

Review Article

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## Therapeutic Benefits and Applications of Whey Protein

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### ABSTRACT

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Whey protein is a derived by-product from cheese manufacturing and has many health benefits due to its high-level content of bioactive peptides, such as  $\beta$ -lactoglobulin,  $\alpha$ -lactalbumin, serum albumin, immunoglobulin, and lactoferrin. These proteins have antioxidant characteristics that reduce hypertension, cancer, hyperlipidemia, and virus contagious. In addition, whey protein is utilized to lessen the inflammatory bowel disease. In this review, we highlighted the characteristics, applications, functional properties of whey proteins.

### Introduction

Whey is a by-product which is produced during cheese making by coagulating the milk by acid or enzymes. The typical composition of bovine milk (Table 1) has approximately 3.5% protein (about 80% of the protein content is casein, while 20% is whey proteins).

Whey proteins have a high nutritional value, and its composition varies based on the coagulation method (acid or enzymes). However, the composition of the final product

is similar which has > 90% water (Table 2). Using advanced technology, such as membrane filtration led to the manufacturing of different whey products (Yalcin, 2006; Guo and Wang, 2019a) (Table 3).

Whey is a good source of bioactive peptides, which are produced from whey by enzymatic hydrolysis during fermentation and gastrointestinal digestion. These bioactive peptides are utilized widely to improve human health and have inevitable roles, such as anti-hypertensive, anti-oxidative, immunomodulant, anti-mutagenic, anti-

microbial, opioid, anti-thrombotic, anti-obesity, and mineral-binding agents. It has been reported that many bioactive peptides help against inflammatory bowel disease in mice (Jayatilake *et al.*, 2014).

Recently, whey proteins have been used in many foods, including ice cream, bread, and infant formula; moreover, whey proteins can replace fat in many products (Hammam and Ahmed, 2019). Furthermore, these dairy products are also associated with lower risks of hypertension, coagulopathy, stroke, and cancer insurgences (Sultan *et al.*, 2018). Additionally, whey proteins have a significant role in muscle-structure complement (Lollo *et al.*, 2011; Josse and Phillips, 2013). Whey proteins also have other applications, such as films and coatings (Hammam, 2019a) that are widely used to enhance the texture and quality of several foods. This work aims to review and highlight whey protein products and functional properties. Furthermore, the health benefits and applications of whey proteins are also discussed in this review.

### **Types of whey**

Milk consists of fat globules and casein micelles that dispersed in the whey solution (Figure 1). The typical composition of whey compared to whole milk is shown in Table 1. Whey is a yellowish or greenish by-product that derived from coagulating the milk by using rennet or acid. As a result, the whey is defined as sweet or acid based on the coagulation method. The composition of sweet whey and acid whey is quietly similar (Table 2) except for lactose, calcium, and pH. In the acid whey case, the pH is decreased during fermentation until the isoelectric point (pH=4.6), and this, in turn, converts the calcium in calcium casein phosphate complex from insoluble to soluble, which resulted in higher calcium content in the acid whey. Lactose is a soluble component and represents

> 69% of the total solids, while minerals represent 12-15% and whey protein or serum protein 8-10% of the total solids.

### **Manufacturing and applications of whey protein products**

Whey protein can be utilized to produce many products that have many applications (Figure 2). As mentioned, there are two types of permeate, namely sweet whey and acid whey. Acid whey is a by-product which is more difficult to utilize and produced from the coagulation of milk by using acid or starter cultures without the use of rennet. On the other hand, sweet whey has advantages as compared to acid whey, since sweet whey (milk-derived whey protein) can be utilized in many applications, particularly making whey protein isolate (WPI).

Nowadays, membrane technology (Figure 3) is utilized widely in the dairy industry to fractionate dairy ingredients, which led to several whey protein products (Table 3). When microfiltration (MF) applied to milk; casein and permeate are fractionated. The MF permeate could be further concentrated by using ultrafiltration (UF) to produce whey protein concentrate (WPC) or whey protein (WP) and permeate as a by-product. The UF permeate could be used to produce fermentation products, or it could be further nanofiltered (NF) to fractionate lactose. The NF by-product could be filtered again by using reverse osmosis (RO) to separate the minerals from the water. These membranes could be used individually or combined based on the required permeate product and its application (Table 4).

