Functional Properties of Tilapia Collagen, a Systematic Review
Propriedades Funcionais do Colágeno de Tilapia, Uma Revisão Sistemática
Propiedades funcionales del colágeno de tilapia, una revisión sistemática

Received: 10/11/2020 | Reviewed: 10/14/2020 | Accept: 12/16/2020 | Published: 12/19/2020

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Abstract
This systematic review aimed to list the functional properties attributed to collagen obtained from tilapia in scientific studies. The results showed that the antioxidant property is related to the form in which the collagen is presented and the method of antioxidant activity evaluation. It was observed a greater antioxidant activity in the collagen hydrolysate extract obtained from the skin, which plays an important role in the skin chronological aging and in the inhibitory capacity of the photoaging. The functional properties of tilapia collagen hydrolysate should be the object of future analysis in order to complement this research, before integrating them into the list of food or ingredients applicable to the food industry.

Keywords: Antiaging; Antioxidant; Food; Hydrolysate; Skin.

Resumo
Esta revisão sistemática teve como objetivo listar as propriedades funcionais atribuídas ao colágeno obtido da tilápia em estudos científicos. Os resultados mostraram que a propriedade antioxidante está relacionada à forma como o colágeno se apresenta e ao método de avaliação da atividade antioxidante. Foi observada uma maior atividade antioxidante no extrato hidrolisado de colágeno obtido da pele, que desempenha um papel importante no envelhecimento cronológico da pele e na capacidade inibitória do fotoenvelhecimento. As propriedades funcionais do hidrolisado de colágeno de tilápia devem ser objeto de análises futuras de forma a complementar esta pesquisa, antes de integrá-las à lista de alimentos ou ingredientes aplicáveis à indústria alimentícia.

Palavras-chave: Antienvelhecimento; Antioxidante; Alimentos; Hidrolisado; Pele.

Resumen
Esta revisión sistemática tuvo como objetivo enumerar las propiedades funcionales atribuidas al colágeno obtenido de la tilapia en estudios científicos. Los resultados mostraron que la propiedad antioxidante está relacionada con la forma en que se presenta el colágeno y con el
método de evaluación de la actividad antioxidante. Se observó una mayor actividad antioxidante en el extracto de colágeno hidrolizado obtenido de la piel, que juega un papel importante en el envejecimiento cronológico de la piel y en la capacidad inhibidora del fotoenvejecimiento. Las propiedades funcionales del hidrolizado de colágeno de tilapia deberían ser objeto de análisis futuros para complementar esta investigación, antes de integrarlas en la lista de alimentos o ingredientes aplicables a la industria alimentaria.

**Palabras clave:** Anti-envejecimiento; Antioxidante; Alimento; Hidrolizado; Piel.

1. Introduction

Over the years, consumers have become more concerned with including healthy food in their diet. Their main goal is to improve quality of life, prevent non-transmissible chronic diseases, and even contribute to esthetic condition. Such interest leads to an increase in the demand for foods with functional properties.

Functional foods contain one or more ingredients with a positive effect on health beyond basic nutrition when consumed on a regular basis as part of a diversified diet. One of these ingredients is the collagen, which plays an important role in the structural integrity of the tissue where it is present (Bordignon, 2010).

Collagen, the most abundant protein in mammals, is the main fibrous component of bone, tendon, cartilage, vein, skin, tooth, muscle, and cornea of the eyes (Silva & Penna, 2012). Campos (2008) and Bordignon (2010) stated that collagen is a structural protein, representing nearly 30% of total protein in the animal body. Collagen is made up of three alpha polypeptide chains with over one thousand amino acids organized in a triple-helix structure. This distribution enables several types of bonds and countless practical application in the foods, cosmetic, and pharmaceutic industry.

Silva and Penna (2012) stated that the usage of collagen in foods as a functional ingredient is due to its emulsifying, foaming, colloids stabilizing, biodegradable layer forming, and microencapsulating properties. Moreover, the antioxidant activity of the collagen peptides has been widely demonstrated in several oxidative systems (Gómez-Guillén et al., 2011). It has been observed that the bioactive collagen peptides are able to eliminate free radical, prevent lipid oxidation, act as chelating agents to assist metal transitions, as well as act as antimicrobial, antioxidant, antihypertensive, antiproliferative, antidiabetic, antithrombotic, opioids agonist, anticancerogenic, and anticoagulant agents (Ennaas et al., 2016, Ferraro, Anton & Santé-Lhoutellier, 2016, Kim & Venkatesan, 2014).
There are several organisms from which collagen can be obtained, for example fish. Fish has a significant economic importance because of its high availability, small risk of disease transmission, no religious barrier and toxicity, and the high yielding collagen in the extraction process (Senaratne, Park & Kim, 2006, Krishnamoorthi et al., 2017). In fact, tilapia (Oreochromis sp.) is a fish which has been widely studied for isolation and extraction of collagen.

