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FOOD SCIENCE & TECHNOLOGY | REVIEW ARTICLE

Whey and protein derivatives: Applications in food products development, technological properties and functional effects on child health

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Abstract: Whey is an industrial by-product with high nutritional value and an extensive use in food products. This study aimed to show some applications of whey and its proteins in food and discuss their effects on child health. The choice of works from the last 10 years was based on the search in databases using relevant descriptors. Few studies were found, a fact that turns this issue into an original one for the development of scientific hypothesis about the functional capability of dairy products. Literature showed that whey proteins enhance various food characteristics sensory. However, the benefits of these proteins in health promotion and prevention of chronic diseases, including the childhood, are controversial. The beneficial actions of these proteins are associated with their high bioavailability of calcium and especially the presence of bioactive peptides, which may modulate allergy and metabolic complications in children. On the other hand, some studies report that infant formulas that have high content of whey proteins are rich in leucine, which would contribute to the early onset of obesity. This review highlighted the need to carry out a greater number of studies in order to elucidate the consequences of the consumption of these proteins on child health.

Subjects: Food Science & Technology; Engineering & Technology; Health and Social Care

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I am from Belo Horizonte, State of Minas Gerais, Brazil. I hold a bachelor's degree in Nutrition in 2006 at UFV, a master's degree in Food Science in 2010 and a PhD in Health Sciences in 2015 at UFMG. At work, I have applied the theory to perform many activities in teaching and researching on clinical nutrition and food science. I want to work with both areas, linking food technology, nutrition, and gut barrier. I am sure that I can contribute extensively worldwide as a researcher, as well as a Nutritionist, because I really like my work and I want to be an expert on gut microbiota and metabolic diseases. At the moment, I am a postdoctoral fellow on Healthy Aging at UFMG focused on immunological factors and gut microbiota during the aging process.

PUBLIC INTEREST STATEMENT

This work was based on the necessity to explain the importance and the applications of whey and protein derivates in food products, besides the benefits on child health, because few studies have evaluated the impacts of their consume on this stage of life. When we eat food containing these ingredients, they release smaller molecules called peptides that can control society, weight, body composition and inflammatory factors related to chronic diseases such as obesity, diabetes, hypertension, high blood cholesterol and even cancer. Also these proteins can rise protein synthesis and recovery of athletes after training and competition and reduce the loss of lean mass in elderly people. On the other hand, whey proteins improve sensory characteristics of food which are the result of their technological properties. Thus, the science shows that we need to study more about the positive effects to add that in food for children with safety.

Keywords: functional food; childhood; novel products; dairy products; whey proteins

1. Introduction

Milk production and processing of dairy products in Brazil has great economic importance and its magnitude can be exemplified by the production of cheese, which corresponded to 896000 (or 896.000) tons in 2010 and it resulted in the production of approximately eight billion liters of whey (Alves et al., 2014; Soares, Fai, Oliveira, Pires, & Stamford, 2011).

Whey constitutes a by-product of cheese manufacturing process, which has in its composition 55% of milk nutrients, including soluble proteins, lactose, vitamins, minerals and traces of fat (Alves et al., 2014; Soares et al., 2011). Despite its significant nutritional value, it is still often discarded in the environment, what causes extensive damage deriving from its high content of organic matter. The increasing number in environmental inspections has reduced the whey disposal in the environment by the dairy industry. However, this inappropriate procedure continues to occur (Alves et al., 2014).

In addition to the strict environmental law, several studies have described the likely functional properties of whey, which presents high biological value (HBV) proteins, that are represented especially by β-lactoglobulin (about 55%) and α-lactalbumin (about 25%) fractions. Bovine serum albumin (BSA), immunoglobulins, and lactoferrin are smaller fractions of globular proteins found in whey too (Alves et al., 2014). Whey also contains components which are attributed some important biological activities, with emphasis on stimulation of immune response, cancer, and cardiovascular disease prevention, among others (Alves et al., 2014; Poppi, Costa, Rensis, & Sivieri, 2010).

According to Alves et al. (2014), whey concentration results in products rich in protein that can be used as ingredients with the aim of improving the technological properties of food, such as solubility, gelling, viscosity, emulsification, and foaming.

Thus, the whey can be widely used in food production, with huge environmental, nutritional, and industrial relevance (Alves et al., 2014), and it has a remarkable potential in the development of functional foods for children. It is noteworthy that few studies that have addressed the development of food products with whey protein, specific to this public, or evaluating their effects on children's health as a whole, were found.

