



Whey proteins and peptides: beneficial effects on immune health

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Over the last decade, natural health products have been the subject of immense infatuation in the scientific community, in particular with immunologists. Numerous recent studies have demonstrated important effects on all facets of immunity – from the stimulation of innate and adaptive immunity, to an anti-inflammatory effect of these products. In many of these enhancing health products, whey proteins and whey peptides are present, which, for many years, have been well known for their benefits on energy, sport endurance, protection against cancers, and serum lipid-lowering effect. Recently, this class of product has gained interest from immunologists who support the ever increasing body of evidence regarding their beneficial effects on the immune system. This article will focus on studies showing immune effects associated with each whey protein and peptide.

Until recently, whey proteins have been mainly studied for their positive effects on endurance by increasing muscle protein balance during sport training [1]. Many studies have also demonstrated that whey proteins possess an excellent lowering effect on serum lipid levels and blood pressure [2]. The discovery of the antioxidant potential of whey protein products [3] was one of the principal studies demonstrating the potential health benefit of these products for cancer and the immune system. Subsequently, many studies have reported a protective effect against different types of cancer by the whey proteins including an important review by Bounous [4].

Currently, most research focuses on the effects whey proteins and peptides have on immune health and their protective roles in immune disorders. Whey is composed mainly of proteins as well as many peptides derived from these proteins. The proteins found in whey are principally β -lactoglobulin, α -lactalbumin, lactoferrin, immunoglobulin (Ig) and bovine serum albumin (BSA). Their biochemical properties, as well as their concentrations in milk and whey, are summarized in Table 1. All of these proteins and peptides possess specific effects on immunity. These effects will be discussed with relation to specific associated proteins or peptides, and are summarized in Table 2.

β -lactoglobulin

β -lactoglobulin is the most abundant protein found in whey, comprising between 55 and 65% of the total whey protein content. This protein possesses numerous physicochemical attributes such as acting as an emulsifier, as well as many reported health effects.

In 1985 Bounous and Kongshavn were among the first researchers to demonstrate an immunoenhancing effect of β -lactoglobulin [5]. They showed that the whey proteins (principally β -lactoglobulin and BSA) increase the number of antibody-forming cells in the spleen of mice immunized with trinitrophenylated ficoll. Subsequently, the team of Wong and colleagues demonstrated that the stimulatory effects of β -lactoglobulin on normal murine spleen cells are more intense than those observed with BSA [6]. The immune effects on murine spleen cells are postulated to be due to an increase in glutathione (GSH) production by splenocytes. This has been confirmed by the addition of *S*-(*n*-butyl)homocysteine sulfoxamine, an inhibitor of glutamylcysteine synthetase, which in this case, blocked the stimulatory effect [6].

Controversially, another study demonstrated that the observed effects of β -lactoglobulin on spleen cells to produce T-helper (Th)-cell 1 cytokines are due to endotoxin contamination [7]. This study was conducted with a commercial β -lactoglobulin product and utilization of a specific isolation technique led to the presence of an endotoxin in the preparation. However, the team of Wong and colleagues have proven that the effect observed with β -lactoglobulin is not due to endotoxin contamination but the utilization of polymixin B, a lipopolysaccharide (LPS) inhibitor [6]. The utilization of this LPS inhibitor markedly reduced the effect of LPS; however, it had no effect on β -lactoglobulin. This study confirms that the β -lactoglobulin really does possess an immunomodulatory effect. It is important to note that preparation is essential in the quality

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Table 1. Specific properties of whey proteins.