Tilapia is a large genus of oreochromine cichlids and is widely distributed in tropical and subtropical regions, such as Israel, southeastern Asia, and America (Ramos, Vidotto-Magnoni & Carvalho, 2008). It is largely cultivated due to its fast reproduction and growth rate, excellent adequacy to the production systems, and high palatability (Bordignon, 2010, Fitzsimmons, 2000).

Due to its importance in the fishing process and to the costumers, this systematic review aimed to list the function properties attributed to the collagen obtained from tilapia in scientific studies.

2. Methods

This research followed the principles of a systematic review where the following criteria were considered: definition of the guiding question; the search for evidence in different databases; delimitation of the research period; and the inclusion and exclusion criteria (MENEZES, 2011).

2.1 Criteria for the selection of articles

The guiding question, the databases and the research period.

For the development of this systematic review, we sought to answer the following guiding question: Can Tilapia collagen be considered a food with functional properties?

From this questioning, the search for documents related to the topic in seven databases was used as a collection instrument: PubMed, EMBASE, MEDLINE, LILACS, Web of Science, SCIELO and Science direct. And the research took place in the period between May 1, 2019 and June 30, 2019.
2.2 Inclusion and exclusion criteria

Original articles, published in English and Portuguese, using quantitative instruments were selected. When searching for articles, the following terms in English were used: “collagenoftilapiaandfood” and “collagenotilapiaandfoodandfunctional”, and Boolean operator "and" to refine the data.

As inclusion criteria of the research, full articles were used, published in the last six years (from 2014 to 2019) and that reported some functionality to the Tilapia collagen. And as exclusion criteria, articles that did not mention in the title, abstract or text the subject addressed in this review and the duplicates were removed from the research.

These criteria were identified in the following research stages:

Stage 1: Titles and abstracts were reviewed in order to determine eligibility. Duplicated results and studies that did not meet the inclusion criteria were removed.

Stage 2: Selected studies were fully reviewed. Studies assessing the functional activity of tilapia collagen were selected.

The studies that met all the inclusion criteria discussing the proposed topic were selected and analyzed through a classification protocol created for this study. The following aspects were registered: authors, country, objective, and results.

3. Results and discussion

The search for articles that characterize the functional properties of Tilapia collagen is essential for making decisions related to innovation and helping to map the gaps for the scientific and technological development of this product. According to the criteria established in this study, in the last six years, a total of 387 publications were found, as shown in Figure 1.

The separate search of the term “tilapia collagen and food” retrieved 242 papers. 220 were retrieved using Science Direct and 22 using PubMed. Of these, seven papers met the inclusion criteria and were used in this review. The search of the term “tilapia collagen and food and functional” resulted in 145 studies. 141 were found using Science Direct and 4 using PubMed. Of these, three papers were selected for this review. No articles were found using EMBASE, MEDLINE, LILACS, Web of Science, and SCIELO databases. Therefore, ten studies in total were identified as eligible for inclusion in this systematic review (Figure 1).
Figure 1. Flow diagram for selection of articles considering inclusion and exclusion criteria.

Source: Own authorship (2019).

The studies included were limited by year (2019-2014). Two studies were published in 2019, two in 2018, three in 2017, one in 2016, one in 2015, and one in 2014. Data regarding author, year, country, effect evaluated, and results are listed in Table 1.