2. Objective

This review aimed to perform a detailed bibliographical survey in databases, with the selection of scientific papers published in journals of Food Science and Nutrition, from the last 10 years, on the main technological applications of whey and its proteins in food products and the possible functional aspects associated with human health and, in particular, child health.

3. Method

The literature search was conducted in the following databases: SciELO, PubMed, Science Direct, and *Periódicos Capes*. The search was conducted with the association between the descriptors in Health Sciences (DeCS) "milk proteins," "cow's milk," "whey," "food production," "dairy," "functional foods" and "child health" in Portuguese, in Spanish and in English. Among the scientific papers found, 32 were chosen to contemplate these descriptors. The search was run from 2005 to 2015. Two resolutions that were published before the time that this review was carried out were mentioned because they are the latest Brazilian resolutions on this topic, totaling 34 citations. After searching and careful selection of the articles, reading and critical discussion were executed.

4. Review

4.1. Technological properties of whey and its protein derivatives in food

Whey is a by-product of cheese making by coagulation of casein. It is obtained through lactic acid bacteria fermentation or directly acid adding to milk (acid whey with isoelectric precipitation of casein) or by enzyme action (sweet whey) (Baldissera, Betta, Penna, & Lindner, 2011; Poppi et al., 2010). This milk derivative has a chemical composition about 93–94% water, 4.5–5.0% lactose, 0.7–0.9% soluble protein, 0.6–1.0% mineral salts and appreciable amounts of vitamins B (Baldissera et al., 2011; Poppi et al., 2010).

Despite being a great source of nutrients, the use of *in natura* whey is limited due to the perishable nature characteristics and the high dilution of its components. Therefore, various processing technologies have been applied in order to add value to this raw product. Whey can be concentrated by processes involving the fluid whey heating and drying (evaporation “spray-dryer” and lyophilization) or by reverse osmosis, while the demineralization can be made by ion exchange resins or electrodialysis (Baldissera et al., 2011; Poppi et al., 2010).

To obtain protein ingredients, membrane separation technologies are commonly employed (ultrafiltration, microfiltration, and diafiltration). The greatest advantage of these separation technologies compared with physicochemical processes is that they are smooth thermally and purely mechanical, in which proteins retain their native structure and consequently its technological and nutritional properties (Baldissera et al., 2011; Poppi et al., 2010).

After proper processing of the fluid whey, many products can be obtained, such as dry sweet whey (DSW); demineralized delactosed whey (DLMW); refined lactose; whey protein concentrate (WPC) with a protein content ranging from 35 to 80%; whey protein isolate (WPI) containing over 90% protein, and whey protein hydrolysate (WPH) (Baldissera et al., 2011; Poppi et al., 2010). Thus, whey demonstrates versatility and a wide application in the food industry as fluid or in the powder aspect, as WPC, WPI, or WPH, representing a rational alternative use of this residue with an excellent nutritional value (Poppi et al., 2010; Vidigal, Minim, Berger, Ramos, & Minim, 2012).

Among those whey derivatives, WPC stands and performs important technological properties in various food products: beverages, desserts, sauces, soups, coffee creams, toppings, meringues, infant food, pasta products, dairy, meat and baking. Thus, in the gelling, this action is associated to its good ability to adsorb water; in the viscosity, for its high solubility in a wide pH range, especially under acidic conditions; in the emulsification, the presence of hydrophilic and hydrophobic regions on its chemical structure; in the foaming and the foam stabilization and in the increasing of the nutritional value of these products, due to its HBV protein content be very significant (Alves et al., 2014; Vidigal et al., 2012; Walczyk et al., 2014).

As can be seen above, the literature has shown the development of many types of food using whey to improve nutritional and sensory characteristics. In Table 1, there are some examples of technological properties imparted to foods by WPC.

Technological functions performed by the whey proteins are associated with their composition, concentration and degree of denaturation. These characteristics were detected by a study conducted with a diet milk dessert. It demonstrated improved firmness, cut resistance, consistency and gumminess attributes with increasing concentration of WPC (Vidigal et al., 2012). The higher the protein content, the more evident are the above aspects, since change occurs in the texture of the gels resulting in an increased firmness and enhancing the retention of water by the matrix. This behavior is attributed mainly to the ß-lactoglobulin, considered a gel-forming agent due to the presence of free sulfhydryl groups. Therefore, the greater the amount of WPC used, the greater the force required to break the gel structure (Vidigal et al., 2012; Walczyk et al., 2014).