Protein	MW (g/mol)	IP	Concentration			Other structural properties
			Milk (g/l)	Whey(g/l)	Whey (%)	
β -lactoglobulin	18,400	5.35–5.49	2.0–4.0	3.3	55–65	Presence of a hydrophobic region capable of binding to vitamin A and helping its absorption.
α -lactalbumin	14,200	4.2–4.5	1.0–1.5	1.2	15–25	Presence of a hydrophobic region that binds galactosyltransferase and aids lactose biosynthesis.
Lactoferrin	80,000	8.4–9.0	0.2	0.2	1–2	Presence of ferric ion binding sites, which permits Lf binding and the transport of iron – an important role in iron assimilation.
Immunoglobulin	80–900,000	5.5–8.3	0.4–1.0	0.5	10–15	Five categories of Igs: IgG1 (0.3–0.6 g/l), IgG2 (0.05–0.1 g/l), IgA (0.05–0.15 g/l), IgM (0.05–0.1 g/l) and IgE.
BSA	69,000	4.7–4.9	0.1–0.4	0.3	5–10	Important capabilities to bind fatty acids.

BSA: Bovine serum albumin; Ig: Immunoglobulin; IP: Isoelectric point; Lf: Lactoferrin; MW: Molecular weight. Adapted from [90–92].

and reliability of results, as demonstrated by Brix and colleagues [7]. An additional control should be included in the study to confirm its validity.

Peptides from β -lactoglobulin

Many studies have been conducted with specific peptides from β -lactoglobulin; however, due to the complex nature of the protein, some of the peptides derived from it are still unknown. Of the β -lactoglobulin peptides, four exhibit antimicrobial activities [8]. β -lactoglobulin is also a carrier of many small hydrophobic molecules, such as retinoic acid, a modulator of lymphocyte responses [9].

A peptide from β -lactoglobulin, known as β -lactotensin, has demonstrated an effect on the contraction of the ileum longitudinal muscle [10]. A study completed with β -lactotensin showed similar results – that this peptide possesses a stimulating effect on smooth muscle *in vitro* [11]. Smooth muscle is responsible for the contractility of hollow organs, such as blood vessels, the gastrointestinal tract, the bladder and the uterus. Many diseases, including allergy, asthma and atherosclerosis, are related to dysfunctions of smooth muscle. Although the role of smooth muscle cells is contraction, they also exhibit extensive phenotypic diversity during normal development, repair of vascular injury and in disease states [12]. The stimulating effect of β -lactotensin on smooth muscle provides information that this peptide can enhance general health.

β -lactoglobulin is the protein responsible for milk allergies in children (2–3% of children suffer from milk allergies); however, in 80% of cases allergy symptoms disappear before the age of 3 years [13]. It has been demonstrated that the peptides from β -lactoglobulin induce oral tolerance and consequently, diminish IgE production specific to β -lactoglobulin [14]. This observation suggests that the consumption of peptides from β -lactoglobulin possesses an important protective role against milk allergies.

α -lactalbumin

α -lactalbumin is the second major protein present in whey, accounting for 15 to 25% of the whey protein content. This protein is rich in essential amino acids and has a low immunogenicity, indicating that α -lactalbumin is a good nutrient for children [15]. It has also been shown that a diet supplemented with α -lactalbumin increases resistance against acute infection caused by *Escherichia coli* [16].

In the 1980s, many studies demonstrated an immunoenhancing effect of α -lactalbumin in mice [17,18]. Despite these studies, it is surprising to observe an absence of research on the immunomodulatory effects of α -lactalbumin. It has been clear since 1997 that α -lactalbumin possesses stimulatory effects. The production of IL-1 β by sheep macrophages issued from bronchoalveolar lavage is increased by the presence of this protein [19].

Table 2. Immunologic effects of whey proteins and peptides.

