International journal of Horticulture, Agriculture and Food science(IJHAF) *Vol-3, Issue-2, Mar-Apr, 2019*
https://dx.doi.org/10.22161/ijhaf.3.2.5 **ISSN: 2456-8635**

Valorization of Cheese whey To "Bio"-value added food Products with Industrial Interest and their Potential Beneficial Health Effects

Charalampia Dimou[1], Koutelidakis E. Antonios[1], Chrysavgi Gardeli[2], Anastasia Papadaki[3], Haralabos C. Karantonis[1] and Charalampia Dimou[1*]

[1]University of the Aegean, Department of Food Science and Nutrition, Lemnos, Greece, Email of principle author and correspondent: xadimxri1983@yahoo.gr
[2]Agricultural University of Athens, Iera Odos, Athens, Greece; Email: agardeli@aua.gr
[3]Technological Educational Institute of Crete, Herakleion, Crete; Email: apapadaki@staff.teicrete.gr
Correspondence: Charalampia Dimou, Department of Food Science and Nutrition, Lemnos, Greece, Email: xadimxri1983@yahoo.gr

***Abstract*— *Cheese whey is a by-product liquid stream that is produced during cheese or casein production process after casein coagulation by enzymes and/or acids. Milk production and processing is increasing continuously, with cheese making being the most abundant dairy product. Thinking that surplus CW's biochemical oxygen demand (BOD_5) varies from 35.000 to 55.000 mg O_2/L and the total worldwide production is estimated at about 180 to 190 million tons/year, its disposal in the environment, could arise several environmental issues. So, valorization of cheese whey to functional value-added products of high industrial interest and nutritional value (such as proteins, oligosaccharides and carotenoids employing either chemical or bio-catalyzed processes), could possibly constitute a novel waste management option while promoting circular economy principles.*

***Keywords*-cheese whey, bio-based ingredients, functional food, health benefits, value-added products, by-products, bioprocesses.**

I. INTRODUCTION

Cheese whey is the major by-product stream, generated during cheese or casein production process. Cheese whey is of relative high importance for the industrial dairy sector, attributed mainly to 1) its high organic load that makes management cost prohibitive, especially for the medium sized cheesemaking industries 2) its high nutritional value (owning to its functional ingredients).

The current total worldwide production of whey is estimated at about 180 to 190 million tons/year. Of that, 40×10^6 tons/year of whey are produced in the European Union. Approximately 70% of whey is converted, by the implementation of processes, into different products, and still approximately the rest 30% of whey is being utilized either for animal feeding, or as fertilizer or even dumped into the rivers or the sea (Koller et al., 2005; Panesar et al., 2007; Jelen et al., 2003).

During industrial cheese-making process, only 10% of the initial raw milk is bio-converted to cheese, while the rest 90% represents cheese whey. More specifically, it has been estimated that for every 1-2 kg of produced cheese, 8-9 kg of whey are generated. That means that for every 100 kg of milk used to produce different types of cheese, 9.3 ± 0.7 kg of fresh cheese and approximately 90.7 kg of both sweet or acid whey are generated (Baldasso et al., 2011). Besides, considering that cheese whey's organic load is high (expressed by high values of COD (60-80 g/L) and BOD_5 (varied from 35.000 to 55.000 mg O_2/L) its disposal into the environment could erase severe environmental issues (Koutinas et al., 2009). In fact, when this thin watery by-product stream is discharged into water bodies, reduces the dissolved oxygen, impeding biodegradability, while erasing major threats to both aquatic organisms as well as environment, putting at risk human health and welfare. Additionally, when cheese whey is disposed of to the land, provokes serious environmental issues, by changing the physicochemical characteristics of cultivated surrounding soil, lowering cultivated crops productivity (Ghaly et al., 2007). Biological treatment of whey is a rather difficult management option, owning mainly to its acidic pH (3.8-6.5), low alkalinity and sodium, free ammonia, potassium and volatile fatty acid contents. Therefore, proper treatment or re-usage of cheese whey before its disposal is required. So, revalorization of cheese whey to value added products such as functional or bioceutical ingredients could offer a sustainable waste management option, promoting circular economy, while protecting human health.

Generally, there are two possible routes for integrating cheese whey to value added products. The first one entails direct process, referring either to physical or thermal treatment of whey. The outcome of these processes is the transformation of cheese whey to several functional value-added fractions such as whey powder, whey protein concentrate, whey protein isolate, whey-permeate and lactose (Nagar et al., 2013). The second possible revalorization route is oriented toward the implementation of proper bioprocessing systems, using cheese whey as raw material for the production of functional foods or bio-based ingredients. In this case, cheese whey is used, as raw material for various microbial or enzymatic bioconversions, leading to the production of several value-added products such as bio-protein (single cell protein-SCP), enzymes, carotenoids or biopigments, bio-preservatives, biological gums, exo-polysaccharides, microbial oil, and bio-plastics (Dimou et al., 2017; Kopsahelis et al., 2017; Smithers et al., 2015; Barilea et al., 2009; Atra et al., 2004). Demand for whey-based products such as whey protein concentrates, reduced lactose whey, whey protein and hydrolyzed whey is growing, due to their high functional and nutritional properties (Gupta et al., 2012). Moreover, biotransformation of whey permeate into protein-rich biomass, galacto-oligosaccharides and carotenoids seems to be other options of whey valorization to functional products with increased industrial interest.