Table 1. Examples of technological properties imparted to foods by WPC*

Technological property	Food sector	Protein percentage (%)	Applications
Viscosity	Desserts	35	Chocolate, marshmallow, nougat, cereal bars and frosting.
Solubility and coloidal stability	Beverages	35	Beverages fortified with protein, isotonic drinks, piña colada, carbonated drinks, carbonated teas, and beverages for children, juices, yogurts and meal replacement drinks.
Emulsification	Soup and infant food	85	Low or fat free soup, salad dressing and processed cheese.
Foaming	Confectionery	35	Frosting, milk cream UHT (*Ultra High Temperature*), chantilly and aerated chocolate.
Gelling	Dairy	65	Yogurt, frozen yogurt and ice cream.
Elasticity	Bakery	65	Brownie, cake, cookies, bread, muffins, dough for pizza, cracker and waffles.
Absorption of water and fat	Meat products	85	Sausage, hamburger steak, ham, nuggets and other meat products.

*WPC = whey protein concentrate.
Source: Adapted from Alves et al. (2014).

In recent decades, the application of WPC in food products has grown largely due to the interest in developing low-fat or fat-free products. It is known that these products have some problems regarding the acceptance, once the reduction of fat interferes adversely on the texture, appearance, flavor and aroma. In this sense, the use of WPC as a fat substitute could be an interesting option for keeping the sensory properties of these products, making them more attractive to consumers (Vidigal et al., 2012).

In addition to preserving the product texture, the use of WPC aids in flavor retention. The bonds between the aromatic components and proteins are generally mild and reversible, as Van der Waals force, hydrogen bonds and hydrophobic interactions. However, they are in great number in the food matrix, what allows greater flavor incorporation in the product (Vidigal et al., 2012). Thus, numerous advantages are reported when using whey protein-based ingredients in food products, such as easy association to aromatic components, moisture maintenance and promotion of the creaminess sensation, enhancing the sensory characteristics of this food (Gurgel, Maciel, & Farias, 2010; Vidigal et al., 2012).

Another way to take advantage of the whey utilization corresponds to its addition in a powdered form to food products, as milk substitute in order to strengthen and to contribute to the micronutrients supply, such as calcium, which is essential in certain stages of life, specifically in childhood (Baldissera et al., 2011). Powdered whey offers economic advantages, but its concentration as a bread ingredient, for example, it is not more than 7.5%, being insufficient to classify this type of product as a calcium food source. This problem can be solved by adding calcium salts in complementary amounts (Gurgel et al., 2010).

Bread is a kind of food that has high-frequency consumption in different populations. A research has observed that with the addition of powdered whey and calcium carbonate in the loaf of bread, it was possible to classify the final product as a protein food source and it was also possible to obtain a calcium-rich product (it had reached 78% of the nutritional recommendations for adults), with good sensory acceptance and purchase intention. The authors mentioned that this product would have significant role for people who do not have access to the main sources of calcium (dairy products). It would also contribute to a better dietary adequacy of this mineral in children, since in this age group the low calcium intake may compromise the genetically pre-determined growth of the peak bone mass, predisposing to osteoporosis, to a later risk of bone fractures and a variety of metabolic complications resulting from chronic non-communicable diseases (CNCDs) (Gurgel et al., 2010).

For this reason, whey proteins exhibit essential technological properties and in general their introduction in food products is well accepted by consumers (Gurgel et al., 2010; Vidigal et al., 2012). This information was confirmed in another study (Gurgel et al., 2010), in which the consumption of yogurt enriched with whey protein showed good acceptance among consumers. These researchers also stated that whey proteins have large applicability for use in food and may be considered a viable strategy to increase the supply of good quality protein in the diet and sustain the protein levels in the human organism (Muza, Peres, & Degáspari, 2014).

4.2. Biological and nutritional functions of whey proteins

Although the exact composition of bovine milk oscillates in response to factors such as the animal nutrition and the stage of lactation, this food is composed of approximately 87% water, 5% lactose, 3% protein, 4% fat and 0.7% mineral salts. Among the minerals, milk contains high amount of phosphorus, potassium, magnesium and calcium, and a small content of vitamin D (Issa et al., 2014; Mezzomo & Nadal, 2014).