Table 1. Overview of the included studies related to the functional properties of collagen obtained from tilapia.

| Study                       | Country | Effect evaluated | Main results                                                                 |
|-----------------------------|---------|------------------|------------------------------------------------------------------------------|
| MEDINA-MEDRANO et al., 2019[12] | Mexico  | Antioxidant capacity of collagen hydrolysate obtained from skin and gills of tilapia. | Higher antioxidant activity for the collagen hydrolysate extract obtained from the skin of tilapia. |
| GÓMEZ et al., 2019[13]      | Colombia| Antioxidant capacity of collagen hydrolysate obtained from the viscera of tilapia | Suppression of intracellular reactive oxygen species accumulation induced by H2O2. |
| Authors                  | Country | Summary                                                                 | Findings                                                                                                                                 |
|-------------------------|---------|-------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| WANG et al., 2018[14]   | China   | Chronological aging of skin capacity using collagen hydrolysate obtained from the skin of tilapia. | Antioxidant capacity, linoleic acid peroxidation, improvement on the color, luster, thickness of hair and reduction of wrinkles formation. |
| QINGYU MA et al., 2018[15] | China   | Inhibitory capacity of photoaging of collagen hydrolysate obtained from the skin of tilapia. | Strong hydroxyl radical scavenging activity, protection of collagen synthesis in under UVB irradiation, oxidative stress inhibition. |
| CHOONPICHARN et al., 2016[16] | India   | Antioxidant capacity of bioactive peptides obtained from the skin of tilapia. | Strong free radical scavenging by the trypsin B fraction.                                                                                   |
| WANG et al., 2017[17]   | China   | Skin antiaging effect with the use of collagen hydrolysate obtained from the skin of tilapia. | Increase in the antioxidant enzymes of the skin, improvement on the color, luster, thickness of hair, improvement on the epidermis structure and distribution of collagen fibers. |
| LEE et al., 2017[18]    | Korea   | Effect of Subcritical water-hydrolyzed fish collagen peptide (SWFCP) of tilapia on the adipogenic differentiation of 3T3-L1 preadipocytes. | Inhibition of lipid accumulation during the adipogenic differentiation of 3T3-L1 preadipocytes; suppression of accumulation of lipid vacuoles in hepatocytes, reduction in adipocytes size; reduction in levels of total cholesterol, triglycerides, low-density lipoprotein; and increase in serum high-density lipoprotein. |
| THUANTHONG et al., 2017[19] | Thailand | ACE-inhibitory activity of collagen hydrolysate peptides obtained from the skin of tilapia. | Low molecular weight ACE-inhibitory peptides.                                                                                               |
| HUANG et al., 2015[20]  | Taiwan  | Extracting bioactive peptides from the structure and the skin of tilapia. | Proteins precursor of antioxidant peptides, peptides with ACE-inhibitory, antithrombotic, and antiamnesic properties.                  |
Several studies point out the antioxidant activity of tilapia collagen obtained from different parts of the animal, such as skin, gills, and viscera. They also demonstrate that the antioxidant property is related to the form in which the collagen is presented (hydrolyzed or not) and to the type of antioxidant activity evaluation (DPPH, ABTS, TAC, and FRAP). For instance, Medina-Medrano et al. (2019) evaluated the antioxidant capacity of the collagen hydrolysate (CH) by pepsin and the non-hydrolyzed collagen from the gills and skin of tilapia using DPPH, ABTS, TAC, and FRAP methods. They observed that the NHC did not present free radical activity, while the HC obtained from the skin had higher extraction yield, free radical scavenging activity, and higher chelation of pro-oxidant metal ions.

Gómez et al. (2019) reported that CH obtained from the viscera of the fish had an antioxidant activity (FRAP, TEAC, ORAC, and CBA). They also observed that, with a degree of hydrolysis (DH) of 42.5%, the low molecular weight of peptides protects Caco-2 cells from oxidative stress induced by hydrogen peroxide (H2O2). Moreover, they reported a decrease in the production of reactive oxygen species (ROS).

The antioxidant capacity of tilapia collagen was also assessed by Liang et al. (2014) in a study with simulated gastrointestinal digestion. They verified that the collagen can be digested almost completely in oligopeptides or amino acids lower surface hydrophobicity. Moreover, collagen could present high antioxidant properties against DPPH radical and linoleic acid peroxidation.

Wang et al. (2017) also assessed collagen activity under simulated gastrointestinal digestion and observed an increase in the collagen content and antioxidant activity in the skin of chronologically aged mice. They observed an improvement in the structure of the epidermis and dermis, density and distribution of collagen fibers and ratio of type I and type III collagen in a dose-dependent fashion. This shows positive influences of collagen matrix homeostasis in chronologically aged mice, since the ratio of type I and type III collagen gradually increases with aging.