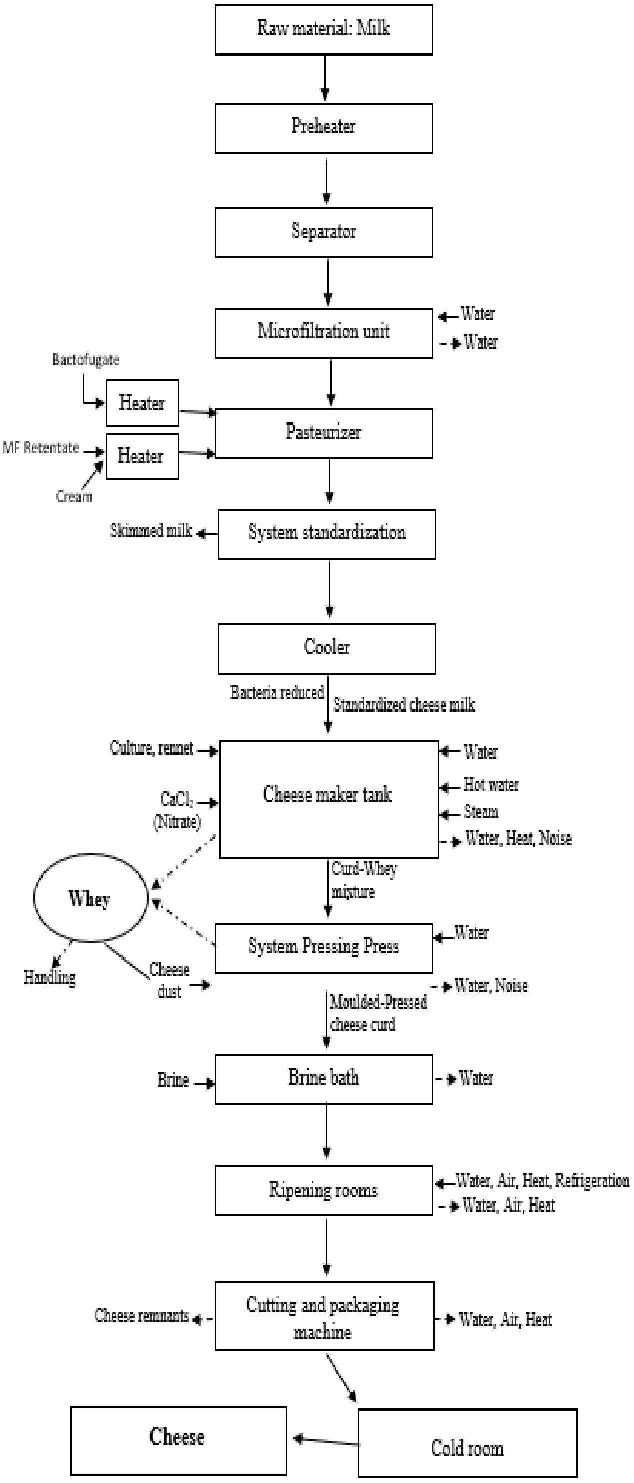
Single cell protein production, using whey as raw material could be carried out by the proper implementation of suitable bioprocessing systems by lactose-consuming yeasts (such as *Kluyveromyces* sp. and *Candida* sp.) and bacteria (such as *Lactobacillus* sp.) bioconversions (Sawin et al., 2015**;** Panesar et al., 2013; Spălăţelu et al., 2012). The produced bio-protein could be used as animal feed or as protein enrichment agent leading to the production of novel rich in protein- functional foods. Also, it should be noted that whey derived proteins hold the highest nutritional quality (Protein Digestibility-Corrected Amino Acid Score=1) among dietary protein sources, while simultaneously have greater biological value than milk protein casein. Besides, most bio-whey based products contain all the spectrum of amino acids including not only the human-essential amino acids but also a large variety of branched chain and sulfur-containing amino acids, which promote metabolic regulation and protein folding (Smithers et al., 2015). Cheese whey-based products (owning to their rich content of bioactive compounds such as protein, lactose, minerals, enzymes and glycomacropeptides) may provide antimicrobial activity, immune modulation, improved muscle strength and body composition, while protecting from the development of cardiovascular diseases and osteoporosis (Smithers et al., 2015; Gupta et al., 2012) Indeed, cheese whey bio-proteins may also possess several in-vivo biological functions with positive effects on digestive, endocrine and nervous system (Gupta et al., 2012; Sawin et al., 2015). However, designing and implementing novel bioderived processing systems leading to the production of carotenoids, using cheese whey as raw material is of high academic interest, aiming at substituting chemical synthesized counterparts. Possible bio-carotenoid production using cheap substrates such as cheese whey, could satisfy the trend towards natural food coloring, not to mention that carotenoids, as functional ingredients fulfill a variety of biological and physiological roles in living organisms, ranging from light harvesting in photosynthesis to protection against light and oxidizing agents (Dimou et al., 2017). Valorization of agroindustrial products toward the production of value-added products of industrial food interest is a current and emerging trend, opening new roads toward the production of novel functional foods of high nutritional value (Dimou et al., 2017; Dimou et al., 2016a; Dimou et al., 2016b; Dimou et al., 2016c; Dimou et al., 2015).

This paper highlights potential valorization routes of cheese whey to value added products of high nutritional value and industrial food interest such as bioproteins and carotenoids. However, beneficial health promoting effects of cheese whey derived products (bioactive peptides or bioproteins) are discussed.

II. CHEESE WHEY AN UNEXPLOITED VALUABLE FEEDSTOCK FOR THE PRODUCTION OF VALUE-ADDED FUNCTIONAL PRODUCTS

Cheese whey is the main liquid watery by product stream generated after the precipitation and removal of milk casein throughout cheese manufacturing process, using milk as raw material. Approximately 33% of the worldwide milk production is used in cheese manufacturing process, yielding about $19x10^6$ tones cheese whey per year (Blaskó et al., 2012). A general flowchart of cheese production process, highlighting cheese whey formulation (after the coagulation of milk caseins), as a by-product stream of cheese processing is presented in Figure-1. Until recently, sweet whey has been discarded or used as animal feed, without further exploited towards the production of valuable functional ingredients. Recovering the solid components of whey is attractive for two main reasons: 1) for reducing organic pollution caused when cheese whey waste streams are disposed of in open areas and 2) for recovering from whey, value added products of high nutritional value as well as functional properties.

https://dx.doi.org/10.22161/ijhaf.3.2.5 ISSN: 2456-8635



Regarding cheese whey physical characteristics; color of whey varies from a dominantly yellow/green to rarely a bluish tinge. As logical, color is strongly influenced by the type of milk used for cheese making. Whey is produced from all types of milk. In Europe, the most usual type of milk used is cow's milk. Also, other types of milk are used for the production of cheese such as goat's, sheep's and camel's milk (Bordenave-Juchereau et al., 2005). It is worth-noting, that the final nutritional value and composition of resulting whey is highly associated with the initial type of milk used for the production of each type of cheese.

Both traditional and modern cheese manufacturing processes, lead to the production of huge watery effluents, which corresponds to approximately 90% of the initial volume of milk used for cheese making. Whey retains more than 55% (w/v) of the bio-compounds contained in the initial milk used as the main raw material for cheese making production process. Cheese whey contains approximately: lactose (4.5-5 % w/v); soluble proteins (0.6-0.8% w/v); lipids (0.4-0.5 w/v) and mineral salts (8-10 w/v, of dried extract) (Nagar et al., 2013). So, this effluent could be regarded as a valuable matrix rather than a waste product stream that could find several potential applications in food, health and pharmaceutical sector.