Whey fraction	Reported effect	Ref.
β-lactoglobulin (proteins)	Stimulatory effect on splenocytes	[5,6]
	Increase GSH	[3]
β-lactoglobulin (peptides)	Carrier of retinoic acid	[9]
	Contraction of ileum muscle	[10,11]
	Increase oral tolerance to whey	[14]
α-lactalbumin (proteins)	Increase IL-1α production by macrophages	[19]
	Induce apoptosis in tumor and immature cells	[20,21]
α-lactalbumin (peptides)	Modulation of B- and T-lymphocyte activities	[5,25]
	Stimulation of adherence and phagocytosis of macrophages	[22,23]
	Stimulation of oxidative burst response	[22]
Lactoferrin (proteins)	Inhibition of cytokines TNF-α, IL-1α and IFN-γ	[19,32,35,36]
	Anti-inflammatory effect on animal model	[33–36]
	Upregulation of cytokine IL-10	[35]
	Stimulatory effect on lymphocyte proliferation	[19]
	Regulatory effect on myelopoiesis	[38–40]
	Promote the differentiation of T- and B-lymphocytes	[42,43]
	Increase NK cells, CD8 ⁺ cells, CD4 ⁺ cells	[44,45,47]
	Bind to CpG and prevent stimulatory effect on B-cells	[37]
	Stimulation of mucosal immunity through Peyer's patches	[46,47]
Lactoferrin (peptides)	Increase phagocytosis activity of neutrophils as well as IL-8	[50,51]
	Bind to CpG and prevent stimulatory effect on B-cells	[37]
	Inhibition of IL-6 production by LPS	[53]
	Increase of apoptosis in leukemic cells lines via production of ROS by phagocytic cells	[54]
Immunoglobulins	Increase of GSH	[58]
	Activation of complement, increase of phagocytosis, prevent adhesion of microbes, neutralize viruses and toxins	[55]
BSAs	Increase of GSH	[3]
	Stimulatory effect on splenocytes	[5]
GMPs	Suppress proliferation of cells upon mitogens stimulation	[59–61]
	Stimulation of macrophages proliferation and phagocytosis	[62]

BSA: Bovine serum albumin; GSH: Glutathione; GMP: Glycomacropeptide; Ig: Immunoglobulin; IL: Interleukin; IFN: Interferon; LPS: Lipopolysaccharide; NK: Natural killer cell; ROS: Reactive oxygen species; TNF: Tumor necrosis factor.

The team of Svanborg and colleagues has identified a variant of α-lactalbumin similar to the modified α-lactalbumin found in the stomach of nursing children, which possess interesting immune effects [20,21]. This protein can protect against cancer by the induction of apoptosis in tumor and immature cells, but has no effect on healthy cells [21].

Peptides from α-lactalbumin

Hydrolyzed α-lactalbumin, which contains unidentified peptides, has demonstrated a modulation of B- as well as T-lymphocyte activities [5].

After this observation, research into the identification of peptides from α-lactalbumin as well as its associated immunomodulatory effects, have been undertaken.

An immunomodulatory tripeptide derived from α-lactalbumin has been discovered [22]. This tripeptide, glycyl-leucyl-phenylalanine (GLF), stimulates the adherence and phagocytosis of human monocytes and macrophages, apparently by a mechanism of binding to the specific receptors for GLF on these cells [22,23]. The same research team evaluated the properties of this tripeptide on human and rat

polymorphonuclear (PMN) cells. GLF increases the production of the superoxide anion by human PMNs, increasing the oxidative burst response in the presence of GLF. Phosphoinositide metabolism is also increased in the presence of GLF, which can be seen by the liberation of a second messenger, IP₃, leading to an enhancement in membrane fluidity [24]. Moreover, a study carried out with another peptide (Tyr–Gly–Gly) from α -lactalbumin revealed a stimulation of human peripheral blood lymphocytes in the presence of this peptide [25]. In relation to antimicrobial activities, Pelligrini and colleagues have identified that these three peptides from α -lactalbumin possess interesting antimicrobial activities [26].

Lactoferrin

Lactoferrin, an antioxidant glycoprotein with iron-binding properties, is the most studied of the whey proteins and also appears to be the best immunomodulator. The antioxidant capacity of lactoferrin is due to its iron-binding site that participates in the generation of hydroxyl radicals [27]. This iron-binding capacity is also partly responsible for its antimicrobial potential [28]. Lactoferrin is found in colostrums [29], mucosal secretions [30] and neutrophil granules [31]. The localization of lactoferrin in important sites implicated in acquiring immunity, suggests an important contribution of lactoferrin in immune health. In whey, the proportion of lactoferrin is 1 to 2%. Numerous studies on the roles of lactoferrin in immunity have been conducted. This paper will review the most significant observations reported to date.

