Nutritional and Functional Importance of Whey Protein in Human Health and Food Applications

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Abstract

Background: Whey protein, a by-product of cheese and casein production, has gained recognition for its nutritional and functional properties. It contains proteins such as β-lactoglobulin and α-lactalbumin, contributing to its use in sports nutrition, weight management, and health supplements. Recent studies have expanded its applications to probiotic development and metabolic health improvements. Methods: This review consolidates findings from key studies on the structural and functional aspects of whey protein. Research focused on its composition, biological activities, and its impact on industrial applications like fermentation and food processing. Results: Whey protein, particularly β-lactoglobulin and α-lactalbumin, has shown positive effects on weight loss, muscle preservation, and metabolic regulation. Studies highlighted its antioxidant and anticancer properties, alongside its potential to enhance probiotic viability. Whey protein supplementation in overweight individuals also improved lipid profiles and insulin sensitivity. Conclusion: Whey protein's versatility extends beyond traditional uses, showing promise in metabolic health, food manufacturing, and probiotic development. Its bioactive properties underscore its importance in both nutritional and industrial applications, warranting further research for optimized health benefits.

Keywords: Whey protein, β-lactoglobulin, α-lactalbumin, Nutrition, Antioxidant properties

Significance | This review discusses the whey protein's role in weight management, protein synthesis, and potential applications in food and health industries.

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Introduction

Whey protein, a by-product of cheese or casein production, has gained widespread recognition due to its diverse applications and high nutritional value. It accounts for approximately 20% of the total protein content in bovine milk and is composed of various proteins, including β-lactoglobulin, α-lactalbumin, serum albumin, immunoglobulins, and proteose peptones (Creamer, 1996). Whey protein's utility spans across multiple industries due to its functional and biological properties, contributing significantly to sectors such as sports nutrition, weight management, food manufacturing, and medical nutrition.

Three main types of whey protein concentrate, isolate, and hydrolysate differ in their compositions and processing methods, providing tailored benefits depending on the application (Qi et al., 1997). β-Lactoglobulin, the major component, comprises 54% of whey proteins and plays a crucial role in milk protein allergies, as well as having a strong interaction with calcium and other ions, which influences its behavior under different environmental conditions (Wong et al., 1996). Other whey protein constituents like α-lactalbumin have been identified as crucial in lactose synthesis and exhibit diverse structural forms based on their calcium-binding properties (Creamer & MacGibbon, 1996). In recent decades, the application of whey proteins has expanded beyond traditional uses to areas such as fermentation, probiotic

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enhancement, and functional foods. Studies have shown their role in metabolic improvements, appetite control, and obesity management (Bowen et al., 2018). The industrial significance of whey proteins is further underscored by their application in dairy probiotics, fermentation processes, and as carriers of probiotics in functional foods (Pereira et al., 2018). Additionally, they exhibit potent biological activities, such as antioxidative and antimicrobial properties, which have found application in health-related sectors (Petit, 2010).

Given the rapid advancements in understanding whey proteins' structural properties and their impact on health and industrial applications, this review aims to consolidate the latest findings on whey proteins, focusing on their compositional, functional, and application-related aspects.

Whey protein

Whey protein is the liquid remaining after milk has been curdled, filtered and strained. It is a by-product of the manufacture of cheese or casein and has several commercial uses. There are 3 types of whey protein on basis of their compositions; Whey protein concentration, Whey protein isolate and Whey protein hydrolysate. Types of whey proteins are shown in Table1.

In milk, there are two major protein types which in bovine milk are defined by acid precipitation: the caseins, which precipitate as a group at pH 4.6, and the whey proteins, which can be subdivided into the major mammary synthesized proteins and the minor, usually blood, proteins. Each of the mammary-synthesized proteins exists in several forms, known as genetic variants, which have slightly different amino acid sequences (Creamer, 1996). Whey proteins are: β-lactoglobulin (β-Lg), α-lactalbumin (α-La), lesser amounts of serum albumin, immunoglobulins, and proteose peptones. Whey proteins give 20% of total protein content in bovine milk. They are globular and are present in milk as discrete molecules with varying numbers of disulfide crosslinks. These proteins are more heat sensitive, and less sensitive to calcium than caseins. They can form disulfide linked dimers or polymers via thiol disulfide interchange e.g. with κ-casein. Composition of Whey Protein is shown in table 2.