III. POTENTIAL INTEGRATION OF CHEESE WHEY TO VALUE ADDED PRODUCTS

Processing of cheese whey, owning to its residual milk constituents, could lead to the production of several value-added products of high commercial value. Nowadays, almost the 50% of the total produced cheese whey, world-widely, is revalorized into different functional and nutritional value-added products, with increased industrial interest. Of these commercialized food products, the 45% are in liquid form, 30% are different types of dried whey powder, 15% is lactose and the remaining fraction consist of by-product streams remained during the production of whey protein concentrates (Panesar et al., 2013; Kossea et al., 2009; Carvalho et al., 2013). Nowadays, several functional whey-based products are produced, using cheese whey as raw material, employing proper developed bioprocesses and physicochemical techniques. The most significant commercially available functional cheese whey-based products are: whey powder, whey concentrate, whey protein isolate, single cell protein, exo-polysaccharides and bio-carotenoids. In fact, physicochemical processes could lead to the production of protein rich whey products such as: 1) whey powder, 2) whey permeate fractions, and 3) concentrated whey proteins. Physicochemical treatment of cheese whey includes the implementation of processing steps such as precipitation with coagulants or thermal/isoelectric precipitation and membrane separation (for instance ultrafiltration, reverse osmosis, ultrafiltration etc.) (Prazeres et al., 2012). More specifically, whey powder could be produced directly from cheese whey (Figure-1). Cheese whey is first pasteurized and then dried. Finishing drying process, a fine white powder, called whey powder is produced (Kargi et al., 2006). Whey concentrate streams are typically filtered (using more frequently ultrafiltration and reverse osmosis), so as to filter cheese or concentrate whey components based on the pore size of the membrane and the molecular weight of the whey filtered

https://dx.doi.org/10.22161/ijhaf.3.2.5 ISSN: 2456-8635

components. Through passing the semi-permeable membrane, cheese whey's lactose and salts (smaller particles) are removed, yielding concentrates of different protein contents. Throughout the aforementioned process leading to protein concentrated, two streams are generated: whey permeate containing mainly lactose and salts and a whey protein isolate fraction (Nasseri et al., 2011). Whey protein isolate in fact is a proteinaceous rich whey-based functional product containing more than 90 % proteins. These functional value-added products could be further exploited by a large variety of processes. Of them, the most usual are microfiltration and ion exchange. Via microfiltration additional fat and lactose are removed so as to facilitate up to 90% (increased) protein concentration in the final whey protein product. Advanced chromatography techniques may then be implemented so as to fractionate individual function protein isolates such as lactoferrin, lactoperixidase (from the main whey proteins: α-lactalbumin, β-lactoglobulin and bovine serum albumin) and glycomacropeptide (Neville et al., 2006; Barile et al. 2009) which are functional ingredients of high nutritional value. Also, several functional products such as peptides, oligosaccharides, single cell protein and carotenoids could be produced, through the implementation of proper bioconversion systems, using cheese whey or cheese permeate as cheap raw material (Table-1). However, several times prior to bioconversions lactose hydrolysis should take place, so as to enhance whey usefulness and product yields, when microorganisms are unable to utilize it. Lactose hydrolysis to monosacharaides (glucose and galactose) could either be catalyzed enzymatically, using β-galactosidase or by acid hydrolysis treatment (Aguirre-Ezkauriatza et al., 2010). Hydrolyzed lactose from whey permeate could be used as a substrate for the production of exopolysaccharides - E.P.S by fermentation. Xanthan gum (a heteropolysaccharide) could be produced by a number of microorganisms such as Xanthomonas sp though the development of proper bioprocessing systems. Xanthan gum find several applications in the production of food products (bakery, prepared foods, and beverages) and drug formulations in tablets and suspensions, owning to its unique rheological properties, such as highly pseudo-plastic behavior (which contributes to its wide-range applications as suspending, stabilizing, thickening and emulsifying agent for food and pharmaceutical applications) (Regenhardt et al., 2013). Hydrolyzed lactose from whey permeate could be used as a substrate for the production of exopolysaccharides - E.P.S by fermentation.

Table-1: Bio-utilization of cheese whey through the implementation of proper bioprocessing systems for the production of several functional products.

Product category	Micro-organism	Product	Fermentation System	Ref
Peptides and proteins	*Lactococcus lactis*	Nicin Bacteriocin	Continuous	Liu et al., 2005
	Kluyveromyces marxianus & Lactobacillus rhamnosus	ACE-Inhibitory Peptides (Antihypertensive)	Shake Flask	Hamme et al., 2009
Oligo-saccharides and biopolymers	*Kluyveromyces marxianus*	Galacto - oligo-saccharides	Shake Flask	Petrova et al., 2009
	Xanthomonas campestris	Xanthan gum	Batch/ Bioreactor	Mesomo et al., 2009
	Lactobacillus rhamnosus	Expoly-saccharides (EPS)	Batch/ Bioreactor	Pham et al., 2000
	Kluyveromyces lactis	d-Arabitol	Shake Flask	Toyoda et al., 2011
Probiotics and Single Cell Protein	Kefir microflora	Single Cell-Protein	Fed Batch/ Bioreactor	Paraskevopoulou et al., 2003
	Lactobacillus casei	Probiotics	Fed Batch/ Bioreactor	Aguirre-Ezkau-riatza et al., 2010
Carotenoids	*Rhodotorula glutinis*	Total-Carotenoids	Shake Flask	Koutelidakis et al., 2019

Xanthan gum (a heteropolysaccharide) could be produced by a number of microorganisms such as *Xanthomonas* sp though the development of proper bioprocessing systems. Xanthan gum find several applications in the production of food products (bakery, prepared foods, and beverages) and drug formulations in tablets and suspensions, owning to its unique rheological properties, such as highly pseudo-plastic behavior (which contributes to its wide-range applications as suspending, stabilizing, thickening and emulsifying agent for food and pharmaceutical applications) (Regenhardt et al., 2013). It has been also reported that whey lactose is also used to produce dextrans (through *Leuconostoc* sp, *Streptococcus* sp, *Rhizobium* sp bioconversions), and biopolymers (such as poly-β-hydroxy butyrate) (Niknezhad et al., 2015; Ribeiro et al., 2015; Kopsahelis et al., 2017; Ramalingam et al., 2014; Purwandari et al., 2007). Regarding dextrans, apart from their usage as food syrup stabilizers and dough improvers these functional ingredients could also find several applications in pharmaceutical and health care

https://dx.doi.org/10.22161/ijhaf.3.2.5 ISSN: 2456-8635

sector (Xue et al., 2016). Clinical dextrans of molecular size ranking from 40 to 100 kDa are used as therapeutic agents to restore blood volume in case of casualties (De Vuyst et al., 2001). Furthermore, since the larger molecular weight dextrans can act as osmotic agents, these biomolecules could be used to treat hypovolemia. Also, a cyclic oligosaccharide derived from dextran, cyclodextrin, could be used as cariostatic, anti-HIV and anti-ulcer agent (De Vuyst et al., 2001). It should be stressed out that E.P.S finds several applications in industrial food and pharmaceutical sector as gelling, thickening and stabilizing agents. Bio-products such as xanthan gum and dextran, commonly used in food processing sector, have been approved by F.D.A to be used as food additives (Ramalingam et al., 2014). In the last years, EPS's prebiotic role has been identified and described. Apart EPS role as prebiotics, *Lactobacillus* sp synthesized EPS have been reported to have several health promoting beneficial effects, acting as anti-tumor, immune-stimulator and blood cholesterol lowering agents (Zannini et al., 2013). Potential carotenoid production (β-carotene, torulene), using microbial strains such as *Rhodotorula glutinis* and cheese whey as raw material, has been reported (Koutelidakis et al., 2019). Humans are unable to biosynthesize carotenoids, and therefore, they must be supplied with diet. Owning to their antioxidant activity, carotenoids protect the skin against the UV light. Furthermore, they strengthen the immune system and accelerate wound healing. Some carotenoids constitute vitamin A precursors, and thus may be protective in eye disease. So, bio-carotenoids hold a great potential to be used as fortifying vitamin "carrier" for the production of nutrient supplements and functional food, preventing and in some cases decreasing the severity of hypovitaminosis-A. Bio-carotenoids are used in food production as food pigments or coloring agents, substituting their chemical synthesized counterparts. Recently, the increasing consumer awareness on the negative effect of synthetic pigments on human health has increased interest in natural pigments. The use of microorganisms as "bioreactors" for the production of carotenoids might serve human health leading to the production of "healthy bio-carotenoids" substituting their chemical synthesized counterparts (Dimou et al., 2017). Microbiological synthesis of different types of carotenoids, using cheese whey as raw material, is of high interest and more research should be carried out.