### **Chemistry of whey proteins**

Milk is utilized as feeding for young animals and humans due to the nutritional value of whey protein (Miller *et al.*, 2002).

Bovine milk contains approximately 3% protein (Fox and McSweeney, 1998), which divided into 80% casein (CN) and 20% whey proteins (Pihlanto and Korhonen, 2003). Whey protein has different fractions, including  $\beta$ -lactoglobulin ( $\beta$ -LG) and  $\alpha$ -lactalbumin ( $\alpha$ -LA), which are the majority of whey proteins and represent 70-80% of the whey protein. Also, there is proteose-peptone that resulted from the proteolysis  $\beta$ -casein ( $\beta$ -CN); besides small amounts of bovine serum albumin, immunoglobulins (Ig), and small

peptides (Whitney, 1988a; Miller *et al.*, 2002). The amino acid profiles in whey proteins are completely different from casein due to their lower content of Glu and Pro and higher amount of sulfur-containing amino acid residues (such as Cys and Met).

These proteins are dephosphorylated, sensitive to high temperature, insensitive to  $Ca^{2+}$ , and liable to the intermolecular bond formation through disulfide bonds between cysteine sulfhydryl groups.

**Table.1** The composition of whole milk and whey.  
Adapted from (Smithers, 2008; Côrtes *et al.*, 2010; Hammam *et al.*, 2017)

Components	Weight (%)	
	Whole milk	Whey
<b>Total solids</b>	11.5 – 12.8	6.3 – 7.0
<b>Lactose</b>	4.6 – 4.9	4.4 – 4.6
<b>Casein</b>	2.5 – 2.8	< 0.1
<b>Whey protein</b>	0.6 – 0.7	0.6 – 0.8
<b>Fat</b>	3.0 – 3.7	0.1
<b>Ash</b>	0.6 – 0.7	0.5

**Table.2** Typical composition of sweet and acid whey.  
Adapted from (Tunick, 2008a; Hammam *et al.*, 2017; Hammam, 2019a)

Components	Weight (%)	
	Sweet whey	Acid whey
<b>Total solids</b>	6.3 – 7.0	6.3 – 7.0
<b>Lactose</b>	4.6 – 5.2	4.4 – 4.6
<b>Protein</b>	0.6 – 1.0	0.6 – 0.8
<b>Calcium</b>	0.04 – 0.06	0.12 – 0.16
<b>Phosphate</b>	0.1 – 0.3	0.2 – 0.45
<b>Chloride</b>	0.11	0.11
<b>pH</b>	> 5.6	< 5.6

**Table.3** Typical composition of whey products; Adapted from (Yalcin, 2006; Tunick, 2008a; Hammam *et al.*, 2017; Guo and Wang, 2019b; Hammam, 2019a)

Product	Weight (%)				
	Protein	Lactose	Fat	Ash	Moisture
Sweet whey powder	11.0 – 14.5	63.0 – 75.0	1.0 – 1.5	8.2 – 8.8	3.5 – 5.0
Acid whey powder	11.0 – 13.5	61.0 – 70.0	0.5 – 1.5	9.8 – 12.3	3.5 – 5.0
Demineralized whey	11.0 – 15.0	70.0 – 80.0	0.5 – 1.8	1.0 – 7.0	3.0 – 4.0
WPC (34% protein)	34.0 – 36.0	48.0 – 52.0	3.0 – 4.5	6.5 – 8.0	3.0 – 4.5
WPC (60% protein)	60.0 – 62.0	25.0 – 30.0	1.0 – 7.0	4.0 – 6.0	3.0 – 5.0
WPC (80% protein)	80.0 – 82.0	4.0 – 8.0	4.0 – 8.0	3.0 – 4.0	3.5 – 4.5
WPI	90.0 – 92.0	0.5 – 1.0	0.5 – 1.0	2.0 – 3.0	3.0 – 5.0