Fluid whey, originating from bovine milk, carries about 50% of the nutrients and 20% of milk protein content, which corresponds on average from 4 to 7 g protein/L. The main proteins in whey are β-lactoglobulin (3.7 g/L), the α-lactalbumin (0.6 g/L), BSA (0.3 g/L) and proteose-peptone fraction (1.4 g/L). Minor whey proteins include, for example, lactoferrins, immunoglobulins, ceruloplasmins and some enzymes (lysozyme, lipase and xanthine oxidase). On the other hand, in human milk, casein (2.5 g/L) corresponds to only 20% of the total nitrogen, whereas the other 70% consists of α-lactalbumin, lactoferrin, lysozyme, gamma globulin and serum albumin (Alves et al., 2014; Muza et al., 2014).

Whey proteins are considered to be a rich source of essential amino acids, especially the branched chain ones (BCAA—leucine, isoleucine and valine). Furthermore, whey proteins digestion and absorption are faster compared to any other type of protein. Its amino-acid profile is very similar to the muscle proteins, offering almost all amino acids in similar proportions (Muza et al., 2014).

Thus, supplementation with whey proteins is a beneficial way to increase the daily protein intake because these proteins exhibit compact globular conformation. This characteristic gives them their own biological properties, what corroborates the fact that the BCAA can minimize the loss of muscle protein under catabolism conditions. The process is explained by the fact that after consumption, these amino acids are quickly released into the bloodstream and, in high concentrations in the blood, they stimulate protein synthesis (Shah, 2014).

Whey proteins are present in milk products, which still have high bioavailability of calcium related to the vitamin D content and the presence of lactose, two factors that increase the intestinal absorption of calcium. The high bioavailability of the mineral is also due to bioactive peptides released during gastrointestinal digestion of milk proteins, especially casein phosphopeptide, which have binding sites with divalent minerals (Ca, Mg, and Fe) and trace elements (Zn, Ba, Cr, Ni, Co and Se). In addition, the bioactive peptides derived from the hydrolysis of whey protein contain about 3 to 20 amino acids and may exhibit opioid, antimicrobial, antithrombotic, immunomodulatory, citomodulatory and antihypertensive activities, as well as modulate the mood and the intestinal microbiota, exerting action in defense against infections, allergies and atopic dermatitis children fed with infant formula (Chung, Yamini, & Trumbom, 2012; Mezzomo & Nadal, 2014; Raikos & Dassios, 2014).

Bioactive peptides derived from whey proteins can also be generated during food processing. Enzymatic hydrolysis is a common method for the production of peptide fragments used in hypoallergenic infant formulas (Chung et al., 2012; Raikos & Dassios, 2014). Although the physiological mechanisms are simulated *in vitro, in vivo* conditions are very complex and require more research with animals and humans to determine under what conditions the peptides exert their bioactivity (Raikos & Dassios, 2014; Shah, 2014). Bioactive peptides were reported for the first time in 1950 and, since then, it has aroused great interest among researchers about their presence in milk and dairy products, as well as their health effects (Raikos & Dassios, 2014; Shah, 2014).

Therefore, according to the scientific literature, dairy and their derived products are the richest source with regard to the provision of a range of nutrients and potentially functional components, mostly coming from the whey proteins.

4.3. Dairy and whey proteins: applications in food products development and functional potential related to child health

The formation of dietary habits is a complex action influenced by many variables. Because of this, ongoing researches have aimed to add benefits to products that are part of the consumer food routine. Development of new products is also considered very important, once the diet-health relationship is a challenge for science and food technology, especially when it concerns functional foods (Baldissera et al., 2011; Soares et al., 2011).

Functional foods are those that ensure adequate nutritional effects and additional benefits in one or more body functions, improving the health, the well-being or reducing the risks of diseases (Baldissera et al., 2011; Shah, 2014). According to the Brazilian law, established by *Agência Nacional* de *Vigilância Sanitária* (ANVISA), the functional property allegation is the one related to the metabolic or physiological role of the nutrient or non-nutrient on growth, development, maintenance and other normal functions of the human body. It is not allowed any indication that refers to the cure or diseases prevention (Brasil, 1999a, 1999b). There is also the health claim property, which states, suggests or implies the existence of relationship between the food or ingredient with disease or health-related condition (Brasil, 1999a, 1999b).

Even with the progressive increase in popularity of functional foods, no universal definition for the category has been developed. However, a food can be considered functional if it satisfactorily demonstrates one or more beneficial effects on target functions in the body consumer/patient, beyond adequate nutritional effects. Beneficial effects could be authorized for use as functional foods claims based on the increase of an effect (type A claim) or reduction of risk of disease (type B claim) (Baldissera et al., 2011).