IV. WHEY PROTEINS: PROPERTIES AND FUNCTIONALITY

Lately, there is a current trend in separating out (concentrate) proteinaceous functional products from cheese whey using sophisticated downstream processes. The common in vitro bottom-up proteomics include the following steps: 1) isolation of proteins or a protein mixture from a food matrix, such as cheese whey, 2) hydrolysis of proteins by different enzymatic proteases. The most common enzymes used are: (a) pepsin, trypsin and chymotrypsin (gastrointestinal enzymes), (b) alcalase, bromelain and ficin, proteases originated from microorganisms or plants, (c) enzymes present in cheese making bioprocessing, by starter *Lactobacillus* or non-starter *Lactobacillus* (3) fractionation, separation, isolation and purification of functional peptides or proteins, (4) bioactivity tests, (5) identification of interesting bioactive peptides (Agyei et al., 2016).

Whey protein consists of several different proteins, including β-lactoglobulin (β-LG), α-lactalbumin (α-LA), the heavy- and light-chain immunoglobulins (Igs), bovine serum albumin (BSA), lactoferrin (LF), lactoperoxidase (LP), and glycomacropeptide (GMP). Whey protein may also contain protease-peptone components and low-molecular-weight products formed during enzymatic casein degradation throughout cheese making process (Madureira et al., 2007). The average individual proteins' concentration in cheese as well as their characteristics is depicted in "Table-2".

Compared to various vegetable proteins sources, whey protein has all the essential amino acids in higher concentrations. It contains all 20 amino acids and all nine essential amino acids. Because of its content of essential amino acids, the biological value of whey protein is high compared to other dietary proteins (Madureira et al., 2007).

Table.2: Average individual protein content of cheese whey and their principal characteristics.

Protein	Content (% w/w)	Molecular mass (kDa)	Isoelectric pH (pI)
β-Lactoglobulin (β-LG)	40.0-50.0	18.3	5.35-5.49
α-Lactalbumin (α-LA)	12.0-15.0	14.0	4.2-4.5
Glycomacropeptide (GMP)	12.0	6.8	4.3-4.6
Immunoglobulins (Igs)	8.0	150-1000	5.5-8.3
Bovine serum albumin (BSA)	5.0	66.0	5.13
Lactoferrin (Lf)	1.0	76.5	9.5-10.0
Lactoperoxidase (LP)	0.5	78.0	9.5

β-Lactoglobulin (β-LG) is one of the most important whey proteins, accounting for approximately either 64% of the heat-coagulable proteins or 51% of the total whey proteins. Its molecular weight varies from 18.20 to 18.36 kDa. Generally, it is consisted of 2 identical subunits, as a dimer. In fact, each monomer consists of one sulfhydryl group and two disulfide bonds. The number of amino acids in the single peptide chain of β-LG is 162. Whey protein isolate is a functional proteinaceous product which in fact is whey isolate enriched with β-LG. It should be noted that enriched with β-LG whey protein isolate products demonstrate enhanced functional properties (such as emulsion stability, activity, viscosity and gelling properties) compared to cheese whey concentrate (Hernández-Ledesma et al., 2011, Madureira et al., 2007). Results of work on β-LG gelation indicated that it may demonstrate gel strength as much as three times greater than that of egg white protein at the same protein concentration. This suggested that β-LG fraction was capable of replacing egg white in the manufacture of processed meat and fish products (Rantamaki et al., 2010).

The bovine serum albumin (BSA) component of whey is a large globular protein with a good essential amino acid profile. More specifically, the number of amino acids in BSA is 582. Whey protein contains approximately 5-6% bovine serum albumin, which is almost suchlike to that included to human milk. The molecular mass of BSA is 66.26 kDa. BSA molecule is consisted of 35 cysteine residues and 17 disulfide linkages. The nature of BSA is very heterogeneous and in fact its content in milk is approximately the same included in bovine blood (Modler et al., 2009). One important feature of BSA is that it could be used as a carrier of fatty acids, owning to its capacity to bind reversibly to several ligands (Markus et al., 2002). Furthermore α-LA and α-LA-peptides could be used as food supplements of essential amino acids demonstrating several beneficial effects either by improving immune system, reducing the stress, enhancing opioid activity or by demonstrating antihypertensive action, as well as by provoking regulation of cell growth (Matsumoto et al., 2001). Furthermore, cheese whey α-La, owning to its high content of amino acids (such as cysteine), promote wound healing, while boosting the immune system, preventing the development of chronic diseases. So, utilization of α-La, as enrichment agent or bioceutical for the production of infant formulas is of high academic interest. Regarding the positive health effects of milk or cheese whey α-La are numerous. It has been revealed that α-La have potential anti-proliferative effects in human adenocarcinoma cell lines such as Caco-2 and HT-29 (Brück et al., 2014). It is well known that human α-lactalbumin and oleic acid (HAMLET), is the first member in a new family of protein-lipid complexes. These complexes were first isolated from human milk. Hamlet may act as a potent anticancer agent, killing tumor cells with high selectivity. Protein-lipid complexes impart tumoricidal properties on a broad basis, targeting novel treatments by identifying death pathways (Brück et al., 2014). BAMLET, which in fact is the bovine milk a-lactalbumin counterpart of HAMLET, remaining also in cheese whey derived from bovine milk cheese making process, triggers in cancer cells a pathway for lysosomal cell death; therefore, alpha-lactalbumin: oleate complexes can kill tumor cells that are highly resistant to apoptosis (Ho et al., 2012; Rammer et al., 2013).

Immunoglobulins (Igs) constitute a complex group of protein molecules. In fact, Ig is an antibody or gamma globulin. It seems that the whey fraction of milk contains Igs, corresponding approximately to 10-15% of total whey proteins. The Igs in whey have demonstrated antimicrobial activity and a great potential to neutralize toxins and viruses. It has been revealed that raw milk from non-immunized cows contains specific antibodies to *Escherichia coli*, *Salmonella enteritidis*, *Salmonella typhimurium* and *human rotavirus* (Gregor et al., 2013; Yolken et al., 1985).