Lactoferrin exhibits a known immunomodulatory potential by its capacity to act as both an immunosuppressive as well as an immunostimulatory agent. Certain studies revealed the anti-inflammatory potential of lactoferrin in some circumstances, while in others the immune status demonstrated its stimulatory potential.

Lactoferrin possesses an anti-inflammatory potential in part by inhibiting cytokines such as tumor necrosis factor (TNF)- α and interleukin (IL)-1 β , which are key inflammatory cytokines [32]. Many animal models demonstrate that lactoferrin can protect against inflammatory conditions. A study by Dial and colleagues shows that lactoferrin protects against gastritis induced by *Helicobacter felis* bacterium in mice [33]. Moreover, local administration of lactoferrin in inflamed joints of two different

arthritis models in mice shows a strong local anti-inflammatory effect not related to the reduction of the proinflammatory cytokine IL-6 [34]. The effect of this protein on arthritis has also been reported in another study in which lactoferrin protected against arthritis in rats induced by adjuvant administration in the right hind paw [35]. In this model, the protective effect against arthritis is due to a downregulation of the proinflammatory cytokine TNF- α and an upregulation of the anti-inflammatory cytokine IL-10 [35].

Lactoferrin also possesses the capacity to inhibit atopic contact dermatitis induced by oxazolone. In this study, lactoferrin applied topically prior to oxazolone sensitization prevents, in a dose-dependent manner, the migration of Langerhan's cells into the lymph nodes and subsequently activates cytotoxic T-cells and the accumulation of dendritic cells in inflamed sites. The mechanism of action seems to be the inhibition of TNF- α production by keratinocytes – the cytokine responsible for delivering the activation signal to Langerhan's cells [36]. Lactoferrin has the ability to bind to the CpG motifs via charge–charge interactions of the N-terminal sequence of lactoferrin. This binding of CpG on lactoferrin inhibits the stimulatory effects of these motifs on immune cells [37]. The binding of CpG and LPS suggests another mechanism for the anti-inflammatory effect of lactoferrin.

The immunosuppressive potential of lactoferrin has also been observed in lymphocyte cells as it demonstrates an inhibitory effect on lymphocyte proliferation upon stimulation by mitogens, as well as on IFN- γ production by these cells [19]. Other studies have reported the regulatory potential of lactoferrin on myelopoiesis by its suppressive activities on many cells including lymphocytes, macrophages and monocytes [38–40]. These processes are regulated by cytokines, indicating that lactoferrin could act as a regulatory nutrient by controlling cytokine production. The potential of lactoferrin to modulate immunity via regulation of cytokines has previously been demonstrated [41].

Lactoferrin also exhibits an immunostimulatory potential. It has been demonstrated that this protein promotes the differentiation of T- and B-lymphocytes [42,43]. The incubation of immature T-lymphocytes in the presence of lactoferrin allows for the differentiation of these cells in CD4⁺ helper T-cells and the immune response of sheep red blood cells increases [42]. Natural killer (NK) cells as well as CD8⁺ T-cells

have also increased in circulating cells after consumption of lactoferrin. This observation reveals a protective role in the control of tumor metastases since NK and CD8⁺ T-cells have important role in tumor inhibition [44,45]. Debbabi and colleagues have investigated the immune responses induced by repeated oral administration of lactoferrin in mice. IgA and IgG secretions are enhanced in the Peyer's patches and spleen from lactoferrin-fed mice but not in serum [46]. Wang and colleagues have also confirmed these observations in a study in which the CD4⁺, CD8⁺, asialoGM1⁺ (marker of NK cells), IgA⁺ and IgM⁺ B-cells have increased in the small intestine of mice treated with lactoferrin [47]. In this study, lactoferrin enhanced production of IL-18, IFN- γ and caspase-1, leading to an important stimulation of intestinal immunity. These results suggested that lactoferrin could act as an immunostimulatory factor on the mucosal immune system [46]. Immune effects occur as a result of the action through gut-associated lymphoid tissue (GALT), where lactoferrin may bind to epithelial cells or interact with M-cells in the Peyer's patches. These interactions of GALT may lead to the production of cytokines being released in the circulation and act systemically on circulating leukocytes.

