	D	D	D	D	D	D	D
Allergen declaration	D	D	D	D	D	D	D
Individual names of nutrients, bioactive substances and enzymes	D	D	D	D	D	D	D
Identification of the collagen source	D	D	ND	D	D	D	ND
Specification for usage	ND	ND	D	D	D	ND	ND
Population for which the product is recommended	ND	D	ND	D	ND	D	ND
Storage instructions (including post-opening)	D	D	D	D	D	D	D
Declared serving size	D	D	D	D	D	D	D
List of ingredients	D	D	D	D	D	D	ND
Preparation instructions	D	D	D	D	D	D	ND
Net content	D	D	D	D	D	D	D

Declared (D) or Not Declared (ND).

The supplements exhibited variations in protein content ranging from 8.76 g·100 g^{-1} to 92.01 g·100 g^{-1} (Table 2). Only supplement D did not declare the protein content on its label, making it impossible to compare with the experimental results. Moreover, this sample contained less than 10% protein, considerably lower than the values obtained for the other supplements analyzed in this study (A, B, C, E, F, and G). It is likely that, due to its low protein content, the manufacturer opted not to disclose this information on the label. Supplements E, F, and G presented protein values lower than those declared on their labels, with sample F showing approximately 28.6% less protein and sample G showing approximately 20.6% less. This deviation exceeds the 20% tolerance limit established by ANVISA under RDC No. 429/2020 (Resolução No 429 - Ministério da Saúde, 2020). The remaining supplements (A, B, and C) presented protein values close to those declared on their labels, falling within the 20% acceptable variation as outlined in the regulation (Resolução No 429 - Ministério da Saúde, 2020). Similarly, dos Santos et al. (2023) quantified the total protein content in commercial whey protein concentrate

supplements and found that many brands presented lower values than those stated on their labels. However, the number of non-compliant samples decreased when applying the 20% tolerance permitted by legislation, even though the actual intake per serving may still have been inaccurate.

Table 2
Comparasion between experimentally quantified protein content and that declared on the label for hydrolyzed collagen supplements

Brands of hydrolyzed collagen supplement	Experimentally quantified protein content ($g.100g^{-1}$)	Protein content declared on the label ($g.100g^{-1}$)
A	32.91 ± 0.62	35.71
B	92.01 ± 5.08	90.00
C	57.60 ± 1.24	55.00
D	8.76 ± 0.35	ND
E	79.16 ± 0.55	90.00
F	62.68 ± 3.87	87.84
G	73.71 ± 0.63	92.83

ND = Not declared.

The total collagen content ranged from 0.043 g to 23.00 g per serving (Table 3). Three supplements (A, E, and G) did not include collagen content on their labels, which made comparison with experimental results impossible. Supplements B and D showed collagen values similar to those declared on their labels, falling within the 20% tolerance limit established by legislation (Resolução No 429 - Ministério da Saúde, 2020). Supplement F presented approximately 35.97% less collagen than declared, likely a result of the lower protein content observed in Table 2. Supplement C stood out by showing the greatest discrepancy: the experimentally obtained value was 11.8 g per serving, whereas the label indicated 0.040 g. Abe-Matsumoto et al. (2021) evaluated 16 hydrolyzed collagen supplements and reported that all samples contained collagen amounts consistent with those declared on their labels.

Table 3
Comparasion between experimentally quantified total collagen content and that declared on the label for hydrolyzed collagen supplements

Brands of hydrolyzed collagen supplement	Experimentally quantified total collagen content (g per serving)	Total collagen content declared on the label (g per serving)
A	3.40 ± 0.07	ND
B	12.13 ± 4.03	9.28
C	11.8 ± 3.69	0.040
D	0.0433 ± 0.006	0.040
E	6.35 ± 0.16	ND
F	0.621 ± 0.016	0.970
G	23.8 ± 0.60	ND

ND = Not declared.

Table 4 shows the vitamin C content in the hydrolyzed collagen supplements, with values ranging from 0.32 mg to 49.97 mg per serving. Two supplements (F and G) did not declare the vitamin C content on their labels, making it impossible to compare with experimentally obtained values. Supplements D and E showed results close to those declared on their labels, within the 20% tolerance limit established by regulation. Supplements A and C showed values higher than those declared. Abe-Matsumoto et al. (2021) found that two collagen supplement samples among 16 evaluated presented results 70% higher than declared by their manufacturers. Supplement B did not allow for accurate quantification of the vitamin C content due to the presence of coloring agents in its formulation, which interfered with endpoint detection in the titration.

Table 4
Comparasion between experimentally quantified vitamin C content and that declared on the label for hydrolyzed collagen supplements

Brands of hydrolyzed collagen supplement	Experimentally quantified vitamin C content (mg per serving)	Vitamin C content declared on the label (mg per serving)
A	34.00 ± 0.00	23.00
B	*	22.50
C	49.97 ± 1.250	45.00
D	42.96 ± 0.434	45.00
E	3.26 ± 0.650	3.4
F	0.32 ± 0.040	ND
G	1.95 ± 0.00	ND

* = Not detected, ND = Not declared.

The market offers a wide variety of hydrolyzed collagen supplements, with variable protein and total collagen content, as well as a lack of essential labeling information for proper consumer use, which may result in economic losses and potential health risks.

Only brand D met all regulatory requirements among the seven evaluated supplements, while brand G failed to comply with five of the mandatory criteria and was the only product that did not list its ingredients or provide preparation instructions. Regarding protein content, supplements E, F, and G presented lower values than those declared on their labels, while brands A, B, and C reported values close to those determined experimentally. The collagen content in brands B and D was consistent with the values stated on their labels, while brand F presented approximately 35.97% less collagen than declared. Moreover, brands A and C exhibited higher vitamin C contents than those reported on their labels, whereas brands D and E presented values similar to those declared.

Conclusion

There is a wide commercial availability of hydrolyzed collagen supplements, many of which lack information required by current legislation and declare amounts of protein, collagen, and vitamin C that do not reflect actual content. This highlights the need for stricter quality control by manufacturers, more rigorous regulatory inspections, and increased consumer awareness.

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