Bioactive components derived from whey fractions, such as Igs, GMP (Glycomacropeptide) and whey-derived minerals have demonstrated specific health benefits, such as enhanced immune function and antioxidant activity, relief of metabolic stress, positive stress responses, improved muscle functionality and greater strength (Philanto-Leppala. 2001). Controlled clinical studies have shown that the oral administration of immune milk preparations containing specific antibodies may have therapeutic value against gastrointestinal infections in humans (Gupta et al., 2017).

Lactoperoxidase (LP) is the most abundant enzyme in whey. Its molecular mass is 78 kDa and in fact is a single polypeptide chain of 612 amino acid residues. It contains 15 cysteines, one heme group and about 10% w/w of carbohydrate moieties (Modler, 2009). It accounts for 0.25-0.50% of total protein found in whey. Actually, LP could possibly act protectively against infectious microbes (Gupta et al., 2017; Shin et al., 2005).

Glycomacropeptide (GMP) is a caseino-macropeptide (CMP), formed during cheese making process from milk k-casein component through the action of the milk-clotting enzyme (e.g. chymosin). The GMP's amino acid residue is 64. Also, its MW and isoelectric pH is equal to 6.8 kDa and varied from 4.3 to 4.6, accordingly (Rajput et al., 2013). GMP molecules have unique attributes owning to the absence of aromatic amino acids (more specifically phenylalanine, tryptophan, tyrosine, histidine, arginine or cysteine) (Philanto-Leppala, 2001). Thus, this glycomacropeptite, if properly isolated from cheese whey could be used as dietary ingredient for the formulation of products suitable for patients who suffer from phenylketonuria (since glycomacropeptide is free of phenylalanine). Phenylketonuria is an inborn error of amino acid (AA) metabolism. This is caused by deficient activity of the enzyme phenylalanine hydroxylase. Phenylalanine hydroxylase is needed to convert the essential AA phenylalanine to tyrosine (Acosta et al., 2010; Baldasso et al., 2011). So, in that case the development of a suitable nutritional program in the form of low-phenylalanine diet, enriching it with GMP functional products, could help patients achieve metabolic control of phenylalanine levels (Rajput, 2013). By the proper free phenylalanine diet, those who suffer of inborn phenylketonuria could normally allow the development of their brain. Indeed, since GMP, is a bioactive peptide whose unique composition and characteristics may offer health-promoting effects, forms a potential ingredient for various functional foods and pharmaceuticals.

V. WHEY PROTEINS: PROPERTIES AND FUNCTIONALITY

Nowadays, it is well known that whey proteins have several functional properties and are characterized by high nutritional value. The functional properties of cheese whey are mainly attributed to physical, chemical and structural characteristics of cheese whey's individual proteins content. Regarding the nutritional value of cheese whey, it should be noted that it is highly associated with the concentration of contained (depending on cheese whey type and milk origin) essential amino acids (especially sulfur-containing ones) as well as branched-chain amino acids (isoleucine, leucine and valine) (Acosta et al., 2010). Moreover, whey proteins are generally recognized as GRAS for food applications. So, cheese whey could find several applications in the production of several functional, rich in whey, food products such as healthy foods, dairy foods, meat products, frozen foods and baby food formulations (Baldasso et al., 2011). Also, it has been reported that whey proteins are already used in bakery, confectionary, meats and seafood leading to the formation of a strong gel with high water-holding capacity (Acosta et al., 2010; Baldasso, et al., 2011, Takayanagi et al., 2011).

The anti-inflammatory effects of cheese whey-based products have been revealed. The beneficial effects of whey-based formula MHN-02; MEIN® (Meiji, Japan) in hepatitis mouse model, have been revealed (Takayanagi et al., 2011). It has been demonstrated that tryptic peptides through the regulation of tumor necrosis factor-a and interferon-g production, in a concanavalin A-induced hepatitis model, prevent the increase of plasma aspartate aminotransferase and alanine aminotransferase (Takayanagi et al., 2011; Kume et al., 2006). It has been demonstrated that tryptic peptides through the regulation of tumor necrosis factor-a and interferon-g production, in a concanavalin A-induced hepatitis model, prevent the increase of plasma aspartate aminotransferase and alanine aminotransferase (Kume et al., 2006). Besides, whey proteins and peptides have shown a hepatoprotective effect in a d-galactosamine-induced hepatitis model, through their preventing action against the increase of plasma levels of hepatic function markers, including bilirubin, alanine aminotransferase aspartate aminotransferase and lactate, dehydrogenase (Salehi et al., 2012). Also, it has been reported that early enteral nutrition with this enriched with cheese whey immune-regulating formula is able of preventing post-transplant bacteremia and hyperglycemia without increasing the potential development of acute cellular rejection in patients (Kaido et al., 2012). The anti-cancer effects of whey have been instigated by the conduction of animal studies. Cheese whey's anticancer potential has been mainly attributed to the antioxidizing, detoxifying, and immune-enhancing effects of lactoferrin. Mice performed studies revealed that, in lactoferrin presence, colon cancer demonstrated reduced tumor expression while cancer metastasis was inhibited (Sekine et al., 1997). Cheese whey could be regarded as an ideal optional source of protein and peptides, owning to its enhanced absorption in the intestines especially for those who suffer from compromised gastrointestinal function, for instance ileostomy patients. It is possible that patients who suffer from cancer, undergoing chemotherapy may benefit from this feature of whey, since anti-cancer therapies influence nutrient intake and absorption (Shariatikia et al., 2017). Besides, the positive effects of milk products in lowering blood pressure and reducing the risk of hypertension have been revealed. An 8-week trial, in which 20 healthy men were administrated by a combination of fermented milk and whey protein concentrate, demonstrated comparatively higher high-density lipoproteins, lower triglycerides and lower systolic blood pressure (Kawase et al., 2000). Besides, the positive effects of milk products in lowering blood pressure and reducing the risk of hypertension have been revealed. An 8-week trial, in which 20 healthy men were administrated by a combination of fermented milk and whey protein concentrate, demonstrated comparatively higher high-density lipoproteins, lower triglycerides and lower systolic blood pressure (Kawase et al., 2000). Also, it has been claimed that certain bioactive peptides, formed throughout the hydrolysis of food proteins, inhibit angiotensin converting enzyme (ACE), acting positively in reducing blood pressure (Korhonen et al., 2007).

VI. CONCLUSION

Valorization of CW to functional ingredients (such as whey proteins, individual peptides, cheese whey concentrates, cheese whey hydrolysates, oligosaccharides, single cell protein and bio-carotenoids) could offer an alternative ecological and sustainable option of addressing waste management issues, promoting circular economy and human health, preventing or sometimes acting therapeutically against the development of diseases including the chronic ones, while providing market with a wide spectrum of functional and health promoting value added products.