ANVISA defines functional foods as “all that food or ingredient that, beyond basic nutritional functions, when consumed as part of the usual diet, produces metabolic and/or physiological and/or beneficial health effects and should be safe for consumption without medical supervision” (Brasil, 1999a, 1999b).

Hence, regarding healthy diet, attention has been focused on functional foods, which are assigned metabolic or physiological effects on physical and mental health. These effects could help to reduce the risk of non-communicable diseases and disorders (NCDs) (Shah, 2014). In this context, it is essential the production of new potentially functional foods for specific groups and the study of their benefits effects in human body.

One of the most prosperous segments of the current market is the functional ready to drink beverage. Through this perspective, dairy products, nutritionally complete food containing bioactive substances, could be improved to meet the growing demand for a specific public: consumers of functional dairy. Among those ingredients with proven functional properties in the dairy sector, can be highlighted the polyunsaturated fatty acids, carotenoids, dietary fiber, phytosterols and especially probiotics (Baldissera et al., 2011).

Milk-based and whey-based drinks, which attest health benefits, as demonstrated by market analysis, account for over 70% of global launches in functional foods. Satiety-enhancing and weight management products, with the protein supplementation purpose, besides those for athletes, have been widely studied and they are equivalent to 20% of the market (Baldissera et al., 2011).

However, in the domestic market there are no options of beverage ready to drink, containing only whey protein as a protein source, and offering for the child public. Recently, a study conducted in Brazil, in the city of Belo Horizonte, State of Minas Gerais, developed a chocolate drink with WPC as the only protein source, for children aged 7 to 10 years. The food product prepared in laboratory scale showed appropriate physical and chemical characteristics and good acceptance among adult judges (Batista et al., 2015). In another phase, the beverage was adapted to follow industrial route with modifications in its chemical composition. The product remained nutritionally balanced, then, it was produced on a pilot scale and examined sensorially by children. It presented excellent results for the acceptance and final chemical composition (unpublished data).

Development of functional foods becomes even more relevant in the face of population surveys, which evidence the close relationship among inadequate dietary habits and lifestyle with obesity and its comorbidities (hypertension, type 2 diabetes mellitus, coronary artery disease and cancer) a global public health issue. In the last decade, it was also observed, the link between childhood obesity and poor quality of life in adulthood (Brasil, 2010).

It is known that the role of food experiences during childhood is crucial for the formation of eating behaviors adopted by individuals. School environment is a place that allows the contact, the construction and the consolidation of healthy eating habits. In addition, the school has to spread good practice in order to control and prevent nutritional deficiencies, child malnutrition and CNCD (Issa et al., 2014).

Proper nutrition is the factor with the greatest impact on children's health, once nutritional status directly influences growth, development and the risks of morbidity and mortality (Issa et al., 2014; Mezzomo & Nadal, 2014). In this context, dairy products emerge, which contribute 47% of calcium intake in the US population. In the Netherlands, 73% of children's calcium intake comes from dairy products (Mezzomo & Nadal, 2014). The consumption of these products contribute about 50% of the calcium daily requirement worldwide and collaborate with bone health and the healthy growth of children over two years old (Mezzomo & Nadal, 2014).

In Brazil, several nutritional inadequacies can be highlighted in the current menu of children and teenagers, especially those associated to calcium and vitamin D intake (Issa et al., 2014). Both at national and global level, the whey components, especially proteins, are emerging as dairy ingredients with high nutritional value that could be used in the development of functional foods (Mezzomo & Nadal, 2014).

Other results presented by population surveys reinforce the urgency of the whey protein inclusion in infant feeding. In Brazil, according to the *Pesquisa* de *Orçamentos Familiares* (POF 2008–2009), milk consumption is proportional to the familiar income. Comparing the highest and lowest income range, dairy products in Brazilian homes are three times upper in higher income families. It is suggested that individuals with higher education make better food choices for their consumption. However, in Brazil, the illiteracy rate is still high (11.4%), when considering the rate of only 1% in the US, UK and Germany. This demonstrates the inability of a part of the population to make appropriate food choices (Brasil, 2010; Mezzomo & Nadal, 2014).