β-lactoglobulin

β-lactoglobulin is the major whey protein, about 54% of whey proteins is βlactoglobulin. Five genetic variants have been characterised. It is a globular protein with a molecular weight of 18,362 Dalton for variant A and 18,276 for variant B. Variant B consists of 162 amino acids. A comparison of the sequences of β-Lg in bovine, ewe's and goat milk shows, that the three proteins are highly homologous. They contain two intrachain disulfides and one sulfhydryl group.

The secondary structure of bovine β-Lg is 15% α-helix, 50% β-sheet and 15-20% reverses turn. The protein is a typical lipocalin whose structure thus contains a β-barrel with eight antiparallel β-strands, labelled A–H and a three-turn α-helix that lies parallel to three of the β 15 strands. Strands A–D form one surface of the barrel while strands E–H form the other. A significant feature in all lipocalins is the bend in strand A that allows it to interact with strand H. The three-turn-α-helix follows strand H and lies on the outer surface of the barrel between the terminal end of the A strand and the H strand. : Structure of β-lactoglobulin (Qi et al., 1997) is shown in figure 1.

The molecule contains two disulfide bonds, which are found between cisteins 106.19 and the cisteins 6.160 respectively. There is one free sulfhydril group in β-Lg, but there is no phosphorus present in this protein.

β-Lg is very acid stable. It is generally in dimer form at the isoelectric pH of 5.2 and alkaline pH range. Bovine β-Lg denatures at temperatures above 65°C at pH 6.7, typically at 70.4±0.5°C, followed by aggregation. Denaturation temperature of β-Lg depends on pH. It is most heat sensitive near pH 4.0 and most stable at pH 6.0.

Temperature affects the three-dimensional structure of β-Lg. Although β-Lg is found mainly in the dimer form in milk, monomers appear when temperature is increased up to 65°C. Critical conformational change occurs around 63°C, where there is 19% net reduction in the βsheet content. Above this temperature, unfolding of β-Lg structure leads to irreversible denaturation in the following order: D-E strand (55-60°C); C-D strand and α-helix (60-65°C); A-B, A-I and E-F strands (65- 70°C); and A-H, B-C and F-G strands (75-80°C). Thermal unfolding of β-Lg is almost complete at 80°C except for the G-H pair of disulfide-linked strands which are the most heat-resistant feature of the structure (Edwards et al., 2002; Doucet, 2004).

β-Lg was found to bind retinol and enhance its fluorescence. One molecule of retinol is bound per β-Lg monomer. Binding of retinol by β-Lg occurs in the interior of the hydrophobic 16 barrel with tryptophan19 at the bottom of the calyx interacting with the β-ionine ring of the retinol molecule (Wong et al., 1996). β-Lg is is one of those milk proteins that are responsible for milk protein intolerance or allergy in humans (Bonomi et al., 2003; Clement et al., 2002).

α-lactalbumin

Bovine α-La is a small globular protein that is relatively stable. It constitutes 21% of whey proteins. Its genetic variant A has a molecular weight of 14,147 Da. Variant B has a molecular weight of 14,175 Da. α-La is composed of 123 amino acid residues. The molecule has an ellipsoid shape with a deep cleft dividing the protein in two parts. Four helices form one side of the cleft and two β-sheets together with a loop-like chain make up the other one. Four disulfide bonds make this protein relatively heat stable.

α-La was found to be a cofactor in lactose synthesis and the concentrations of this protein and of lactose in milk are correlated.

It is a strong binder of calcium and other ions, including Zn, Mn, Cd, Cu, and Al, and changes conformation markedly on calcium binding (Wong et al., 1996). One interesting feature of α-La is that it seems to exist in three different structures: the calcium-bound, the calcium-free and the low pH or A form. Recently, this latter form has been studied intensely as it may constitute a new protein structure. This 'molten globule' structure may be intermediate between the native and denatured forms of the protein (Creamer& MacGibbon). Figure 2 shows the structure of α-lactalbumin (1996).