Controversially, lactoferrin shows an absence of stimulation in B- or T-cells or in cytokine production (IL-6, TNF- α , INF- γ) in Peyer's patches of newborn mice [48]. The consumption of nutrients by newborns in these studies probably leads to oral tolerance due to the supposed absence of early consumption of whey proteins prior to the experiment. The immune system of newborns was not completely developed and they do not have effective cells for the development of the same immunomodulation as an adult mouse [49].

The phagocytic activity of human neutrophils is increased by the presence of lactoferrin. This activation appears to be a result of the specific binding of lactoferrin to neutrophils [50]. Following binding, lactoferrin is thought to be transported into the nucleus where it activates gene expressions responsible for the activation of the phagocytosis mechanism. It is also demonstrated that lactoferrin stimulates the production of IL-8 (a chemokine implicated in the activation of neutrophil activities) from human neutrophils [51]. In contrast, consumption of lactoferrin by newborn calves does not seem to change the production of the superoxide by PMN cells [52]. However, this

study was completed with newborn calves that received lactoferrin only over a 9-day period; it is possible that the immunity of these young animals was not stimulated to activate their PMN cells over such a brief time period.

Peptides from lactoferrin

The main lactoferrin-derived peptide studied is lactoferricin, which corresponds to 25 amino acids from its N-terminus. This peptide appears to be responsible for the majority of immune benefits reported for lactoferrin. The activation of phagocytosis, as well as the production of IL-8 from neutrophils when treated with lactoferrin, is also observed when treated with the lactoferricin fraction [50,51]. It is mentioned above that the production of IL-18, IFN- γ and caspase-1 is increased by lactoferrin; a response also observed with lactoferricin [47]. Lactoferricin is capable of binding CpG motifs and preventing their immunostimulatory effects on B-cells [37], suggesting a potential anti-inflammatory role of lactoferricin similar to lactoferrin. Moreover, the lactoferricin peptide has been found to suppress the IL-6 response in a monocytic cell line upon stimulation by lipopolysaccharide [53].

Lactoferricin demonstrates an induction of apoptotic in human monocytic leukemic cells in a dose- and time-dependent manner. The apoptosis effect of lactoferricin remains present even if various cytokines and mitogens are added. This effect is correlated with high levels of intracellular reactive oxygen species (ROS), suggesting that the apoptosis-inducing activity is related to the production of intracellular ROS by phagocytic cells [54].

Immunoglobulins

Igs are present in whey at a rate of approximately 10%. IgG1 is the major Ig found in whey (~75%), followed by IgM, IgA and IgG2. In general, the Igs possess several immune benefits. The principal role of Igs is to defend organisms against pathogens and viruses. They are responsible for the activation of complement, increasing phagocytosis by leukocytes, preventing adhesion of microbes and neutralizing viruses and toxins [55]. All of these activities can likely be attributed to whey Igs. Effectively, Roos and colleagues have demonstrated that ingested Igs retain these immunological activities in the human ileum [56]. It has also been demonstrated that an Ig-like receptor isolated from milk inhibits HIV integrase as well as HIV protease [57].

The immunoenhancing effects often demonstrated in animals fed with whey proteins can be attributed in part to an increase in intracellular glutathione [58]. A study of animals fed with defined whey products has demonstrated that the product containing a higher proportion of Igs (and BSA) exhibited a better GSH-enhancing effect [3]. GSH is an intracellular antioxidant, which requires cysteine, glycine and glutamine for its synthesis. It is important to note that the Igs possess high levels of cysteine and glutamine.

Bovine serum albumine

BSA is a good source of essential amino acids and is found in approximately 5 to 10% of the whey protein content. Only a few studies have demonstrated the immunologic effects of BSA. GSH production increases when animals are fed with a whey diet containing a higher proportion of BSA. This explains the positive effect of BSA since GSH is responsible for some of the immune benefits observed with whey products [3]. As with the Igs, serum albumin fractions contain glutamine and cysteine amino acids that provide an enhancing effect on GSH production.