ACKNOWLEDGEMENTS

This project has received funding from the Hellenic Foundation for Research and Innovation (HFRI) and the General Secretariat for Research and Technology (GSRT), under grant agreement No 2342 (Principle director Dr Dimou Charalampia).

REFERENCES

[1] Acosta, P.B.; Matalon, K.M. Nutrition management of patients with inherited disorders of aromatic amino acid metabolism. In: Acosta PB, editor. Nutrition Management of Patients with Inherited Metabolic Disorders, Boston, Jones and Bartlett Publishers, 2010; pp 119-174.

[2] Aguirre-Ezkauriatza, E.; Aguilar-Yáñez, J.; Ramírez-Medrano, A.; Alvarez, M. Production of probiotic biomass *Lactobacillus casei* in goat milk whey: comparison of batch, continuous and fed-batch cultures. Bioresour Technol, **2010**, *101*, 2837-2844. https://doi.org/10.1016/j.biortech.2009.10.047

[3] Agyei, D.; Ongkudon, C.M.; Wei, C.Y; Chan, A.S.; Danquah, M.K. Bioprocess challenges to the isolation and purification of bioactive peptides. Food Bioprod Processing **2016**, *98*, 244-256. https://doi.org/10.1016/j.fbp.2016.02.003

[4] Atra, R.; Vatai, G.; Bekassy-Molnar E, Balint A. Investigation of ultra and nanofiltration for utilization of whey protein and lactose. *J Food Eng* 2004, 67, 3, 325-332. https://doi.org/10.1016/j.jfoodeng.2004.04.035

[5] Baldasso, C.; Barros, T.C.; Tessaro I.C. Concentration and purification of whey proteins by ultrafiltration. *Desalination* **2011**, *278*, 1-3, 381-386. https://doi.org/10.1016/j.desal.2011.05.055

[6] Barile, D.; Tao, N.; Lebrilla, C.B.; Coisson J.D, Arlorio, M.; Germana J. B. Permeate from cheese whey ultrafiltration is a source of milk oligosaccharides. *Int Dairy J* **2009**, *19*, 9, 524-530. https://doi.org/10.1016/j.idairyj.2009.03.008

[7] Barilea, D.; Tao, N.; Carlito, Lebrilla B.; Jean-Daniel Coisson.; Arlorio M., Bruce German, G. Permeate from cheese whey ultrafication is a source of milk oligosaccharides. *Int Dairy J* **2009**, 524-530. https://doi.org/10.1016/j.idairyj.2009.03.008

[8] Bordenave-Juchereau, S.; Almeida, B.; Piot, J.M.; Sannier F. Effect of protein concentration, pH, lactose content and pasteurization on thermal gelation of acid caprine whey protein concentrates. *J. Dairy Res* **2005**, *72*, 34-38.

[9] Brück, WM.; Gibson, GR.; Brück, TB. The effect of proteolysis on the induction of cell death by monomeric alpha-lactalbumin. *Biochem* 2014, 97, 138-143. https://doi.org/10.1016/j.biochi.2013.10.007

[10] Blaskó, B. World importance and present tendencies of dairy sector. Applied Studies in Agribusiness and Commerce – APSTRACT. Budapest, Hungary: *Agroinform Publishing House*, **2012**, 119-23.

[11] Carvalho, F., Prazeres, A.R., Rivas J. Cheese whey wastewater: characterization and treatment. *Sci. Total Environ* **2013**, *445*, 385-396. https://doi.org/10.1016/j.scitotenv.2012.12.038

[12] De Vuyst, L.; De Vin, F.; Vaningelgem, F.; Degeest, B. Recent developments in the biosynthesis and applications of heteropolysaccharides from lactic acid bacteria. *International Dairy J* **2001**, *11*, 687-707. https://doi.org/10.1016/S0958-6946(01)00114-5

[13] Dimou, C.; Koutelidakis, E.A.; Nasopoulou, C.; Karantonis, H. Current trends and emerging technologies in biopigment production processes: Industrial food and health applications. *Inte J Horticult, Agricult and Food Science* **2017b**, *1*, 2, 33-46.

[14] Dimou, C.; Koutelidakis, E.A. Value added alternatives of winemaking process residues: A health based oriented perspective. *BAOJ Biotechnol* **2016a**, *2*, 3, 016. https://bioaccent.org/biotechnology/biotechnology16.pdf

[15] Dimou, C.; Koutelidakis, E.A. Grape pomace: A challenging renewable resource of bioactive phenolic compounds with diversified health benefits. MOJ *Food Processing and Techn* **2016b**, *3*, 1, 262-265. https://medcraveonline.com/MOJFPT/MOJFPT-03-00065

[16] Dimou, C.; Vlysidis, A.; Kopsahelis, N.; Papanikolaou, S.; Koutinas, A.A, Kookos, I.K. 2016. Techno-economic analysis of wine lees valorisation for the production of high value-added products. *Biochem Eng J* **2016c,** *116*, 157-165.

[17] Dimou, C.; Koutelidakis, E.A. 2017. From pomegranate processing by-products to innovative value-added functional ingredients and biobased products with several applications in food sector. *BAOJ Biotechnol*. 3:025.

[18] Gregor, Mc.; Poppitt, S.D. Milk protein for improved metabolic health: a review of the evidence. *Nutr Metab (Lond)* **2013**, *10*, 46. https://doi.org/10.1186/1743-7075-10-46

[19] Ghaly, A..; Mahmoud, N. S.; Rushton, D. G.; Arab, F. Potential Environmental and health impacts of high land application of cheese whey. *American J Agricult Biologic Science* **2007**, *2*, 106-117. https://doi.org/10.3844/ajabssp.2007.106.117

[20] Gupta, C.; Prakash, D.; Garg, A.P; Gupta, S. Whey proteins: A novel source of bioceuticals. Middle-East *J Sci Res* **2012**, *12*, 3, 365-375.

[21] Gregor, Mc.; Poppitt, S.D. Milk protein for improved metabolic health: a review of the evidence. *Nutr Metab (Lond)* **2013**, *10*, 46. https://doi.org/10.1186/1743-7075-10-46

[22] Hamme, V.; Sannier, F.; Piot, J.M.; Didelot, S.; Bordenave-Juchereau. S. Crude goat whey fermentation by *Kluyveromyces marxianus* and *Lactobacillus rhamnosus*: contribution to proteolysis and ACE inhibitory activity. J. Dairy Res **2009**, *76* 152-157. https://doi.org/10.1017/S0022029908003877

[23] Hernández-Ledesma, B.; Ramos, M.; Gómez-Ruiz, J.Á. Bioactive components of ovine and caprine cheese whey. *Small Rumin Res* **2011**, *101*, 196-204. https://doi.org/10.1016/j.smallrumres.2011.09.040

[24] Ho, C.S.J.; Rydström, A.; Trulsson, M.; Bålfors, J.; Storm, P. HAMLET: functional properties and therapeutic potential. *Future Oncol* **2012**, *8*, 1301-1313.