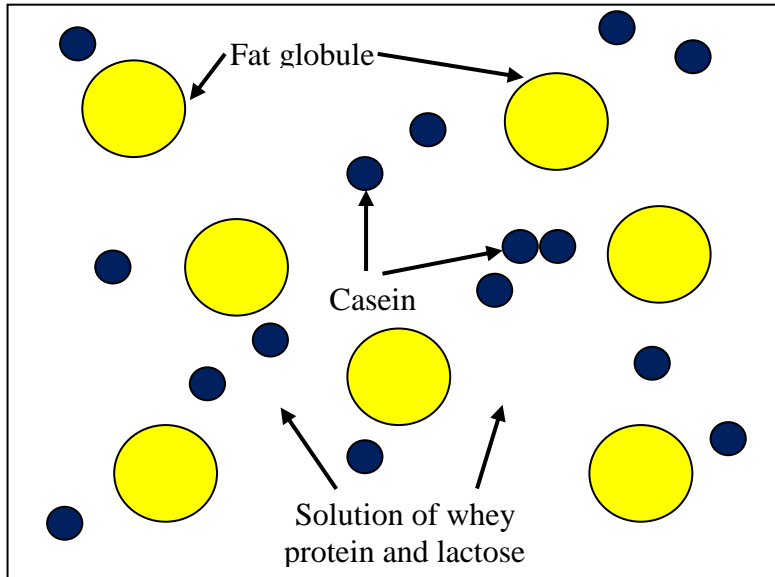
WPC=Whey protein concentrate; WPI=Whey protein isolate

**Table.4** Application of whey proteins in dairy-based foods; Adapted from (Mulvihill and Ennis, 2003)

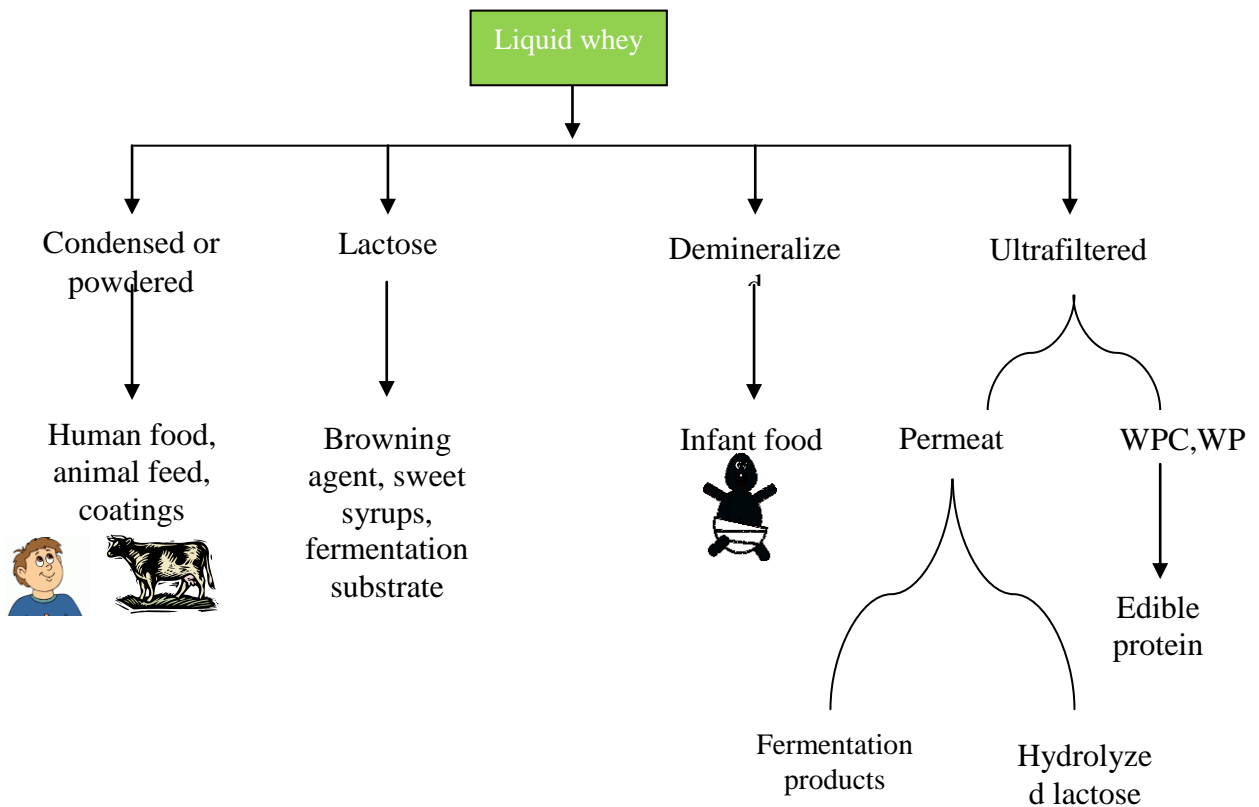
Product	The benefit of whey products
Yogurt, cheese (Quarg, Ricotta)	Yield; nutritional, consistency, curd cohesiveness
Cream cheese and cheese spreads, sliceable/squeezable cheeses, cheese filling and dips	Emulsifier, gelling, sensory properties
Soft drinks, fruit juices, powdered or frozen orange beverages	Nutritional
Milk-based flavored beverages	Viscosity, colloidal stability
Ice cream, frozen desserts coating, frozen juice bars	Skimmed milk solid replacement, whipping properties, emulsifying properties, body and texture