According to the data mentioned above, educating and assisting the population in food choices are extremely effective strategies to stimulate the choice of new and healthier food in the diet. It emphasizes the need for such measures, showing how milk and dairy products consumption is necessary, because they are classified as a type of food with high functional potentiality, once they are composed by: whey proteins and their bioactive peptides, probiotic bacteria, antioxidants, high calcium bioavailability, conjugated linoleic acid and other biologically active compounds that may prevent various diseases in childhood (Brasil, 2010; Mezzomo & Nadal, 2014).

Regarding to its functional properties, whey proteins play an immunomodulatory role for their high concentration of IgG and IgA immunoglobulins, and cysteine, the amino acid responsible for increasing the production of glutathione. Glutathione is the centerpiece of the body antioxidant system, preventing oxidative stress and cellular aging. Thus, the whey protein acts on the immune system through stimulating the lymphocyte production of antibodies (Shah, 2014). Their immunomodulating and antimicrobial properties are related to the stimulation of immune cells of the immune system and the proliferation of protective microflora in the animals and humans gastrointestinal tract (Raikos & Dassios, 2014), showing the possible role of whey protein in strengthening the immunity in children.

Whey bioactive peptides also have mineral binding property and the regulation of intestinal microbiota encourages the mineral absorption by digestive tract (Raikos & Dassios, 2014), what can be checked in infant beverages fortified with iron and calcium and containing whey proteins in their composition. In this case, peptides promote smaller inhibitory effect of calcium on iron absorption and act synergistically with ascorbic acid when it is added, amplifying the iron bioavailability (Walczyk et al., 2014).

Opioid peptides are small molecules synthesized *in vivo* that act as hormones and neurotransmitters in the nervous system. These peptides are generated during whey protein hydrolysis but the mechanism of action in the human body (Raikos & Dassios, 2014) and, consequently in the children's health, is not fully elucidated.

When it concerns the prevention of childhood diseases, the consumption of high amounts of dairy products, especially those with low-fat and containing whey proteins, can prevent insulin resistance, precursor of type 2 diabetes. Other studies associate these products with weight and blood pressure control due to greater satiety stimulus, reducing the incidence of coronary diseases and dental caries in children (Shah, 2014).

More fully described, the effects on the cardiovascular system may include reduction on blood pressure, through the release of peptide inhibitors of angiotensin-converting enzyme (ACE), proven in *in vitro* mechanism (Morais et al., 2014; Raikos & Dassios, 2014; Silva et al., 2014). A review article also highlighted that infant formulas based on enzymatically hydrolyzed whey proteins exhibit greater ACE inhibitory effect in relation to those not hydrolyzed formulas. Low molecular weight peptides (< 3,000 Da) are the main responsible for this activity (Raikos & Dassios, 2014). Thus, the size of the hydrolyzed fragments could be critical in terms of antihypertensive activity, since di- and tripeptides are readily absorbed in the intestine and reach the blood and other target sites quickly (Morais et al., 2014; Raikos & Dassios, 2014; Silva et al., 2014).

Whey proteins antioxidant property is also well documented and it can be beneficial *in situ*ations that predispose to oxidative stress, as occurs in preterm neonates and in CNCD (Raikos & Dassios, 2014; Silvestre, Morais, Silva, & Silva, 2013). This activity is due to the high content of sulfur-containing amino acids such as cysteine and methionine, which are incorporated into enzymes and other antioxidants systems of the organism (Shah, 2014) and it could be associated with amelioration of inflammation and oxidative stress reported by researches with premature infants and/or chronic disorders.

In relation to CNDC, besides antioxidant property, whey proteins have gained popularity and literature has emphasized the role of these bioactive peptides in the regulation of food intake,

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Table 2. Main components and actions of whey proteins

Components	Actions
β-lactoglobulin (45–57%)	It has a high content of branched chain amino acids (~ 25.1%). It binds hydrophobic molecules, participating in the reduction of intestinal absorption of lipids.
α-lactalbumin (15–25%)	It has the highest tryptophan content (6%) of all dietary proteins. It is rich in lysine, leucine, threonine and cysteine. It has the ability to bind minerals such as Ca and Zn, positively affecting their absorption.
Immunoglobulin (10–15%)	Four classes of immunoglobulins are present in whey: IgG, IgA, IgM, and IgE. Their functions are antioxidant protection and increased immunity.
Lactoferrin (~ 1%)	It inhibits the production of proinflammatory cytokines and it protects against hepatitis development.
Lactoperoxidase (< 1%)	It plays antimicrobial properties.
Glycomacropeptide (10–15%)	It is form from the digestion of κ-casein during cheese making. It contains high content of essential amino acids that facilitate minerals absorption.
Bovine serum albumin (BSA)	This protein fraction has good amino-acid profile and lipid binding property.