Scope or usefulness

Whey is biological mixture of heterogenous of secreted proteins which have wide function in nutritional, biological, food purpose and some characteristics of major whey proteins and polypeptides are summarized. Protein concentration and number per molecule of reactive amino acids such as half-cystine (cys/2) and lysine-residuesare important characteristics during heat treatments. Whey protein is a popular choice among athletes, fitness enthusiasts and people wanting to build muscles or lose weight. It is also complete source of protein and contains all the essential amino acids. Dietary whey proteins have several putative biological effects when ingested, including an anti- cancer action. This study compared the ability of several common dietary protein sources, including whey, casein, meat, and soybean, to prevent the development of colon cancer.

Applications

Importance in industrial and fermentation process

The use of whey in dairy probiotics is a topic of great interest to the scientific community and the food industries. However, few studies address the effect of ohmic heating (OH) on cell metabolism and growth parameters of probiotic microorganisms. Despite of this, OH under sub-lethal conditions presents promising results regarding the enhancement of growth rate and bacteriocin activity, leading to considerable improvements in the fermentation process. Thus, this review highlights the main findings and advances on the effect of OH on probiotic metabolism, while addressing the modification of whey protein structure as potential carrier of probiotic entities, aiming at stimulating interest and encouraging the development of functional products using OH (Pereira in drugi, 2018).

Role in overweight and obesity

A study by Bowen et al. (9) suggested that the whey and casein protein components of dairy appear to be more important for weight loss than Ca in overweight adults due to their high concentrations of branched-chain amino acids. However, there is little evidence of beneficial effects of casein beyond it being a good quality source of protein and having a likely hypotensive effect (10 – 12). In another article, it's shown that both whey and casein proteins consumed over 12 weeks significantly reduced diastolic and systolic blood pressure from baseline in overweight individuals; however, whey protein consumption also significantly reduced arterial stiffness (12). Some studies demonstrate that dairy whey proteins have a better effect on appetite control than other protein sources such as egg and casein (13 – 15). In addition, convincing evidence indicates that dairy whey proteins and their bioactive components such as lactalbumin, angiotensin-converting enzyme inhibitor and branched-chain amino acids may have an insulinotrophic effect (16 – 20), hypotriacylglycerolaemic effect (21), muscle-sparing effect (22 – 24) and cholesterol-lowering effect (25). However, most of these studies using whey proteins have been conducted in healthy individuals or animals, with limited studies in overweight/ obese individuals. Given the effect of whey proteins on appetite control, muscle sparing and lipid metabolism demonstrated previously in healthy adults, our hypothesis was that whey protein consumption would also have a beneficial effect on metabolic risk factors in overweight and obese individuals, a population highly susceptible to the metabolic syndrome. Therefore, the aim of the present study was to compare the effect of whey and casein consumption on lipids, insulin, and glucose and body composition in overweight / obese individuals.

Previous studies have demonstrated the effect of whey proteins on appetite control, muscle sparing and lipid metabolism in healthy adults, but limited data are available for the effect of whey protein consumption on metabolic risk factors in overweight and obese individuals. While in recent studies the whey protein also decreased plasma TAG, insulin and homeostasis model assessment of insulin resistance scores compared with the control. There was no effect of casein supplementation on any metabolic risk parameter compared with control supplementation. Overall, the present study demonstrated that whey protein supplementation can significantly improve metabolic risk factors associated with chronic diseases in overweight and obese individuals.

Role in cell growth:

Whey proteins can play a role in reducing these social and economic costs. Dietary whey proteins have a number of putative biological effects when ingested, including an anticancer action. Among the many minor protein constituents of whey are several that display antimicrobial activity. Lactoferrin, present at low concentrations in whey (50 to 150 mg/L), exhibits both bacteriostatic and bactericidal activity against a range of microorganisms, including those responsible for gastroenteric infections, food poisoning, listeriosis, and mastitis. Whey contains proteins that serve as potent growth stimulants for a number of mammalian cell lines in culture. These growth factors have a dramatic impact on cell growth by promoting synthesis of DNA and protein and by inhibiting degradation of protein.