**Table.5** The chemical and physiological properties of whey protein fractions and their relative molecular weight. Adapted from (Whitney, 1988b; Zydney, 1998; Hammam *et al.*, 2017; Hammam, 2019a)

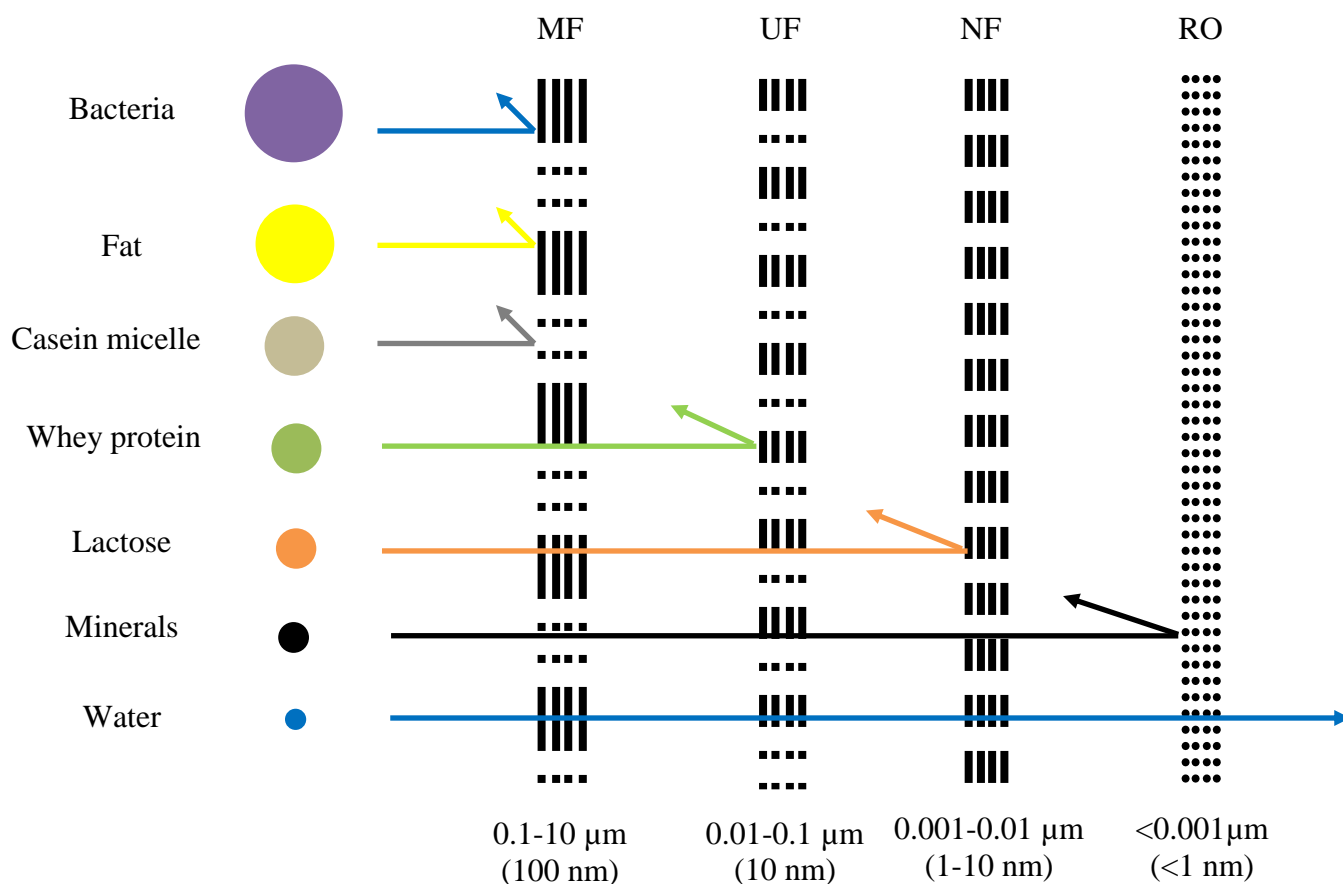
Whey protein fractions	Concentration (g/L)	MW (kDa)	Isoelectric point (pI)
$\beta$ -Lactoglobulin	3.0 – 4.0	18.4	5.2
$\alpha$ -Lactalbumin	0.7 – 1.5	14.2	4.7 – 5.1
Bovine serum albumin	0.3 – 0.6	69	4.7 – 4.9
IgG, IgA, IgM	0.6 – 0.9	150 – 1000	5.5 – 8.3
Lactoperoxidase	0.006	89	9.6
Lactoferrin	0.05 – 0.35	78	8.0
Protease-peptone	0.5 – 1.0	4 – 20	
Caseinomacropptide	0.0 – 1.5	7	