Moreover, as with β -lactoglobulin, BSA increases the amount of antibody-forming cells in the spleen of mice immunized with trinitrophenylated ficoll [5].

Glycomacropeptide

Glycomacropeptide (GMP) is released during the digestion of casein with the chymosin enzyme has been found in whey at a rate of approximately 10%. This is the only casein-derived peptide to be found in whey; all of the other peptides derived from casein remain in the cheese fraction. The GMP is present in whey only when chymosin is used during the cheese fabrication process. GMP is known to inhibit proliferation of mouse splenocytes as well as in cells from Peyer's patches isolated from a rabbit upon stimulation with LPS and phytohemagglutinin (PHA) [59–61]. These results indicate that this peptide downregulates the immune system by suppressing T-lymphocytes (stimulated by PHA) as well as B-lymphocytes (stimulated by LPS). Li and Mine demonstrated that GMP is a potent immunoenhancer of macrophage proliferation as well as phagocytic activity *in vitro* [62]. The second part of this study demonstrated that the immunomodulatory effects of GMP are essentially due to sialic acid. Effectively, when enzymatic treatment removes this fragment, the effects are abolished.

Other effects of whey proteins

The majority of the studies concerning the immunomodulatory potential of whey proteins used whey directly and not one of individual whey proteins; the effects are therefore associated with whey proteins in general and not a specific protein.

The immunoenhancing effect of whey proteins on the formation of specific antibodies is well documented [5,63–66]. For example, one study demonstrated that mice fed with whey protein concentrate (WPC) express an elevated level of antibodies after the administration of different vaccines via different routes [66]. The same immunoenhancing effect was observed by Wong and Watson, when they reported higher concentrations of anti-ovalbumin antibodies in the presence of whey proteins [65]. The same study also demonstrated an increase in cell-mediated immunity after a period of 5 weeks in contrast with another study [5]. This difference; however may be as a result of different whey sources as well as the dose and duration of feeding. Variable effects of whey can be attributed to the whey source [67]. It is also demonstrated that whey enhances the proliferation of non-stimulating (mitogens) splenocytes [68].

A hypothesis suggests that whey proteins may act via the GALT system for the production of antibodies. This hypothesis is supported by results demonstrating that WPC increases the antibody response in the intestinal tract of mice upon immunization with ovalbumin [69].

Roth and colleagues demonstrated that ultra-filtered bovine whey increases the *in vitro* neutrophil functions of cattle cells as well as cytochromeC reduction in cells of dexamethasone-treated cattle [70]. This finding indicates that whey proteins increase the oxidative metabolism of cattle treated with dexamethasone. However, in this study, the whey came from hyperimmunized cows and it is possible that these effects are due to the cytokines present and not by the whey proteins.

Until now, the only immunostimulating properties of whey proteins have been discussed; however, some studies indicate that whey can be an immunosuppressive agent in some circumstances. *In vitro* studies show an immunosuppression of T- and B-lymphocyte proliferation upon stimulation with mitogens [19,71,72]. Whey proteins also show an immunoregulatory effect in spleen cells, since the activation of these cells is downregulated by oral administration of whey [73]. The increase

in transforming growth factor (TGF)- β production in cells after whey treatment may explain this regulation. TGF- β is a cytokine secreted during the tolerance induction and is responsible for the downregulation against food antigens [49]. These results show that whey proteins might be a good nutritive supplement due to their capabilities to modulate immunity, which may help in many different immune diseases.

Other effects of whey peptides

Some effects of whey peptides have been reported; however, the characterization of these peptides have not yet been investigated, thus the protein associated with the effective peptides is unknown. A hydrolyzed whey protein isolate composed of β -lactoglobulin, α -lactalbumin and GMP has been shown to possess a stimulatory effect on lymphocyte proliferation *in vitro* [68]. Another peptide, a glycoposphopeptide isolated from cheese whey, has demonstrated a mitogenic activity on splenocytes [74]. It has also been demonstrated that the peptides issued from whey and milk possess a good immunostimulatory effect on keratinocyte growth *in vitro* [75].