Source: Adapted from Sousa et al. (2012).

increasing the satiety and therefore in weight control and modulation of the body composition in animals and adult humans. According to the review work of Sousa et al. (2012), studies have suggested that whey proteins may assist in the management of type 2 diabetes by lowering blood glucose in healthy subjects; improve glucose tolerance in diabetic and obese patients; reduce body weight; maintain lean mass; increase the release of anorectic hormones such as cholecystokinin, leptin and GLP-1 (glucagon-like peptide-1) and decrease orexigenic hormone as ghrelin. In children, these effects are not fully elucidated, but we consider that these peptides, along with its antioxidant role, modulate the inflammatory and oxidative parameters, key elements that trigger these diseases (Raikos & Dassios, 2014). So, it is possible to check the most important whey proteins fractions and their functions which are simplified in Table 2.

Dietary proteins seem to induce weight loss and whey proteins are known to be insulinotropic, once they can stimulate the insulin synthesis and release, in adults. On the other hand, in children, the interaction between the energy and macronutrients intake and physiological factors regulating this process and also the satiety in short time has still been little reported (Bellissimo et al., 2008). A clinical trial conducted with children and adolescents aged 9–14 years had evaluated the effects of the consumption of a beverage containing carbohydrate and another containing isolated whey protein. It showed that the intake is affected by diet composition, the time until the next meal and boy's body fat. The main result was that whey protein suppressed food intake in normal weight boys, but not in obese boys. Therefore, this study suggested that the satiety signals coming from protein, but not from carbohydrates, are reduced in obese children. These data are relevant and can guide the physiological basis for the formulation of diets and snacks which aim to maximize satiety signals in a short period of time and monitor the children weight (Socha et al., 2011).

One issue that has already been discussed refers to the fact that the ingestion of high amounts of milk protein derived from infant formulas during the first year of life, can induce excessive weight gain in early childhood (Socha et al., 2011). Infant formulas are developed according to the composition of breast milk, but as the main ingredients of these formulas are milk and dairy products, they usually contain more whey proteins in their composition and high leucine content, an amino acid that stimulates cell growth factors, specifically the mTORC1 (mammalian target of rapamycin complex 1). Compared to the breastfeeding, infant formulas containing whey proteins express excessive leucine levels, which increase thereby the release of insulin and IGF-1 (insulin-like growth factor 1), explaining the immature and exaggerated adipogenic schedule dependent of the mTORC1, which represents the trigger of the early childhood obesity (Melnik, 2012; Melnik, John, & Schmitz, 2015).

Adjustment of the leucine content to breast milk physiological levels, in infant formulas, may indicate a promising new chance for preventing adipogenic programming and the epidemic of childhood obesity (Melnik, 2012; Melnik et al., 2015). Also, in overweight adolescents, consumption of large amounts of non-fat milk, whey protein and casein raised the body mass index (BMI) for age and the C-reactive protein concentration, an important inflammation marker. Whey proteins and casein further exacerbated insulin release (Arnberg et al., 2012), transmitting to the juvenile body an insulinotropic response too.

Moreover, experimental study in mice demonstrated that whey proteins attenuate the metabolic risk in animals treated with high-fat diet (Shertzer, Woods, Krishan, Genter, & Pearson, 2011). This hypothesis was also supported in a review article that proposed, according to experimental and observational epidemiological studies, that the yogurt and dairy products consumption may be associated with the improvement of diverse characteristics of the metabolic syndrome, such as insulin resistance, high blood pressure, dyslipidemia and abdominal obesity (Astrup, 2014). These foods are also linked to lower risk of weight gain and obesity, as well as cardiovascular disease development, due to the decrease of parameters such as LDL cholesterol and triglycerides, among others, attributed to calcium and other bioactive components (Astrup, 2014; Marette & Picard-Deland, 2014; Tremblay, Doyon, & Sanchez, 2015). Recent researches confirm the positive findings, since demonstrated that WPI ingestion reduced weight gain, plasma cholesterol and glucose intolerance and improved insulin sensitivity in C57BL/6J mice fed a high-fat diet (McAllan et al., 2013; Tranberg et al., 2013), through modulating the energy intake and the expression of hypothalamic and adipose tissue genes related to the energy balance (McAllan et al., 2013), as well as the intestinal microbiota (McAllan et al., 2014).