Role as antioxidant

Flaxseed contains approximately 55% of total fatty acids of the oil aslinolenic acid and is rich in lignans, which are strong antioxidants. Diets rich in omega-3 fatty acids and antioxidants are known to have beneficial effects on human health such as a decrease in the incidence of cancer, cardiovascular diseases, hypertension, and arthritis. Flaxseed could then be an interesting natural feed to consider for changing milk composition. Cyanogenic glycosides (linustatin and neolinustatin) are present in flaxseed, but the concentration of hydrocyanic acid is very low in milk and ruminal fluid of cows fed flaxseed products. In general, feeding up to 15% of the total dry matter as whole flaxseed has a limited effect on dry matter intake. Heat treatments such as micronization and extrusion have no effect on dry matter intake and the effect of formaldehyde treatment on feed intake is unclear. The effects of flaxseed supplementation on milk production of dairy cows in the early stage of lactation have been neutral. Diet supplementation with whole flaxseed has had no effect on milk yield and composition of dairy cows in the mid or late stages of lactation. Physical processing of flaxseed increased milk production although heat treatment did not. Results on the effect of flaxseed processing on overall milk fat concentration have been controversial, but heat and formaldehyde treatments had no effect. Flaxseed supplementation had no effect on milk fat and protein concentrations, and processing of flaxseed had little effect. The extent of change in the concentration of fatty acids in milk is generally proportional to the level of inclusion of flaxseed in the diet. In conclusion, feeding flaxseed does not affect milk production or composition in most studies, but its long-term effects on health of cows and productivity still need to be determined (Petit, 2010).

The economic output of the dairy industry is to a great extent dependent on the processing of milk into other milk-based products such as cheese. The yield and quality of cheese are dependent on both the composition and technological properties of milk. Milk parameters of the protein, lipid, and carbohydrate profiles as well as minerals were used to obtain correlations with native CN micelle size and gelation characteristics. Milk pH and protein, CN, and lactose contents were found to affect milk gelation. Smaller native CN micelles were shown to form stronger gels when poorly coagulating milk was excluded from the correlation analysis. In addition, milk pH correlated positively, whereas Mg and K correlated negatively with native CN micellar size. The milk from the elite dairy cows was shown to have good gelation characteristics. Furthermore, genetic progress in relation to CN micelle size was found for these cows as a correlated response to selection for the Swedish breeding objective if optimizing for milk gelation characteristics. The results indicate that selection for smaller native CN micelles and lower milk pH through breeding would enhance gelation properties and may thus improve the initial step in the processing of cheese (Glantz in drugi, 2010).

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Role in food application

Whey proteins are well known for their high nutritional value and versatile functional properties in food products. Estimates of the worldwide production of whey indicate that about 700,000 tonnes of true whey proteins are available as valuable food ingredients. Nutritional and functional characteristics of whey proteins are related to the structure and biological functions of these proteins. During recent decades, interest has grown in the nutritional efficacy of whey proteins in infant formula and in dietetic and health foods, using either native or pre-digested proteins. This paper focuses attention on the differences and similarities in composition of human and bovine milks with reference to infant formula. More desirable milk protein composition for consumption by humans is obtained by the addition of lactoferrin and more specific fractionations of proteins from bovine milk. Optimization of heating processes is important to minimize the destruction of milk components during fractionation and preservation processes. Some functional characteristics of whey proteins are discussed in relation to their properties for application in food products. Information obtained from functional characterization tests in model systems is more suitable to explain retroactively protein behaviour in complex food systems than to predict functionality (De Wit, 1998).

Conclusion

Whey protein is an essential dietary component with diverse applications, ranging from supporting muscle growth to combating obesity and enhancing food products. Its unique composition of β-lactoglobulin and α-lactalbumin provides numerous health benefits, including antioxidant, anticancer, and immune-boosting effects. Moreover, whey proteins show potential for improving metabolic risk factors in overweight and obese individuals. These findings underscore the importance of whey protein in both nutritional and industrial contexts, providing valuable insights for further research and product development.

Author contributions

N.S. conceptualized the project and developed the methodology. U.N. and I. conducted a formal analysis and drafted the original writing and contributed to the methodology. S.Z. conducted investigations, provided resources, visualized the data and contributed to reviewing and editing the writing.

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Competing financial interests

The authors have no conflict of interest.

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