Some whey peptides also possess an inhibitory effect on the angiotensin-converting enzyme (ACE) [76]. ACE is responsible for inactivation of bradykinin. Bradykinin exhibits an essential role in inflammatory defence by the stimulation of macrophage and cytokine production [55]. Consequently, the peptides that act as ACE inhibitors stimulate the immune system via macrophage activation.

As mentioned previously, β -lactoglobulin is principally responsible for milk allergies in children. It has been postulated that peptides from β -lactoglobulin diminish the allergic reaction to this protein [14]. Many studies have also demonstrated a preventive role against milk allergies from hydrolyzed whey proteins [77–79].

Moreover, many other constituents in milk and whey are known to possess immunomodulatory effects, such as cytokines, growth factors, enzymes and hormones [80–82]. A growth factor derived from whey has been shown to have a protective effect in a colitis animal model [83,84]. Francis and colleagues have demonstrated that a growth factor isolated from whey improved the growth rate of cells such as epithelials and fibroblasts [85,86]. These results led them to postulate that whey could be an interesting product against many diseases, not only due to the protein or peptide content.

Expert commentary & outlook

It has been known for many years that the consumption of nutraceuticals is important in maintaining general health. Statistics confirming the important rise in the consumption of nutraceutical products by the general population show that this is indeed the case [87,88]. For example, some reviews have already demonstrated the immunologic effects of milk-derived products such as yogurt [89].

This article, which emphasizes the reported immune effects of whey proteins and derived peptides, demonstrates an important therapeutic potential of whey products, not only for maintaining good general health but also in guarding against many immune diseases, such as inflammatory disorders and autoimmune diseases. All the proteins and peptides present in whey possess an immunomodulatory potential, in both innate and acquired immunity, which provide an excellent mechanism of defence against all infections. The potential of enhancing GSH, NK cells, cytotoxic T-cells and the phagocytic process, leads to an enhancement in its capacity to defend against cancer.

Moreover, it is now reported that lactoferrin (and lactoferricin) provides whey with an important effect against bacterial and autoimmune inflammatory diseases. Many studies have proven that whey (and especially lactoferrin) plays a protective role against gastritis, asthma, colitis, arthritis and atopic contact dermatitis. The antiallergy properties of whey with regard to milk reactions were also reported in a study involving peptides derived from β -lactoglobulin. These peptides appear to protect against allergies by the stimulation of oral tolerance. This observation is very important, as it presents an encouraging perspective that children, having consumed whey early on in life, can consume milk (an important nutrient) without the onset of allergies.

Whey products appear to have essential properties and could be used in the treatment of many diseases. Their effects could be comparable with the effects observed with many medicines and drugs, whilst still acting as a unique natural product. Further studies are needed to compare whey products with medicines in the treatment and prevention of disease.

These products or derived products from part of a future solution in obtaining and maintaining a healthy general immune system and in providing a natural, nutritive and non-chemical supplement against numerous diseases and immune disorders.

Highlights

- The most important immune effect reported for the majority of whey proteins and peptides is the stimulation of innate immunity via an increase in macrophage activity and interleukin-8 production.
- Lactoferrin is the most studied of the whey proteins and its immune effects are diverse and dependent on the conditions for which it is used. For example, lactoferrin stimulates innate immunity in some conditions and could also exert anti-inflammatory effects in others.
- Lactoferrin also exhibits effect on mucosal immunity via stimulation of Peyer's patches. This mucosal immunomodulation could be responsible for multiple reported systemic effects.
- The ability of whey proteins and peptides to enhance glutathione, natural killer cells, cytotoxic T-cells and the phagocytic process, fortifies the immune system against the development of cancers.
- Many studies demonstrated that whey plays a protective role against diseases such as gastritis, asthma, colitis, arthritis and atopic contact dermatitis.

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