Afterwards, it was observed that adding 5% and 10% of CH with the average molecular weight of 624.72 Da presented a protective effect on the chronologically aged skin.
of mice. Moreover, this administration significantly increased the collagen content, improved the color, luster, thickness of hair, prevented the loss of whisker and reduced the formation of wrinkles. Thus, the bioactive peptides of tilapia CH could be developed into new functional foods (Lee et al., 2017).

Huang et al. (2015) stated that the processing co-products from tilapia can be great sources of potential bioactive peptides. After isolation and hydrolysis of structural proteins from tilapia frame and skin using enzyme action tool (papain, bromelain, chymotrypsin C, ficain, pancreatic elastase, and proteinase K), they obtained peptides (mostly from glycoproteins) with ACE-inhibitory, antithrombotic and antiamnesic properties. It was proposed that these peptides could be applicable to food, cosmetic and biomedical industry.

Bioactive peptides vary in size from 2 to 50 amino acids residues and present several biological functions or physiological effects, such as anti-hypertensive, antioxidant, immunomodulatory, antimicrobial, antithrombotic, prebiotic, opioid agonist, among others (Dias, 2010). These peptides are derived from a great number of proteins of bacterial, vegetal, and animal origin, such as milk, soy, chicken, and fish (Wang & De Mejia, 2005).

Choonpicharn et al. (2016) assessed the identification of bioactive peptides from Oreochromis niloticus skin gelatin through trypsin hydrolysis. They identified two peptide sequences, GPEGPAGAR (MW 810.87 Da) and GETGPAGPAGPAGPR (MW 1490.61 Da), with high radical scavenging (TEAC value of 8.156 ± 2.182 μg trolox/mg peptide) and ACE inhibitory (59.325 ± 9.971% inhibition) activities. Moreover, Qingyu Ma et al. (2018) observed that tilapia skin gelatin hydrolysates Leu-Ser-Gly-Tyr-Gly-Pro (LSGYGP) inhibited photoaging induced by ultraviolet B (UVB) in mouse embryonic fibroblasts (MEFs). In addition, it inhibited oxidative stress and regulated matrix metalloproteinase activity.

Furthermore, tilapia collagen peptides proved to be effective in obese mouse in several variables, such as body weight reduction, adipogenesis, inhibition of lipid accumulation during the differentiation of 3T3-L1 preadipocytes, suppression of lipidic accumulation, presence of palmitate in the hepatocytes vacuoles, reduction in total serum cholesterol and low-density lipoprotein, and increase in serum high-density lipoprotein (Doan et al. 2017).

Thuanthong et al. (2017) hydrolyzed (with pepsin and pancreatin) and lyophilized tilapia skin collagen using an enzymatic membrane reactor. They verified the effectiveness in the conversion process of collagen into low molecular weight peptides ACE-inhibitory hydrolysate, which can be used as ingredients in functional foods against moderate hypertension. Moreover, it can be used as a general supplement of peptides to prevent sarcopenia or improve recovery from physical performance.
It is worth noting that there are several evidences supporting the functional properties of collagen and its use for prevention of diseases and/or health promotion. On the other hand, Schadow et al. (2013) stated that, despite the therapeutically useful peptides of the CH, their biomedical properties must be thoroughly examined before being applied as safe and effective nutriceuticals in patients.

4. Final Considerations

The studies analyzed demonstrated that the functional properties of tilapia collagen, both in prevention of diseases and health promotion, rely on its form of presentation (hydrolyzed or not) and the tests system (in vitro or in vivo).

Regarding the clinical trials in vitro for the antioxidant activity, CH affects not only the free radical scavenging activity but also the chelation of pro-oxidant metal ions. On the other hand, non-hydrolyzed collagen presented only free radical scavenging property.

In addition to the oxidative stress protective effect, CH inhibits chronological aging, cardiovascular diseases, thrombosis, amnesia, weight gain, adipogenesis, decreases cholesterol, triglycerides, blood pressure, sarcopenia, and improves physical performance.

Therefore, further study is needed to determine in depth the functional properties of tilapia collagen before embracing its development and application in the food industry.

Further studies are suggested to make it possible to reuse tilapia fillet residues in the preparation of different co-products, such as hydrolysates, which act in health promotion. This will imply, in the environment, a reduction of fillet waste discarded without treatment. To the economic sector, other possibilities of income. To the food sector, the elaboration of co-products with functional properties. And to research, greater knowledge about the hydrolysates of tilapia collagen.

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