[25] Jelen, P. Whey processing. In: Encylcopedia of dairy sciences. Roginski, H.; Fuquay, J. W.; P. F. Fox. ed; Academic Press. London, **2003**, pp 2739-2751. ISBN: 0122272358

[26] Kargi, F.; Ozmihci S. Utilization of cheese whey powder for ethanol fermentations: effect of operating marameters. Enz Microb Technol **2006**, *38*, 5, 711-718. https://doi.org/10.1016/j.enzmictec.2005.11.006

[27] Kaido, T.; Ogura, Y.; Ogawa, K.; Hata, K.; Yoshizawa, A. Effects of post-transplant enteral nutrition with an immunomodulating diet containing hydrolyzed whey peptide after liver transplantation. *World J Surg* **2012**, *36*, 1666-1671. https://doi.org/10.1007/s00268-012-1529-9

[28] Kawase, M.; Hashimoto, H.; Hosoda, M.; Morita, H.; Hosono, A. Effect of administration of fermented milk containing whey protein concentrate to rats and healthy men on serum lipids and blood pressure. *J Dairy Sci* **2000**, *83*, 2, 255-63.https://doi.org/10.3168/jds.S0022-0302(00)74872-7

[29] Koller, M; Bona, R.; Braunegg, G.; Hermann, C.; Horvat, P.; Kroutil, M.; Martinz, J.; Neto, J.; Pereira, L.; Varila, P. Production of Polyhydroxyalkanoates from Agricultural Waste and Surplus Materials. *Biomacromolecules* **2005**, *6*, 561-565. https://doi.org/10.1021/bm049478b

[30] Kopsahelis, N.; Dimou, C.; Papadaki, A.; Xenopoulos, E.; Kuraleou, M.; Kalithraka, S.; Kotseridis, Y.; Papanikolaou, S.; Koutinas AA. Refining of wine lees and cheese whey for the production of microbial oil, polyphenol-rich extracts and value-added co-products. *J Chem Technol Biotechnol* **2017**, *93*, 1. https://doi.org/10.1002/jctb.5348

[31] Koutelidakis EA, Mavropoulou R, Karantonis HC, Yanniotis S, Charalampia Dimou. Exploiting cheese whey potential bio-conversion to several value-added functional bio-based compounds with nutritional and industrial food interest. Accepted for poster presentation (21/1/2019). 3rd International Conference on Food and Nutritional Sciences. Paris. France.

[32] Koutinas, A.A.; Papastolou, H.; Dimitrellou, D.; Kopsahelis, N.; Katechaki, E.; Bekatorou, A.; Bosnea, L.A. Whey valorisation: a complete and novel technology development for dairy industry starter culture production. *Bioresour Technol* **2009**, 100, *15*, 3734-9. https://www.ncbi.nlm.nih.gov/pubmed/19254836

[33] Korhonen, H.; Pihlanto, A. Technological options for the production of health-promoting proteins and peptides derived from milk and colostrum. *Curr Pharm Des* **2007**, *13*, 8, 829-43. https://doi.org/10.2174/138161207780363112

[34] Kossea, M.R.; Panesar, P.S.; Kaur, G.; Kennedy, J.F. Use of immobilized biocatalysts in the processing of cheese whey. *Int. J. Biol. Macromol* **2009**, *45*, 437-447. https://doi.org/10.1016/j.ijbiomac.2009.09.005

[35] Kume, H.; Okazaki, K.; Sasaki, H. Hepatoprotective effects of whey protein on D-galactosamine-induced hepatitis and liver fibrosis in rats. *Biosci Biotechnol Biochem* **2006**, *70*, 1281-1285. https://doi.org/10.1271/bbb.70.1281

[36] Liu, X.; Chung, Y.K.; Yang, S.T.; Yousef, A.E. Continuous nisin production in laboratory media and whey permeate by immobilized *Lactococcus lactis*. *Process Biochem* **2005**, *40*, 13-24. https://doi.org/10.1016/j.procbio.2003.11.032

[37] Madureira, A.R.; Pereira, C.I.; Gomes, A.M.P.; Pintado, M.E.; Malcata F. Xavier. Bovine whey proteins - overview on their main biological properties. *Food Res. Int*, **2007**, *40*, 1197-1211. https://doi.org/10.1016/j.foodres.2007.07.005

[38] Markus, C.R.; Olivier, B.; Haan, E.H. de. Whey protein rich in alpha-lactalbumin increases the ratio of plasma tryptophan to the sum of the other large neutral amino acids and improves cognitive performance in stress-vulnerable subjects. *Am J Clin Nutr* **2002**, *75*, 1051-1056. https://doi.org/10.1093/ajcn/75.6.1051

[39] Matsumoto, H.; Shimokawa, Y.; Ushida, Y.; Toida, T.; Hayasawa, H. New biological function of bovine α-lactalbumin: Protective effect against ethanol- and stress-induced gastric mucosal injury in rats. *Biosci, Biotechnol and Biochem* **2001**, 65, 1104-11. https://doi.org/10.1271/bbb.65.1104

[40] Mesomo, M.; Silva, M.F.; Boni, G.; Padilha, F.F.; Mazutti, M.; Mossi, A. *et al*. Xanthan gum produced by *Xanthomonas campestris* from cheese whey: production optimization and rheological characterization. *J Sci Food Agric* **2009**, *89*, 2440-2445. https://doi.org/10.1002/jsfa.3743

[41] Modler, W. Pioneer paper: Value-added components derived from whey. American Dairy Science Association **2009**, 1-33.

[42] Neville, J. Developments in whey protein and lactose permeate production processes and their relationship to specific product attributes. *Int. J. Dairy Techn* **2006**, *59*, 2, 67-69. https://doi.org/10.1111/j.1471-0307.2006.00244.x

[43] Nasseri, A.T.; Rasoul-Amini, S.; Morowvat M.H.; Ghasemi Y. Single Cell Protein: Production and Process. *Am. J. F. Techn* **2011**, *6*,103-116. https://doi.org/10.3923/ajft.2011.103.116

[44] Nagar, S.; Nagal, S. Whey: composition, role in human health and its Utilization in preparation of value- added products. *Int J Food Ferment Technol* **2013**, 3, *2*. https://doi.org/10.5958/2277-9396.2014.00336.5

[45] Niknezhad S.V.; Asadollahi. M.A.; Zamani, A.; Biria, D.; Doostmohammadi, M. Optimization of Xanthan Gum Production Using Cheese Whey and Response Surface Methodology. *Food Sci. Biotechnol* **2015**, *24*, 2, 453-460. https://doi.org/10.1007/s10068-015-0060

[46] Purwandari, U.; Shah, N. P.; Vasiljevic, T. Effects of exopolysaccharide-producing strains of *Streptococcus thermophilus* on technological and rheological properties of set-type yoghurt. *Int. Dairy J* **2007**, *17*, 1344-1352. https://doi.org/10.1016/j.idairyj.2007.01.018

[47] Panesar, PS., Kennedy J.F., Gandhi D.N., Bunko K. Bio-utilisation of whey for lactic acid production. *Food Chem* **2007**, *105*, 1-14. https://doi.org/10.1016/j.foodchem.2007.03.035

[48] Pham, P.L.; Dupont, I.; Roy, D.; Lapointe, G.; Cerning. J. Production of exopolysaccharide by *Lactobacillus rhamnosus* R and analysis of its enzymatic degradation during prolonged fermentation. *Appl. Environ. Microbiol*, **2000**, *66*, 2302-2310.