**Figure.1** Milk contains fat globules and casein micelles colloidal in a solution of whey protein and lactose



**Figure.2** Liquid whey processing (Marwaha and Kennedy, 1988; Siso, 1996; Tunick, 2008b)



**Figure.3** Filtration spectrum and size of major components in milk

### Therapeutic applications of whey proteins

Whey protein has a high amount of bioactive components, including  $\alpha$ -lactalbumin,  $\beta$ -lactoglobulin, bovine serum albumin, immunoglobulins, lactoferrin, and lactoperoxidase (Table 5). These proteins have been used as ingredients in pharmaceuticals, nutraceuticals, and cosmeceuticals applications (Pihlanto and Korhonen, 2003; Etzel, 2004) due to their bioactive characteristics (Korhonen and Pihlanto, 2003). Many studies have been reported that these bioactive peptides have many health benefits, such as improving the immune system (Mann *et al.*, 2019), inhibiting infections due to the antiviral

activity of lactoferrin (Drago-Serrano *et al.*, 2017; Hammam, 2019b), reducing oxidative stress and human immunodeficiency virus (HIV) infection (Gupta and Prakash, 2017), anticancer activity (Patel, 2015; Hammam *et al.*, 2017), lessen anxiety (Yalcin, 2006), assist with the reduction in blood pressure (Fekete *et al.*, 2018), positive effects on hepatitis (Ng *et al.*, 2015), reduce cardiovascular risk (Pal *et al.*, 2019), and osteoporosis (Mangano *et al.*, 2019).

### Nutritional applications of whey protein products

Whey protein products are widely used in many applications, including infant formulas,

dietetic foods, and animal feeds (Fitzsimons *et al.*, 2008). Polymerized whey protein, which has different commercial names, such as preheated whey protein, process whey protein, heat-denatured whey proteins, or denatured whey proteins (Vardhanabhuti *et al.*, 2001), has shown improved functional properties, including gelatin agents, films (Hammam, 2019a), thickness agents, stabilizers, microencapsulation, and coatings that are widely used to enhance the texture and quality of several foods, such as sausages, dairy products, desserts, bakery products, cold sauces (Elofsson *et al.*, 1997; Hammam, 2019a), beverages, bars, and fruits (Ferreira *et al.*, 2007).

Milk whey or whey protein has tremendous therapeutic properties, including antimicrobial, anticancer, anticarcinogenic effects, immune-enhancer, prebiotic property, anti-inflammatory, anti-hypertensive actions, binding of toxins, cardiovascular, antioxidant activity, gastro-intestinal health, physical strength, obesity control and weight-management, HIV, diabetes, anti-viral effects, promotion of cell growth, platelet binding, appetite suppression, ageing, and wound healing. Several whey products are available nowadays in the market, which can be utilized as attractive health-promoting food supplements.

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