In this scenario, the yogurt is an eclectic dairy food, since it combines the benefits of whey protein to its quick absorption, low fat content and easy digestibility, representing a substantial source of protein, calcium, phosphorus, vitamins and carbohydrates (Arnberg et al., 2012; Astrup, 2014; Gurgel et al., 2010). However, the effect of whey proteins in child health remains inconclusive because the literature also shows the relationship between the consumption of cow's milk and the occurrence of anemia, food allergies and type 2 diabetes among children (Mezzomo & Nadal, 2014). Some general mechanisms were described and show how whey proteins may act preventing metabolic diseases (Figure 1).

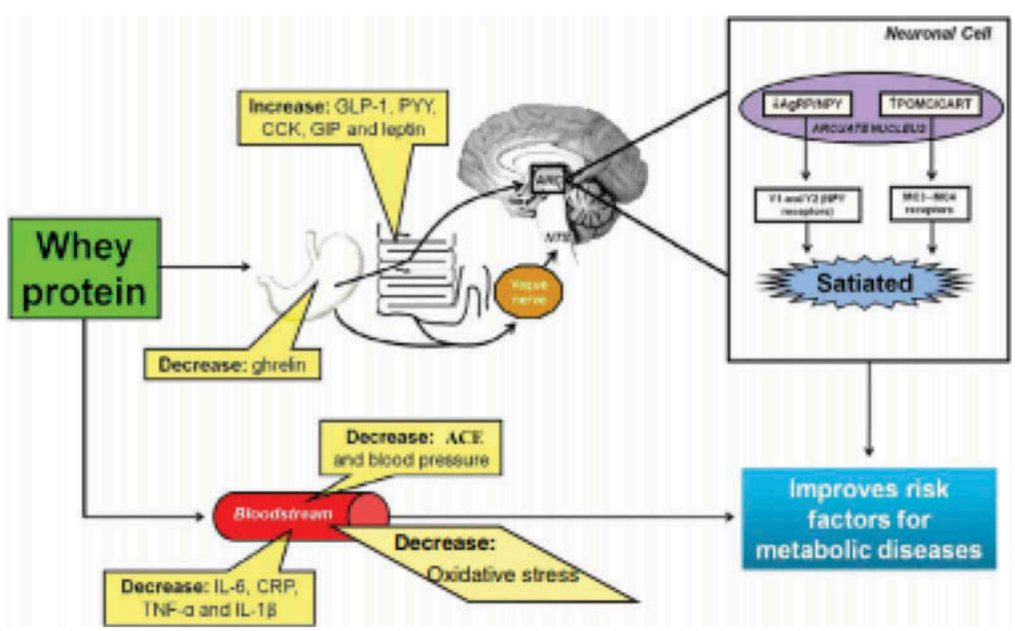

Figure 1. Mechanisms of action of whey proteins on reducing risk factors for metabolic diseases, such as obesity, type 2 diabetes mellitus, hypertension, oxidative stress and metabolic syndrome.

ACE, angiotensin-converting enzyme; AgRP, agouti-related protein; CCK, cholecystokinin; CRP, C-reactive protein; IL-6, interleukin-6; *GIP*, gastric inhibitory polypeptide; GLP-1, glucagon-like peptide-1; *GIP*, gastric inhibitory polypeptide; NPY, neuropeptide Y; POMC, proopiomelanocortin; PYY, peptide YY. **Source**: Adapted from Sousa et al. (2012).

In sum, research on this population group, with emphasis on schoolchild, is still being carried out on a small scale, limiting to arrive at concrete scientific evidence about the effective actions of the whey proteins in the health of individuals in childhood.

5. Conclusions

Whey proteins have numerous nutritional benefits and food technological applications. Positive factors and potential health benefits are clear and mostly determined *in vitro*. However, the optimal physiological conditions for the performance of their bioactive peptides *in vivo* remain unclear, especially in the human body.

Thus, further studies should be conducted in order to associate the whey proteins properties with child health. Some of these studies could involve the development of new food products containing these proteins, for health promotion and disease prevention at early ages. Besides, aiming to elucidate the effects of whey proteins on the health of this population group, clinical trials in children should also be performed, since the controversies about the mechanisms of action in the NCD are due to the lack of studies that discuss the purpose of this review manuscript.

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