[49] Petrova, V.Y.; Kujumdzieva A.V. Thermotolerant yeast strains producers of galacto-oligosaccharides. Biotechnoly Biotechnologic. Equip, **2014**, *24*, 1612-1619. https://doi.org/10.2478/V10133-010-0014-6

[50] Prazeres, A.R.; Carvalho, F.; Rivas, J. Cheese whey management. *J Environ Manag* **2012**, *110*, 48-68. https://doi.org/10.1016/j.jenvman.2012.05.018

[51] Rajput, Y.S.; Sharma, R.; Mann B. Chemical and functional properties of glycomacropeptide (GMP) and its role in the detection of cheese whey adulteration in milk: a review. *Dairy Sci. Technol* **2013**, *93*, 21-43.

[52] Ramalingam, C., Priya, J., Mundra, S. Applications of microbial polysaccharides in food industry. *Int J Pharmaceut Sci Review and Research*., **2014**, *27*, 1, 322-324.

[53] Rammer, P.; Groth-Pedersen, L.; Kirkegaard, T.; Daugaard, M.; Rytter A. BAMLET activates a lysosomal cell death program in cancer cells. *Mol Cancer Ther* **2010**, *9*, 24-32. https://doi.org/10.1158/1535-7163

[54] Rantamaki, O.; Tossavainen, O.; Outinen, M.; Tupasela, T.; Koskela, P.; Kaunismaki, M. Functional properties of the whey protein fractions produced in pilot plant processes. Foaming, water-holding capacity and gelation. *Milchwissenschaft*, **2010**, *200055*, *10*, 569-572.

[55] Ribeiro, V.A.; Burkert, C.A.V. Exopolysaccharides Produced by Rhizobium: Production, Composition and Rheological Properties. *J. Pol. And Biophysics Chem* **2016**, *4*, 1, 1-6. https://doi.org/10.12691/jpbpc-4-1-1

[56] Regenhardt, S.A.; Mammarella, E.J.; Rubiolo, A.C. Hydrolysis of lactose from cheese whey using a reactor with β-galactosidase enzyme immobilized on a commercial UF membrane. *Chem and Eng Process*, **2013**, *34*, *3*, 375-385. https://doi.org/10.2478/cpe-2013-0030

[57] Salehi, A.; Gunnerud, U.; Muhammed, SJ.; Ostman, E.; Holst JJ. The insulinogenic effect of whey protein is partially mediated by a direct effect of amino acids and GIP on Î²-cells. *Nutr Metab (Lond)* **2012**, 9, *48*. https://doi.org/10.1186/1743-7075-9-48

[58] Shariatikia, M.; Behbahani, M.; Mohabatkar, H. Anticancer activity of cow, sheep, goat, mare, donkey and camel milks and their caseins and whey proteins and in silico comparison of the caseins. *Mol Biol Res Commun* **2017**, 6, *2*, 57-64.

[59] Sawin, E.A.; De Wolfe, T.J.; Aktas, B.; Stroup, B.M.; Murali, S.G.; Steele J.L.; Ney, D.M. Glycomacropeptide is a prebiotic that Reduces De-sulfovibrio bacteria, increases cecal short-chain fatty acids and is anti-inflammatory in mice. *Am J Physiol-Gastrointestinal Liver Physiol* **2015**, *309*, 7, G590-G60. https://doi.org/10.1152/ajpgi.00211.2015

[60] Sekine, K.; Watanabe, E.; Nakamura, J.; Takasuka, N.; Kim, DJ.; Asamoto, M.; Krutovskikh, V.; Baba-Toriyama, H.; Ota, T.; Moore, MA.; Masuda, M.; Sugimoto, H.; Nishino, H.; Kakizoe, T.; Tsuda H. Inhibition of azoxymethane-initiated colon tumor by bovine lactoferrin administration in F344 rats. *Jpn J*

Cancer Res., **1997**, *88*, 6, 23-6. https://doi.org/10.1111/j.1349-7006.1997.tb00413.x

[61] Shin, K.; Wakabayashi, H.; Yamauchi, K.; Teraguchi, S.; Tamura, Y.; Kurokawa, M. et al. Effects of orally administered bovine lactoferrin and lactoperoxidase on influenza virus infection in mice. *J Med Microbiol* **2005**, *54*, 717-723.

[62] Smithers, G.W. Whey-ing up the options. Yesterday, today and Tomorrow. *Int Dairy J* **2015**, *48*, 2-14. https://doi.org/10.1016/j.idairyj.2015.01.011

[63] Spălăţelu, C. Biotechnological valorization of whey. *Innov. Rom Food Biotechnol* **2012**, *10*,1-8.

[64] Takayanagi, T.; Sasaki, H.; Kawashima, A.; Mizuochi, Y.; Hirate, H. A new enteral diet, MHN-02, which contains abundant antioxidants and whey peptide, protects against carbon tetrachloride-induced hepatitis. *JPEN J Parenter Enteral Nutr.* **2011**, *35*, *516-522*. https://doi.org/10.1177/0148607110381599

[65] De Vuyst, L.; De Vin, F.; Vaningelgem, F.; Degeest, B. Recent developments in the biosynthesis and applications of heteropolysaccharides from lactic acid bacteria. *International Dairy J* **2001**, *11*, 687-707. https://doi.org/10.1016/S0958-6946(01)00114-5

[66] Xue, Han.; Yang, Z.; Jing, X.; Peng, Yu.; Huaxi, Y.; Zhang L. Improvement of the Texture of Yogurt by Use of Exopolysaccharide Producing Lactic Acid Bacteria. *Biomed Res Int* **2016**, *11*, 687-707. https://doi.org/10.1155/2016/7945675

[67] Yolken, R.H.; Losonsky, G.A.; Vonderfecht, S.; Leister, F.; Wee SB. Antibody to human rotavirus in cow's milk. *N Engl J Med* **1985**, *312*, 605-610. https://doi.org/10.1056/NEJM198503073121002

[68] Zannini, E.; Waters Deborah, M.; Coffey, A.; Arendt, Elke K. Production, properties, and industrial food application of lactic acid bacteria-derived exopolysaccharides. *Appl Microbiol and Biotechnol* **2016**, *100*, 3. 1121-1135. https://doi.org/10.1007/s00253-015-7172-2